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Preeminent experts of different profiles and with different scientific titles publish their scientific and research papers in the journal. By means of conveying the selected texts, the pages of **Health Care** represent the testimony, of both the pioneering work of the Chamber, and a kind of history of health care in Serbia alike.

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AUTHOR: PROFESSOR NELA PUSKAS, MD, PhD, INSTITUTE OF HISTOLOGY AND EMBRYOLOGY "PROF. DR ALEKSANDAR DJ. KOSTIC" OF THE FACULTY OF MEDICINE UNIVERSITY OF BELGRADE.....8 - 15

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## IZLOŽBA „TAJNE IZ ZABORAVLJENE ARHIVE“ U GALERIJI NAUKE I TEHNIKE SANU

**AUTOR: PROF. DR NELA PUŠKAŠ, INSTITUT ZA HISTOLOGIJU I EMBRIOLOGIJU „PROF. DR ALEKSANDAR Đ. KOSTIĆ“ MEDICINSKI FAKULTET UNIVERZITETA U BEOGRADU**

**Milica Labudović Borović<sup>1\*</sup>**

<sup>1</sup> Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“, Medicinski fakultet Univerziteta u Beogradu, Beograd, Republika Srbija; e-mail: milica.labudovic-borovic@med.bg.ac.rs

Izložba „Tajne iz zaboravljenih arhive“, autora prof. dr Nele Puškaš je tematska izložba posvećena osnivaču Instituta za histologiju i embriologiju Medicinskog fakulteta u Beogradu, prof. dr Aleksandru Đ. Kostiću.

Izložba je pripremana kao deo proslave važnog i velikog jubileja, stote godišnjice osnivanja Medicinskog fakulteta Univerziteta u Beogradu i stote godišnjice osnivanja Instituta za histologiju i embriologiju Medicinskog fakulteta Univerziteta u Beogradu.

Cilj izložbe bio je i jeste, pre svega, da predstavi javnosti i vrati iz zaborava prof. dr Aleksandra Đ. Kostića, velikana srpske nauke i medicine, osnivača Instituta za histologiju i embriologiju i jednog od osnivača Medicinskog, Farmaceutskog i Veterinarskog fakulteta, autora brojnih udžbenika iz histologije i embriologije, potom Medicinskog rečnika sa 140.000 pojmove na osam jezika, autora prvog atlasa histoloških mikrofotografija, pionira medicinskog filma i osnivača Foto-filmskog zavoda Medicinskog fakulteta Univerziteta u Beogradu, studenta čuvenog Pola Buena i nosioca francuske Legije časti.

Izložba je proistekla iz zajedničkog projekta Audiovizuelnog arhiva i centra za digitalizaciju SANU, Muzeja nauke i tehnike i Instituta za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“.

Tim Audiovizuelnog arhiva i centra za digitalizaciju SANU, uz ogroman entuzijazam akademika Aleksandara Kostića, upravnika Audiovizuelnog arhiva i centra za digitalizaciju i uz stručnu ekspertizu gospodina Branislava Vojnovića, saradnika ovog centra, digitalizovao je dragocenu zaostavštinu prof. Kostića, koja se nalazila na Institutu za histologiju i embriologiju Medicinskog fakulteta Uni-

verziteta u Beogradu i na Katedri za histologiju i embriologiju Fakulteta veterinarske medicine u Beogradu. Postavka ove izložbe predstavlja prvo javno predstavljanje rezultata vrlo predanog rada.

Osnove projekta i ideju postavke, uz prof. dr Nelu Puškaš, postavila je i dr Jelena Jovanović Simić, viši kustos Muzeja nauke i tehnike koja je stalni i vrlo posvećeni saradnik i saborac u naporima da se zaostavština brojnih velikana medicinske profesije očuva i zaštitи, uključujući i zaostavštinu profesora Aleksandra Đ. Kostića (slika 1.).

Prva postavka izložbe otvorena je 7. oktobra 2022. godine u galeriji Rančićeva kuća Centra za kulturu Grocka, u Grockoj. Na otvaranju su govorili: gospođa Zorica Atić, direktorka Centra za kulturu Grocka, gospodin Zoran Lević, direktor Muzeja nauke i tehnike, prof. dr Milica Labudović-Borović, urednica kataloga i prof. dr Nela Puškaš, autorka izložbe.

U periodu od 7. oktobra do 31. oktobra izložbu je posetio veliki broj poštovaoca dela prof. Kostića, zainteresovanih građana, učenika i studenata u okviru obilazaka koje su vodili kustosi galerije i sama autorka.

U periodu od 4. novembra 2022. godine do 26. novembra 2022. godine, materijal izložbe, uz nove eksponate, postavljen je u Galeriji nauke i tehnike SANU (slika 2). Na otvaranju, 4. novembra, govorili su akademik Zoran Petrović, upravnik Galerije nauke i tehnike SANU, dr Jelena Jovanović Simić, viši kustos u Muzeju nauke i tehnike, prof. dr Ivanka Marković, prodekan za KME Medicinskog fakulteta i prof. dr Nela Puškaš, autorka izložbe. Pored autora i kustosa Galerije, ulogu domaćina i kustosa ove postavke preuzeли su i studenti medicine, članovi Centra za stručni i naučno-istraživački rad

## EXHIBITION “SECRETS FROM THE FORGOTTEN ARCHIVE” AT THE GALLERY OF SCIENCE AND TECHNOLOGY OF THE SERBIAN ACADEMY OF SCIENCES AND ARTS – SASA

**AUTHOR: PROFESSOR NELA PUSKAS, MD, PhD, INSTITUTE OF HISTOLOGY AND EMBRYOLOGY “PROF. DR ALEKSANDAR DJ. KOSTIC” OF THE FACULTY OF MEDICINE UNIVERSITY OF BELGRADE**

**Milica Labudović Borović<sup>1\*</sup>**

<sup>1</sup> Institute of Histology and Embryology „Prof. dr Aleksandar Đ. Kostić”, Faculty of Medicine, University of Belgrade, Belgrade, Republic of Serbia; e-mail: milica.labudovic-borovic@med.bg.ac.rs

The exhibition “Secrets from the Forgotten Archive” authored by Professor Nela Puskas is a thematic exhibition dedicated to the founder of the Institute of Histology and Embryology of the Faculty of Medicine in Belgrade, Professor Aleksandar DJ. Kostic.

The exhibition was prepared as part of the celebration of an important and great jubilee, the hundredth anniversary of the establishment of the Faculty of Medicine of the University of Belgrade and the hundredth anniversary of the founding of the Institute of Histology and Embryology of the Faculty of Medicine of the University of Belgrade.

The aim of the exhibition was, first of all, to present to the public and bring back from silence Professor Aleksandar DJ. Kostić, a great man of Serbian science and medicine, the founder of the Institute of Histology and Embryology and one of the founders of the Faculty of Medicine, the Faculty of Pharmacy and the Faculty of Veterinary Medicine, the author of numerous textbooks on histology and embryology, then the Medical Dictionary with 140,000 terms in eight languages, the author of the first Atlas of Histological Microphotography, the pioneer of medical film and the founder of the Photo-film Institute of the Faculty of Medicine, the University of Belgrade, a student of the famous Pol Bouin, and the holder of the French Legion of Honor.

The exhibition resulted from the joint project of the Audiovisual Archive and Center for Digitalization of SASA, the Museum of Science and Technology and the Institute of Histology and Embryology “Prof. dr Aleksandar DJ. Kostic”.

The team of the Audiovisual Archive and the Center for Digitalization of SASA, with the enormous enthusiasm of academician Aleksandar Kostic, the director of the Audiovisual Archive and the Center for Digitalization and with the professional expertise of Mr. Branislav Vojnovic, an associate of this Center, digitalized the valuable legacy of Professor Kostic, gathered or obtained from the Institute of Histology and Embryology of the Faculty of Medicine of the University of Belgrade and from the Department of Histology and Embryology of the Faculty of Veterinary Medicine in Belgrade. The exhibition represents the first public presentation of the results of very dedicated work.

The basics of the project and the idea of the exhibition was set by the author, Professor Nela Puskas, and Dr. Jelena Jovanovic Simic, senior curator of the Museum of Science and Technology, who is a constant and very dedicated fellow associate in efforts to preserve and protect the legacy of numerous great men of medical profession, including the legacy of Professor Aleksandar DJ. Kostic (Picture 1).

The first display of the exhibition was opened on October 7<sup>th</sup>, 2022, in the Gallery “Ranciceva kuca” of the Cultural Center Grocka, in Grocka. The following spoke at the opening: Ms. Zorica Antic, the director of the Cultural Center Grocka, Mr. Zoran Levic, the director of the Museum of Science and Technology, Professor Milica Labudovic-Borovic, the editor of the catalog and Professor Nela Puskas, the author of the exhibition.



**Slika 1.** Katalog izložbe otvorene u Galeriji nauke i tehnike SANU koji je štampan u formi monografije, čiji je autor prof. dr Nela Puškaš

Medicinskog fakulteta u Univerzitetu Beogradu.

Postavku izložbe čini osam tematskih postera, dvanaest postera histoloških mikrofotografija, potom osamnaest postera sa fotografijama enterijera Histološkog instituta, zgrada Medicinskog fakulteta i starog Beograda, kao i fotografске staklene ploče, crno-beli dijapositivi, dijapositivi u boji (autochromi), albumi sa histološkim mikrofotografijama i Mikrofotografski atlas normalne histologije iz 1925. godine (slike 3-5). Među eksponatima se nalazi i knjiga naredbi i originalni rukopis članka prof. dr Aleksandra Đ. Kostića o osnivanju Histološkog instituta (slika 6). Izložena su različita izdanja rečnika prof. Kostića: Rečnik histoloških izraza, Rečnik srpskih medicinskih izraza, kao i prvi Medicinski rečnik iz 1956. godine. Posebno su dragoceni i interesantni sačuvani parafinski blokovi tkiva i histološki preparati iz 1952. godine, kao i mikroskop i lični fotoaparat prof. Kostića. Izložbu prati film o procesu digitalizacije fotografike zaostavštine u AVA SANU pod nazivom „Projekat digitalizacije zaostavštine prof. dr Aleksandra Kostića”, čiji je autor prof. dr Nela Puškaš.

Izložba je privukla veliku pažnju, te će zbog ogromnog interesovanja publike, biti postavljena ponovo u Galeriju nauke i tehnike SANU 26. decembra 2022. i biće otvorena sve do 31. januara 2023. godine.

Kao prateći deo postavke izložbe u Galeriji nauke i tehnike SANU dizajnirana je video igrica



**Slika 2.** Otvaranje izložbe u Galeriji nauke i tehnike SANU

„100 godina Histološkog instituta”, koja nas vodi u virtuelni svet u kome pod budnim okom prof. Kostića njegova asistentkinja pravi histološke preparate, a mikrofotografije tako nastalih preprata snima Aleksandar Šafranski, ruski vojni fotograf i saradnik prof. Kostića u Fotografskom odeljenju. Autori igrice su mladi dizajneri gospodica Tatjana Gadža i gospodin Branko Gadža, *TeamG Game & Art Studio*.

Izložbu prati i katalog koji je štampan u formi monografije, čiji je autor prof. dr Nela Puškaš. Monografija je štampana na ukupno 89 strana i obuhvata pet poglavlja: 1. Histološki institut pod rukovodstvom prof. dr Aleksandra Đ. Kostića; 2. Pronađena zaostavština profesora Kostića; 3. Biografija profesora Aleksandra Đ. Kostića; 4. Zahvalnice; 5. Literatura i izvori. Prva tri poglavlja ilustrovana su sa ukupno 65 fotografija (27 fotografija u prvom poglavlju, 37 fotografija u drugom poglavlju i 1 fotografija u trećem poglavlju), nastalih u periodu između dva svetska rata i u toku osnivanja Histološkog instituta, Medicinskog fakulteta, ali i tokom transformacija kroz koje je prolazio Beograd u tom istorijskom periodu. Sve originalne fotografije, od neprocenjivog kulturnog i istorijskog značaja, sačuvane su postupkom digitalizacije u Audiovizuelnom arhivu i centru za digitalizaciju SANU. Nadahnutu recenziju monografije napisao je predsednik Srpskog lekarskog društva, akademik Radoje Čolović.



**Picture 1.** Catalog of the exhibition opened in the Gallery of Science and Technology of SASA printed in the form of a monograph, whose author is Professor Nela Puskas

In the period from October 7<sup>th</sup> to October 31<sup>st</sup>, 2022, the exhibition was visited by numerous admirers of the work of Professor Kostic, interested citizens, pupils, and students, as part of the tours led by the curators of the Gallery and the author herself.

In the period from November 4<sup>th</sup> to November 26<sup>th</sup>, 2022, the exhibition material, along with new exhibits, was displayed at the Gallery of Science and Technology of the Serbian Academy of Sciences and Arts (Picture 2). Academician Zoran Petrovic, the director of the Gallery of Science and Technology of SASA, Dr. Jelena Jovanovic Simic, senior curator at the Museum of Science and Technology, Professor Ivanka Markovic, vice dean for continuing medical education of the Faculty of Medicine and Professor Nela Puskas, the author of the exhibition spoke at the opening on November 4<sup>th</sup>, 2022. In addition to the author and curator of the Gallery, the role of a host and curator of this exhibition was eagerly accepted by medical students, members of the Center for Professional and Scientific Research of the Faculty of Medicine of the University of Belgrade.

The exhibition consists of eight thematic posters, twelve posters of histological microphotographs, then eighteen posters with photos of the interior of the Histological Institute, the buildings of the Faculty of Medicine and old Belgrade, as well as photographic glass plates,



**Picture 2.** The opening of the exhibition in the Gallery of Science and Technology of SASA

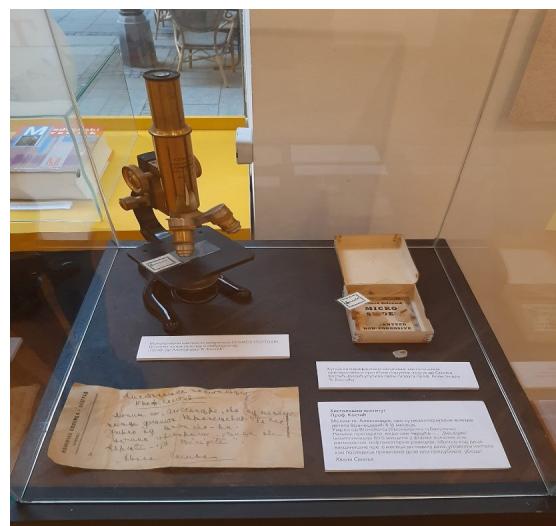
black and white slides, color slides (autochromes), albums with histological microphotographs and the 1925 Microphotographic Atlas of Normal Histology (Pictures 3-5). Among the exhibits is the book of orders and the original manuscript of the article by Prof. Dr. Aleksandar Đ. Kostić on the establishment of the Histological Institute (Picture 6). Different editions of the dictionary of prof. Kostić: Dictionary of histological terms, Dictionary of Serbian medical terms, as well as the first Medical Dictionary from 1956 are presented. Particularly valuable and interesting are the preserved paraffin tissue blocks and histological preparations from 1952, as well as the microscope and personal camera of prof. Kostic. The exhibition is accompanied by a film about the process of digitization of the photographic heritage at the Audiovisual Archive and the Center for Digitalization entitled "Project of Digitalization of the Legacy of Prof. Dr. Aleksandar Kostić", authored by prof. Dr. Nela Puskas.

The exhibition attracted significant attention, and due to the enormous interest of the audience, it will be presented again in the Gallery of Science and Technology of SASA on December 26<sup>th</sup>, 2022, and it will be open until January 31<sup>st</sup>, 2023.

A video game „100 years of the Histological Institute“ was designed as an accompanying part of the exhibition in the Gallery of Science



Slika 3. Rad prof. Kostića na Medicinskoj terminologiji (Evolucija medicinskog rečnika)



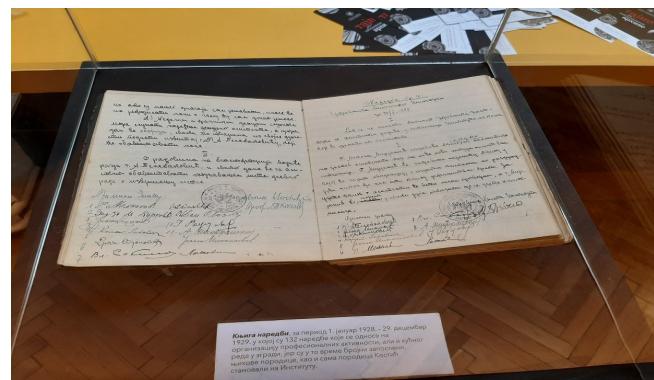
Slika 4. Monokularni svetlosni mikroskop COSMOS STUTTGART i kutija sa parafinskim kalupima



Slika 5. Crno beli dijapositivi i dijapositivi u boji

Postavljanje izložbe, rad na pripremi eksponata, otvaranje izložbe i štampanje monografije podržali su Medicinski fakultet Univerziteta u Beogradu, uz posebno zlaganje članova dekanskog kolegijuma, pre svega prof. dr Lazara Davidovića, dekana i prof. dr Ivane Marković, potom Srpska akademija nauka i umetnosti, a posebno Galerija nauke i tehnike i Audiovizuelni arhiv i centar za digitalizaciju i direktori ovih uglednih institucija, akademik Zoran Petrović i akademik Aleksandar Kostić, zatim Centar za kulturu Grocka uz stalno posvećeno angažovanje direktorke centra, gospođe Zorice Atić, kao i Laboratorija iz oblasti patohistologije Supremalab iz Beograda.

Kolektiv Instituta za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ je prihvatio ideju izložbe i monografije sa velikim poštovanjem i



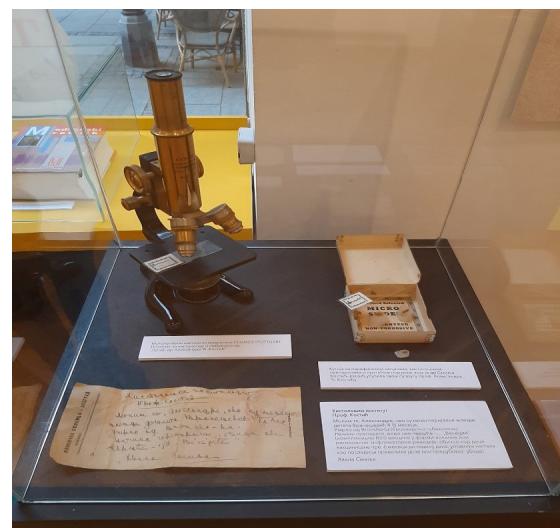
Slika 6. Knjiga naredbi koje se odnose na organizaciju profesionalnih aktivnosti

posebnim piletetom. Uz prof. dr Nelu Puškaš, projektu su doprineli i mladi članovi kolektiva Histološkog instituta asistent dr Aleksandra Milosavljević i asistent dr Katarina Milutinović, kao i prethodni upravnik, prof. dr Milica Labudović Borović. Aktuelni kolektiv Instituta za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ ovim projektima postavlja delo prof. Kostića u istorijski kontekst na mesto u istoriji medicine koje je prof. Kostić odavno zasluzio svojim životom i delom i počinje rad na zajedničkom legatu naše generacije za buduće generacije.

Fotografije: Galerija nauke i tehnike SANU



**Picture 3.** Work of Professor Kostić on medical terminology (Evolution of medical dictionary)



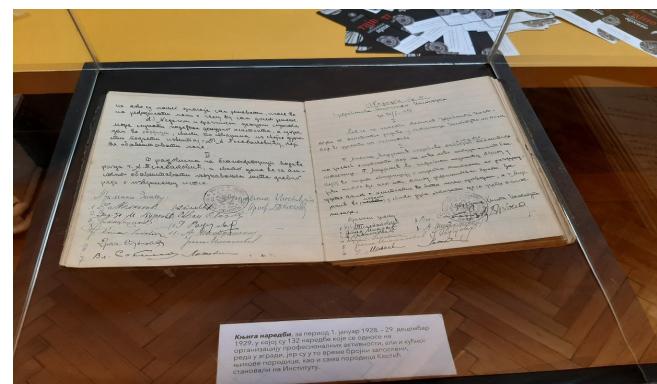
**Picture 4.** Monocular light microscope COSMOS STUTTGART and the box with paraffin blocks (of tissue)



**Picture 5.** Black (and) white diapositives and colored diapositives

and Technology of SASA, and it takes us to the virtual world, where under the watchful eye of Professor Kostic, an assistant makes histological preparations, while the microphotographs of these preparations are taken by Aleksandar Safranski, a Russian military photographer and associate of Professor Kostic at the Photography Department. The authors of the game are young designers Ms. Tatjana Gadza and Mr. Branko Gadza from the Team G Game & Art Studio.

The exhibition is accompanied by a catalog printed in the form of a monograph, authored by Professor Nela Puskas. The monograph is printed on a total of eighty-nine pages and includes five chapters: 1. Histological Institute under the leadership of Professor Aleksandar DJ. Kostić; 2. Found legacy of Professor Kostić; 3.



**Picture 6.** Book of orders related to the organization of professional activities

Biography of Professor Aleksandar DJ. Kostic; 4. Acknowledgements; 5. Literature and sources. The first three chapters are illustrated with a total of 65 photographs (27 photographs in the first chapter, 37 photographs in the second chapter and 1 photograph in the third chapter) that were created in the period between the two world wars during the establishment of the Institute of Histology and the Faculty of Medicine, but also during transformations through which Belgrade passed in that historical period. All original photographs of inestimable cultural and historical significance have been preserved by the digitalization process in the Audiovisual Archive and the Center for Digitalization of SASA. The inspired review of the monograph was written by the president of the Serbian Medical Society, academician Radoje Colovic.



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The installation of the exhibition, work on the preparation of the exhibits, the opening of the exhibition and the printing of the monograph were supported by the Faculty of Medicine of the University of Belgrade, with the special efforts of the dean's collegium, first of all, Professor Lazar Davidovic, dean and Professor Ivanka Markovic, then the Serbian Academy of Sciences and Arts, and especially the Gallery of Science and Technology and the Audiovisual Archive and Center for Digitalization and the directors of these distinguished institutions, academician Zoran Petrovic and academician Aleksandar Kostic, then the Cultural Center Grocka with the constant commitment of the director of the Center, Mrs. Zorica Antic, as well as the Pathohistology Laboratory Supremalab from Belgrade.

The collective of the Institute of Histology and Embryology „Prof. dr Aleksandar DJ. Kostic“ accepted the idea of the exhibition and monograph with profound respect and special piety. With Professor Nela Puskas, young members of the team of the Institute of Histology, assistant Aleksandra Milosavljevic, MD and Katarina Milutinovic MD as well as the previous director, Professor Milica Labudovic Borovic contributed to the project. With these projects, the current staff of the Institute of Histology and Embryology „Prof. dr Aleksandar DJ Kostic“, sets the work of Professor Kostic in the historical context and to the place in the history of medicine that Professor Kostic deserved a long time ago with his life time work and achievements, and begins the efforts on the joint legacy of our generation for future generations.

Photographs: Gallery of Science and Technology of SASA



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## FOTOGRAFSKO ODELJENJE PROFESORA ALEKSANDRA KOSTIĆA – OSNIVANJE, DOMETI I ZNAČAJ

Nela Puškaš<sup>1\*</sup>, Ivana Arađanin<sup>2</sup>

<sup>1</sup> Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić”, Medicinski fakultet Univerziteta u Beogradu, Beograd, Republika Srbija

<sup>2</sup> Narodni muzej Zrenjanin, Zrenjanin, Republika Srbija

\* Korespondencija: Nela Puškaš, Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić”, Medicinski fakultet Univerziteta u Beogradu, Višegradska 26 Beograd, Republika Srbija; e-mail: nela.puskas@med.bg.ac.rs

### SAŽETAK

Godine 1924. dr Aleksandar Đ. Kostić, prvi profesor histologije i embriologije i osnivač Histološkog instituta Medicinskog fakulteta u Beogradu, u sastavu Instituta je oformio i Fotografsko odeljenje. Prve fotografije su bile mikrofotografski snimci histoloških preparata, od kojih je izvestan broj objavljen već 1925. godine u Mikrofotografskom atlasu normalne histologije. Veći broj snimaka, međutim, iskorišćen je za izradu mikrofotograma, odnosno crno-belih dijapositiva, koji su prikazivani na predavanjima i vežbama. U narednim godinama profesor Kostić je proširio fotografske teme i na patohistološke preparate, mokraćne kristale i bakteriološke uzorke, operativni i obdukcioni materijal, embriološke i teratološke uzorke. Posebno važna aktivnost Odeljenja bilo je i snimanje pacijenata. Pacijenti su fotografisani u bolnicama ili u ateljeu Fotografskog odeljenja. Pored fotografija, tu su snimljeni i prvi filmovi pod nazivom *Krvotok u trbušnoj opni žabe* i *Krvotok u međuprstnoj opni žabe*. Tokom okupacije u Drugom svetskom ratu, Nemci su odneli fotografsku opremu i potrošni materijal, ali je nakon oslobođenja, već početkom 1946. godine, rad bio obnovljen. Pored fotografisanja, profesor Kostić je organizovao snimanje i režirao prve medicinske filmove u prvim posleratnim godinama. Odeljenje je i dalje bilo centar za medicinsku fotografiju na Fakultetu, a profesor Kostić je bio rukovodilac sve do 1952, kada je iz političkih razloga udaljen sa Medicinskog fakulteta.

**Ključne reči:** Fotografsko odeljenje, Aleksandar Đ. Kostić, mikrofotografski snimci, *Mikrofotografski atlas normalne histologije*, mikrofotogrami, medicinski filmovi

### Uvod

Razvoj medicinske fotografije u Srbiji počinje četiri godine nakon osnivanja Medicinskog fakulteta u Beogradu i dve godine nakon početka rada Histološkog instituta (1,2). Glavnu ulogu u tom poduhvatu imao je dr Aleksandar Kostić, prvi profesor histologije i embriologije i prvi upravnik Histološkog instituta na Medicinskom fakultetu u Beogradu (2,3). Naime, on je u prostorijama Škole za nudilje Društva Crvenog krsta, gde je Histološki institut bio privremeno smešten, formirao Fotografsko odeljenje. U početku je izrađivao mikrofotografske snimke histoloških preparata, dok je kasnije proširio spektar tema i interesovanja i na patohistološke preparate, mokraćne kristale

i bakteriološke uzorke, operativni i obdukcioni materijal, embriološke i teratološke uzorke i pacijente, a zatim i na snimanje medicinskih dokumentarnih filmova. Prema Kostićevim rečima, Odeljenje je na Međunarodnoj izložbi medicinske fotografije, održanoj 1950. godine u Londonu, od strane „merodavnih” označeno „pionirem medicinske fotografije u svetu”, uz objašnjenje da su „slični zavodi osnivani u Engleskoj tek pred rat, a mnogi tek posle poslednjeg rata”. Kao primer je navedeno Fotografsko odeljenje Medicinskog fakulteta pri Vestminsterskoj bolnici koje je osnovano „tek 1946. godine” (4).

## PHOTOGRAPHY DEPARTMENT OF PROFESSOR ALEKSANDAR KOSTIĆ – ESTABLISHMENT, ACHIEVEMENTS AND SIGNIFICANCE

Nela Puskas<sup>1\*</sup>, Ivana Aradjanin<sup>2</sup>

<sup>1</sup> Institute of Histology and Embryology „Prof. dr Aleksandar Đ. Kostić”, Faculty of Medicine, University of Belgrade, Belgrade, Republic of Serbia

<sup>2</sup> National Museum Zrenjanin, Zrenjanin, Republic of Serbia

\* Correspondence: Nela Puskas, Institute of Histology and Embryology „Prof. dr Aleksandar Đ. Kostić”, Faculty of Medicine, University of Belgrade, Višegradska 26, 11000 Belgrade, Republic of Serbia; e-mail: nela.puskas@med.bg.ac.rs

### SUMMARY

In 1924, Dr. Aleksandar Đ. Kostić, the first Professor of Histology and Embryology and the founder of the Institute of Histology at the Faculty of Medicine in Belgrade, formed the Photography Department within the Institute. The first photographs were microphotographs of histological specimens and a certain number of them were published in 1925 in the *Microphotographic Atlas of Normal Histology*. However, a greater number of photographs were used for the preparation of microphotograms, that is, black and white diapositives which were shown during lectures and laboratory practices. In the following years, Professor Kostić expanded his photographic topics to pathohistological specimens, urine crystals, and bacteriological samples, operative and autopsy material, and embryological and teratological samples. A particularly important activity of the Department was making photographs of patients. Patients were photographed in hospitals or in the studio of the Photography Department. In addition to photographs, the first films entitled *Blood flow in the peritoneal membrane of a frog* and *Blood flow in the interdigital membrane of a frog* were made there. During the Second World War occupation, the Germans took away the photographic equipment and consumables, but after the liberation, at the beginning of 1946, the work was restored. In addition to photography, Professor Kostić organized filming and he directed the first medical films in the first post-war years. The Department was still the center of medical photography at the Faculty, while Professor Kostić was the head until 1952, when he was removed from the Faculty of Medicine due to political reasons.

**Keywords:** Photography Department, Aleksandar Đ. Kostić, microphotographs, *Microphotographic Atlas of Normal Histology*, microphotograms, medical films

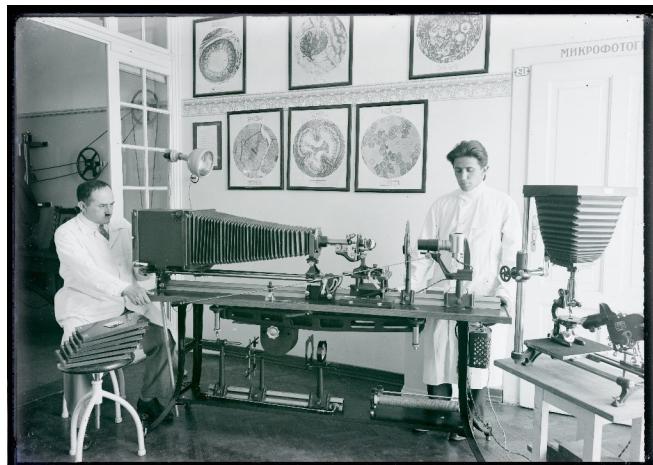
### Introduction

The development of medical photography in Serbia began four years after the establishment of the Faculty of Medicine in Belgrade and two years after the establishment of the Institute of Histology (1,2). Dr. Aleksandar Kostić, the first Professor of Histology and Embryology and the first director of the Institute of Histology at the Faculty of Medicine in Belgrade, played a major role in that endeavor (2,3). Namely, he formed the Photography Department in the premises of the Red Cross Society Nursing School, where the Institute of Histology was temporarily located. In the beginning, he made microphotographs of

histological specimens, while he later expanded the range of topics and interests to pathohistological specimens, urine crystals, bacteriological samples, operative and autopsy material, embryological and teratological samples and patients, and then to making medical documentaries. According to Kostić, at the International exhibition of medical photography held in London in 1950, the Department was marked as “the pioneer of medical photography in the world” by the “authorities”, with the explanation that “similar institutes were founded in England only before the war, and many were founded only after the last

## Aleksandar Đ. Kostić, osnivač Fotografskog odeljenja

Aleksandar Đ. Kostić (1893 – 1983) je još kao gimnazijalac snimio svoje prve fotografije (5). Po završetku osnovne škole i Druge muške gimnazije u Beogradu (danас Filološka gimnazija), upisao je Medicinski fakultet u Nansiju u Francuskoj. Kao student medicine i dobrovoljni hospitant na Histološkom institutu u Nansiju, 1913. godine je snimio prve mikrofotografije, ali su one nestale tokom Prvog svetskog rata (5). Inače, dva puta je prekidao studije medicine, kako bi se vraćao u zemlju i kao dobrovoljac učestvovao u Balkanskim i Prvom svetskom ratu. Završio je Medicinski fakultet u Strazburu odbranivši doktorsku tezu u julu 1921. godine. Iste godine, 21. novembra, postavljen je za profesora normalne histologije na novoosnovanom Medicinskom fakultetu u Beogradu. Po povratku u Beograd, u januaru 1922. otpočeo je pripreme na organizaciji nastave da bi već u martu održao svoje prvo predavanje studentima. Do useljenja u sopstvenu, namenski sazidanu zgradu 1927. godine, Histološki institut se nekoliko puta selio. Najpre je radio u dvema sobama upravne zgrade Glavne vojne bolnice, potom neko vreme u Fizičkom institutu Filozofskog fakulteta, pa u prostorijama Škole za nudilje Društva Crvenog krsta.



**Slika 1.** Profesor Kostić i dr Aleksandar Telebакović sa mikrofotografskim aparatom *Uma* u Fotografskom odeljenju 1927. godine. Iza profesora Kostića se vidi deo mikrokinematografskog aparata *Ascania*, a na zidu u centru fotografije nekoliko postera urađenih u samom Odeljenju. Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ Medicinskog fakulteta Univerziteta u Beogradu.

Upravo u toj školi, 1924. godine Kostić je osnovao Fotografsko odeljenje (6) i svoja znanja stečena u Nansiju na polju mikrofotografije primenio u uspostavljanju rada u Beogradu (slika 1).

## Prve tekovine Fotografskog odeljenja

Prvi snimci napravljeni u Fotografskom odeljenju bili su mikrofotografski snimci histoloških preparata, urađeni mikrofotografskim aparatom *Uma* firme Lajc (*Leitz*) (1,6,7). Rezultati tog rada su bili vidljivi stručnoj javnosti već 1925. godine, kada je izašao iz štampe *Mikrofotografski atlas normalne histologije*. Kako je navedeno u predgovoru, Atlas sadrži 150 originalnih mikrofotografija jer je cilj autora bio da što vernije predstavi mikroskopski sastav i sklop organa i tkiva iz kojih je jedan organizam sagrađen i da na taj način doprinese razumevanju teorijskih pojmove. Kostić u predgovoru ukaže i na manjkavost crteža kao jedinog sredstva koje se do tada koristilo u nastavi i na problematiku verodostojnosti crteža kod određenih preseka tkiva. Odlučio se za korak dalje u korist nauke i crtež zamjenio nečim što verno reprodukuje original, a to je – mikrofotografija (7).

Da Atlas ne bi premašio obim koji je prvobitno zamišljen, određeni snimci organa i tkiva „manje važnosti“ su bili izostavljeni, ali je Znanstveni zavod



**Slika 2.** Crno-beli dijapositiv (mikrofotogram) „Razvoj folikula“. Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ Medicinskog fakulteta Univerziteta u Beogradu, Zbirka histoloških mikrofotograma prof. dr A. Kostića.

war". The Photography Department of the Faculty of Medicine at the Westminster Hospital, which had been founded "only in 1946", was mentioned as an example (4).

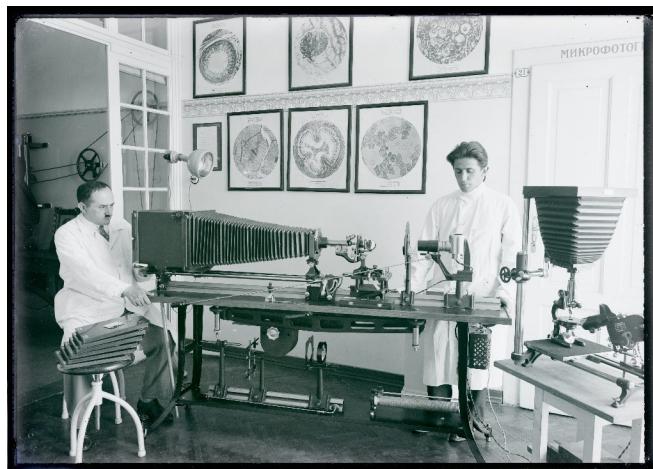
## Aleksandar Đ. Kostić, the founder of the Photography Department

Aleksandar Đ. Kostić (1893-1983) took his first photographs as a high school student (5). After he finished primary school and the Second Male High School in Belgrade (today the Philological High School), he enrolled at the Faculty of Medicine in Nancy, France. As a medical student and volunteer at the Institute of Histology in Nancy, he took the first microphotographs in 1913, but they disappeared during the First World War (5). Otherwise, he interrupted his medical studies twice, in order to return to the country and take part in the Balkans and the First World War as a volunteer. He graduated from the Faculty of Medicine in Strasbourg and defended his doctoral thesis in July, 1921. In the same year, on November 21<sup>st</sup>, he was appointed professor of Normal Histology at the newly founded Faculty of Medicine in Belgrade. After he returned to Belgrade, in January 1922, he began preparations for the organization of classes in order to give his first lecture to students

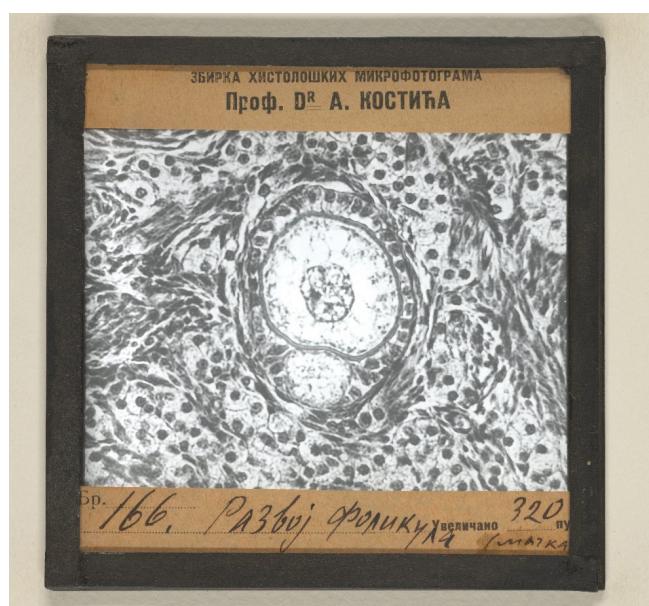
in March. Until moving into its own purpose-built building in 1927, the Institute of Histology had moved several times. First, it worked in two rooms of the administration building of the Main Military Hospital, then for some time in the Institute of Physics of the Faculty of Philosophy, and then in the premises of the Red Cross Society Nursing School. It was precisely in that school that Kostić founded the Department of Photography in 1924 (6) and applied the knowledge acquired in Nancy in the field of microphotography to establish the work in Belgrade (Picture 1).

## The first acquirements of the Photography Department

The first photographs made in the Photography Department were microphotographs of histological specimens, made with the Leitz microphotographic camera *Uma* (1,6,7). The results of that work were visible to the professional public as early as 1925, when the *Microphotographic Atlas of Normal Histology* was published. As it was stated in the preface, the Atlas contains 150 original microphotographs, because the author's aim was to present as faithfully as possible the microscopic composition of organs and tissues, which one organism is made from,



**Picture 1.** Professor Kostić and Dr. Aleksandar Telebакović with the *Uma* microphotographic camera in the Photography Department in 1927. A part of the Askania microcinematography camera can be seen behind Professor Kostić, as well as the photos of several posters in the center of the wall. The Institute of Histology and Embryology "Prof. dr Aleksandar Đ. Kostić" of the Faculty of Medicine, University of Belgrade.



**Picture 2.** Black and white diapositive (microphotogram) "Follicle development". The Institute of Histology and Embryology "Prof. dr Aleksandar Đ. Kostić" of the Faculty of Medicine, University of Belgrade. Collection of histological microphotograms of Prof. A. Kostić.

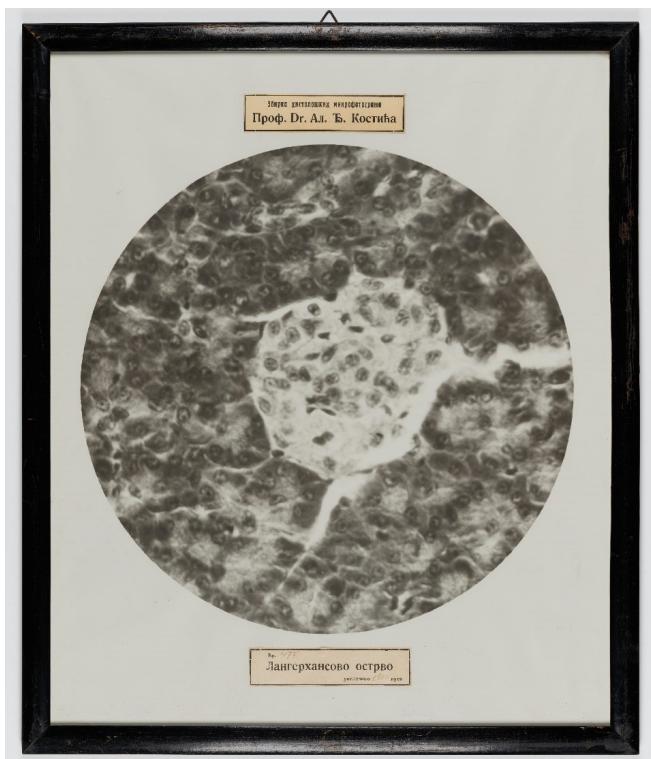
prof. Breslera (*Brössler*) preuzeo na sebe obavezu da na osnovu njih izradi mikrofotograme, tj. crno-bele dijapoitive, koji su se i prodavali naučnim i nastavnim ustanovama (7). Dijapoitive su bili intenzivno korišćeni u nastavi, projektovani su tokom predavanja i nakon uvodnih časova na vežbama. Predstavljeni su drugu veliku tekovinu Fotografskog odeljenja (slika 2).

Kao eventualni uzor u pristupu i ideji koja je vodila Kostića ka Mikrofotografskom atlasu normalne histologije, može se izdvojiti prvi udžbenik iz histologije na švedskom jeziku iz 1920. godine, autora Emila Holmgrena (*Emil Holmgren*), profesora histologije sa Karolinska instituta u Stokholmu (8). Važno je istaći da se prof. Holmgren tada, kao i Kostić nekoliko godina kasnije, nije zadovoljavao čisto morfološkim opisom, već je gradivo analizirao sa razvojnog i sa funkcionalnog, tj. fiziološkog aspekta. Na osnovu trenutno dostupne literature, može se zaključiti da je to bio prvi udžbenik iz histologije koji je u potpunosti bio ilustrovan mikrofotografijama – čak 782. Pojedina tkiva, poput nervnog, bila su znatno verodostojnija na fotografijama, nego na bilo kom crtežu koji je izrađen tih godina. Ova činjenica nas navodi na zaključak da su težnje prof. Holmgrena da se napusti forma crteža i uvede mikrofotografija u službu nauke uspele. Taj put u razmišljanjima i radu je sledio i prof. Kostić.

Treća velika tekovina Fotografskog odeljenja, kojom se profesor Kostić ponosio bila je serija uveičanih mikrofotografskih snimaka, štampanih u formatu postera (slika 3). Za uveičavanje snimaka Odeljenje je imalo posebnu prostoriju, a radilo se na aparatu *Furor II* (1,6).

Važno je naglasiti da su u Odeljenju snimane prve mikrofotografije u Kraljevini Srba, Hrvata i Slovenaca, te se ono s pravom označava prvim jugoslovenskim centrom za naučnu fotografiju (1).

Početkom marta 1925. godine, u Fotografsko odeljenje Histološkog instituta dolazi Aleksandar Šafranski, ruski vojni fotograf. Šafranski je dao izuzetan doprinos u oblasti teorijskih razmatranja fotografije tokom treće i četvrte decenije 20. veka. On je zajedno sa profesorom Kostićem razvijao Fotografsko odeljenje. Bio je i aktivni član Beogradskog foto-kluba, koji je 1928. godine osnovao prof. Kostić sa ciljem razvijanja umetničke i naučne fotografije, popularisanja fotografije u turističke svrhe i edukacije (9).



Slika 3. Mikrofotografki snimak u formatu postera „Langerhansovo ostrvo“. Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ Medicinskog fakulteta Univerziteta u Beogradu, Zbirka histoloških postera prof. dr A. Kostića.

## Fotografsko odeljenje u novoj zgradbi Histološkog instituta

Kada je 1927. godine Histološki institut preseljen u svoju novu zgradu, Fotografsko odeljenje je dobilo značajan prostor od skoro 160m<sup>2</sup> i dodatnu opremu. Nalazilo se na prvom spratu centralnog dela zgrade Fiziološkog i Histološkog instituta, pored amfiteatra, i raspolaгало је низом prostorija (1,6).

U velikom hodniku, duž jedne strane bili su smešteni: ormani za sušenje negativa toplim vazduhom, za čuvanje negativa, za fotografsku biblioteku i čuvanje fotografiskog materijala, za aparate i optiku, као и велики сто за хемikalije. На другој strani hodnika bio je montiran mikrokinematografski aparat *Ascania* са „ubrzavajućim aparatom“, који је omogућавао 200 snimaka у секundi (6,10). Управо на овом uređaju profesor Kostić je snimio seriju sekvenci за prve filmove *Krvotok u trbušnoj opni žabe* и *Krvotok u međuprstnoj opni žabe*. Међутим, о njima се данас, осим назива, не зна готово ништа јер су уништени током Drugog svetskog rata (11).

and thus, contribute to understanding theoretical concepts. In the preface, Kostić points out the shortcomings of drawings as the only means used for teaching until that time and the problem of the credibility of drawings in the case of some tissue sections. He decided to go a step further in favor of science and he replaced drawings with something that faithfully reproduces the original, which is a microphotograph (7).

Certain images of organs and tissues that were “less important” were omitted so that the Atlas would not exceed the scope that was originally conceived, but the Scientific Institute of Professor Brössler took upon himself the obligation to create microphotograms, that is, black and white diapositives, which were sold to scientific and educational institutions (7). Diapositives were intensively used in classes, they were projected during lectures and after the introductory lessons during exercises. This represented the second major asset of the Photography Department (Picture 2).

The first histology textbook in the Swedish language from 1920, written by Emil Holmgren, Professor of Histology at the Karolinska Institute in Stockholm can be singled out as a possible model for the approach and idea that led Kostić towards the *Microphotographic Atlas of Normal Histology* (8). It is important to point out that professor Holmgren then, like Kostić a few years later, was not satisfied with a purely morphological description, but analyzed the material from a developmental and functional point of view, i.e. physiological aspect. Based on the currently available literature, it can be concluded that it was the first textbook in histology that was completely illustrated with microphotographs – even 782. Certain tissues, such as the nervous, were much more faithful in photographs than in drawings that were made at that time. This fact leads us to the conclusion that the aspirations of professor Holmgren to abandon the form of a drawing and introduce microphotography in the service of science succeeded. This way of thinking and work was also followed by professor Kostić.

The third major achievement of the Photography Department, which professor Kostić was proud of, was a series of enlarged microphotographs, printed in poster format (Picture 3). The Department had a special room for magnifying the images and a *Furor II* camera was used (1,6).



**Picture 3.** Microphotograph in the poster format “Island of Langerhans”. Institute of Histology and Embryology “Prof. dr Aleksandar Đ. Kostić” of the Faculty of Medicine, University of Belgrade, Collection of histological posters of Professor A. Kostić.

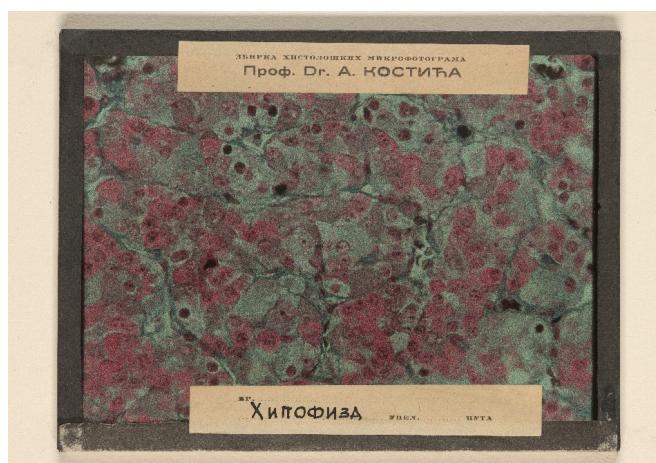
It is important to emphasize that the first microphotographs in the Kingdom of Serbs, Croats and Slovenes were taken in the Department, and it is rightly called the first Yugoslav center for scientific photography (1).

At the beginning of March 1925, Aleksandar Shafransky, the Russian military photographer, came to the Photography Department of the Institute of Histology. Shafransky made a significant contribution to the field of theoretical considerations of photography during the third and fourth decades of the 20th century. Together with Professor Kostić, he developed the Department of Photography. He was also an active member of the Belgrade Photo Club, which was founded in 1928 by professor Kostić with the aim of developing artistic and scientific photography, popularizing photography for tourist purposes and education (9).

Hodnikom se dalje dolazilo do ateljea u kome su snimani pacijenti, preparati i drugi predmeti. Atelje je bio prilagođen snimanju kako pri dnevnoj, tako i pri veštačkoj svetlosti. Dovoljan priliv dnevne svetlosti omogućavao je veliki prozor sa mutnim staklom i plavim pokretnim zavesama, dok su veštačku svetlost obezbeđivali jaki reflektori. Dobro osvetljenje je bilo posebno potrebno prilikom snimanja pojedinih patoloških promena kod pacijenata, posebno onih na koži (6,10).

Iz ateljea se nadesno ulazilo u sobu za hromofotografiju u kojoj su izrađivani snimci u boji, pozitivi i dijapositivi. Pozitivi u boji rađeni su po sistemu *Jos-pe*, a snimano je sa specijalnim aparatom, sa dimenzijom snimaka 9 x 12 cm. Dijapositivi u boji radili su se po sistemu autochromnog procesa po Limijeru. Na Institutu je sačuvano 43 dijapositiva u boji i oni danas predstavljaju izuzetno retke primerke svoje vrste ne samo kod nas, već i u svetu (slika 4). Razlog za tako mali broj sačuvanih autohroma leži u činjenici da su bili izuzetno osetljivi na svetlost i vlagu. Levo od ateljea bila je prostorija za mikrofotografiju opremljena velikim mikrofotografskim aparatom *Uma* firme *Leitz*. Iz nje se ulazilo u dve mračne komore izuzetno moderno opremljene, koje su u zidovima imale uzidana korita od armiranog betona obložena keramičkim pločicama (6,10).

Pored mračnih komora bila je soba za uveličavanje opremljena aparatom *Furor II*. Tu je bio instaliran i aparat za kopiranje kinematografskih filmova, kao i uređaj za „izazivanje“ i sušenje filmova.



**Slika 4.** Dijapositiv u boji (autohrom) „Hipofiza“. Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ Medicinskog fakulteta Univerziteta u Beogradu, Zbirka histoloških mikrofotograma prof. dr A. Kostića.

Iz sobe za uveličavanje ulazilo se u sobu za ispiranje. Na jednom zidu ove prostorije bila su ugrađena korita za ispiranje negativa i pozitiva, a iznad korita bile su žice sa štipaljkama za sušenje pozitiva (1,6).

Opremu za Fotografsko odeljenje profesor Kostić je nabavio od Znanstvenog zavoda prof. Breslera (*Brössler*), koji je osnovan 1923. godine u Zagrebu, sa podružnicama u Beogradu i Ljubljani. Saradnja Kostića sa pomenutim zavodom navodi se i u tekstu objavljenom u Vesniku kulture iz 1927. godine pod nazivom *Znanstveni zavod profesora dr Breslera Zagreb – Beograd*. U tekstu se navodi: „Isto tako institut g. Dr. Kostića za znanstvenu fotografiju izrađen je od strane ovog preduzeća savršeno“ (12).

U ovako moderno opremljenom Fotografskom odeljenju stekli su se uslovi da Kostić napravi veliki iskorak u pogledu drugih tema snimanja. Počeo je sa izradom mikrobioloških i patohistoloških, kao i mikrofotografskih snimaka mokraćnih kristala, zatim embrioloških i teratoloških snimaka. Fotografsko odeljenje je bilo i prva ustanova u Srbiji za medicinska snimanja, a imala je i urednu fotografsku dokumentaciju, takozvanu fototeku (3). Pojedini snimci pacijenata su dragoceni za istoričare medicine jer su na njima zabeležene patološke promene koje se zahvaljujući napretku dijagnostičkih i terapijaskih protokola u medicini, kao i otkriću i uvođenju vakcina, danas više ne viđaju u medicinskoj praksi.

Ideja profesora Kostića o izuzetno savremenom opremanju prostora Fotografskog odeljenja bila je posledica njegove spoznaje o značaju takve službe, ne samo za potrebe Histološkog instituta i Medicinskog fakulteta, već i drugih ustanova van Fakulteta. Kostić je već do 1935. godine uspostavio saradnju sa kolegama iz čak 47 obrazovnih i drugih institucija. Iz te saradnje je proistekao veliki broj snimaka sa motivima biljaka, različitih životinja, paleontoloških preparata, fosilnih ostataka, arheoloških artefakata, različitih instrumenata i drugih tema (1,6).

Razmera i bogatstva snimljenih motiva postali smo svesni tek nedavnim otkrićem fotografске zaostavštine profesora Kostića, za koju se decenijama nije znalo da postoji. Zaostavštinu čini nekoliko hiljada fotografskih staklenih ploča, zatim teratološka kolekcija, kao i (pred)ratna arhiva i brojni naučni separati i dokumenta (13).

Pored izrade fotografija, Odeljenje je omogućilo i mnogim nastavnicima Univerziteta u Beogradu

## The Photography Department in the new building of the Institute of Histology

When the Institute of Histology was moved to its new building in 1927, the Photography Department received a significant space of almost 160 m<sup>2</sup> and additional equipment. It was located on the first floor of the central part of the building of the Institute of Histology and Physiology, next to the amphitheatre and it had a series of rooms (1,6).

In the large corridor, along one side, there were: cabinets for drying negatives with warm air, for storing negatives, for the photographic library and storing photographic material, for apparatuses and optics, as well as a large desk for chemicals. On the other side of the corridor, *Ascania* microcinematographic camera with an "accelerating mechanism" was mounted, and it enabled 200 shots per second (6,10). It was precisely on this device that Professor Kostić recorded a series of sequences for the first films *the Blood flow in the peritoneal membrane of a frog* and *the Blood flow in the interdigital membrane of a frog*. However, apart from the name, almost nothing is known about them today because they were destroyed during the Second World War (11).

The corridor led to the studio where patients, preparations and other objects were filmed. The studio was adapted to shooting in both daylight and artificial light. Sufficient daylight was provided by a large window with opaque glass and blue

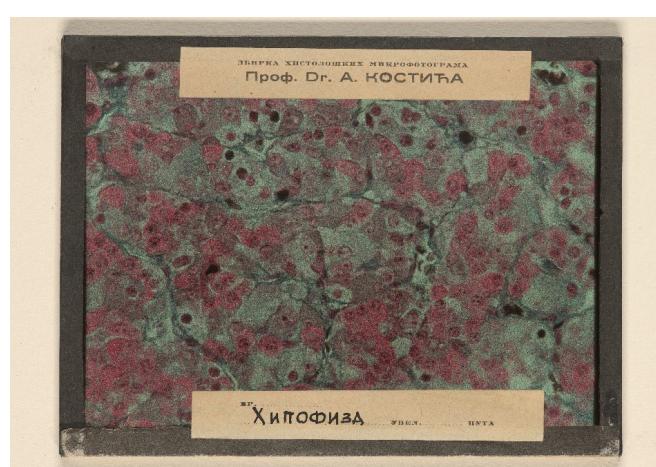
movable curtains, while the artificial light was provided by strong reflectors. Good light was particularly necessary when recording certain pathological changes in patients, especially those on the skin (6,10).

From the studio, on the right side was the chromophotography room, where colored images, positives and diapositives were made. Positives were made based on the system *Jos-pe*, and a special camera was used while the dimension of the images was 9 x 12 cm. Colored diapositives were made based on the system of autochrome process patented by Lumier. Forty-three colored diapositives were preserved at the Institute and today they represent extremely rare examples of their kind not only in our country, but in the world, as well (Picture 4). The reason for such a small number of preserved autochromes lies in the fact that they were extremely sensitive to light and moisture. On the left of the studio was a room for microphotography equipped with a large *Uma* microphotographic camera made by the Leitz company. This room led to two dark chambers that were modernly equipped, and had built-in troughs made of reinforced concrete coated with ceramic tiles (6,10).

In addition to dark chambers, there was a room for magnifying that was equipped with camera *Furor II*. There was also a device for copying cinematographic movies, as well as a device for "provoking" and drying movie tape. The room for magnifying led to the room for rinsing. Built-in troughs for rinsing negatives and positives were on one wall of this room, while wires with clippers for drying positives were above the troughs (1,6).

Professor Kostić got the equipment for the Photography department from the Scientific Institute of professor Brössler, which was founded in Zagreb in 1923, with branches in Belgrade and Ljubljana. The collaboration between Kostić and the aforementioned Institute is described in the text that was published in the magazine „Vesnik kulture“ in 1927 under the name "The Scientific Institute of Professor Brössler Zagreb-Beograd". It is also stated in the text: "the Institute of Professor Kostić for scientific photography was made by this company perfectly" (12).

In such a modern photographic department, the conditions enabled Kostić to make a large step forward in terms of other filming themes. He started



**Picture 4.** Colored diapositive (autochrome) "Pituitary gland". Institute of Histology and Embryology "Prof. dr Aleksandar Đ. Kostić" of the Faculty of Medicine, University of Belgrade, Collection of histological microphotograms of Professor A. Kostić.

savladavanje fotografске tehnike i tehnike izrade fotografija i slajdova. Takođe, bilo je i uzor u organizovanju prostora i nabavci opreme mnogim kasnije uspostavljenim fotografskim laboratorijama na Univerzitetu (1).

## Fotografsko odeljenje prof. Kostića u posleratnom periodu

Tokom aprilskog bombardovanja Beograda 1941. godine, pogodjena je zgrada Fiziološkog i Histološkog instituta, i tom prilikom je delimično oštećen inventar Fotografskog odeljenja. Aparate i opremu koji su „preživeli“ bombardovanje, odneo je nemački okupator, pa je Odeljenje bilo potpuno opustošeno (2). Međutim, ubrzo po oslobođenju, počinje obnova Fotografskog odeljenja i nabavka odgovarajuće opreme za izradu fotografija, ali i moderne kamere i kompletna oprema za izradu filmova.

U radu u Fotografskom odeljenju prof. Kostiću su od kraja 1945. pomagala i dva saradnika: fotograf Vladimir Jelovac i kinooperater Milisav Jakovljević, koji su u prvim mesecima rada, dok nije stigla sva naručena oprema, svoju fotografsku opremu stavljali besplatno na raspolaganje Odeljenju (14). Vladimir Jelovac je bio magistar farmacije i odličan poznavalac fotohemije, ali i konstruktor dodataka za Lajkine kamere. Sa druge strane, Milisav Jakov-

ljević je bio dugogodišnji kino-operater sa velikim iskustvom u inostranstvu (slika 5) (15).

Profesor Kostić je prvim posleratnim godinama režirao i nekoliko medicinskih filmova, međutim, njihov tačan broj u ovom momentu nije poznat. Naime, sam Kostić u jednom rukopisu pominje da ih je bilo dvanaest, ali navodi naslove njih šest (5, 11). U svakom slučaju, bili su to prvi medicinski filmovi u Jugoslaviji, neki od njih snimljeni čak i preigranih filmova (5,11). Na normalnoj traci (35 mm) je 1945. (ili 1946.) snimljen film *Izrada histoloških preparata* (u dva dela), a snimatelj je bio Milisav Jakovljević. Na uzanoj (16 mm) traci između 1946. i 1949. snimljeno je preostalih 5 filmova, čiji naslovi su nam poznati: *Tumor kičmene moždine* (operator prof. Slobodan Kostić), *Perikardioliza* (operator prof. Vojislav Stojanović), *Resekcija želuca* (operator prof. Milivoje Kostić), *Litlova bolest/Fersterova operacija* (operator prof. Dimitrije Jovčić) i *Judinova operacija jednjaka/Plastika jednjaka* (operator prof. Isidor Papo, u to vreme sanitetski pukovnik, kasnije general) (5,11). Za snimanje je korišćena *Roloflex* kamera, a snimatelj je bio Kosta Novaković, pionir jugoslovenske kinematografije, inače magistar farmacije (5,11). Svi filmovi su bili dužine između 250 i 260 metara. Kostićeva uloga u režiji se, prema njegovim sopstvenim rečima, više svodi na dirigovanje i organizovanje uveličanja, dok su



Slika 5. Profesor Kostić sa saradnicima Foto-filmskog zavoda, oko 1950. godina.  
Institut za histologiju i embriologiju „Prof. dr Aleksandar Đ. Kostić“ Medicinskog fakulteta Univerziteta u Beogradu.

making microbiological and pathohistological, as well as microphotographic images of urine crystals, then embryological and teratological records. The Photography Department was the first institution in Serbia for medical recordings, and had neat photographic documentation, the so-called photo archive (3). Some images of patients are valuable for medical historians because they present some pathological changes that are not seen today in medical practice thanks to the advance of diagnostic and therapeutic protocols in medicine, as well as the discovery and introduction of vaccines.

The idea of Professor Kostić about equipping the Photography Department with modern equipment was the result of his realization of the significance of such a service, not only for the needs of the Institute of Histology and the Faculty of Medicine, but also for other institutions outside the faculty. Until 1935, Kostić had established collaboration with colleagues from even 47 educational and other institutions. A large number of recordings with the motifs of plants, different animals, paleontological preparations, fossil remains, archeological artifacts, different instruments and other topics resulted from that collaboration (1,6).

We only became aware of the scale and richness of the captured motifs with the recent discovery of Professor Kostić's photographic heritage, which was not known for decades. The legacy consists of several thousand photographic glass plates, then a teratological collection, as well as a (pre)war archive and numerous scientific papers and documents (13).

In addition to making photographs, the Department also enabled many teachers of the University of Belgrade to master photographic techniques of making photographs and slides. Also, it was a role model regarding the organization of space and the procurement of equipment for many later-established photographic laboratories at the University (1).

### **Professor Kostić's Photography Department in the post-war period**

During the bombing of Belgrade in April, 1941, the building of the Institute of Histology and Physiology was hit, and on that occasion, the inventory of the Photography Department was partially damaged. The devices and equipment that "survived" the bombing were taken away by the German soldiers, so the Department was completely devastated (2). However, shortly after



**Picture 5.** Professor Kostić with associates of the Photo-film Institute around 1950.  
The Institute of Histology and Embryology "Prof. dr Aleksandar Kostić" of the Faculty of Medicine, University of Belgrade.

„neprikosnoveni reditelji“ bili profesori koji su izvodili operacije. Inače, svi pomenuti profesori su bili velikani srpske i jugoslovenske hirurgije.

Pored pomenutih filmova, snimljena je i serija od pet ili šest kratkih informativnih filmova, takozvanih *Medicinskih žurnala*, dužine oko 120 metara. U njima su prikazani karakteristični slučajevi sa klinika Medicinskog fakulteta. Snimatelj žurnala bio je takođe Kosta Novaković (11). Nije poznato da li su sačuvni do danas.

Ideja je bila i da se nastavi sa snimanjem takvih kratkih edukativnih filmova namenjenih studentima i lekarima, i da se snimanje interesantnih slučajeva radi u svim većim bolnicama, ali i domovima zdravlja u Srbiji. Bili su urađeni i scenariji za izradu filmova o pravilnom pregledu bolesnika, davanju injekcija, izvođenju punkcija, transfuzija i drugog, ali do realizacije nije došlo (11).

Prema Kostićevim rečima, zastoj u izradi medicinskih filmova je nastao kada je Fotografsko odeljenje izdvojeno iz sastava Histološkog instituta i pretvoreno u samostalnu ustanovu pod nazivom Foto-filmski zavod, pod neposrednom upravom Medicinskog fakulteta (16).

## Međunarodna izložba medicinske fotografije u Londonu

Profesor Kostić je 1950. godine učestvovao na Međunarodnoj izložbi medicinske fotografije u Londonu. Pored fotografija, te godine je na izložbi bio prijavljen tek jedan film biološkog odeljenja fabrike Ciba iz Bazela pod nazivom *Xenopus laevis*. Iako Kostić nije bio prijavio ni jedan svoj medicinski film, bilo mu je omogućeno da pred Savetom Kraljevskog društva (*Royal Society*) i njegovim predsednikom, nobelovcem ser Henri Delom (*Sir Henry Dale*) prikaže jedan od *Medicinskih žurnala*. Film je naišao na veliko interesovanje i vrlo pozitivne komentare. Stoga je usledio dogovor da se između Društva i Foto-filmskog zavoda uspostavi saradnja i razmena filmova. Za svaki film ustupljen Društvu Zavod je trebalo da dobije medicinski film u boji. Međutim, nije došlo do realizacije te saradnje. Moguće da je uklanjanje profesora Kostića sa Medicinskog fakulteta bilo uzrok tome (11,17). Na pozitivne komentare u Londonu su naišli i filmovi *Operacija tumora kičmene moždine* i *Perikardiektomija*, koji su prikazani pred gospodinom Wilsonom (*Wilson*), direktorom Fotografskog instituta.

## Foto-filmski zavod

U proleće 1950. godine Fotografsko odeljenje je izdvojeno u zasebnu ustanovu pod nazivom Foto-filmski zavod Medicinske velike škole u Beogradu. U to vreme, tačnije od 21.6.1948. do 28.7. 1954. godine, tri fakulteta – Medicinski, Farmaceutski i Stomatološki, bila su izdvojena iz sastava Univerziteta u Beogradu i organizovana u okviru Medicinske velike škole, ustanove u rangu univerziteta (18). Cilj Zavoda bio je da organizuje i obavlja celokupnu foto-filmsku aktivnost Medicinske velike škole u oblasti nastave i naučno-istraživačkog rada, da prati razvoj opšte i naučne fotografije i kinematografije i obučava mlade kadrove za Foto-filmsku službu u medicini (3). Za upravnika Foto-filmskog zavoda je određen prof. Kostić. Međutim, on je u martu 1952. godine udaljen sa Medicinskog fakulteta iz političkih razloga, a za upravnika je imenovan prof. Mileta Magarašević. Foto-filmski zavod je nakon prof. Magaraševića vodio dr Miodrag Mile Đorđević, zatim Dragan Pantelić, a 1998. godine je na inicijativu prof. Vesne Lačković, tadašnje upravnice Histološkog instituta, vraćen u sastav Instituta. Međutim, u januaru 2006. godine Zavod je prestao sa radom (2). Bio je to danak razvoju savremene fotografске tehnologije, dostupnosti fotografije i video zapisa putem mobilnih telefona, dostupnosti različitih fotografskih i filmskih sadržaja i brze razmene podataka putem interneta.

Fotografsko odeljenje koje je osnovao prof. dr Aleksandar Kostić imalo je istorijsku ulogu u naučno-obrazovnom sistemu Medicinskog fakulteta i njegovih instituta, naročito za samu histologiju. Kostićev doprinos razvoju medicinske dokumentarne fotografije je nemerljiv i zavređuje posebnu pažnju, jer je on na Fotografskom odeljenju Instituta za histologiju, kako sam navodi „izradio prve fotomikrograme u Jugoslaviji, a među prvima i u Evropi“ (19).

Fotografsko odeljenje bilo je i pionir medicinskog filma na ovim prostorima. Duboko svestan značaja naučnih filmova za potrebe edukacije studenata medicine, ali i lekara, profesor Kostić je i po uklanjanju sa fakulteta nastavio da se bori i zalaže za njihovo snimanje i uvođenje u praksu kroz brojne tekstove koje je objavljivao u inostranim i domaćim naučnim i stručnim časopisima, kao i u stampi gotovo do kraja života (11,16,17,20).

the liberation, the restoration of the Photography Department began and the acquisition of appropriate equipment for making photographs, as well as modern cameras and complete equipment for making films.

In his work in the Photography Department, from the end of 1945, Professor Kostić was assisted by two assistants: photographer Vladimir Jelovac and cinematographer Milisav Jakovljević, who in the first months of work, made their photographic equipment available to the Department until all the ordered equipment arrived (14). Vladimir Jelovac was a master of Pharmacy and an expert in photochemistry, as well as a designer of accessories for Leica cameras. Milisav Jakovljević, on the other hand, was a long-time cinema operator with great international experience (Picture 5) (15).

Professor Kostić also directed several medical films in the first post-war years, however, their exact number is not known at the moment. Namely, Kostić himself mentions in one manuscript that there were twelve of them, but he lists the titles of six of them (5,11). In any case, they were the first medical films in Yugoslavia, and some of them were filmed before feature films (5,11). In 1945 (or 1946), the film *Making histological specimens* (in two parts) was shot on normal film tape (35 mm), and the cinematographer was Milisav Jakovljević. Between 1946 and 1949, the remaining 5 films were shot on narrow (16 mm) tape, and their titles are known: *Tumor of the spinal cord* (operator Prof. Slobodan Kostić), *Pericardiolysis* (operator Prof. Vojislav Stojanović), *Gastric Resection* (operator Prof. Milivoje Kostić), *Little's disease/Ferster's operation* (operator Prof. Dimitrije Jovčić) and *Yudin's surgery of esophagus/esophagoplasty* (operator prof. Isidor Papo, at that time, medical colonel, later general) (5,11). *Roloflex* camera was used for filming, while the cameraman was Kosta Novaković, a pioneer in Yugoslav cinematography, who also had a master's degree in pharmacy (5,11). All films were between 250 and 260 meters long. According to Kostić, his role in directing was more related to managing and organizing the magnifications, while "the true directors" were the professors who performed the operations. Otherwise, all of the mentioned professors were great men of Serbian and Yugoslav surgery.

In addition to the mentioned films, a series of five or six short informational films, so-called *Medical journals*, was shot and they were 120

meters long. Characteristic cases from the clinics of the Faculty of Medicine were presented in them. The cameraman of the journal was Kosta Novaković (11). It is not known whether they have been preserved to this day.

The idea was to continue filming such short educational films intended for students and doctors, and to film interesting cases in all major hospitals and health centers in Serbia. Scenarios were also prepared for the production of films about the proper examination of patients, giving injections, performing punctures, transfusions and others, but they were not realized (11).

According to Kostić, the production of medical films was interrupted when the Photography Department was separated from the Institute of Histology and turned into an independent institution under the name Photo-Film Institute, under the direct management of the Faculty of Medicine (16).

## International Exhibition of Medical Photography in London

In 1950, Professor Kostić participated in the International Exhibition of Medical Photography in London. In addition to the photographs, only one film from the biological department of the Ciba factory in Basel was submitted for the exhibition that year, under the name *Xenopus laevis*. Although Kostić had not registered any of his medical films, he was given an opportunity to present one of his *Medical Journals* before the Council of the Royal Society and its president, Nobel laureate Sir Henry Dale. The film caused great interest and positive comments. Therefore, the agreement was made to establish the cooperation and exchange of films between the Royal Society and the Photo-Film Institute. The Institute was supposed to receive colored medical film for each film given to the Society. However, that cooperation was not realized. It is possible that the removal of Professor Kostić from the Faculty of Medicine was the reason for this (11,17). The films *The Operation of spinal cord tumor* and *Pericardectomy* which were shown in front of Mr. Wilson, director of the Photographic Institute received also positive comments in London.

## Photo-Film Institute

The Photography Department was separated from the Institute of Histology in the spring of

Fotografsko odeljenje Aleksandra Kostića je sinonim za uvođenje i upotrebu fotografije i filma u nauku i medicinu. Činjenica da je ono živelo decenijama nakon Kostićevog udaljavanja sa Medicinskog fakulteta je dokaz koliko je bio ispred svoga vremena u razmišljanjima kada ga je uspostavlja i koliko je čvrste temelje postavio.

## Zahvalnica

Neizmernu zahvalnost za pomoć u prikupljanju podataka prikazanih u ovom radu i stručnu pomoć i podršku autorke duguju dr Vesni Lačković, profesorki histologije i embriologije u penziji, dr Jeleni Jovanović Simić, višem kustosu Muzeja nauke i tehnike i Milanki Todić, profesorki istorije umetnosti u penziji. Zahvalnost za pomoć u pronalaženju podataka o postojanju i radu firme prof. Breslera duguju Milošu Jurišiću, fotografu Muzeja nauke i tehnike. Za pomoć u realizaciji procesa digitalizacije fotografskih staklenih negativa profesora Kostića duguju zahvalnost akademiku Aleksandru Kostiću, upravniku Audiovizuelnog arhiva i centra za digitalizaciju SANU i svim saradnicima AVA SANU.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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1950 to form the Photo-Film Institute of the Great School of Medicine in Belgrade. At that time, more precisely from June 21<sup>st</sup>, 1948 to July 28<sup>th</sup>, 1954, three faculties – Medicine, Pharmacy and Dentistry, were separated from the University of Belgrade and organized within the Great School of Medicine, an institution at the level of a university (18). The aim of the Institute was to organize and carry out the entire photo-film activity of the Great School of Medicine in the field of teaching and scientific research, to follow the development of general and scientific photography and cinematography and to train young personnel for the photo-film service in medicine (3). Professor Kostić was appointed the manager of the Photo-film Institute. However, he was removed from the Faculty of Medicine in March 1952 due to political reasons, and Professor Mileta Magarašević was appointed to the position of manager. After Professor Magarašević, the Photo-Film Institute was led by Dr. Miodrag Mile Đorđević, then by Dragan Pantelić, before being returned to work within the Institute of Histology in 1998, on the initiative of Professor Vesna Lačković, then the director of the Institute of Histology. However, in January 2006, the Institute was closed (2). It happened due to the development of modern photographic technology, the availability of photography and videos via mobile phones, the availability of different photographic and film contents and the rapid exchange of data via the Internet.

The Photography Department, founded by Professor Aleksandar Kostić, had a historical role in the scientific and educational system of the Faculty of Medicine and its Institutes, especially for Histology itself. Kostić's contribution to the development of medical documentary photography is immeasurable and deserves special attention, because according to his own words, he "created the first photomicrograms in Yugoslavia, and among the first in Europe" at the Photographic Department of the Institute of Histology (19).

The Photography Department was also a pioneer of medical film in this region. Deeply aware of the significance of scientific films for the educational needs of medical students, as well as doctors, Professor Kostić, even after his removal from the faculty, continued to fight and advocate for their recording and introduction into practice through numerous texts that he published in

foreign and domestic scientific journals, as well as in magazines almost until the end of his life (11,16,17,20).

Aleksandar Kostić's Photography Department is a synonym for the introduction and use of photography and film in science and medicine. The fact that it lived decades after Kostić's removal from the Faculty of Medicine proves how far ahead of his time he was when he founded it and how solid the foundations were.

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## Competing interests

Authors declare no competing interests.

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## POST-EKSPOZICIONA I PRE-EKSPOZICIONA PROFILAKSA KAO MERE PREVENCIJE HIV INFEKCIJE

Slađana Baroš<sup>1\*</sup>, Sandra Grujičić<sup>2</sup>

<sup>1</sup> Centar za kontrolu i prevenciju bolesti, Odeljenje za HIV, PPI, virusne hepatitise i tuberkulozu, Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut”, Beograd, Republika Srbija

<sup>2</sup> Institut za epidemiologiju, Medicinski fakultet Univerziteta u Beogradu, Beograd, Republika Srbija

\* Korespondencija: Slađana Baroš, MPH, Centar za prevenciju i kontrolu bolesti, Odeljenje za HIV, PPI, virusne hepatitise i tuberkulozu, Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut”, Dr Subotića 5, Beograd, Republika Srbija; e-mail: sladjana.baros@gmail.com

### SAŽETAK

Hemioprofilaksa u prevenciji HIV infekcije praktično počinje da se koristi od registrovanja prvog leka za lečenje AIDS-a odnosno od 1987. godine. Post-eksponirana profilaksa (PEP) koju koriste osobe akcidentalno eksponirane HIV infekciji uglavnom je vezana za profesionalnu akcidentalnu izloženost HIV infekciji (primarno zdravstvenih radnika). Procenjuje se da PEP smanjuje rizik za 81% od HIV infekcije. Pre-eksponirana profilaksa (PrEP) je počela više da se ispituje i primenjuje pre desetak godina. PrEP je namenjena osobama koje nisu inficirane HIV-om, ali su u kontinuiranom riziku od HIV-a usled svog rizičnog ponašanja. Procenjuje se da PrEP smanjuje rizik od nastanka HIV infekcije za 75% i više u zavisnosti od populacije i adherencije propisanom terapijskom režimu. U Srbiji PEP i PrEP i dalje nisu potpuno regulisane, ali je rad na tome počeo 2022. godine. U zemljama sa neregulisanom PrEP prisutan je rizik od neformalne upotrebe terapije bez medicinskog nadzora, što može da dovede do manje efikasnosti PrEP i razvoja rezistentnih oblika HIV infekcije u slučaju prethodno nedijagnostikovane HIV infekcije. Obe intervencije pripadaju biomedicinskim intervencijama vezanim za prevenciju HIV infekcije i od značaja su za dosezanje globalnih ciljeva usmerenih na okončanje AIDS-a kao „javnozdravstvene pretnje” do 2030. godine. Međutim, da bi biomedicinske intervencije bile maksimalno efikasne, potrebno je da budu praćene adekvatnim bihevioralnim intervencijama u cilju povećanja informisanosti, adherencije propisanom terapijskom režimu i periodične kontrole zdravstvenog stanja u skladu sa definisanim preporukama za PEP i PrEP.

**Ključne reči:** post-eksponirana profilaksa, pre-eksponirana profilaksa, HIV infekcija, AIDS, zdravstveni radnici, biomedicinske intervencije

### Uvod

Po procenama Udruženog programa Ujedinjenih nacija za HIV/AIDS (engl. *Joint United Nations Programme on Human Immunodeficiency Virus - HIV/Acquired ImmunoDeficiency Syndrome - AIDS*), u daljem tekstu: UNAIDS), od početka epidemije pa do kraja 2021. godine 84,2 miliona (64,0-113,0 miliona) ljudi je inficirano HIV-om, a 40,1 milion (33,6 - 48,6 miliona) osoba je umrlo od bolesti i stanja povezanih sa AIDS-om (1). Samo u regionu Evrope, kako je definisano od strane Svetske zdravstvene organizacije (SZO), u 2021. godini ukupno je kod 106.508 osoba novodijagnostikova-

na HIV infekcija. Od toga, kod 5.940 osoba je HIV novodijagnostikovan u regionu Centralne Evrope, gde pripada i Srbija (sa 172 osobe kojima je HIV novodijagnostikovan). Kumulativno, od početka registrovanja HIV slučajeva do kraja 2021. godine, HIV-om je inficirano oko 2,3 miliona osoba u regionu Evrope (od kojih 106.411 u regionu Centralne Evrope, sa 4.372 osobe u Srbiji). Na kraju 2021. godine, od bolesti i stanja povezanih sa AIDS-om u regionu Evrope je umrlo 3.354 osobe (kumulativno od početka registrovanja do kraja 2021. godine 270.374), od kojih je njih 229 umrlo u regionu Cen-

## POST-EXPOSURE AND PRE-EXPOSURE PROPHYLAXIS AS HIV PREVENTIVE MEASURES

Slađana Baros<sup>1\*</sup>, Sandra Grujicic<sup>2</sup>

<sup>1</sup> Centre for Disease Prevention and Control, Department for HIV, STI, viral hepatitis and tuberculosis, Institut of Public Health of Serbia „Dr Milan Jovanovic Batut”, Belgrade, Republic of Serbia

<sup>2</sup> Institute of Epidemiology, Faculty of Medicine, Belgrade University, Belgrade, Republic of Serbia

\* Correspondence: Sladjana Baros, MPH, Centre for Disease Prevention and Control, Department for HIV, STI, viral hepatitis and tuberculosis, Institut of Public Health of Serbia „Dr Milan Jovanovic Batut”, 5 Dr Subotića Street, Belgrade, republic of Serbia; e-mail: sladjana.baros@gmail.com

### SUMMARY

HIV chemoprophylaxis started to be used since the first AIDS drug was registered, i.e. in 1987. Post-exposure prophylaxis (PEP), used by persons accidentally exposed to HIV, is mostly related to professional accidental exposure to HIV (mostly among healthcare workers). It is estimated that PEP decreases HIV risk by 81%. Research and implementation of pre-exposure prophylaxis (PrEP) started about 10 years ago. PrEP is intended for use among those who are HIV negative, and in the continuous HIV risk due to their behavior. It is estimated that PrEP use decreases HIV risk by 75% or more, depending on the population and adherence to treatment. In Serbia, PEP and PrEP are still not fully regulated. However, in 2022, the work on regulations has started. In countries with unregulated PrEP, there is a risk from informal therapy use without medical supervision, which can lead to the development of resistant HIV cases among those with previously undiagnosed HIV infection. Both interventions belong to the biomedical HIV preventive interventions, and both are relevant for reaching the global AIDS target – to end AIDS as a “public health threat” by 2030. Nevertheless, for biomedical interventions to be at maximum efficacy, they have to be integrated with adequate behavioral ones, aiming to increase information, adherence to the therapy, and to periodical medical supervision, in line with defined PEP and PrEP recommendations.

**Keywords:** post-exposure prophylaxis, pre-exposure prophylaxis, HIV infection, AIDS, healthcare workers, biomedical interventions

### Introduction

According to the estimates of the Joint United Nations Program on Human Immunodeficiency Virus - HIV/ Acquired Immunodeficiency Syndrome AIDS, from the beginning of the epidemic until the end of 2021, 84.2 million (64.0-113.0 million) people were infected with HIV, and 40.1 million (33.6-48.6 million) people died from AIDS-related diseases and conditions (1). Only in the European region, as defined by the World Health Organization (WHO), in 2021, a total of 106,508 people were newly diagnosed with HIV infection. Of these, 5,940 people were newly diagnosed with HIV in the region of Central Europe, which includes Serbia as well (with 172 people newly diagnosed with HIV). Cumulatively, from the beginning of registration of HIV cases until the end of 2021, about 2.3 million

people in the European region were infected with HIV (of whom 106,411 in the Central European region with 4,372 people in Serbia). At the end of 2021, 3,354 people died from AIDS-related diseases and conditions in the European region (cumulatively from the beginning of registration until the end of 2021, 270,374 people), while 229 of them died in the Central European region (cumulatively 9,936) with 14 persons from Serbia (cumulatively 1,186). In the Central European region, the dominant way of transmission of HIV infection is sexual, where the transmission of HIV infection is equally shared by unprotected sexual intercourse between women and men and between men. In Serbia, sexual transmission of HIV infection is dominant, primarily the unprotected sexual intercourse among men (2).

tralne Evrope (kumulativno 9.936), sa 14 osoba iz Srbije (kumulativno 1.186). U regionu Centralne Evrope dominantan način transmisije HIV infekcije je seksualnim putem, gde je podjednako učešće transmisije HIV infekcije nezaštićenim seksualnim odnosom između muškaraca i žena i između muškaraca. U Srbiji dominira seksualni način transmisije HIV infekcije, primarno nezaštićenim seksualnim odnosom među muškarcima (2).

Od početaka HIV/AIDS epidemije, nacionalne politike i mere za suzbijanje i prevenciju HIV/AIDS-a su bile usmerene preporukama centralnih međunarodnih organizacija koje su bile posvećene borbi protiv HIV/AIDS-a. Uspešnost odgovora je praćena dosezanjem zacrtanih ciljeva na globalnom i na nacionalnim nivoima. Globalni ciljevi definisani za 2020. godinu, određeni strategijom UNAIDS-a za 2016–2021. godinu, nisu dosegnuti. Na kraju 2020. godine, procenjuje se da je 1,5 miliona (1,2–2,0 miliona) osoba bilo novoinficirano HIV-om, što je tri puta više od strateškog cilja od 500.000 novih infekcija globalno, kao i da je 690.000 (540.000–900.000) osoba umrlo od bolesti i stanja povezanih sa AIDS-om, što je za 140.000 više osoba od strateškog cilja da bude manje od 500.000 osoba preminulih od bolesti i stanja povezanih sa AIDS-om (3). Kada je reč o dosezanju operativnog cilja 90-90-90 (da 90% osoba koje žive sa HIV-om znaju da su inficirane HIV-om, da 90% osoba koje znaju da žive sa HIV-om bude na lečenju antiretrovirusnom (ARV) terapijom i da 90% osoba koje su na lečenju ARV terapijom ima nedetektibilnu viremiju u krvi), nije ni on u potpunosti dosegnut. Na kraju 2020. godine, na globalnom nivou 83% osoba koje žive sa HIV-om su znale da su inficirane HIV-om, 87% od onih osoba koje znaju da žive sa HIV-om se lečilo ARV terapijom, a kod 90% osoba koje se leče ARV terapijom bila je postignuta nedetektibilna viremija u krvi (3).

U regionu Centralne Evrope, po podeli SZO, kao i u Srbiji, na kraju 2020. godine cilj „90-90-90“ nije dosegnut. U regionu centralne Evrope 87% osoba koje žive sa HIV-om je dijagnostikovano, 67% osoba sa dijagnostikovanom HIV infekcijom je bilo na lečenju ARV terapijom, a kod 81% osoba koje se leče ARV terapijom postignuta je supresija virusa u krvi do nedetektabilnosti (4). Na kraju 2020. godine, prema UNAIDS procenama, u Srbiji je 85% od osoba koje žive sa HIV-om znalo da su inficirane HIV-om, a 75% onih osoba koje znaju da žive sa HIV-om bilo je na lečenju ARV terapijom

(3). Na žalost, naša zemlja ne raspolaže podatkom o uspešnosti lečenja ARV terapijom, odnosno da li je dosegnuta željena supresija virusa u krvi (ispod 50 kopija/ml).

Na sastanku visokog nivoa o AIDS-u redefinišani su ciljevi i UNAIDS postavljaju nove, jednako ambiciozne, za 2025. godinu: da bude manje od 370.000 osoba novoinficiranih HIV-om, kao i manje od 250.000 onih koji su umrli od bolesti i stanja povezanih sa AIDS-om, što bi vodilo ka tome da do 2030. godine ne bude novih infekcija, kao ni smrti od bolesti i stanja povezanih sa AIDS-om (5). Nedosegnuti cilj „90-90-90“ postaje ambiciozniji i prelazi u „95-95-95“ (da 95% onih koji žive sa HIV-om zna da su inficirani HIV-om, da se 95% onih koji znaju da žive sa HIV-om leče ARV terapijom, i da se kod 95% onih koji su na lečenju ARV terapijom postigne nedetektibilna viremija u krvi) (5). Ovako ambiciozni ciljevi zahtevaju i uvođenje novih intervencija, kako bihevioralnih, tako i biomedicinskih i strukturalnih. U ovom radu detaljnije ćemo predstaviti hemioprofilaktične intervencije za prevenciju HIV infekcije, primarno post-eksponicionu i pre-eksponicionu hemioprofilaksu.

## Biomedicinske intervencije za prevenciju HIV infekcije

U poslednjih 15-ak godina biomedicinske intervencije sve više zauzimaju primat u prevenciji HIV infekcije. Ove intervencije se odnose na primenu terapije i medicinskih tehnika u cilju sprečavanja infekcije HIV-om (6). Obuhvataju muški i ženski kondom kao fizičku barijeru za inficiranje HIV-om, zatim cirkumciziju, dijagnostikovanje i lečenje polno prenosivih infekcija, hemioprofilaksu pre ili posle eksponicije HIV infekciji ili u okviru prevencije vertikalne transmisije, lečenje ARV terapijom kao preventivnu meru kod seksualnih partnera različitog HIV statusa, i slično.

### Post-eksponiciona profilaksa

Profilaktična upotreba ARV terapije nakon eksponicije HIV infekciji je započela već krajem 80-tih godina 20. veka, sa registrovanjem prvog leka za terapijsko lečenje AIDS-a (zidovudine, AZT) 1987. godine od strane američke Administracije za hranu i lekove (engl. *Food and Drug Administration*) (7). AZT se za prevenciju HIV infekcije najpre počeo koristiti u slučaju profesionalne eksponicije HIV infekciji zdravstvenih radnika. Već početkom 1990. godine Centri za suzbijanje i prevenciju bolesti

Since the beginning of HIV/AIDS epidemic, national policies and measures for the suppression and prevention of HIV/AIDS have been directed by recommendations of central international organizations dedicated to the fight against HIV/AIDS. The success of the response is monitored by reaching the set goals at the global and national level. Global goals defined for the year 2020, which were determined by the UNAIDS strategy for 2016-2021, have not been reached. At the end of 2020, it was estimated that 1.5 million people (1.2-2.0 million people) were newly infected with HIV, which is three times more compared to the strategic target of 500,000 new infections globally, as well as that 690,000 (540,000-900,000) people died from AIDS-related diseases and conditions, which is 140,000 more people than the strategic goal of less than 500,000 dying from AIDS-related diseases and conditions (3). When it comes to reaching the operational goal of 90-90-90 (that 90% of people living with HIV know that they are infected with HIV, that 90% of people who know they are living with HIV are treated with antiretroviral (ARV) therapy and that 90% of people on ARV therapy have undetectable viremia in the blood), it has not been fully reached either. At the end of 2020, globally 83% of people living with HIV knew they were infected with HIV, 87% of people who knew they were living with HIV were being treated with ARV therapy, and in 90% of people treated with ARV therapy, undetectable viremia was achieved in the blood (3).

In the Central European region, according to the division of the WHO, as well as in Serbia, at the end of 2020, the "90-90-90" goal was not achieved. In the region of Central Europe, 87% of people living with HIV were diagnosed, 67% of people with diagnosed HIV infection were treated with ARV therapy, and in 81% of people treated with ARV therapy, suppression to the undetectable virus in the blood was achieved (4). At the end of 2020, according to UNAIDS estimates, 85% of people living with HIV in Serbia knew they were infected with HIV, and 75% of those people who knew they were living with HIV were treated with ARV therapy (3). Unfortunately, our country does not have data on the success of treatment with ARV therapy, that is, whether the desired suppression of the virus in the blood (below 50 copies/ml) has been achieved.

At the high level meeting on AIDS, the goals have been redefined and UNAIDS has set the

new, equally ambitious goals for 2025: fewer than 370,000 newly infected people, as well as fewer than 250,000 people who died from AIDS-related diseases and conditions, which would lead to no new infections and no deaths from AIDS-related diseases and conditions by 2030 (5). The unachieved goal of "90-90-90" becomes more ambitious and turns into "95-95-95" (which means that 95% of those living with HIV know they are infected with HIV, that 95% of those who know they are living with HIV are treated with ARV therapy and that in 95% of those who are on ARV therapy, undetectable viremia in the blood is achieved) (5). Such ambitious goals require the introduction of new behavioral interventions, as well as biomedical and structural. In this paper, we will present chemoprophylactic interventions for the prevention of HIV infection in more detail, primarily post-exposure and pre-exposure chemoprophylaxis.

## Biomedical interventions for the prevention of HIV infection

In the last 15 years, biomedical interventions have increasingly taken precedence in the prevention of HIV infection. These interventions refer to the application of therapy and medical techniques in order to prevent HIV infection (6). They include the male and female condom as a physical barrier to HIV infection, then circumcision, diagnosis and treatment of sexually transmitted infections, chemoprophylaxis before and after exposure to HIV infection or as part of the prevention of vertical transmission, treatment with ARV therapy as a preventive measure in partners of different HIV status, and similarly.

### *Post-exposure prophylaxis*

The prophylactic use of ARV therapy after exposure to HIV infection started already at the end of 1980s, with the registration of the first drug for therapeutic treatment of AIDS (zidovudine, AZT) in 1987 by the US Food and Drug Administration (7). AZT was first used for the prevention of HIV infection in the case of occupational exposure to HIV infection of healthcare workers. Already at the beginning of 1990, the Centers for Disease Prevention and Control (CDC) published recommendations for the prevention of HIV infection among accidentally exposed healthcare workers using post-exposure

(engl. *Centers for Disease Prevention and Control - CDC*) objavljaju preporuke za prevenciju HIV infekcije među akcidentalno eksponiranim zdravstvenim radnicima koristeći post-ekspozicionu profilaksu (PEP) AZT-om (8). Kasnijim studijama je ustanovljeno da je rizik od inficiranja HIV-om kod zdravstvenih radnika nakon perkutane ekspozicije krvi inficiranoj HIV-om 0,3% (9,10), odnosno 0,09% nakon kontaminacije sluzokože kroz kontakt sa krvlju inficiranom HIV-om (10), kao i da post-ekspoziciona profilaksa nakon perkutanih povreda smanjuje rizik za 81% od inficiranja HIV-om (9).

Među zdravstvenim radnicima profesionalni rizik predstavljaju primarno perkutane povrede (ubod na iglu ili ubodi i posekotine oštrim instrumentima), kontaminacija sluzokoža (usta, konjunktiva) i kontaminacija ledirane kože (rane, abrazijske, dermatitis) kroz kontakt sa krvlju inficiranom HIV-om u trajanju minimum 15 minuta. Izvori HIV infekcije koji mogu dovesti do njenog prenošenja su primarno krv, ali i telesne tečnosti i tkiva u kojima se može naći HIV (telesne tečnosti koje imaju vidljive tragove krvi, vaginalni sekret, semena, amniotska, pleuralna, cerebrospinalna, perikardna i peritonealna tečnost). Kada je reč o stepenu rizika koji nosi sama ekspozicija, on zavisi od vrste igle i/ili oštrog instrumenta (dimenzije) s kojim je došlo do povrede, težine ozlede (dubina), količine infektivne doze kojoj je eksponiran zdravstveni radnik i stepena viremije kod pacijenta čijom krvlju je eksponiran zdravstveni radnik (11,12).

CDC prvi put preporučuje PEP za neprofesionalnu ekspoziciju HIV infekciji 2005. godine (13). Neprofesionalna ekspozicija je podrazumevala izlaganje riziku od inficiranja HIV-om putem seksualnog odnosa (posebno adresirajući seksualne napade/silovanje), injektiranja, transfuzije krvi i perkutanih povreda (primarno ubod na iglu) kada je poznato da je izvor ekspozicije inficiran HIV-om. Takođe, preporučuje se primena PEP-a do 72 sata nakon izlaganja riziku, kao i individualna procena rizika za svaki pojedinačni slučaj ekspozicije radi donošenja odluke o primeni PEP-a (13). Dve godine kasnije SZO, zajedno sa Međunarodnom organizacijom rada, publikuje vodič za PEP koji obuhvata i profesionalnu i neprofesionalnu ekspoziciju HIV infekciji (posebno adresirajući silovanje/seksualno nasilje), sa preporukom da PEP bude deo nacionalnih politika primarno u zemljama sa visokom prevalencijom HIV infekcije (14). Treba istaći da je već krajem 90-tih godina 20. veka veliki broj zemalja

Evrope imao PEP procedure za profesionalnu ekspoziciju HIV infekciji primarno kod zdravstvenih radnika (15). Generalno, razvoj vodiča i preporuka je kasnio za praksom. Tako npr. tek 2007. godine se u vodiču za lečenje HIV/AIDS-a Evropskog kliničkog društva za AIDS (engl. *European AIDS Clinical Society - EACS*) definiše i protokol za PEP (16).

Da bi imao rezultate, po najnovijim preporukama EACS-a, PEP treba započeti unutar idealno 4 sata posle ekspozicije, a najkasnije unutar 72 sata nakon ekspozicije, u trajanju od 4 nedelje (28 dana). Serološka kontrola kojom se utvrđuje prisustvo HIV infekcije se vrši unutar 72 sata po ekspoziciji, a zatim nakon završetka PEP režima i ponavlja se 6 do 8 nedelja nakon završenog režima. Pre započinjanja PEP režima, potrebno je utvrditi prisustvo HIV infekcije kod izvora potencijalne infekcije, odnosno viremiju ukoliko je izvor nosilac HIV infekcije, kao i dodatna ispitivanja izvora i izložene osobe u skladu sa individualnim slučajem (12).

I pored ranog prepoznavanja PEP-a kao efikasne mere za prevenciju HIV infekcije, PEP primarno za neprofesionalnu upotrebu nije u velikoj meri implementiran. Jedna od glavnih prepreka, pored onih vezanih za razvoj i implementaciju nacionalnih politika i protokola vezanih za PEP, je bila informisanost osoba iz ključnih populacija u riziku od HIV-a (muškaraca koji imaju seks sa muškarima, osoba koje injektiraju droge, seks radnika/ica, transrodnih osoba, zatvorenika) o postojanju i benefitima PEP-a, pravilno i pravovremeno identifikovanje izlaganja riziku od HIV infekcije, kao i pravovremeno javljanje u zdravstvenu službu radi dobijanja terapije (unutar 72 sata) (17).

### Pre-ekspoziciona profilaksa

Prva ispitivanja uspešnosti upotrebe ARV terapije u preventiji HIV infekcije, pre same ekspozicije HIV infekciji, krenula su oko 2005. godine, sa sve intenzivnijim istraživanjima oko 2010. godine. Pre-ekspoziciona profilaksa (PrEP) podrazumeva upotrebu definisane ARV terapije od strane osobe koja nije inficirana HIV-om, a koja svesno ulazi u rizik od izlaganja HIV infekciji. Jedna od prepostavki je bila da uspešna PrEP HIV infekcije može doprineti njenom suzbijanju u ključnim populacijama, tj. onim koje su u kontinuiranom riziku od HIV infekcije. Prve randomizirane kontrolisane studije su rađene mahom u heteroseksualnoj populaciji u Africi. Jedna od prvih studija sprovedena među ženama u Africi (Gana, Kamerun i Nigerija) zbog

prophylaxis (PEP) with AZT (8). Later studies found that the risk of HIV infection in healthcare workers after percutaneous exposure to HIV-infected blood was 0.3% (9,10), that is, 0.09% after mucosal contamination through contact with HIV-infected blood (10), as well as that post-exposure prophylaxis after percutaneous injuries reduces the risk of HIV infection by 81% (9).

Among healthcare workers, the occupational risk relates primarily to percutaneous injuries (needle sticks, or punctures and cuts with sharp instruments), contamination of mucous membranes (mouth, conjunctiva), and contamination of injured skin (wounds, abrasions, dermatitis) through contact with HIV-infected blood lasting at least 15 minutes. Sources of HIV infection that lead to its transmission are primarily blood, as well as body fluids and tissues in which HIV may be present (body fluids with visible traces of blood, vaginal secretions, semen, amniotic, pleural, cerebrospinal, pericardial and peritoneal edema). When it comes to the degree of risk of exposure itself, it depends on the type of needle and/or sharp instrument (dimension) with which the injury occurred, the severity of the injury (depth), the amount of infectious dose to which the healthcare worker was exposed and the degree of viremia in the patient whose blood the healthcare worker was exposed to (11,12).

The CDC first recommended PEP for non-occupational exposure to HIV infection in 2005 (13). Non-occupational exposure included the exposure to the risk of HIV infection through sexual intercourse (specifically addressing sexual assault/rape), injection, blood transfusion and percutaneous injuries (primarily needle stick), when the source of exposure is known to be HIV-infected. Also, the application of PEP is recommended up to 72 hours after exposure to the risk, as well as the individual risk assessment for each individual case of exposure in order to make a decision on applying PEP (13). Two years later, the WHO together with the International Labor Organization, published guidelines for PEP that includes both occupational and non-occupational exposure to HIV infection (specifically addressing rape/sexual violence), with the recommendation that PEP should be part of national policies, primarily in countries with a high prevalence of HIV infection (14). It should be emphasized that already at the end of 1990s, a large number of European countries had

PEP procedures for occupational exposure to HIV infection, primarily among healthcare workers (15). Generally, the development of guidelines and recommendations has lagged behind practice. For example, it was only in 2007 that the protocol for PEP was defined within the Guidelines for the treatment of HIV/AIDS of the European AIDS Clinical Society (EACS) (16).

In order to be effective, according to the latest EACS recommendations, PEP should be started ideally within 4 hours after exposure and no later than 72 hours after exposure during 4 weeks (28 days). Serological control, which determines the presence of HIV infection, is performed within 72 hours after exposure, and then after the completion of the PEP regimen, and it is repeated 6 to 8 weeks after the completed regimen. Before starting the PEP regimen, it is necessary to determine the presence of HIV infection in the source of potential infection, that is, viremia if the source is the carrier of HIV infection, as well as additional tests of the source and exposed person in accordance with each individual case (12).

Despite the early recognition of PEP as an effective measure used for the prevention of HIV infection, PEP primarily for non-occupational use has not been widely implemented. One of the main obstacles, in addition to those related to the development and implementation of national policies and protocols that consider PEP, was informing people from key populations at risk of HIV (men who have sex with men, people who inject drugs, sex workers, transgender persons, prisoners) about the existence and benefits of PEP, correct and timely identification of exposure to the risk of HIV infection, as well as timely reporting to the healthcare service in order to receive therapy (within 72 hours) (17).

### **Pre-exposure prophylaxis**

The first studies of the success of ARV therapy in the prevention of HIV infection, before exposure to HIV infection, began around 2005, with increasingly intensive research around 2010. Pre-exposure prophylaxis (PrEP) involves the use of defined ARV therapy by a person who is not infected with HIV, and who knowingly enters the risk of exposure to HIV infection. One of the assumptions was that successful PrEP of HIV infection can contribute to its suppression in key populations, i.e. those who are at continuous risk of HIV infection. The first

malog broja slučajeva serokonverzije u eksperimentalnoj i kontrolnoj grupi nije mogla da evaluira efektivnost PrEP-a (18). Međutim, studije koje su usledile su pokazale visoku efektivnost PrEP-a na bazi tenofivir disoproxil fumarate (TDF), kasnije tenofivir alafenamide (TAF), u prevenciji HIV infekcije, kako u heteroseksualnoj populaciji, tako i među muškarcima koji imaju seks sa muškarcima i osobama koje injektiraju drogu. Tako *Partners PrEP* studija koja je realizovana 2010. godine među heteroseksualnim partnerima različitog HIV statusa nalazi da PrEP u kombinaciji TDF i emtricitabine (FTC) prevenira HIV infekciju u 75% slučajeva, dok samo TDF prevenira 67% (19). Jedna od prvih multinacionalnih randomiziranih kontrolnih studija u populaciji muškaraca koji imaju seks sa muškarcima (*Preexposure Prophylaxis Initiative - iPrEx*) je pokazala sprečavanje HIV infekcije u 44% slučajeva kod onih koji su koristili PrEP u kombinaciji TDF i FTC, ali su ukazali i na to da je efikasnost bila veća kod onih koji su koristili redovno terapiju (17). Kasnije studije su našle da je redovno korišćenje (na dnevnoj bazi ili pre i posle sekualnog odnosa) kombinacije TDF/FTC sprečava čak 86% slučajeva HIV infekcije među muškarcima koji imaju seks sa muškarcima (20,21). Studije među osobama koje injektiraju drogu su takođe ukazale da redovno korišćenje PrEP-a (na dnevnoj bazi) utiče na smanjenje rizika od HIV infekcije za čak 83,5% kod onih sa najvećom adherencijom (22). Studije među transrodnim ženama pokazuju ograničenja u efikasnosti PrEP-a usled verovatne inetrakcije sa hormonskom terapijom kod onih transrodnih osoba koje je koriste. Neke studije su ukazale na bolje rezultate TAF/FTC terapije kada su transrodne žene u pitanju (23). Dokazana uspešnost PrEP-a u prevenciji HIV infekcije uticala je na to da američka FDA već 2012. godine odobri upotrebu TDF/FTC za prevenciju HIV infekcije kod odraslih (24). Već 2015. godine prvo Evropski centar za prevenciju i kontrolu bolesti (engl. *European Center for Disease Prevention and Control - ECDC*), a zatim SZO daju svoje preporuke da se PrEP integriše u preventivne mere na nacionalnim nivoima za ključne populacije (25).

Prema najnovijim preporukama SZO i EACS, PrEP može da se koristi na dva načina: 1) neposredno pre i posle rizičnog seksualnog odnosa (oralna upotreba duple doze leka baziranog na TDF dva do 24 sata pre rizičnog seksualnog kontakta i po jedna doza u naredna dva dana po rizičnom događaju) ili 2) kontinuirano na dnevnom nivou. SZO navodi

da je prvi način prilagođeniji muškarcima, uključujući i transrodne žene koje ne koriste hormone i druge trans osobe koje su muškog pola po rođenju, a drugi im je alternativni, dok je drugi način prilagođen ženama i transrodnim osobama koje koriste određene hormonske terapije. Pre i tokom upotrebe PrEP-a potrebno je sprovesti odgovarajuće medicinske pregledе i periodični monitoring određenih zdravstvenih parametara, uključujući i HIV status (12,26). Ono što je presudno za uspešnost PrEP-a jeste adherencija propisanom režimu i periodična medicinska supervizija zdravstvenog stanja (26).

Međutim, i pored svega, implementacija PrEP-a na nacionalnim nivoima u Evropi nije na zadovoljavajućem nivou. U 2021. godini, u većini zemalja Zapadne Evrope PrEP je dostupan, a individualni troškovi vezani za nabavku terapije u potpunosti ili delimično finansirani od strane nacionalnih fondova. Istovremeno, u većini zemalja Centralne i Istočne Evrope, PrEP nije bio formalno uveden (27).

Posebni rizici vezani za korišćenje PrEP-a vezani su za uzimanje PrEP-a bez medicinske supervizije. Ovi rizici su posebno zastupljeni u zemljama gde nije regulisana upotreba PrEP-a, odnosno gde osobe koje procenjuju da su u (kontinuiranom) riziku od HIV infekcije lekove za PrEP nabavljaju na neformalne načine, često bez prethodne medicinske procene i zdravstvenih pregleda. Prema jednoj studiji sprovedenoj u Nemačkoj, neformalna upotreba PrEP-a je bila povezana sa većim šansama da se osobe koje na taj način nabavljaju i koriste PrEP nisu prethodno testirale na HIV, što dalje povećava rizik od razvoja rezistencije na TDF i FTC u slučaju postojanja nedijagnostikovane HIV infekcije (28). Ove nalaze podržavaju i druge studije, dodajući i da postoji rizik od neadekvatne upotrebe ARV lekova, što smanjuje efektivnost PrEP-a (29,30).

### **PEP i PrEP u Srbiji**

Mada je potreba za uvođenjem PEP-a i PrEP-a prepoznata praktično od početaka primene hemioprofilakse za prevenciju HIV infekcije, do sada još uvek nije formalizovana i regulisana primena ARV terapije u preventivne svrhe u Srbiji. U „Strategiji za kontrolu i prevenciju HIV infekcije i AIDS-a Republike Srbije, 2018-2025. godine“ (Strategija), prepoznaje se kao posebna mera obezbeđivanje dostupnosti PEP-a i PrEP-a svima koji su imali akidentalnu ekspoziciju HIV infekciji ili su u kontinuiranom (seksualnom) riziku od HIV infekcije

randomized studies were conducted mainly in heterosexual populations in Africa. One of the first studies conducted among women in Africa (Ghana, Cameroon, and Nigeria) could not evaluate the effectiveness of PrEP due to the small number of seroconversion cases in the experimental and control group (18). However, subsequent studies have shown the high effectiveness of PrEP based on tenofovir disoproxil fumarate (TDF), later tenofovir alafenamide (TAF) in the prevention of HIV infection, both in the heterosexual population and among men who have sex with men, as well as among people who inject drugs. Thus, the Partners PreEP study that was realized in 2010 among heterosexual partners of different HIV status found that PrEP in combination with TDF and emtricitabine (FTC) prevents HIV infection in 75% of cases, while TDF alone prevents 67% (19). One of the first multinational randomized controlled studies in the population of men who have sex with men (Preexposure Prophylaxis Initiative – iPrEx) showed the prevention of HIV infection of 44% cases in those who used PrEP in combination with TDF and FTC, but also indicated that the effectiveness was higher in those who used regular therapy (17). Later studies found that regular use (daily or before and after sexual intercourse) of the TDF/FTC combination prevented as many as 86% of HIV infections among men who have sex with men (20,21). Studies that were conducted among people who inject drugs have also shown that regular use of PrEP (on a daily basis) reduces the risk of HIV infection by as much as 83.5% among those with the highest adherence (22). Studies that were conducted among transgender women have showed limitations in the effectiveness of PrEP due to the possible interaction with hormone therapy in those transgender people who use it. Some studies have pointed out better results of TAF/FTC therapy in transgender women (23). The proven success of PrEP in the prevention of HIV infection influenced the US FDA to approve the use of TDF/FTC for the prevention of HIV infection in adults as early as 2012 (24). Already in 2015, first the European Center for Disease Prevention and Control, and then the WHO gave their recommendations to integrate PrEP into preventive measures at the national level for key populations (25).

According to the latest recommendations of the WHO and EACS, PrEP can be used in two ways: 1) immediately before and after risky sexual

intercourse (oral use of a double dose of drug based on TDF two to 24 hours before the risky sexual contact and one dose in the following two days after the risky event) or 2) continuously on a daily basis. The WHO states that the first method is more suitable for men, including transgender women who do not use hormones and other trans people who are male at birth and the second is alternative to them, while the second method is suitable for women and transgender people who use certain hormone therapies. Before and during the use of PrEP, certain medical examinations and periodical monitoring of certain health parameters, including the HIV status, should necessarily be done (12, 26). What is crucial for the success of PrEP is adherence to the prescribed regimen and periodical medical supervision of health condition (26).

However, despite everything, the implementation of PrEP at national levels in Europe is not at a satisfactory level. In 2021, PrEP was available in most Western European countries, and individual costs related to the acquisition of therapy were fully or partially financed by national funds. At the same time, PrEP was not formally introduced in most countries of Central and Eastern Europe (27).

Special risks related to the use of PrEP are associated with taking PrEP without medical supervision. These risks are especially present in countries, where the use of PrEP is not regulated, that is, where people who assess that they are at (continuous) risk of HIV infection get PrEP drugs in informal ways, often without prior medical evaluation and health examinations. According to a study that was conducted in Germany, the informal use of PrEP was associated with higher chances that individuals who obtained and used PrEP in this way had not been previously tested for HIV, which further increases the risk of developing resistance to TDF and FTC in case of the presence of undiagnosed HIV infections (28). These findings have been supported by other studies, adding that there is a risk of inadequate use of ARV drugs, which reduces the effectiveness of PrEP (29,30).

#### **PEP and PrEP in Serbia**

Although the need for the introduction of PEP and PrEP has been recognized practically since the beginning of the application of chemoprophylaxis for the prevention of HIV infection, the use of ARV therapy for preventive purposes has not been formalized and regulated in Serbia yet. In

(31). Pravilnik o imunizaciji i načinu zaštite lekovima (32) identificuje potrebu za hemioprofilaksom (pre ili posle ekspozicije) za HIV infekciju prema epidemiološkim indikacijama. Međutim, treba istaći da je, bez obzira na nedostatak pune formalne regulacije hemioprofilakse, tj. protokola za korišćenje hemioprofilakse za HIV infekciju, u našoj zemlji moguće kupiti lekove za PrEP, registrirane od strane Agencije za lekove i medicinska sredstva Srbije za osobe u riziku od seksualne transmisije HIV infekcije. Ovo je uticalo da se u većoj meri u definisanje privremenih operativnih procedura uključe zdravstveni radnici i predstavnici nevladinih organizacija, kako bi smanjili rizik od neadekvatne primene PrEP terapije primarno u populaciji muškaraca koji imaju seks sa muškarima. Takođe, u skladu sa strateškim merama, Ministarstvo zdravlja Republike Srbije je tokom 2022. godine formiralo Radnu grupu za izradu nacionalnog vodiča za lečenje osoba sa HIV-om i korišćenje PEP i PrEP terapije. Posledično, možemo očekivati skoru regulaciju ovih preventivnih mera i u našoj zemlji i njihovu integraciju u postojeće programe prevencije HIV infekcije u ključnim populacijama u riziku od HIV-a, odnosno među zdravstvenim radnicima i drugim osobama izloženim riziku od akidentalnog izlaganja HIV infekciji.

## Zaključak

Kako je prihvaćeno da će uvek biti osoba koje ne žele ili ne mogu da promene svoje ponašanje i smanje rizik od HIV infekcije, biomedicinske intervencije sve više dobijaju na značaju. Ovo važi i za PEP i PrEP koje pripadaju grupi biomedicinskih intervencija u prevenciji HIV infekcije. Pri tome, PEP je ostao više vezan za prevenciju HIV infekcije nakon akidentalnog izlaganja riziku od HIV-a primarno zdravstvenih radnika, ali i drugih profesionalaca, kao i žrtava seksualnog nasilja (silovanja). PrEP je više usmeren na prevenciju neprofesionalnih ekspozicija HIV infekciji osoba koje nisu inficirane HIV-om, a u kontinuiranom su riziku od HIV infekcije. Ipak, da bi biomedicinske intervencije bile efikasne, potrebno je njihovo povezivanje sa bihevioralnim intervencijama. Odnosno, bitno je adekvatno savetovanje vezano za adherenciju propisanoj terapiji i periodične zdravstvene preglede, kako bi PrEP i PEP mogli uspešno da preveniraju HIV infekciju.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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the "Strategy for control and prevention of HIV infection and AIDS of the Republic of Serbia, 2018-2025" (Strategy), ensuring the availability of PEP and PrEP to all those who had an accidental exposure to HIV infection or who are at continuous (sexual) risk of HIV infection is recognized as a specific measure (31). The Rulebook on Immunization and Protection with Drugs (32) identifies the need for chemoprophylaxis (before or after exposure) for HIV infection according to epidemiological indications. However, it should be noted that, regardless of the lack of full formal regulation of chemoprophylaxis, i.e. lack of protocol for chemoprophylaxis for HIV infection, in our country, it is possible to buy drugs for PrEP, which are registered by the Agency for Medicines and Medical Devices of Serbia for persons at risk of sexual transmission of HIV infection. This influenced to a great extent the involvement of healthcare workers and representatives of non-governmental organizations in defining the temporary operating procedures, in order to reduce the risk of inadequate application of PrEP therapy primarily in the population of men who have sex with men. Also, in accordance with the strategic measures, the Ministry of Health of the Republic of Serbia formed in 2022 the Working group for development of national guideline for HIV treatment and use of PEP and PrEP therapy. Consequently, we can soon expect the regulation of these preventive measures in our country and their integration into the existing prevention programs for HIV infection in key populations at risk of HIV, that is, among healthcare workers and other persons exposed to the risk of accidental exposure to HIV infection.

## Conclusion

Since it is accepted that there will always be people who are unwilling or unable to change their behavior and reduce the risk of HIV infection, biomedical interventions are getting more and more importance. This also applies to PEP and PrEP, which belong to the group of biomedical interventions in the prevention of HIV infection. At the same time, PEP remained more related to the prevention of HIV infection after the accidental exposure to the risk of HIV, primarily of healthcare workers, but also of other professionals, as well as victims of sexual violence (rape). PrEP is more focused on the prevention of non-occupational

exposure to HIV infection of people who are not infected with HIV and who are at a continuous risk of HIV infection. However, in order for biomedical interventions to be effective, it is necessary to combine them with behavioral interventions. That is, adequate counseling related to adherence to prescribed therapy and periodic health examinations is essential, so that PrEP and PEP could successfully prevent HIV infection.

## Competing interests

Authors declare no competing interests.

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## SINDROM SAGOREVANJA LEKARA I MEDICINSKIH SESTARA/TEHNIČARA ZAPOSLENIH U OPŠTOJ BOLNICI ZDRAVSTVENOG CENTRA U BRČKOM

Aleksandra Nikolić<sup>1</sup>, Anđa Nikolić<sup>2</sup>, Sandra Grujičić<sup>1\*</sup>

<sup>1</sup> Institut za epidemiologiju, Medicinski fakultet Univerziteta u Beogradu, Beograd, Republika Srbija

<sup>2</sup> Pododjeljenje za javno zdravstvo, Odjeljenje za zdravstvo i ostale usluge Vlade Brčko distrikta, Bosna i Hercegovina

\* Korespondencija: Sandra Grujičić, Institut za epidemiologiju, Medicinski fakultet Univerziteta u Beogradu, Višegradska 26a, Beograd, Republika Srbija; e-mail: sandra.grujicic@med.bg.ac.rs

### SAŽETAK

**Uvod/Cilj:** Sindrom sagorevanja može se definisati kao prolongirani odgovor na hronične emocionalne i interpersonalne stresore koji se dovode u vezu sa radnim mestom. Obično se manifestuje emocionalnom iscpričenosti, osećajem male lične ostvarenosti i depersonalizacijom. Najčešće se javlja kod radnika koji intenzivno rade sa ljudima, posebno kod lekara, učitelja i nastavnika, gde čak 20-30% zaposlenih ispoljava neke od simptoma sindroma sagorevanja na poslu. Cilj rada je procena prevalencije sindroma sagorevanja među zdravstvenim radnicima (lekariма i medicinskim sestrama/tehničarima) u opštoj bolnici JZU Zdravstveni centar Brčko i da se identifikuju prediktori emocionalne iscpričenosti, depersonalizacije i osećaja male lične ostvarenosti.

**Metode:** Ova studija preseka je sprovedena, tokom juna i jula 2018. godine, u opštoj bolnici JZU Zdravstveni centar Brčko. U istraživanje su uključeni lekari (61) i medicinske sestre/tehničari (155), od 18 i više godina, koji su zaposleni sa punim radnim vremenom. Svi ispitanici dobrovoljno su pristali da anonimno učestvuju u istraživanju. Podaci su od ispitanika dobijeni upitnicima. Pored opšteg upitnika korišćen je Maslašev upitnik za procenu sindroma sagorevanja na poslu (eng. *Maslach Burnout Inventory - Human Services Survey*, MBI-HSS). U statističkoj analizi podataka primenjene su metode deskriptivne statistike: srednja vrednost, standardna devijacija. Za poređenje dve grupe ispitanika korišćen je t-test za nezavisne uzorce, univariatna i multivariatna logistička regresiona analiza. U modele multivariatne logističke analize uključene su varijable koje su prema vrednostima univariatne analize imale  $p < 0,1$ .

**Rezultati:** Prevalencija emocionalne iscpričenosti, kao komponente sindrom sagorevanja, bila je prisutna kod 51% zdravstvenih radnika, depersonalizacija kod 33%, i niska lična ostvarenost kod 54% ispitanika. Ukoliko kao kriterijum ukupnog sindroma sagorevanja odaberemo prisustvo bar jedne od tri komponente sindroma, sindrom sagorevanja je bio prisutan kod 59% ispitanika. Prema Maslaš upitniku, lekari su značajno češće imali umerene i visoke vrednosti emocionalne iscpričenosti i umerene vrednosti lične ostvarenosti, a medicinske sestre/tehničari značajno češće umerene vrednosti depersonalizacije.

**Zaključak:** Visoka učestalost sindroma sagorevanja kod zdravstvenih radnika, zahteva dalja istraživanja u ovoj oblasti sa ciljem uvođenja adekvatnih preventivnih mera radi unapređenja zdravlja zdravstvenih radnika, pogotovo lekara.

**Ključne reči:** sindrom sagorevaja, zdravstveni radnici, studija preseka

### Uvod

U svim radovima sindrom sagorevanja (engl. *burn out syndrome*) definiše se kao prolongirani odgovor na hronične emocionalne i interpersonalne stresore koji su u vezi sa radnim mestom. Karakteriše ga: emocionalna iscpričenost, depersonalizacija i osećaj male lične ostvarenosti. Nastaje kao posledica neusaglašenih odnosa između zaspolenih i radne sredine (1).

Dosadašnja istraživanja pokazuju da preko 3% ljudi u opštoj populaciji ima razvijenu formu „sindroma sagorevanja“ (2). Ovaj sindrom je prvo uočen kod medicinskog osoblja zaposlenog na odeljenjima psihijatrije i intenzivne nege, a potom kod hirurga i anesteziologa (1,3,4). Studije su pokazale da je najizraženiji kod radnika koji intenzivno rade sa ljudima, posebno kod lekara, učitelja i nastavnika,

## BURNOUT SYNDROME OF DOCTORS AND NURSES/TECHNICIANS EMPLOYED IN THE GENERAL HOSPITAL OF THE HEALTH CENTER IN BRCKO

Aleksandra Nikolic<sup>1</sup>, Andja Nikolic<sup>2</sup>, Sandra Grujicic<sup>1\*</sup>

<sup>1</sup>Institute of epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Republic of Serbia

<sup>2</sup>Subdivision for Public Health, Department for Health and Other Services of Brcko District Bosnia and Herzegovina

\* Correspondence: Sandra Grujicic, Institute of epidemiology, Faculty of Medicine, University of Belgrade, Višegradska 26a, Belgrade, Republic of Serbia; e-mail: sandra.grujicic@med.bg.ac.rs

### SUMMARY

**Introduction/Aim:** Burnout syndrome can be defined as a prolonged response to chronic emotional and interpersonal stressors associated with the workplace. It is usually manifested as emotional exhaustion, a feeling of reduced personal accomplishment and depersonalization. It most often occurs in people who work intensively with people, especially doctors, teachers, where even 20-30% of employees show some of the symptoms of burnout syndrome at work. The aim of the study is to evaluate the prevalence of burnout syndrome among healthcare workers (doctors and nurses/technicians) in the general hospital of the Health Center Brcko and to identify the predictors of emotional exhaustion, depersonalization and a feeling of reduced personal accomplishment.

**Methods:** This cross-sectional study was conducted during June and July 2018, in the general hospital of the Health Center Brcko. The research included doctors (61) and nurses/technicians (155), aged 18 and older, who were employed full time. All respondents voluntarily agreed to participate anonymously in the research. The data were obtained from the respondents with the help of questionnaires. In addition to the general questionnaire, Maslach Burnout Inventory – Human Services Survey (MBI-HSS) was used to assess burnout syndrome at work. In the statistical analysis of data, the following methods of descriptive statistics were applied: mean value, standard deviation. T-test for independent samples, univariate and multivariate logistic regression analysis were used to compare the two groups of respondents. Variables that had  $p < 0.1$ , according to univariate analysis, were included in the multivariate logistic analysis models.

**Results:** The prevalence of emotional exhaustion, as a component of burnout syndrome, was present in 51% of health workers, depersonalization in 33%, and reduced personal accomplishment in 54% of respondents. If we choose the presence of at least one of three components of the syndrome as a criterion of the total burnout syndrome, the burnout syndrome was present in 59% of respondents. According to the Maslach questionnaire, doctors significantly more often had moderate and high values of emotional exhaustion and moderate values of personal accomplishment, while nurses/technicians significantly more often had moderate values of depersonalization.

**Conclusion:** The high incidence of burnout syndrome in healthcare workers requires further research in this field with the aim of introducing adequate preventive measures to improve the health of healthcare workers, especially doctors.

**Key words:** burnout syndrome, healthcare workers, cross-sectional study

### Introduction

In all papers, burnout syndrome is defined as a prolonged response to chronic emotional and interpersonal stressors connected with the workplace. It is characterized by: emotional exhaustion, depersonalization and a feeling of reduced personal accomplishment. It occurs as a consequence of disharmonic relations between the employees and the working environment (1).

Previous research shows that over 3% of people in the general population have a developed form of "burnout syndrome" (2). This syndrome was first observed in medical staff employed at psychiatric departments and in intensive care units, and then in surgeons and anesthesiologists (1,3,4). Studies have shown that it is most pronounced in workers who work intensively with people, especially

advokata, sudija i radnika u drugim društvenim delatnostima, gde čak 20-30% ovih zaposlenih ispoljava neke od simptoma sindroma sagorevanja na poslu (2). U Japanu i Tajvanu sindrom sagorevanja na radu je zabeležen kod 48 do 69% ljudi, u državama Evropske zajednice kod 28% ljudi, a u Sjedinjenim Američkim Državama kod 20% ljudi (3). Sindrom sagorevanja umereno do izraženog stepena javlja se kod 60% zdravstvenih radnika oba pola srednje, više i visoke spreme, zaposlenih u hitnoj službi u Sremskoj Kamenici, a kod 27% zaposlenih zdravstvenih radnika u Institutu za neurologiju, psihijatriju i mentalno zdravlje u Novom Sadu (3).

Studije preseka pokazale su povezanost sagorevanja lekara sa nižim nivoom nege pacijenta (5), ali i sa duplo većim rizikom od medicinske greške (6). IMWELL studija je pokazala povezanost višeg stepena sagorevanja sa većom mogućnošću prijavljivanja krupne medicinske greške u narednom periodu od 3 meseca. Takođe, uočeno je da su samo veće medicinske greške bile povezane sa pogoršanjem depresivnih simptoma i smanjenjem kvaliteta života (7). Rezultati istraživanja koja su sprovedena u Evropi i Aziji podržavaju rezultate IMWELL studije (8). Veća emocionalna iscrpljenost lekara koji rade u jedinicama intenzivne nege povezana je sa većom standardizovanom stopom mortaliteta pacijenata (9) i nižim kvalitetom timskog rada (10), dok je povećan nivo depersonalizacije povezan sa dužim vremenom oporavka pacijenata nakon hospitalizacije (11). Pojedine studije preseka pokazale su značajnu korelaciju između stepena sagorevanja lekara i zadovoljstva pacijenata bolničkom negom (11), između zadovoljstva lekara i zadovoljstva pacijenata njihovom zdravstvenom zaštitom, i između zadovoljstva lekara i pacijentovog pridržavanja medicinskih saveta (8,12). Sve ove studije ukazuju na negativni uticaj sindroma sagorevanja na zadovoljstvo pacijenata i odnos lekar-pacijent, sa konačnim efektom koji se ogleda u smanjenom kvalitetu zdravstvene zaštite.

Cilj rada je procena prevalencije sindroma sagorevanja među zdravstvenim radnicima (lekariма i medicinskim sestrama/tehničarima) u opštoj bolnici JZU Zdravstveni centar Brčko i da se identifikuju prediktori emocionalne iscrpljenosti, depersonalizacije i osećaja male lične ostvarenosti.

## Metode

Ova studija preseka je sprovedena, tokom juna i jula 2018. godine, u opštoj bolnici JZU Zdravstveni

centar Brčko. U istraživanje su uključeni zaposleni lekari (61 – 81,3% zaposlenih) i medicinske sestre/tehničari (155 – 70,1% zaposlenih), od 18 i više godina, sa punim radnim vremenom, koji su u trenutku anketiranja dobrovoljno pristali da anonimno učestvuju u istraživanju. Kriterijumi za isključivanje iz studije su bili: diskontinuitet u radu duži od jedne godine (duža bolovanja, studijskih boravci u inostranstvu); izloženost većoj fizičkoj i/ili psihičkoj traumi, nezavisno od profesionalnog okruženja, kao i odbijanje učestvovanja u istraživanju.

Za potrebe ovog istraživanja konstruisan je opšti upitnik o ispitanicima, kojim su prikupljeni podaci o demografskim karakteristikama ispitanika (pol, uzrast, bračni status, deca, broj članova domaćinstva, posedovanje sopstvenog stana/kuće), socijalno-ekonomskom statusu, karakteristikama radnog mesta, dužini radnog staža i dr.

Pored opšteg upitnika korišćen je Maslašov upitnik za procenu sindroma sagorevanja na poslu (eng. *Maslach Burnout Inventory- Human Services Survey*, MBI-HSS). Maslašov upitnik za procenu sindroma sagorevanja na poslu je instrument koji se najčešće koristi za merenje stepena sindroma sagorevanja. Upitnik ima tri verzije, namenjene različitim grupama: 1) za opštu populaciju (eng. *General Survey*, MBI-GS) sa 16 varijabli; 2) za zaposlene u ustanovama, koji su u neposrednom kontaktu sa ljudima (eng. *Human Services Survey*, MBI-HSS) sa 22 varijable; 3) za zaposlene u obrazovnim ustanovama (eng. *Educators Survey*, MBI-ES) sa 22 varijable. Za potrebe ovog istraživanja, korišćen je upitnik namenjen zaposlenima koji su u neposrednom kontaktu sa ljudima MBI-HSS. Od autora je dobijena dozvola za upotrebu 100 upitnika koji su prevedeni, adaptirani i validirani na srpski jezik. Upitnikom je anketirano 50 lekara i 50 medicinskih sestara/tehničara. Ovaj upitnik se sastoji od ukupno 22 stavke koje se potom koriste u izračunavanju tri sumarne skale: skale emocionalne iscrpljenosti (eng. *Emotional Exhaustion*, EE-9 varijabli), skale depersonalizacije (eng. *Depersonalization*, DP-5 varijabli) i skale lične ostvarenosti (eng. *Personal Accomplishment*, PA-8 varijabli). Kategorije odgovora su date kroz šestostepenu Likertovu skalu. Ukupan stav svakog ispitanika dobija se sumiranjem odgovora pomoću specifičnog ključa, za svaku od tri skale pojedinačno. Granične vrednosti skorova za skale su različite i iznose: skala emocionalne iscrpljenosti: visoka EE je 27 poena i

doctors, teachers, lawyers, judges and workers in other social professions, where as many as 20-30% of these employees show some of the symptoms of burnout syndrome at work (2). In Japan and Taiwan, burnout syndrome at work has been noted in 48 to 69% of people, in the countries of the European Union, in 28% of people, and in the United States of America, in 20% of people (3). Moderate to severe burnout syndrome occurs in 60% of healthcare workers of both genders with secondary, post-secondary or university education, employed in the emergency service in Sremska Kamenica, and in 27% of healthcare workers employed at the Institute of Neurology, Psychiatry and Mental Health in Novi Sad (3).

Cross-sectional studies showed that doctors' burnout was associated with a lower level of patient care (5), but also with a double risk of medical error (6). The IMWELL study showed the association of a higher degree of burnout with a greater possibility of reporting a major medical error in the following three-month period. Also, it was observed that only major medical errors were associated with worsening of depressive symptoms and reduced quality of life (7). The results of the research conducted in Europe and Asia support the results of the IMWELL study (8). Greater emotional exhaustion of doctors working in intensive care units is associated with a higher standardized mortality rate of patients (9) and lower quality of teamwork (10), while the increased level of depersonalization is associated with longer recovery time of patients after hospitalization (11). Some cross-sectional studies have shown a significant correlation between the level of burnout of doctors and patients' satisfaction with healthcare (11), as well as between the satisfaction of doctors and patients with the healthcare, and between the satisfaction of doctors and patients' adherence to medical advice (8,12). All these studies point to the negative impact of burnout syndrome on the patients' satisfaction and the doctor-patient relationship, with the final effect reflected in the reduced quality of health care.

The aim of this study is to assess the prevalence of burnout syndrome in healthcare workers (doctors and nurses/technicians) in the general hospital of the Health Center Brcko and to identify the predictors of emotional exhaustion, depersonalization and a feeling of reduced personal accomplishment.

## Methods

This cross-sectional study was conducted during June and July, 2018 in the general hospital of the Health Center Brcko. The study included doctors (61 – 81.3% of employees) and nurses/technicians (155 – 70.1% of employees), aged 18 and older, with the full-time employment, who voluntarily agreed to participate anonymously in the study. Exclusion criteria were the following: discontinuity in work longer than one year (longer sick leave, study stays abroad), exposure to greater physical and/or psychological trauma, regardless of the professional environment, as well as refusal to participate in the study.

For the purposes of this study, a general questionnaire was created, which collected data on the demographic characteristics of the respondents (gender, age, marital status, children, number of household members, owning their own apartment/house), social-economic status, workplace characteristics, length of service etc.

In addition to the general questionnaire, the Maslach Burnout Inventory – Human Services Survey (MBI-HSS) was used to assess the burnout syndrome at work. Maslach Burnout Inventory is the instrument which is most often used to measure the degree of burnout. The questionnaire has three versions, intended for different groups: 1) for the general population (General Survey, MBI-GS) with 16 variables; 2) for employees in institutions, who are in direct contact with people (Human Services Survey, MBI-HSS) with 22 variables; 3) for employees in educational institutions (Educators Survey, MBI-ES) with 22 variables. For the purposes of this study, a questionnaire intended for employees, who are in direct contact with people, was used (MBI-HSS). Permission was obtained from the author to use 100 questionnaires that were translated into the Serbian language, adapted and validated. 50 doctors and 50 nurses/technicians were surveyed with the questionnaire. This questionnaire consists of a total of 22 items, which are then used to calculate three summary scales: the scale of emotional exhaustion (EE-9 variables), the scale of depersonalization (DP-5 variables) and the scale of personal accomplishment (PA-8 variables). Categories of answers were given through the 6-point Likert scale. The overall attitude of each respondent is obtained by summarizing the answers using a specific key, for each of the three scales individually. The threshold values of scores

više, umerena EE je 17-26 poena i niska EE je od 0 do 16; skala depersonalizacije: visok nivo DP je 13 i više, umeren nivo DP je 7-12 i nizak nivo DP je od 0 do 6; skala lične ostvarenosti: visok nivo PA je 39 i više, umeren nivo PA je od 32 do 38 i nizak nivo PA je u opsegu od 0 do 31. Visoke učestalosti iscrpljenosti i depersonalizacije doprinose sindromu sagorevanja, dok ga visoka učestalost profesionalne ostvarenosti umanjuje (22).

Za statističku obradu podatka korišćen je program SPSS 17 (*SPSS Inc., Chicago, IL, USA*). U statističkoj analizi podataka korišćene su metode deskriptivne statistike: srednja vrednost, standardna devijacija, parametarski ili neparametarski test (ukoliko nisu ispunjeni uslovi za primenu parametarskog testa). Za poređenje dve grupe ispitanika

korišćen je t-test za nezavisne uzorce, univarijantna i multivarijantna logistička regresiona analiza. Za ispitivanje korelacija između skorova različitih skala korišćen je Pearson-ov koeficijent korelacijske. Razlika je označena kao signifikantna ukoliko je  $p < 0,05$ . U modele multivarijantne logističke analize uključene su varijable koje su prema vrednostima univarijantne analize imale  $p < 0,1$ .

## Rezultati

U ovu studiju preseka uključen je 61 lekar (33 muškarca i 28 žena) i 155 medicinskih sestara/tehničara (25 muškaraca i 125 žena) (tabela 1). Na tabeli 1 prikazana je distribucija lekara i medicinskih sestara/tehničara u odnosu na njihove demografske karakteristike. Prosečna starost lekara bila je  $45,1 \pm$

**Tabela 1.** Distribucija lekara i medicinskih sestara/tehničara u odnosu na njihove demografske karakteristike

Karakteristike	Lekari N=61 Broj (%)	Medicinska sestra/tehničar N=155 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Pol</b>				
Muškarci	33 (54,1)	26 (16,7)		
Žene	28 (45,9)	130 (83,3)	0,163 (0,08-0,32)	< 0,001
<b>Starost (<math>\bar{x} \pm SD</math>)</b>	$45,1 \pm 12,2$	$45,9 \pm 12,2$		0,880*
<b>Starosne grupe(godine)</b>				
20-30	9 (16,1)	24 (15,7)	1 (Ref)	
31-40	15 (26,8)	26 (17,0)	1,54 (0,57- 4,16)	
41-50	11 (19,6)	34 (22,2)	0,86 (0,31-2,40)	
51-60	13 (23,2)	60 (39,2)	0,58 (0,22-1,53)	
61+	8 (14,3)	9 (5,9)	2,37 (0,70 -8,05)	0,610
<b>Bračni status</b>				
U braku	48 (82,8)	116 (75,8)		
Bez partnera	10 (17,2)	37 (24,2)	0,65 (0,30-1,42)	0,282
<b>Deca</b>	44 (77,2)	129 (84,3)	0,63 (0,29-1,34)	0,231
<b>Broj dece</b>				
1	18 (40,9)	35 (27,1)	1 (Ref)	
2	23 (52,3)	91 (70,5)	0,49 (0,24-1,02)	
3	3 (6,8)	3 (2,3)	1,94 (0,36-10,62)	0,305
<b>Broj članova domaćinstva</b>				
1	6 (10,7)	8 (5,2)	1 (Ref)	
2	10 (17,9)	12 (7,8)	1,11 (0,29-4,29)	
3+	40 (71,4)	133 (86,9)	0,40 (0,13-1,22)	0,020
<b>Socio-ekonomski status</b>				
Dobar	7 (11,5)	1 (0,6)	1 (Ref)	
Srednji	53 (86,9)	146 (94,2)	0,05 (0,01-0,43)	
Loš	1 (1,6)	8 (5,2)	0,02 (0,00-0,34)	0,003
<b>Sopstvena kuća/stan</b>	56 (86,1)	150 (96,8)	0,93 (0,18-4,95)	0,935

\*p vrednost za t test,  $\bar{x}$  - aritmetička sredina, SD - standardna devijacija, UO - unakrsni odnos, 95%IP - 95% interval poverenja, ULRA – univarijantna logistička regresiona analiza

for the scales are different and they amount to: scale of emotional exhaustion – high EE is 27 points and more, moderate EE is 17-26 points and low EE is from 0 to 16; depersonalization scale – high level of DP is 13 and more, moderate level of DP is 7-12 and low level of DP is from 0 to 6; scale of personal accomplishment – high PA is 39 and more, moderate PA is from 32 to 38 and low PA ranges from 0 to 31. The high incidence of exhaustion and depersonalization contribute to burnout syndrome, while the high incidence of professional accomplishment reduces it (22).

The SPSS 17 program (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis of data. In the statistical analysis of data, the following methods of descriptive statistics were used: mean value, standard deviation, parametric or non-

parametric test (if the conditions for the application of the parametric test were not fulfilled). T-test for independent samples, univariate and multivariate logistic regression analysis were used to compare the two groups of respondents. Pearson's correlation coefficient was used to examine the correlations between scores of different scales. The difference was marked as significant if  $p < 0.05$ . Variables that had  $p < 0.1$ , according to univariate analysis, were included in the multivariate logistic analysis models.

## Results

This cross-sectional study included 61 doctors (33 men and 28 women) and 155 nurses/technicians (25 men and 125 women) (Table 1). Table 1 shows the distribution of doctors and nurses/technicians

**Table 1.** Distribution of doctors and nurses/technicians in relation to their demographic characteristics

Characteristics	Doctors N=61 Number (%)	Nurse/technician N=155 Number (%)	OR (95%CI)	p value ULRA
<b>Gender</b>				
Men	33 (54.1)	26 (16.7)		
Women	28 (45.9)	130 (83.3)	0.163 (0.08-0.32)	< 0.001
<b>Age (<math>\bar{x} \pm SD</math>)</b>	45.1±12.2	45.9±12.2		0.880*
<b>Age group (years)</b>				
20-30	9 (16.1)	24 (15.7)	1 (Ref)	
31-40	15 (26.8)	26 (17.0)	1.54 (0.57- 4.16)	
41-50	11 (19.6)	34 (22.2)	0.86 (0.31-2.40)	
51-60	13 (23.2)	60 (39.2)	0.58 (0.22-1.53)	
61+	8 (14.3)	9 (5.9)	2.37 (0.70 -8.05)	0.610
<b>Marital status</b>				
Married	48 (82.8)	116 (75.8)		
Single	10 (17.2)	37 (24.2)	0.65 (0.30-1.42)	0.282
<b>Children</b>	44 (77.2)	129 (84.3)	0.63 (0.29-1.34)	0.231
<b>Number of children</b>				
1	18 (40.9)	35 (27.1)	1 (Ref)	
2	23 (52.3)	91 (70.5)	0.49 (0.24-1.02)	
3	3 (6.8)	3 (2.3)	1.94 (0.36-10.62)	0.305
<b>Number of household members</b>				
1	6 (10.7)	8 (5.2)	1 (Ref)	
2	10 (17.9)	12 (7.8)	1.11 (0.29-4.29)	
3+	40 (71.4)	133 (86.9)	0.40 (0.13-1.22)	0.020
<b>Socio-economic status</b>				
Good	7 (11.5)	1 (0.6)	1 (Ref)	
Average	53 (86.9)	146 (94.2)	0.05 (0.01-0.43)	
Poor	1 (1.6)	8 (5.2)	0.02 (0.00-0.34)	0.003
<b>Owns apartment/house</b>	56 (86.1)	150 (96.8)	0.93 (0.18-4.95)	0.935

\*p value for t test,  $\bar{x}$  - mean, SD - standard deviation, OR-odds ratio, 95%CI - 95% confidence interval, ULRA – univariate logistic regression analysis

12,2 godine, a medicinskih sestara/tehničara 45,9 ± 12,2 godine. U braku je bilo 82,8% lekara i 75,8% medicinskih sestara/tehničara. Decu je imalo 77,2% lekara i 84,3% medicinskih sestara/tehničara. Najveći broj ispitanika živeo je u domaćinstvima sa 3 i više članova (71,4% lekara i 86,9% medicinskih sestara/tehničara). Ispitanici obe grupe u najvećem broju su se izjasnili da imaju prosečan socio-ekonomski status (86,1% lekara i 96,8% medicinskih sestara/tehničara. Sopstveni stan/kuću imalo je 86,1% lekara i 96,8% medicinskih sestara/tehničara). Medicinske sestre/tehničari su značajno češće bile ženskog pola, češće su živele u domaćinstvu sa 3 i više članova i imale srednji i loš socio-ekonomski status. Između ispitivanih grupa nije bilo značajne razlike u odnosu na uzrast, bračni status, roditeljstvo i broj dece, kao i posedovanje sopstvenog stana/kuće.

Najveći broj lekara (74,0%) i medicinskih sestara/tehničara (73,7%) imalo je radni staž od 11 i više godina i najveći procenat njih je bio zaposlen na trenutnom random mestu više od 10 godina (tabela 2). Između ispitivanih grupa nije bilo značajne razlike u odnosu na dužinu radnog staža i dužinu rada na trenutnom random mestu. Lekari

i medicinske sestre/tehničari najčešće su bili sa odeljenja hirurgije, ginekologije i akušerstva i interne medicine.

Na tabeli 3 prikazana je distribucija lekara i medicinskih sestara/tehničara u odnosu na vrednosti skorova MBI (*Maslach Burnout Inventory*) komponenti. Lekari su značajno češće imali umerene i visoke vrednosti emocionalne iscrpljenosti, umerene vrednosti za ličnu ostvarenost, dok su sestre značajno češće imale umerene vrednosti depersonalizacije.

Lekari i medicinske sestre/tehničari sa visokim skorom za emocionalnu iscrpljenost značajno češće su imali decu i više od 10 godina radnog staža (tabela 4). Između ispitivanih grupa nije bilo značajne razlike u odnosu na pol, stručnu spremu, bračni status, broj dece, broj članova domaćinstva, socio-ekonomski status, posedovanje sopstvene kuće/stana, i dužinu radnog staža na trenutnom random mestu. Kada se u model multivarijantne logističke regresione analize uključe sve varijable koje su prema univariantnoj imale  $p < 0,1$  (odnosno bračni status, deca i godine staža), onda se kao značajan nezavisan prediktor emocijalne iscrpljenosti izdvajaju deca ( $p=0,016$ ;  $UO=5,32$ ;  $95\%IP=1,37-20,66$ ).

**Tabela 2.** Distribucija lekara i medicinskih sestara/tehničara u odnosu na karakteristike radnog mesta

Karakteristike	Lekari N=61 Broj (%)	Medicinska sestra/tehničar N=155 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Dužina radnog staža (godine)</b>				
≤5	9 (15,8)	21 (14,0)	1 (Ref)	
6-10	6 (10,5)	18 (12,0)	0,78 (0,23-2,61)	
11+	42 (73,7)	111 (74,0)	0,88 (0,37-2,08)	0,853
<b>Dužina rada na trenutnom radnom mestu (godine)</b>				
≤10	21 (36,8)	40 (26,7)		
>10	36 (63,2)	110 (73,3)	0,62 (0,33-1,19)	0,153
<b>Odeljenje</b>				
Hirurgija	11 (18,3)	28 (19,2)		
Ginekologija/akušerstvo	7 (11,7)	22 (15,1)		
Otorinolaringologija	2 (3,3)	4 (2,7)		
Interno	6 (10,0)	20 (13,7)		
Anestezija/ Reanimacija/ Intenzivna nega	5 (8,3)	17 (11,6)		
Fizikalna medicina	1 (1,7)	6 (4,1)		
Pedijatrija	4 (6,7)	7 (4,8)		
Plućne bolesti i TBC	2 (3,3)	6 (4,1)		
Služba za dijagnostiku	4 (6,7)	7 (4,8)		
Centralni prijemni šalter	0 (0,0)	4 (2,7)		
Drugo	18 (30,0)	25 (17,1)		

Ȑ - aritmetička sredina, UO - unakrsni odnos, 95%IP - 95% interval poverenja, ULRA – univariantna logistička regresiona analiza

in relation to their demographic characteristics. The average age of doctors was  $45.1 \pm 12.2$  years, while the average age of nurses was  $45.9 \pm 12.2$  years. 82.8% of doctors and 75.8% of nurses/technicians were married. 77.2% of doctors and 84.3% of nurses/technicians had children. The largest number of respondents lived in households with 3 or more members (71.4% of doctors and 86.9% of nurses/technicians). Most respondents of both groups stated that they have an average socio-economic status (86.1% of doctors and 96.8% of nurses/technicians). 86.1% of doctors and 96.8% of nurses/technicians had their own apartment/house. Nurses/technicians were significantly more often female, they lived more frequently in households with 3 or more members and they had average and poor socio-economic status. There was no significant difference between the examined groups regarding age, marital status, parentage and number of children, as well as ownership of their own apartment/house.

The largest number of doctors (74.0%) and nurses/technicians had 11 years of service and more, while the largest percentage of them were employed in the current work position for more than 10 years (Table 2). There was no significant

difference between the examined groups regarding the years of service and the length of service in the current position. Doctors and nurses/technicians were most frequently from the departments of surgery, gynecology and obstetrics and internal medicine.

Table 3 shows the distribution of doctors and nurses/technicians in relation to the scores of MBI components. Doctors significantly more often had moderate and high levels of emotional exhaustion, moderate values of personal accomplishment, while nurses significantly more often had moderate values of depersonalization.

Doctors and nurses/technicians with the high score for emotional exhaustion significantly more often had children and more than 10 years of service (Table 4). There was no significant difference between the examined groups regarding gender, education, marital status, number of children, number of household members, socio-economic status, ownership of their own house/apartment, and years of service in the current work position. When all variables that had  $p < 0.1$  according to the univariate model are included in the multivariate logistic regression analysis model (that is, marital status, children and years of service), then children

**Table 2.** Distribution of doctors and nurses/technicians in relation to workplace characteristics

Characteristics	Doctors N=61 Number (%)	Nurse/technician N=155 Number (%)	OR (95%CI)	p value ULRA
<b>Years of service (years)</b>				
≤5	9 (15.8)	21 (14.0)	1 (Ref)	
6-10	6 (10.5)	18 (12.0)	0.78 (0.23-2.61)	
11+	42 (73.7)	111 (74.0)	0.88 (0.37-2.08)	0.853
<b>Length of service in the current position (years)</b>				
≤10	21 (36.8)	40 (26.7)		
>10	36 (63.2)	110 (73.3)	0.62 (0.33-1.19)	0.153
<b>Department</b>				
Surgery	11 (18.3)	28 (19.2)		
Gynecology/obstetrics	7 (11.7)	22 (15.1)		
Otorhinolaryngology	2 (3.3)	4 (2.7)		
Internal	6 (10.0)	20 (13.7)		
Anesthesiology/ Reanimation/Intensive care	5 (8.3)	17 (11.6)		
Physical medicine	1 (1.7)	6 (4.1)		
Pediatrics	4 (6.7)	7 (4.8)		
Pulmonary diseases i TBC	2 (3.3)	6 (4.1)		
Service for diagnostics	4 (6.7)	7 (4.8)		
Central admission registration desk	0 (0.0)	4 (2.7)		
Other	18 (30.0)	25 (17.1)		

̄ - mean, SD - standard deviation, OR-odds ratio, 95%CI - 95% confidence interval, ULRA – univariate logistic regression analysis

**Tabela 3.** Distribucija lekara i mediinskih sestara/tehničara u odnosu na vrednosti komponenata Maslaš skora (eng. *Maslach Burnout Inventory - MBI*)

MBI komponente	Lekari N=61 Broj (%)	Medicinska sestra/tehničar N=155 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Emocionalna iscrpljenost</b>				
Niska	5 (10,0)	18 (36,0)	1 (ref)	
Umerena	20 (40,0)	6 (12,0)	12,00 (3,12-46,14)	
Visoka	25 (50,0)	26 (52,0)	3,46 (1,11-10,75)	0,143
<b>Depersonalizacija</b>				
Niska	18 (36,0)	17 (34,0)	1 (Ref)	
Umerena	8 (16,0)	24 (48,0)	0,32 (0,11-0,89)	
Visoka	24 (48,0)	9 (18,0)	2,52 (0,91-6,94)	0,092
<b>Lična ostvarenost</b>				
Niska	21 (42,0)	33 (66,0)	1 (Ref)	
Umerena	25 (50,0)	13 (26,0)	3,02 (1,27-7,18)	
Visoka	4 (8,0)	4 (8,0)	1,57 (0,35-6,97)	0,064

\*p vrednost za ULRA, ULRA – univariantna logistička regresiona analiza

Lekari i medicinske sestre/tehničari sa visokim skorom za depersonalizaciju značajno češće su bili muškarci, medicinske sestre/tehničari, osobe koje su imale partnera i decu, kao i više od 10 godina radnog staža (tabela 5). Između ispitivanih grupa nije bilo značajne razlike u odnosu na broj dece, broj članova domaćinstva, socio-ekonomski status, posedovanje sopstvene kuće/stana, i dužinu rada na trenutnom random mestu. Kada se u model multivariantne logističke regresione analize uključe varijable koje su prema univariantnoj imale p < 0,1 (odnosno pol, stručna spremja, bračni status, deca, dužina radnog staža, dužina rada na trenutnom random mestu), onda je značajan nezavisan prediktor pol (p < 0,001; UO= 0,16; 95%IP=0,06-0,45).

Lekari i medicinske sestre/tehničari sa niskim skorom za ličnu ostvarenost su značajno češće bili medicinske sestre/tehničari, sa partnerom, imali su decu, više od 10 godina radnog staža i više od deset godina rada na trenutnom random mestu (tabela 6). Između ispitivanih grupa nije bilo značajne razlike u odnosu na broj dece, broj članova domaćinstva, socio-ekonomski status i posedovanje sopstvene kuće/stana. Kada se u model multivariantne logističke regresione analize uključe varijable koje su prema univariantnoj imale p < 0,1 (odnosno stručna spremja, bračni status, deca, dužina radnog staža, dužina rada na trenutnom random mestu), onda značajan nezavisan prediktor su deca (p = 0,004; UO=9,72; 95%IP=2,03-46,59).

## Diskusija

U našoj studiji medicinske sestre/tehničari su značajno češće bile ženskog pola, iz domaćinstava sa 3 i više članova i imale srednji i loš socioekonomski status. Između lekara i medicinskih sestara nije bilo značajne razlike u odnosu na uzrast, bračni status, roditeljstvo i broj dece, posedovanje sopstvenog stana/kuće, dužinu radnog staža i dužinu rada na trenutnom radnom mestu. Ispitivanjem stavova po pitanju posla, uočeno je da su medicinske sestre/tehničari uvođenje novih tehnologija doživljavale značajno stresnijim ( $3,0 \pm 1,0$ ) nego lekari ( $2,6 \pm 1,1$ ).

Stresni uslovi na radnom mestu mogu biti uzrok iscrpljenosti, profesionalnog sagorevanja i smanjenja radnog učinka. Takođe, mogu biti uzrok brojnih drugih negativnih posledica, kao što su preterano konzumiranje alkohola, kafe, pušenje, neredovna ishrana i dr. (13). Zdravstveni radnici izloženi su velikom stresu zbog ogromne odgovrnosti prema ljudskom životu i zdravlju, ali mogu biti profesionalno izloženi infekciji, zračenju, štetnom dejstvu citotoksičnih lekova itd. Kod zdravstvenih radnika može doći do povećanog obolevanja od različitih psihičkih poremećaja i psihosomatskih bolesti usled specifičnih uslova rada (npr. produženog radnog vremena, rada u smenama, nočnog rada, kontakta sa obolelima i njihovim porodicama, itd.) (14). Jedna od čestih negativnih posledica profesionalnog stresa kod osoba koje su u neposrednom kontaktu sa ljudima jeste upravo sindrom sagorevanja

**Tabela 3.** Distribucija lekara i mediinskih sestara/tehničara u odnosu na vrednosti komponenata Maslaš skora (eng. *Maslach Burnout Inventory - MBI*)

MBI components	Doctors N=61 Number(%)	Nurse/technician N=155 Number (%)	OR (95%CI)	p value ULRA
<b>Emotional exhaustion</b>				
Low	5 (10.0)	18 (36.0)	1 (ref)	
Moderate	20 (40.0)	6 (12.0)	12.00 (3.12-46.14)	
High	25 (50.0)	26 (52.0)	3.46 (1.11-10.75)	0.143
<b>Depersonalization</b>				
Low	18 (36.0)	17 (34.0)	1 (Ref)	
Moderate	8 (16.0)	24 (48.0)	0.32 (0.11-0.89)	
High	24 (48.0)	9 (18.0)	2.52 (0.91-6.94)	0.092
<b>Depersonalization</b>				
Low	21 (42.0)	33 (66.0)	1 (Ref)	
Moderate	25 (50.0)	13 (26.0)	3.02 (1.27-7.18)	
High	4 (8.0)	4 (8.0)	1.57 (0.35-6.97)	0.064

\*p value for ULRA, ULRA – univariate logistic regression analysis

stand out as a significant independent predictor of emotional exhaustion ( $p=0.016$ ; OR=5.32; 95% CI=1.27-20.66).

Doctors and nurses/technicians with a high score for Depersonalization were significantly more often men, nurses/technicians, people who had a partner and children, as well as more than 10 years of service (Table 5). There was no significant difference between the examined groups regarding the number of children, number of household members, socio-economic status, ownership of their own house/apartment, and length of service in the current work position. When the variables that had  $p<0.1$ , according to the univariate analysis, are included in the model of the multivariate logistic regression analysis (i.e. gender, education, marital status, children, years of service, length of service in the current position), then gender is a significant independent predictor ( $p < 0.001$ , OR=0.16; 95% CI=0.06-0.45).

Doctors and nurses/technicians with a low score for Personal Accomplishment were significantly more often nurses/technicians with a partner, had children, more than 10 years of service and more than ten years of work in the current position (Table 6). There was no significant difference between the examined groups regarding the number of children, the number of household members, socio-economic status and ownership of their own house/apartment. When the variables that had  $p<0.1$ , according to the univariate model, are included in the multivariate logistic regression

analysis model (that is, professional qualifications, marital status, children, years of service, length of service in the current position), then a significant independent predictor is children ( $p=0.004$ ; OR=9.72; 95% CI=2.03-46.59).

## Discussion

In our study, nurses/technicians were significantly more often female, from households with 3 or more members and had average or poor socio-economic status. There was no significant difference between doctors and nurses regarding age, marital status, parentage and number of children, owning of their own apartment/house, years of service and length of service in the current position. Examining attitudes about work, it was noted that the introduction of new technologies was more stressful for nurses/technicians ( $3.0 \pm 1.0$ ) than for doctors ( $2.6 \pm 1.1$ ).

Stressful conditions in the workplace may be the cause of exhaustion, professional burnout and reduced work performance. Also, they can be the cause of numerous other negative consequences, such as excessive consumption of alcohol, coffee, smoking, irregular diet, etc. (13). Healthcare workers are exposed to great stress due to their huge responsibility for human life and health, but they can be professionally exposed to infection, radiation, harmful effects of cytotoxic drugs, etc. The increased incidence of different mental disorders and psychosomatic diseases may appear in healthcare workers due to specific

**Tabela 4.** Distribucija lekara i medicinskih sestara/tehničara prema vrednostima skora za MBI komponentu emocionalna iscrpljenost

Karakteristike	Niska/umerena N=49 Broj (%)	Visoka N=51 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Pol</b>				
Muškarci	18 (36,7)	21 (41,2)		
Žene	31 (63,3)	30 (58,8)	0,78 (0,34-1,77)	0,556
<b>Stručna spremam</b>				
Sestre	25 (51,0)	25 (49,0)		
Lekari	24 (49,9)	26 (51,0)	0,92 (0,42-2,02)	0,841
<b>Bračni status</b>				
Sa partnerom	34 (73,9)	34 (73,9)		
Bez partnera	12 (26,1)	12 (26,1)	0,39 (0,13-1,14)	0,084
<b>Deca</b>	34 (75,6)	46 (92,0)	3,72 (1,09-12,69)	0,028
<b>Broj dece</b>				
1	14 (41,2)	14 (30,4)	1 (Ref)	
2	19 (55,9)	29 (63,0)	1,53 (0,59-3,91)	
3	1 (2,9)	3 (6,5)	3,00 (0,28-32,46)	0,258
<b>Broj članova domaćinstva</b>				
1	3 (6,7)	3 (6,0)	1 (Ref)	
2	11 (24,4)	6 (12,0)	0,54 (0,08-3,59)	
3+	31 (68,9)	41 (82,0)	1,32 (0,25-7,00)	0,255
<b>Socio-ekonomski status</b>				
Dobar	3 (6,4)	4 (7,8)	1 (Ref)	
Srednji	41 (87,2)	45 (88,2)	0,82 (0,17-3,90)	
Loš	3 (6,4)	2 (3,9)	0,50 (0,05-5,15)	0,580
<b>Sopstvena kuća/stan</b>	43 (93,5)	48 (96,0)	1,67 (0,27-10,5)	0,582
<b>Dužina radnog staža (godine)</b>				
≤5	8 (18,6)	2 (4,1)	1 (Ref)	
6-10	6 (14,0)	4 (8,2)	0,17 (0,03-0,85)	
11+	29 (67,4)	43 (87,8)	1,45 (1,12-1,73)	0,018
<b>Dužina rada na trenutnom random mestu (godine)</b>				
≤10	16 (37,2)	11 (22,4)		
>10	27 (62,8)	38 (77,6)	2,05 (0,82-5,10)	0,124

MBI - *Maslach Burnout Inventory* – Upitnik o sagorevanju, p vrednost prema univariatnoj logističkoj regresionoj analizi, UO-unakrsni odnos, 95%IP - 95% interval poverenja, ULRA – univariatna logistička regresiona analiza

na poslu. Sindrom sagorevanja može se definisati kao prolongirani odgovor na hronične emocionalne i interpersonalne stresore koji se dovode u vezu sa radnim mestom. Obično se manifestuje emocionalnom iscpriljenošću, osećajem male lične ostvarenosti i depersonalizacijom (1).

Pored lekara, na kojima je odgovornost i od kojih društvo očekuje da budu nepogrešivi profesionalci, i sestrinstvo je stresna profesija. Sestrinstvo je profesija koja zahteva dobre odnose sa osobama kojima se pruža zdravstvena nega, porodicama obolelih, kolegama i nadređenima. Mnoge studije spovedene u populaciji medicinskih sestara ukazale su da postoji veza između određenih poremećaja

zdravlja (npr. emocionalna i fizička iscrpljenost, bol u donjem delu leđa, koronarna bolest) i stresa na random mestu (15-17). Doživljaj stresa na poslu često je vezan za preopterećenost (preveliki zahtevi, kratki rokovi), konflikt i nejasnu radnu ulogu (18,19). Sve ovo vodi nesigurnosti, nezadovoljstvu poslom, smanjenju radnog učinka i željom da se napusti radno mesto (20).

U našoj studiji prevalencija emocionalne iscrpljenosti kao komponente sindroma sagorevanja bila je prisutna kod 51% zdravstvenih radnika, depersonalizacija kod 33%, i niska lična ostvarenost kod 54% ispitanika. Ukoliko kao kriterijum ukupnog sindroma sagorevanja odaberemo prisustvo bar

**Table 4.** Distribution of doctors and nurse/technicians according to the values of the score for MBI component emotional exhaustion

Characteristics	Low/moderate N=49 Number (%)	High N=51 Number (%)	OR (95%CI)	p value ULRA
<b>Gender</b>				
Men	18 (36.7)	21 (41.2)		
Women	31 (63.3)	30 (58.8)	0.78 (0.34-1.77)	0.556
<b>Education</b>				
Nurses	25 (51.0)	25 (49.0)		
Doctors	24 (49.9)	26 (51.0)	0.92 (0.42-2.02)	0.841
<b>Marital status</b>				
With a partner	34 (73.9)	34 (73.9)		
Single	12 (26.1)	12 (26.1)	0.39 (0.13-1.14)	0.084
<b>Children</b>	34 (75.6)	46 (92.0)	3.72 (1.09-12.69)	0.028
<b>Number of children</b>				
1	14 (41.2)	14 (30.4)	1 (Ref)	
2	19 (55.9)	29 (63.0)	1.53 (0.59-3.91)	
3	1 (2.9)	3 (6.5)	3.00 (0.28-32.46)	0.258
<b>Number of household members</b>				
1	3 (6.7)	3 (6.0)	1 (Ref)	
2	11 (24.4)	6 (12.0)	0.54 (0.08-3.59)	
3+	31 (68.9)	41 (82.0)	1.32 (0.25-7.00)	0.255
<b>Socio-economic status</b>				
Good	3 (6.4)	4 (7.8)	1 (Ref)	
Average	41 (87.2)	45 (88.2)	0.82 (0.17-3.90)	
Poor	3 (6.4)	2 (3.9)	0.50 (0.05-5.15)	0.580
<b>Owns house/apartment</b>	43 (93.5)	48 (96.0)	1.67 (0.27-10.5)	0.582
<b>Years of service (years)</b>				
≤5	8 (18.6)	2 (4.1)	1 (Ref)	
6-10	6 (14.0)	4 (8.2)	0.17 (0.03-0.85)	
11+	29 (67.4)	43 (87.8)	1.45 (1.12-1.73)	0.018
<b>Length of service in the current position (years)</b>				
≤10	16 (37.2)	11 (22.4)		
>10	27 (62.8)	38 (77.6)	2.05 (0.82-5.10)	0.124

MBI - Maslach Burnout Inventory – questionnaire on burnout, p value according to univariate logistic regression analysis, OR-odds ratio, 95%CI - 95% confidence interval, ULRA – univariate logistic regression analysis

working conditions (e.g. extended working hours, working in shifts, night shifts, contact with patients and their families, etc.) (14). One of the frequent negative consequences of professional stress in persons who are in direct contact with people is burnout syndrome at work. Burnout syndrome can be defined as a prolonged response to chronic emotional and interpersonal stressors associated with the workplace. It is usually manifested as emotional exhaustion, a feeling of reduced personal accomplishment and depersonalization (1).

In addition to doctors, who have responsibility and from whom society expects to be infallible professionals, nursing profession is also a stressful

profession. Nursing is a profession that requires good relations with the persons who receive healthcare, the families of the sick, colleagues and superiors. Many studies conducted in the population of nurses indicated that there is a connection between certain health disorders (e.g. emotional and physical exhaustion, lower back pain, coronary disease) and stressors at the workplace (15-17).

Experiencing stress in the workplace is often related to overload (excessive demands, short deadlines), conflict and unclear work role (18,19). All this leads to insecurity, job dissatisfaction, reduced work performance and wish to leave the workplace (20).

**Tabela 5.** Distribucija lekara i medicinskih sestara/tehničara prema vrednostima skora za MBI komponentu depersonalizacija

Karakteristike	Niska/umerena N=67 Broj (%)	Visoka N=33 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Pol</b>				
Muškarci	19 (28,4)	20 (60,6)		
Žene	48 (71,6)	13 (39,4)	0,26 (0,11-0,62)	0,002
<b>Stručna spremam</b>				
Sestre	26 (38,8)	24 (72,7)		
Lekari	41 (61,2)	9 (27,3)	4,21 (1,69-10,45)	0,002
<b>Bračni status</b>				
Sa partnerom	47 (72,3)	31 (100)		
Bez partnera	18 (27,7)	0 (0,0)	0,09 (0,01-0,69)	0,025
<b>Deca</b>	49 (76,6)	31 (100)	9,18 (1,15-73,11)	0,036
<b>Broj dece</b>				
1	30 (40,8)	8 (25,8)	1 (Ref)	
2	27 (55,1)	21 (67,7)	1,94 (0,72-5,28)	
3	2 (4,1)	2 (6,5)	2,50 (0,29-20,92)	0,178
<b>Broj članova domaćinstva</b>				
1	6 (9,4)	0 (0,0)	1 (Ref)	
2	12 (18,8)	5 (16,1)	2,50 (0,236-26,48)	
3+	46 (71,9)	26 (83,9)	3,26 (0,37-28,62)	0,106
<b>Socio-ekonomski status</b>				
Dobar	4 (6,1)	4 (6,1)	1 (Ref)	
Srednji	57 (86,4)	57 (86,4)	0,65 (0,13-3,13)	
Loš	5 (7,6)	5 (7,6)	0,27 (0,02-3,65)	0,158
<b>Sopstvena kuća/stan</b>	59 (92,2)	32 (100,0)	2,63 (0,29-23,49)	0,387
<b>Dužina radnog staža (godine)</b>				
≤5	9 (14,8)	1 (3,2)	1 (Ref)	
6-10	9 (14,8)	1 (3,2)	0,16 (0,02-1,37)	
11+	43 (70,5)	29 (93,5)	0,16 (0,02-1,37)	0,034
<b>Dužina rada na trenutnom random mestu (godine)</b>				
≤10	22 (36,1)	5 (16,1)		
>10	39 (63,9)	26 (83,9)	2,93 (0,99-8,73)	0,053

MBI - *Maslach Burnout Inventory* – Upitnik o sagorevanju, p vrednost prema univarijantnoj logističkoj regresionoj analizi, UO-unakrsni odnos, 95%IP - 95% interval poverenja, ULRA – univarijantna logistička regresiona analiza

jedne komponente sindroma, sagorevanje je prisutno kod 59% ispitanika. Prema rezultatima multivarijantne logističke regresione analize, značajan nezavisan prediktor emocionalne iscrpljenosti i lične ostvarenosti su deca, a za depersonalizaciju pol.

Tri osnovne dimenzije ispoljavanja sindroma sagorevanja su emocionalna iscrpljenost profesionalca, depersonalizacija i lična neostvarenost (21). Osim ova tri osnovna simptoma, sindrom sagorevanja na poslu može biti povezan sa pojmom niza drugih tegoba, koje se najčešće karakterišu kao psihosomatske (na primer povišen krvni pritisak, glavobolja, bolesti srca, pojačano lučenje hormona stresa i drugi hormonski poremećaji, stomačne

tegobe), i različitih tegoba psihičke prirode, kao što su hronična anksioznost, bes, depresija, apatija, česte promene raspoloženja i drugi problem (22). Takođe, pominju se i poremećaji sna, podložnost raznim drugim bolestima, prehladi ili alergiji. Ponekad se može javiti osećaj unutrašnje praznine i tuge.

Sindrom sagorevanja na radu kod lekara je poslednjih godina dobio povećanu pažnju jer su stopi prevalence simptoma sagorevanja koje su oko 50% dokumentovane u nacionalnim studijama u Sjedinjenim Američkim Državama (23,24). Nacionalni podaci za druge zemlje su manje dostupni, ali prema postojećim podacima sličan problem je pri-

**Tabela 5.** Distribucija lekara i medicinskih sestara/tehničara prema vrednostima skora za MBI komponentu depersonalizacija

Characteristics	Niska/umerena N=67 Broj (%)	Visoka N=33 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Gender</b>				
Men	19 (28.4)	20 (60.6)		
Women	48 (71.6)	13 (39.4)	0.26 (0.11-0.62)	0.002
<b>Education</b>				
Nurses	26 (38.8)	24 (72.7)		
Doctors	41 (61.2)	9 (27.3)	4.21 (1.69-10.45)	0.002
<b>Marital status</b>				
With a partner	47 (72.3)	31 (100)		
Single	18 (27.7)	0 (0.0)	0.09 (0.01-0.69)	0.025
<b>Children</b>	49 (76.6)	31 (100)	9.18 (1.15-73.11)	0.036
<b>Number of children</b>				
1	30 (40.8)	8 (25.8)	1 (Ref)	
2	27 (55.1)	21 (67.7)	1.94 (0.72-5.28)	
3	2 (4.1)	2 (6.5)	2.50 (0.29-20.92)	0.178
<b>Number of household members</b>				
1	6 (9.4)	0 (0.0)	1 (Ref)	
2	12 (18.8)	5 (16.1)	2.50 (0.236-26.48)	
3+	46 (71.9)	26 (83.9)	3.26 (0.37-28.62)	0.106
<b>Socio-economic status</b>				
Good	4 (6.1)	4 (6.1)	1 (Ref)	
Average	57 (86.4)	57 (86.4)	0.65 (0.13-3.13)	
Poor	5 (7.6)	5 (7.6)	0.27 (0.02-3.65)	0.158
<b>Owns house/apartment</b>	59 (92.2)	32 (100.0)	2.63 (0.29-23.49)	0.387
<b>Years of service (years)</b>				
≤5	9 (14.8)	1 (3.2)	1 (Ref)	
6-10	9 (14.8)	1 (3.2)	0.16 (0.02-1.37)	
11+	43 (70.5)	29 (93.5)	0.16 (0.02-1.37)	0.034
<b>Length of service in the current position (years)</b>				
≤10	22 (36.1)	5 (16.1)		
>10	39 (63.9)	26 (83.9)	2.93 (0.99-8.73)	0.053

MBI - Maslach Burnout Inventory – questionnaire on burnout, p value according to univariate logistic regression analysis, OR-odds ratio, 95%CI - 95% confidence interval, ULRA – univariate logistic regression analysis

In our study, the prevalence of emotional exhaustion as a component of burnout syndrome was present in 51% of healthcare workers, depersonalization in 33%, and low personal accomplishment in 54% of respondents. If we choose the presence of at least one component of the syndrome as a criterion of the total burnout syndrome, burnout is present in 59% of respondents. According to the results of the multivariate logistic regression analysis, a significant independent predictor of emotional exhaustion and personal accomplishment are children, and for depersonalization gender.

Three basic dimensions of burnout syndrome

manifestations are emotional exhaustion of the professional, depersonalization and personal accomplishment (21). In addition to these three basic symptoms, burnout syndrome at work can be associated with the appearance of a number of other problems, which are most often characterized as psychosomatic (for example, high blood pressure, headache, heart disease, increased secretion of stress hormones and other hormonal disorders, stomach problems), and various ailments of a psychological nature, such as chronic anxiety, anger, depression, apathy, frequent mood swings and other problems (22). Also, sleep disorders, susceptibility to other diseases, colds or

**Tabela 6.** Distribucija lekara i medicinskih sestara/tehničara prema vrednostima skora za MBI komponentu lična ostvarenost

Karakteristike	Niska/umerena N=46 Broj (%)	Visoka N=54 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Pol</b>				
Muškarci	17 (37,0)	22 (40,7)		
Žene	29 (63,0)	32 (59,3)	0,85 (0,38-1,91)	0,699
<b>Stručna spremja</b>				
Sestre	17 (37,0)	33 (61,1)		
Lekari	29 (63,0)	21 (38,9)	0,37 (0,17-0,84)	0,017
<b>Bračni status</b>				
Sa partnerom	31 (72,1)	47 (88,7)		
Bez partnera	12 (27,9)	6 (11,3)	0,33 (0,11-0,97)	0,044
<b>Deca</b>	30 (71,4)	50 (94,3)	6,67 (1,74-25,5)	0,006
<b>Broj dece</b>				
1	11 (36,7)	17 (34,0)	1 (Ref)	
2	18 (60,0)	30 (60,0)	1,08 (0,41-2,81)	
3	1 (3,3)	3 (6,0)	1,94 (0,18-21,12)	0,679
<b>Broj članova domaćinstva</b>				
1	4 (9,5)	2 (3,8)	1 (Ref)	
2	9 (21,4)	8 (15,1)	1,78 (0,25-12,45)	
3+	29 (69,0)	43 (81,1)	2,97 (0,51-17,26)	0,145
<b>Socio-ekonomski status</b>				
Dobar	3 (6,7)	4 (7,5)	1 (Ref)	
Srednji	40 (88,9)	46 (86,8)	0,86 (0,18-4,09)	
Loš	2 (4,4)	3 (5,7)	1,12 (0,11-11,59)	0,968
<b>Sopstvena kuća/stan</b>	40 (93,0)	51 (96,2)	1,912 (0,30-12,00)	0,489
<b>Dužina radnog staža (godine)</b>				
≤5	8 (18,6)	2 (4,1)	1 (Ref)	
6-10	6 (14,0)	4 (8,2)	0,17 (0,03-0,85)	
11+	29 (67,4)	43 (87,8)	0,45 (1,12-1,73)	0,018
<b>Dužina rada na trenutnom random mestu (godine)</b>				
≤10	18 (41,9)	9 (18,4)		
>10	25 (58,1)	40 (81,6)	3,20 (1,25-8,22)	0,016

MBI - Maslach Burnout Inventory – Upitnik o sagorevanju, p vrednost prema univariantnoj logističkoj regresionoj analizi, UO-unakrsni odnos, 95%IP - 95% interval poverenja, ULRA – univariantna logistička regresiona analiza

sutan širom sveta (26). Pored toga što u nekim starijim studijama u Norveškoj (26) i Danskoj (27) prevalencija sindroma sagorevanja među lekarima nije bila veća nego kod profesionalaca drugih struka, novija studija iz Sjedinjenih Američkih Država pokazala je da je prevalencija sagorevanja veća kod lekara nego u drugim profesijama, čak i kad se koriguje za broj radnih sati i druge faktore (28). U studiji sprovedenoj kod anesteziologa u Beogradu detektovan je značajan stepen sindroma sagorevanja: visoka emocionalna iscrpljenost 52,7%, visoka depersonalizacija 12,2% i niska lična ostvarenost 28,2%. Kod lekara opšte prakse emocionalna iscrpljenost bila je prisutna kod 24% lekara,

depersonalizacija kod 7,3% ispitanika, a niska lična ostvarenost kod 51,7% ispitanika (29). Ortopedski hirurzi imali su 24,5% emocionalne iscrpljenosti, 9,9% depersonalizacije, i 35,7% niske lične ostvarenosti (30). Kod psihijatara je emocionalna iscrpljenost bila prisutna sa 29,1%, depersonalizacija sa 12,2% i niska lična ostvarenost sa 22,4% (31).

Studije preseka na populacijama lekara su pokazale da postoji povezanost između sindroma sagorevanja i pola lekara, uzrasta, obrazovanja, bračnog statusa, uzrasta dece i zanimanja partnera (32). Iako pol nije konzistentno nezavisan prediktor sindroma sagorevanja nakon adžastiranja za uzrast i druge faktore, prema nekim studijama žene lekari

**Table 6.** Distribution of doctors and nurses/technicians according to the values of the score for MBI component personal accomplishment

Characteristics	Niska/umerena N=46 Broj (%)	Visoka N=54 Broj (%)	UO (95%IP)	p vrednost ULRA
<b>Gender</b>				
Men	17 (37.0)	22 (40.7)		
Women	29 (63.0)	32 (59.3)	0.85 (0.38-1.91)	0.699
<b>Education</b>				
Nurses	17 (37.0)	33 (61.1)		
Doctors	29 (63.0)	21 (38.9)	0.37 (0.17-0.84)	0.017
<b>Marital status</b>				
With a partner	31 (72.1)	47 (88.7)		
Single	12 (27.9)	6 (11.3)	0.33 (0.11-0.97)	0.044
<b>Children</b>	30 (71.4)	50 (94.3)	6.67 (1.74-25.5)	0.006
<b>Number of children</b>				
1	11 (36.7)	17 (34.0)	1 (Ref)	
2	18 (60.0)	30 (60.0)	1.08 (0.41-2.81)	
3	1 (3.3)	3 (6.0)	1.94 (0.18-21.12)	0.679
<b>Number of household members</b>				
1	4 (9.5)	2 (3.8)	1 (Ref)	
2	9 (21.4)	8 (15.1)	1.78 (0.25-12.45)	
3+	29 (69.0)	43 (81.1)	2.97 (0.51-17.26)	0.145
<b>Socio-economic status</b>				
Good	3 (6.7)	4 (7.5)	1 (Ref)	
Average	40 (88.9)	46 (86.8)	0.86 (0.18-4.09)	
Poor	2 (4.4)	3 (5.7)	1.12 (0.11-11.59)	0.968
<b>Owns house/apartment</b>	40 (93.0)	51 (96.2)	1.912 (0.30-12.00)	0.489
<b>Years of service (years)</b>				
≤5	8 (18.6)	2 (4.1)	1 (Ref)	
6-10	6 (14.0)	4 (8.2)	0.17 (0.03-0.85)	
11+	29 (67.4)	43 (87.8)	0.45 (1.12-1.73)	0.018
<b>Length of service in the current position (years)</b>				
≤10	18 (41.9)	9 (18.4)		
>10	25 (58.1)	40 (81.6)	3.20 (1.25-8.22)	0.016

MBI - Maslach Burnout Inventory – questionnaire on burnout, p value according to univariate logistic regression analysis, OR-odds ratio, 95%CI - 95% confidence interval, ULRA – univariate logistic regression analysis

allergies are mentioned. Sometimes, the feeling of inner emptiness and sadness may appear.

Burnout syndrome among doctors has gained increased attention in recent years because prevalence rates of burnout symptoms of around 50% have been documented in national studies in the United States (23,24). National data for other countries are less available but according to existing data, a similar problem is present worldwide (25). In addition to the fact that in some older studies in Norway (26) and Denmark (27) the prevalence of burnout syndrome among doctors was not higher among professionals of other professions, a recent study from the United States of America has

shown that the prevalence of burnout is higher in doctors than in other professions, even when adjusted for the number of working hours and other factors (28). In a study conducted among anesthesiologists in Belgrade, a significant degree of burnout syndrome was detected: high emotional exhaustion 52.7%, high depersonalization 12.2% and low personal accomplishment 28.2%. In general practitioners, emotional exhaustion was present in 24% of doctors, depersonalization in 7.3% of respondents, and low personal accomplishment in 51.7% of respondents (29). Orthopedic surgeons had 24.5% of emotional exhaustion, 9.9% of depersonalization, and 35.7%

imaju 20-60% veće šanse za sindrom sagorevanja (33). Norveška studija koja je objavila rezultate sindroma sagorevanja pronašla je veći nivo iscrpljenosti kod žena, kod kojih je sagorevanje bilo povezano sa konfliktima na radnom mestu i višim nivoima povlačenja među muškarcima, kod kojih je sagorevanje najjače povezano sa radnim opterećenjem (34). Povećan rizik od pojave simptoma sagorevanja prisutan je kod mlađih lekara, kod lekara mlađih od 55 godina rizik je dvostruko veći od onih starijih od 55 godina. Utvrđeno je da lekari koji imaju dete mlađe od 21 godine imaju povećan rizik od sagorevanja 54% i supružnik / partner koji radi kao zdravstveni radnik koji nije lekar pokazalo se da povećava rizik od sagorevanja za 23%. Individualne karakteristike, kao što su ličnost i interpersonalne veštine i lična iskustva mogu uticati na to kako se lekari nose sa stresom (35).

Ograničenje ove studije je u vezi sa pristrasnošću izbora ispitanika, koja je rezultat uzorkovanja ispitivane populacije iz jedne zdravstvene ustanove, uključujući nisku stopu regrutovanja, i relativno malu veličinu uzorka, što može ograničiti generalizaciju rezultata na širu populaciju zdravstvenih radnika.

## Zaključak

Prevalencija emocionalne iscrpljenosti, kao komponente sindroma sagorevanja, bila je prisutna kod 51% zdravstvenih radnika, depersonalizacija kod 33%, i niska lična ostvarenost kod 54% ispitanika. Ukoliko kao kriterijum ukupnog sindroma sagorevanja odaberemo prisustvo bar jedne od tri komponente sindroma, sindrom sagorevanja je prisutan kod 59% ispitanika. Prema rezultatima multivarijantne logističke regresione analize, značajan nezavisan prediktor emocionalne iscrpljenosti i lične ostvarenosti prema MBI su deca, a za depersonalizaciju prema MBI je pol. Neophodna su dalja istraživanja prevalencije sindroma sagorevanja među zdravstvenim radnicima drugih ustanova, kao i identifikovanje faktora koji doprinose sindromu sagorevanja u cilju njegovog prevenranja.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Zahvalnica

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of reduced personal accomplishment (30). In psychiatrists, emotional exhaustion was present in 29.1%, depersonalization in 12.2% and low personal accomplishment in 22.4% (31).

Cross-sectional studies of the populations of doctors have shown that there is a connection between burnout syndrome and doctors' gender, education, marital status, children's age and partner's occupation (32). Although gender is not a consistent independent predictor of burnout, after adjusting for age and other factors, some studies indicate that female doctors are 20-60% more likely to experience burnout (33). A Norwegian study that published the results of burnout syndrome found a higher level of burnout in women, in whom burnout was associated with conflicts at work, and higher levels of withdrawal in men, in whom burnout was most strongly associated with workload (34). An increased risk of burnout is present in younger doctors, in doctors younger than 55 the risk is twice as high in comparison to those older than 55. It was found that doctors who had a child under the age of 21 had a 54% increased risk of burnout, and that a spouse/partner who worked as a healthcare worker, but who was not a doctor, increased the risk of burnout by 23%. Individual characteristics, such as personality and interpersonal skills and personal experiences can influence how doctors cope with stress (35).

The limitation of this study is related to respondent selection bias, which is the result of sampling the study population from a single healthcare institution, including a low recruitment rate, and a relatively small sample size, which may limit the generalization of results applied to a wider population of healthcare professionals.

## Conclusion

The prevalence of emotional exhaustion, as a component of burnout syndrome, was present in 51% of healthcare workers, depersonalization in 33%, and low personal accomplishment in 54% of respondents. If we choose the presence of at least one of the three components of the syndrome as a criterion of the total burnout syndrome, burnout syndrome is present in 59% of respondents. According to the results of the multivariate logistic regression analysis, a significant independent predictor of emotional exhaustion and personal

accomplishment, according to MBI, is children, and for depersonalization, according to MBI, is gender. Further research on the prevalence of burnout syndrome in healthcare workers from other institutions is necessary, as well as the identification of factors that contribute to burnout syndrome aimed at its prevention.

## Competing interests

Authors declare no competing interests.

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## ZNANJE, STAVOVI I PONAŠANJE STUDENATA VISOKE ZDRAVSTVENE ŠKOLE U BEOGRADU O ZNAČAJU HPV INFEKCIJE, HPV VAKCINE I DRUGIH PREVENTIVNIH MERA

Marijana Dabić <sup>1\*</sup>

<sup>1</sup> Akademija strukovnih studija Beograd, Odsek Visoka zdravstvena škola, Beograd, Republika Srbija

\* Korespondencija: Marijana Dabić, Akademija strukovnih studija, Odsek Visoka zdravstvena škola, Katedra za zdravstvenu negu, Cara Dušana 254, 11080 Beograd, Republika Srbija; e-mail: dabicmarijana26@gmail.com

### SAŽETAK

**Uvod/Cilj:** Znanje i informisanost o važnosti HPV vakcine protiv humanog papiloma virusa (HPV) u velikoj meri mogu doprineti redukciji obolenja od raka grlića materice i drugih malignih tumora. Cilj ove studije je da se procene znanje, stavovi i ponašanja studenata o HPV infekciji i vakcini, kao i da se predlože mere za bolji obuhvat mlađih HPV vakcinom.

**Metode:** Studijom preseka obuhvaćeno je 449 studenata zdravstvene nege Visoke zdravstvene škole u Beogradu u periodu mart/maj 2019. godine. Upitnikom su prikupljeni podaci. U statističkoj analizi podataka korišćen je hi kvadrat test i Fišerov egzaktni test.

**Rezultati:** Prosečna starost studenata iznosila je  $21,02 \pm 2,59$  godine. Svoje znanje o HPV vakcini 86,0% studenata je ocenilo kao zadovoljavajuće. Na znanje o HPV vakcini u najvećem procentu su uticali nastavnici (79,7%), a zatim elektronski mediji (10,7%). Medicinske platforme za informisanje o HPV vakcini koristilo je samo 9% studenata. Prve informacije i određen stepen znanja o HPV infekciji i HPV vakcini studenti su usvojili u srednjoj školi (80,4% i 65,6%). Samo 3,4% studenata smatra da su mlađi u Srbiji dovoljno informisani o HPV infekciji, a 0,4% o HPV vakcini. Svaki drugi student smatra da je jedan od načina za bolju informisanost mlađih vršnjačka edukacija u školama. Oko 94% studenata zna da u našoj zemlji postoji organizovani skrining za rak grlića materice. Samo 10,2% studenata je želelo da vakciniše svoje dete HPV vakcinom, a oni koji to ne bi učinili kao glavni argument navode nedovoljnu informisanost o bezbednosti i efikasnosti vakcine (81,6%). Osobe koje su bile za HPV vakcincu su se značajno ređe podvrgavale redovnim ginekološkim pregledima.

**Zaključak:** Studenti Visoke zdravstvene škole u Beogradu smatraju da treba da postoji bolja edukacija o HPV infekciji i vakcini, što bi najbolje moglo da se realizuje sprovođenjem vršnjačke edukacije.

**Ključne reči:** HPV vakcina, studenti, znanje, stavovi

### Uvod

Infekcija humanim papiloma virusima (HPV) je jedna od najčešćih polno prenosivih infekcija (1). Smatra se da skoro svi seksualno aktivni muškarci i žene u nekom trenutku svog života mogu da budu zaraženi nekim od preko 200 tipova humanog papiloma virusa (HPV)(2). Podaci Svetske zdravstvene organizacije (SZO) ukazuju da mlađi uzrasta do 24 godine čine oko 60% ukupno obolelih od polno prenosivih infekcija (3). Rano stupanje u seksualne odnose uz nedovoljno znanja o polno prenosivim infekcijama, kontracepciji i planiranju porodice, kao i o značaju vakcine u prevenciji HPV infekcije i virusnog hepatitis B, doprinose evidentnom narušavanju reproduktivnog zdravlja.

Imajući u vidu ozbiljne posledice hronične HPV infekcije među kojima je i pojava raka grlića materice, vulve, vagine, penisa, orofarinks i anusa, HPV vakcina predstavlja sigurnu i efikasnu javno-zdravstvenu meru u prevenciji ove infekcije (4). Kao poseban značaj primene ove vakcine ogleda se i u redukciji javljanja genitalnih kondiloma (čak u 90% slučajeva). Vakcinacija takođe doprinosi smanjenju zdravstvenih troškova lečenja i postizanju ekonomskih isplativosti u sistemu zdravstvene zaštite (5). Do 2018. na globalnom nivou 84 države (42% zemalja članica Ujedinjenih nacija) su u svoje nacionalne programe imunizacije uvele vakcinaciju protiv HPV-a (uključujući i 33 zemlje u Evropskom regionu

## KNOWLEDGE, ATTITUDES AND BEHAVIOR OF STUDENTS OF THE MEDICAL COLLEGE OF APPLIED SCIENCES IN BELGRADE RELATED TO THE SIGNIFICANCE OF HPV INFECTION, THE HPV VACCINE AND OTHER PREVENTIVE MEASURES

**Marijana Dabic<sup>1\*</sup>**

<sup>1</sup> Medical College of Applied Sciences, Department of Health Care, Belgrade, Republic of Serbia

\* Correspondence: Marijana Dabic, Medical College of Applied Sciences, Department of Health Care, Cara Dusana 254, 11080 Belgrade, Republic of Serbia; e-mail: dabicmarijana6@gmail.com

### SUMMARY

**Introduction/Aim:** Knowledge and awareness of the importance of the HPV vaccine against human papillomavirus (HPV) can greatly contribute to the reduction of cervical cancer and other malignant tumors. The aim of this study is to assess the knowledge, attitudes and behavior of students about HPV infection, as well as to propose measures for the better coverage of young people with the HPV vaccine.

**Methods:** A cross-sectional study included 449 students of healthcare of the Medical College of Applied Sciences in Belgrade in the period from March to May, 2019. Data were collected using a questionnaire. Chi-square test and Fisher's exact tests were used for the statistical analysis of data.

**Results:** The average age of students was  $21.02 \pm 2.59$  years. 86.0% of students assessed their knowledge about the HPV vaccine as satisfactory. Teachers had the greatest influence on their knowledge about the HPV vaccine (79.7%), followed by the electronic media (10.7%). Medical platforms for information about the HPV vaccine were used by only 9% of students. Students acquired the first information and a certain degree of knowledge about HPV infection and the HPV vaccine in high school (80.4% and 65.6%). Only 3.4% of students think that young people in Serbia are sufficiently informed about HPV infection and 0.4% about the HPV vaccine. Every second student believes that peer education in schools is one of the ways to better inform young people. About 94% of students know that there is an organized screening for cervical cancer in our country. Only 10.2% of students wanted to vaccinate their child with the HPV vaccine, and those who would not do so cite the insufficient information about the safety and effectiveness of the vaccine as their main argument (81.6%). Respondents who were for the HPV vaccine significantly less frequently underwent regular gynecological examinations.

**Conclusion:** Students of the Medical College of Applied Sciences in Belgrade believe that there should be better education about HPV infection and the vaccine, which could be best realized by conducting peer education.

**Keywords:** HPV vaccine, students, knowledge, attitudes

### Introduction

Human papillomavirus (HPV) infection is one of the most common sexually transmitted infections (1). It is believed that almost all sexually active men and women may, at some point in their lives, get infected with one of more than 200 types of human papillomavirus (HPV) (2). Data of the World Health Organization (WHO) indicate that young people under the age of 24 make up about 60% of all cases of sexually transmitted diseases (3). Early sexual intercourse with insufficient knowledge about sexually transmitted infections, contraception and family planning, as well as the

significance of the vaccine and the prevention of HPV infection and viral hepatitis B contribute to the evident impairment of reproductive health.

Having in mind the serious consequences of chronic HPV infection, including the cancer of cervix, vulva, vagina, penis, oropharynx and anus, the HPV vaccine represents a safe and effective public health measure in the prevention of this infection (4). The special significance of this vaccine is reflected in the reduction of occurrence of genital warts (in up to 90% of cases). Vaccination also contributes to the reduction in the cost of

od ukupno 44 zemlje) (4). U zemljama sa visokim obuhvatom HPV vakcinom uočena je smanjena učestalost patoloških promena na grliću materice. Tako je studija Lei i saradnika pokazala da je praćenjem 1.672.983 devojčica i žena starosti od 10 do 30 godina od 2006. do 2017 u Švedskoj došlo do redukcije kumulativne incidencije raka grlića materice među vakcinisanim kvadrivalentnom HPV vakcynom (47 obolelih na 100.000 ispitanika) u odnosu na ne-vakcinisane (94 na 100.000 ispitanika) (6).

Cilj naše studije je da se procene znanje, stavovi i ponašanje studenata zdravstvene nege Visoke zdravstvene škole u Beogradu o HPV infekciji i vakcini, kao i da se predlože mere za bolji obuhvat mladih HPV vakcynom.

## Metode

Istraživanje je dizajnirano kao studija preseka koja je sprovedena u periodu od marta do maja 2019. godine u Visokoj zdravstvenoj školi u Beogradu. U studiju je uključeno 449 studenata sve tri godine osnovnih strukovnih studija koji su dobrovoljno prihvatali anonimno učešće u studiji. Od svih ispitanika prikupljeni su podaci upitnikom. Na osnovu pregleda literature i prethodnih istraživanja u ovoj oblasti, konstruisan je upitnik koji se sastojao iz 3 dela sa 30 pitanja (otvorenog i zatvorenog tipa).

Prvi deo upitnika odnosio se na demografske karakteristike (uzrast, pol, mesto stanovanja, zaposlenost, godina studija, prethodno završena škola, studijski program), a drugi na znanje i stavove o HPV infekciji i HPV vakcini. Trećim delom upitnika obuhvaćeno je ponašanje ispitanika (pušenje, konzumiranje alkohola, korišćenje psihoaktivnih supstanci, seksualno ponašanje, korišćenje kontracepcije, odlazak na ginekološke pregledе, učešće u Papanikolau skrining programu za rano otkrivanje karcinoma grlića materice, vakcinalni status po pitanju HPV).

U deskriptivnoj analizi podataka korišćeni su apsolutni brojevi, procenti i aritmetičke sredine sa standardnom devijacijom. Za pripremu baze podataka, kao i za statističku obradu, korišćen je softverski paket programa Statistical Package for the Social Science, SPSS 20.0 (SPSS Inc., Chicago, IL, USA). U statističkoj analizi podataka korišćen je hi kvadrat test i Fisherov egzaktni test.

## Rezultati

Ovom studijom preseka (engl. *cross-sectional study*) obuhvaćeno je 449 studenata zdravstvene nege Visoke zdravstvene škole u Beogradu (5,3% muškaraca i 94,7% žena), uzrasta od 18 do 38 godina (tabela 1). Prosečna starost svih studenata iznosila je 21,02 godine ( $SD=2,59$ ). Skoro  $\frac{1}{3}$  je bilo iz Beograda, a 87,8% je bilo zaposleno. Najveći broj studenata je bio sa prve (42,8%), a zatim sa druge (30,5%) i treće godine studija (26,7%). Među studentima zdravstvene nege, najviše je bilo studenata sa odseka Strukovna medicinska sestra (57,9%), a zatim Strukovna medicinska sestra – babica (33,2%) i Strukovna medicinska sestra – vaspitač (8,9%). Većina studenata (95,1%) je imala završenu srednju medicinsku školu.

Svoje znanje o HPV vakcini 86,0% studenata je ocenilo kao zadovoljavajuće (tabela 2). Na znanje o HPV vakcini u najvećem procentu su uticali nastavnici (79,7%), a zatim elektronski mediji (10,7%). Medicinske platforme za informisanje o HPV vakcini koristilo je 9% studenata. Prve informacije i određen stepen znanja o HPV infekciji i HPV vakcini studenti su usvojili u srednjoj školi (80,4% i 65,6%). Samo 3,4% studenata smatra da su mlađi u Srbiji dovoljno informisani o HPV infekciji, a 0,4% o HPV vakcini. Svaki drugi student smatra da je jedan od načina za bolju informisanost mlađih vršnjačka edukacija u školama. Oko 94% studenata zna da u našoj zemlji postoji organizovani skrining za rak grlića materice. Oko 10% studenata ima stav da bi vakcinisali svoje dete HPV vakcynom, a oni koji to ne bi učinili kao glavni argument navode nedovoljnju informisanost o bezbednosti i efikasnosti vakcine (81,6%).

Ponašanje ispitanika pokazuju da  $\frac{1}{4}$  studenata svakodnevno puši, oko 50% povremeno ili svakodnevno konzumira alkohol i 1,1% povremeno ili svakodnevno upotrebljava psihoaktivne supstance (tabela 3). Seksualni odnos je imalo 78,3% ispitanika, a kondom koristi skoro pri svakom seksualnom odnosu 77,2% studenata. Prosečna starost pri prvom seksualnom odnosu je bila 18,03 godina ( $SD=1,41$ ), a prosečan broj partnera je bio 2,21 ( $SD=2,14$ ). Kontracepciju je koristilo 85,1% studenata koji upražnjavaju seksualne odnose (78,3%) i najčešće korišćeni metod kontracepcije je prezervativ (91,8%). Na redovne ginekološke pregledе odlazi 75,8% ispitanica. Na skriningu karcinoma grlića materice u Srbiji je učestvovalo 30,6% stu-

treatment and the achievement of economic profitability in the healthcare system (5). By 2018, at the global level, 84 countries (42% of the United Nations member states) had introduced HPV vaccination into their national immunization programs (including 33 of 44 countries in the European region) (4). A decrease in the frequency of pathological changes of the cervix was observed in the countries with the high HPV vaccination coverage. Thus, the study of Lei and associates showed that by following up 1,672,983 girls and women aged between 10 and 30 from 2006 to 2017 in Sweden, there came to a reduction in the cumulative incidence of cervical cancer among those vaccinated with the quadrivalent HPV vaccine (47 cases per 100,000 respondents) in comparison to the unvaccinated (94 per 100,000 respondents) (6).

The aim of our study is to assess the knowledge, attitudes and behavior of healthcare students of the Medical College of Applied Sciences in Belgrade about the HPV infection and vaccine, as well as to propose measures for the better coverage of young people with the HPV vaccine.

## Methods

The research was designed as a cross-sectional study which was conducted at the Medical College of Applied Sciences in the period from March to May 2019. The study included 449 students of all three years of professional studies who voluntarily accepted the anonymous participation in the study. Data were collected from all respondents with the help of a questionnaire. The questionnaire was designed based on the literature review and previous research in this field, and it consisted of 3 parts with 30 questions (open and closed questions).

The first part of the questionnaire was related to demographic characteristics (age, gender, place of residence, employment, year of studies, previously completed school, study program), while the second part was related to the knowledge and attitudes about HPV infection and HPV vaccine. The third part of the questionnaire covered the behavior of respondents (smoking, alcohol consumption, use of psychoactive substances, sexual behavior, use of contraception, going to gynecological examinations, participation in the Papanicolaou screening program for the

early detection of cervical cancer, HPV vaccination status).

Absolute numbers, percentages and arithmetic mean with standard deviation were used for the descriptive data analysis. The Statistical Package for the Social Science, SPSS 20.0 (SPSS Inc, Chicago, IL, USA) was used for the preparation of the database, as well as for the statistical analysis. Chi-square test and Fisher's exact test were used for the statistical analysis of data.

## Results

This cross-sectional study included 449 healthcare students of the Medical College of Applied Sciences in Belgrade (5.3% of men and 94.7% of women) aged 18 to 38 (Table 1). The average age of all students was 21.02 years ( $SD=2.59$ ). Almost two-thirds were from Belgrade, while 87.8% were employed. The largest number of students was first year students (42.8%), followed by the second year students (30.5%) and third year students (26.7%). Among healthcare students, the majority was from the vocational nurse department (57.9%), followed by vocational nurse – midwife (33.2%) and vocational nurse – pre-school teacher (8.9%). The majority of students (95.1%) had completed secondary medical school.

86.0% of students assessed their knowledge about the HPV vaccine as satisfactory (Table 2). Teachers (79.7%) had the greatest influence on knowledge about the HPV vaccine, followed by the electronic media (10.7%). Medical platforms for the information about the HPV vaccine were used by 9% of students. Students acquired the first information and a certain degree of knowledge about the HPV infection and vaccine in high school (80.4% and 65.6%). Only 3.4% of students believe that young people in Serbia are sufficiently informed about HPV infection, and 0.4% about the HPV vaccine. Every second student believes that peer education in schools is one of the ways to better inform young people. About 94% of students know that there is an organized screening for cervical cancer in our country. About 10% of students think that they would vaccinate their child with the HPV vaccine, while those who would not do so state insufficient information about the safety and effectiveness of the vaccine as the main argument (81.6).

**Tabela 1.** Demografske karakteristike studenata Visoke zdravstvene škole

Karakteristike	Broj (%) N=449
<b>Pol</b>	
Muški	4 (5,3)
Ženski	425 (94,7)
<b>Uzrast (godine) (<math>\bar{x} \pm SD</math>):</b>	$21,02 \pm 2,59$
<b>Mesto stanovanja:</b>	
Beograd	264 (58,9)
Centralna Srbija	72 (16,1)
Vojvodina	112 (25,0)
<b>Godina studija</b>	
Prva	192 (42,8)
Druga	137 (30,5)
Treća	120 (26,7)
<b>Prethodno završena škola</b>	
Medicinska škola	427 (95,1)
Gimnazija	19 (4,2)
Drugo	3 (0,7)
<b>Studijski program</b>	
Strukovna medicinska sestra	260 (57,9)
Strukovna medicinska sestra-babica	149 (33,2)
Strukovna medicinska sestra-vaspitač	40 (8,9)
<b>Zaposlenost u oblasti zdravstvene struke</b>	55 (12,2)

$\bar{x}$  - aritmetička sredina; SD - standardna devijacija

dentkinja, koje su bile seksualno aktivne. U periodu izvođenja studije nijedan od ispitanika nije bio vakcinisan HPV vakcinom.

Osobe koje su bile za primenu HPV vakcine i one koje su bile protiv nisu se značajno razlikovale u odnosu na sledeće životne navike: svakodnevno pušenje cigareta, konzumiranje alkohola povremeno ili svakodnevno, seksualni odnos, korišćenje kondoma pri skoro svakom seksualnom odnosu i zadovoljavajućem znanju o HPV infekciji (tabela 4). Osobe koje su bile za HPV vakcini su se značajno ( $p < 0,001$ ) ređe podvrgavale redovnim ginekološkim pregledima.

## Diskusija

Rezultati naše studije pokazuju da studenti Visoke zdravstvene škole u Beogradu ukazuju na deficit znanja i informisanosti mladih o HPV infekciji (3,4%) i vakcini (0,4%). Međutim, oko 10% studenata bi vakcinisalo svoje dete HPV vakcinom, ali ni jedan student nije dobio HPV vakcini do početka sprovođenja ovog istraživanja. Protiv HPV vakcine, u poređenju sa studentima koji su bili za HPV vakcini, bili su studenti koji su značajno češće isli na redovni ginekološki pregled. Protiv HPV vakcine

bile su osobe koje su kao glavni razlog takvog stava navodile nedovoljno informacija o efikasnosti i bezbednosti vakcine.

U studiji koja je rađena među studentima Visoke medicinske škole u Čupriji o humanom papiloma virusu i HPV vakcini, gde je korišćena provera znanja pre i posle edukacije o HPV infekciji i primeni HPV vakcine (7). Rezultati su pokazali nezadovoljavajući nivo znanja i pre i posle testa, naročito u oblasti prevencije HPV infekcije (7). Sagledavajući rezultate brojnih evropskih i svetskih istraživanja u populaciji studenata sestrinstva, medicine i drugih fakulteta, ali i među zaposlenim zdravstvenim radnicima, uočen je i deficit znanja o HPV vakcini, efektima primene, ali i nedovoljno primenjenih postojećih znanja o prevenciji HPV infekcije u praksi (8-13). Jedno od takvih istraživanja je sistemski pregled literature za period od 2006. do 2017. godine gde su sumirani rezultati o faktorima koji su povezani sa znanjem o HPV-u i prihvatanju vakcine kod adolescenata i njihovih roditelja u 16 evropskih država (14). Najviši nivo znanja o HPV infekciji i vakcini, pokazali su adolescenti u Španiji (93%), Belgiji (67%) i Italiji (61%), dok je najveća zainteresovanost za primenu vakcine bila kod adolescenata u Švedskoj (90,5%)

**Table 1.** Demographic characteristics of students of Medical College of Applied Sciences

Characteristics	Number (%) N=449
<b>Gender</b>	
Male	4 (5.3)
Female	425 (94.7)
<b>Age (years) (<math>\bar{x} \pm SD</math>)</b>	$21.02 \pm 2.59$
<b>Place of residence</b>	
Belgrade	264 (58.9)
Central Serbia	72 (16.1)
Vojvodina	112 (25.0)
<b>Year of studies</b>	
First	192 (42.8)
Second	137 (30.5)
Third	120 (26.7)
<b>Previously finished school</b>	
Medical School	427 (95.1)
High School	19 (4.2)
Other	3 (0.7)
<b>Study program</b>	
Vocational nurse	260 (57.9)
Vocational nurse - midwife	149 (33.2)
Vocational nurse – pre-school teacher	40 (8.9)
<b>Employment in the field of healthcare</b>	55 (12.2)

$\bar{x}$  - arithmetic mean; SD – standard deviation

The respondents' behavior shows that one fourth of students smoke every day, about 50% consume alcohol occasionally or every day and 1.1% uses psychoactive substances occasionally or daily (Table 3). 78.3% of respondents had sexual intercourse, while 77.2% of students use condoms almost every time they have sex. The average age at first sexual intercourse was 18.03 years ( $SD=1.41$ ), while the average number of partners was 2.21 ( $SD=2.14$ ). Contraception was used by 85.1% of students who have sexual relations (78.3%), and the most frequently used method of contraception was a condom (91.8%). 75.8% of respondents go to regular gynecological examinations. 30.6% of students who had sexual intercourse participated in cervical cancer screening in Serbia. None of the respondents were vaccinated with the HPV vaccine at the time when this study was conducted.

There were no significant differences between persons who were for the application of the HPV vaccine and those who were against, regarding the following lifestyle habits: daily smoking of cigarettes, occasional or daily consumption of alcohol, sexual intercourse, use of condoms almost during each sexual intercourse, and satisfactory knowledge

about the HPV infection (Table 4). Persons who were for the application of the HPV vaccine ( $p < 0.001$ ) underwent regular gynecological examinations significantly less frequently.

## Discussion

The results of our study show that the students of the Medical College in Belgrade indicate a deficit of knowledge and information among young people about HPV infection (3.4%) and the vaccine (0.4%). However, about 10% of students would vaccinate their child with the HPV vaccine, but none of the students had received the HPV vaccine by the time this study began. The students, who went to regular gynecological examinations significantly more often, were against the HPV vaccine in comparison to those students who were for the HPV vaccine. There were persons against the HPV vaccine who cited insufficient information about the effectiveness and safety of the vaccine as the main reasons for such an attitude.

In a study which was conducted among the students of the Medical College in Ćuprija about the human papillomavirus and the HPV vaccine, the assessment test was used to assess knowledge

**Tabela 2.** Znanje i stavovi studenata o HPV infekciji i vakcini

Karakteristike	Broj (%)
<b>Zadovoljavajuće znanje o HPV infekciji (N=449)</b>	386 (86,0)
<b>Izvori informacija o HPV vakcini (N=449)</b>	
Nastavnici	358 (79,7)
Roditelji	14 (3,1)
Prijatelji	14 (3,1)
Elektronski mediji (društvene mreže, web sajtovi)	48 (10,7)
Medijske kampanje (TV, štampa)	12 (2,7)
Nisam znao/la da postoj	3 (0,7)
<b>Koristim medicinske platforme za dobijanje informacije o HPV vakcini (N=449)</b>	40 (9,0)
<b>Prvi put čula/čuo sam o HPV infekciji (N=449)</b>	
U osnovnoj školi	55 (12,2)
U srednjoj školi	361 (80,4)
U toku studija	27 (6,0)
Nisam bio/la informisan/a	6 (1,3)
<b>Prvi put čula/čuo sam o HPV vakcini (N=448)</b>	
U osnovnoj školi	18 (4,0)
U srednjoj školi	294 (65,6)
U toku studija	115 (25,7)
Nisam bio/la informisan/a	21 (4,7)
<b>Mladi u Srbiji su dovoljno informisani o HPV infekciji (N=449)</b>	15 (3,4)
<b>Mladi u Srbiji su dovoljno informisani o HPV vakcini (N=449)</b>	2 (0,4)
<b>Boljoj informisanosti o HPV vakcini može da doprinese (N=449)</b>	
Vršnjačka edukacija u školama	240 (53,8)
Medijske kampanje	76 (17,0)
Preventivni pregledi	82 (18,4)
Učešće roditelja u edukaciji	42 (9,4)
Drugo	6 (1,3)
<b>U našoj zemlji sprovodi se organizovani skrining program za rak grlića materice (N=449)</b>	398 (93,9)
<b>Vakcinisala bih svoje dete (N=441)</b>	45 (10,2)
<b>Argumenti protiv vakcinacije HPV vakcinom (N=396)*</b>	
Visoka cena	56 (14,4)
Nedovoljna informisanost o bezbednosti i efikasnosti vakcine	323 (81,6)
Strah od igala	2 (0,5)
Seksualna inhibicija ili stigma promiskuiteta	12 (3,0)
Interesi farmaceutskih kompanija	28 (7,1)
Vakcine smatram štetnim u svakom smislu	3 (0,7)
Drugo (saglasnost roditelja, strah od bolesti)	4 (1,0)

\* Bio je moguć izbor više ponuđenih odgovora

i na Islandu (90,9%). U studiji preseka rađenoj 2020. godine u Saudijskoj Arabiji među studentima medicinskih i nemedicinskih koledža, utvrđeno je da bi više od polovine studenata medicinskih nauka (60,5%) pristalo na imunizaciju HPV vakcinom, a znatno manje studenata drugih fakulteta. S obzirom da naša studija nije obuhvatila studente drugih fakulteta nemedicinskih fakulteta, bilo bi značajno u perspektivi uraditi i ovo istraživanje.

Podaci Svetske zdravstvene organizacije (SZO) ukazuju da mladi uzrasta do 24 godine života čine oko 60% ukupno obolelih od polno prenosivih infekcija i da su u 50% slučajeva nosioci HIV infekcije (4). U okviru našeg istraživanja prosečna starost stupanja u seksualne odnose kod studenata iznosi  $18,03 \pm 1,41$  godina, dok među onima koji imaju seksualne odnose čak 11,5% njih uopšte ne koristi kontracepciju. U studiji preseka koja je rađena

**Table 2.** Knowledge and attitudes of students towards HPV infection and vaccine

Characteristics	Number (%)
<b>Satisfactory knowledge about HPV infection (N=449)</b>	386 (86.0)
<b>Sources of information about the HPV vaccine (N=449)</b>	
Teachers	358 (79.7)
Parents	14 (3.1)
Friends	14 (3.1)
Electronic media (social networks, websites)	48 (10.7)
Media campaigns (TV, press)	12 (2.7)
I did not know it exists	3 (0.7)
<b>I use medical platforms for obtaining information about the HPV vaccine (N=449)</b>	40 (9.0)
<b>I heard about HPV infection for the first time (N=449)</b>	
In elementary school	55 (12.2)
In secondary school	361 (80.4)
During studies	27 (6.0)
I was not informed	6 (1.3)
<b>I heard about the HPV vaccine for the first time (N=448)</b>	
In elementary school	18 (4.0)
In secondary school	294 (65.6)
During studies	115 (25.7)
I was not informed	21 (4.7)
<b>Young people in Serbia are sufficiently informed about HPV infection (N=449)</b>	15 (3.4)
<b>Young people in Serbia are sufficiently informed about the HPV vaccine (N=449)</b>	2 (0.4)
<b>The following can contribute to better awareness of HPV vaccine (N=449)</b>	
Peer education in schools	240 (53.8)
Media campaigns	76 (17.0)
Preventive examinations	82 (18.4)
Participation of parents in the education	42 (9.4)
Other	6 (1.3)
<b>Organized screening for cervical cancer is conducted in our country (N=449)</b>	398 (93.9)
<b>I would vaccinate my child (N=441)</b>	45 (10.2)
<b>Arguments against the vaccination with the HPV vaccine (N=449)*</b>	
High price	56 (14.4)
Insufficient information about the safety and effectiveness of the vaccine	323 (81.6)
Fear of needles	2 (0.5)
Sexual inhibition of the stigma of promiscuity	12 (3.0)
Interests of pharmaceutical companies	28 (7.1)
I think that vaccines are harmful in any sense	3 (0.7)
Other (parents' consent, fear of disease)	4 (1.0)

\* multiple-choice answers were offered

before and after the education on HPV infection and the use of the HPV vaccine (7). The results showed an unsatisfactory level of knowledge both before and after the test, especially in the field of HPV infection prevention (7). Looking at the results of numerous European and world studies in the population of students of nursing, medicine and other faculties, as well as among employed health workers, a deficit of knowledge about the HPV vaccine, effects of its application was observed, as

well as the insufficiently applied existing knowledge about the prevention of HPV infection in practice (8-13). One of such studies is a systematic review of the literature for the period from 2006 to 2017, where the results about factors that are associated with the knowledge on HPV and acceptance of the vaccine among adolescents and their parents in 16 European countries are summarized (14). The highest level of knowledge about HPV infection and the vaccine was shown by adolescents in

**Tabela 3.** Distribucija studenata u odnosu na ponašanje

Karakteristike	Broj (%) N=449
Pušenje cigareta (svakodnevno)	114 (25,6)
Konsumiranje alkohola (povremeno ili svakodnevno)	235 (48,2)
Korišćenje psihoaktivnih supstanci (povremeno ili svakodnevno)	5 (1,1)
Seksualni odnos	343 (78,3)
Uzrast pri stupanju u prvi seksualni odnos (godine) ( $\bar{x} \pm SD$ )	18,03 $\pm$ 1,41
Prosečan broj partnera ( $\bar{x} \pm SD$ )	2,21 $\pm$ 2,14
Redovan ginekološki pregled studentkinja (N=343)	322 (75,8)
Korišćenje kontracepcije (studentkinje) (N=343)	292 (85,1)
Vrsta kontraceptiva (studentkinje koje su imale seksualni odnos) (N=292)	
Spirala	5 (1,7)
Prezervativ	268 (91,8)
Metod prekinutog snošaja	16 (5,5)
Kontraceptivne pilule	3 (1,0)
Podvrgnute Papanikolau skrining testu (studentkinje) (N=343)	130 (30,6)

$\bar{x}$  - aritmetička sredina; SD - standardna devijacija

na teritoriji opštine Indija i kojom je obuhvaćeno 490 adolescenata uzrasta 15-19 godina, uzrast pri stupanju u prvi seksualni odnos za adolescente je bio 16,33 godine dok je polno prenosivu infekciju imalo oko 2% devojčica i oko 5% mladića (15). U poređenju sa populacijom adolescenata u Brazilu na osnovu Nacionalne ankete o zdravlju iz 2009. godine, utvrđeno je da adolescenti rano stupaju u seksualne odnose. Čak trećina mlađih uzrasta 14 godina imala je prvi seksualni odnos u 12. godini života ili ranije što se povezuje sa nezaštićenim odnosima i

većim brojem partnera tokom života (16).

Uvođenje novih vakcina na tržište i u nacionalne programe imunizacije predstavlja složen i delikatan postupak. Rezultati dosadašnjih istraživanja ukazuju na to da je zaštita koju pruža HPV vakcina dugotrajna i u toku su studije praćenja kako bi se ustanovilo koliko dugo traje imunitet (17-19). Postmarketinškim praćenjem neželjenih događaja utvrđeno je da je vakcina protiv HPV-a visoko bezbedna. Od 2006. godine, od kada se prvi put primenjuje pa do danas, nije registro-

**Tabela 4.** Životne navike studenata u odnosu na stav prema HPV vakcini

Karakteristike	Za primenu HPV vakcine (N=45) Broj (%)	Protiv primene HPV vakcine (N=396) Broj (%)	p vrednost*
Pušenje cigareta (svakodnevno)	10 (22,2)	104 (26,5)	0,539
Konsumiranje alkohola (povremeno ili svakodnevno)	22 (48,9)	207 (52,5)	0,642
Korišćenje psihoaktivnih supstanci (povremeno ili svakodnevno)	1 (2,2)	6 (1,5)	0,073
Seksualni odnos	34 (75,6)	306 (77,2)	0,951
Korišćenje kondoma pri skoro svakom seksualnom odnosu***	23 (67,6)	242 (76,3)	0,108
Zadovoljavajuće znanje o HPV infekciji	42 (93,3)	338 (85,4)	0,142**
Redovni ginekološki pregledi (studentkinje)***	5 (14,7)	300 (98,0)	< 0,001

\*  $\chi^2$  test; \*\*Fisher-ov test; \*\*\*odnosi se samo na one koje su imali seksualni odnos.

**Table 3.** Distribution of students in relation to behavior

Characteristics	Number (%) N=449
<b>Smoking (daily)</b>	114 (25.6)
<b>Alcohol consumption (occasionally or every day)</b>	235 (48.2)
<b>Use of psychoactive substances (occasionally or every day)</b>	5 (1.1)
<b>Sexual intercourse</b>	343 (78.3)
<b>Age at the time of the first sexual intercourse (years) (<math>\bar{x} \pm SD</math>)</b>	$18.03 \pm 1.41$
<b>Average number of partners (<math>\bar{x} \pm SD</math>)</b>	$2.21 \pm 2.14$
<b>Regular gynecological examination of students (N=343)</b>	322 (75.8)
<b>Use of contraception (female students) (N=343)</b>	292 (85.1)
<b>Type of contraceptives (female students that had sexual relations) (N=292)</b>	
Spiral	5 (1.7)
Preservative	268 (91.8)
Method of coitus interruptus	16 (5.5)
Contraceptive pills	3 (1.0)
<b>Underwent Papanicolaou screening test (female students) (N=343)</b>	130 (30.6)

$\bar{x}$  - arithmetic mean; SD – standard deviation

Spain (93%), Belgium (67%) and Italy (61%), while the greatest interest in the application of vaccine was observed among the adolescents in Sweden (90.5%) and Iceland (90.9%). In a cross-sectional study that was conducted in Saudi Arabia in 2020 among medical and non-medical college students, it was found that more than half of medical students (60.5%) would agree to immunization with the HPV vaccine, and significantly fewer students of other faculties. Given that our study did not include students from other faculties, non-

medical faculties, it would be significant to do this research in the future as well.

Data of the World Health Organization (WHO) indicate that young people under the age of 24 make up about 60% of all cases of sexually transmitted infections and that in 50% of cases they are carriers of HIV infection (4). In our study, the average age of entering into sexual relations among students is  $18.03 \pm 1.41$  years, while among those who have sexual relations, even 11.5% do not use contraception at all. In a cross-sectional study that

**Table 4.** Life habits of students in relation to the attitude towards the HPV vaccine

Characteristics	For the administration of HPV vaccine (N=45) Number (%)	Against the administration of HPV vaccine (N=396) Number (%)	p value*
<b>Smoking (daily)</b>	10 (22.2)	104 (26.5)	0.539
<b>Alcohol consumption (occasionally or every day)</b>	22 (48.9)	207 (52.5)	0.642
<b>Use of psychoactive substances (occasionally or every day)</b>	1 (2.2)	6 (1.5)	0.073
<b>Sexual intercourse</b>	34 (75.6)	306 (77.2)	0.951
<b>Use of condoms almost during each sexual intercourse ***</b>	23 (67.6)	242 (76.3)	0.108
<b>Satisfactory knowledge about HPV infection</b>	42 (93.3)	338 (85.4)	0.142**
<b>Regular gynecological examinations (female students) ***</b>	5 (14.7)	300 (98.0)	< 0.001

\*  $\chi^2$  test; \*\*Fisher's test; \*\*\*only those who had sexual intercourse.

van nijedan slučaj teže neželjene reakcije u vezi sa prethodnom imunizacijom HPV vakcinom (20-22). U zemljama sa visokim obuhvatom HPV vakcinom, kao što je slučaj u Australiji, smanjena je učestalost patoloških promena na grliću materice a isto se očekuje kada je u pitanju i pojava karzinoma (23,24). SZO u svom izveštaju za 2022. godinu navodi da je u Evropskom regionu 38 od 53 zemlje, uključujući i Srbiju, uvelo HPV vakcinu do kraja 2021. godine. Sa ovim rezultatom, preko polovine zemalja sa srednjim prihodima u regionu sada ima pristup ovoj vakcini (25). U Srbiji se sprovođi aktivna preporučena imunizacija za oboljenja izazvana HPV-om i to za lica određenog uzrasta što je bliže određeno Pravilnikom o programu obavezne i preporučene imunizacije stanovništva protiv određenih zaraznih bolesti (26,27). Prema Stručnom metodološkom uputstvu Instituta za javno zdravlje Srbije, ova imunizacija se preporučuje kod dece starije od devet godina, pre prvih seksualnih odnosa, a prvenstveno deci šestih razreda osnovne škole u dve ili tri doze što zavisi od uzrasta i vrste vakcine (28).

Naša studija preseka ima nekoliko ograničenja koje se odnose na samu vrstu studije, subjektivnu samoprocenu znanja studenata koja se različito može interpretirati i uticati na kvalitet odgovora, kao i mogućnost dobijanja socijalno poželjnih odgovora kada je reč o životnim stilovima i navikama. Prednosti ove studije predstavljene su u reprezentativnosti i veličini uzorka.

## Zaključak

Edukacija mladih o putevima prenošenja HPV infekcije i mogućnostima prevencije (sa akcentom na HPV vakcincu) je prioritet. Potreban je multidisciplinarni pristup i uključivanje relevantnih društvenih, zdravstvenih i obrazovnih institucija koje bi, svojim dobro isplaniranim i organizovanim akcijama, kontinuirano radile na unapređivanju reproduktivnog zdravlja. Samim tim bi se ukazao javnozdravstveni značaj ovog problema i proširio prostor za podizanje nivoa znanja o značaju imunizacije HPV vakcinom u bližoj budućnosti.

## Konflikt interesa

Autor je izjavio da nema konflikta interesa.

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was conducted in the territory of the municipality of Indjija and which included 490 adolescents aged 15-19, the age at the time of first sexual intercourse for adolescents was 16.33 years, while 2% of girls and about 5% of young men had sexually transmitted infections (15). In comparison with the adolescent population in Brazil based on the National Health Survey in 2009, it was found that adolescents entered sexual relations early. As many as a third of young people aged 14 years had their first sexual intercourse at the age of 12 or earlier, which is associated with unprotected relations and a greater number of partners during life (16).

Introducing new vaccines to the market and into national immunization programs is a complex and delicate process. The results of previous research indicate that the protection provided by the HPV vaccine is long-lasting and follow up studies are in progress in order to determine how long the immunity lasts (17-19). Post-marketing monitoring of side effects has shown that the HPV vaccine is highly safe. Since 2006, when it was first administered, no severe side effects related to previous immunization with the HPV vaccine have been registered (20-22). In countries with a high coverage of the HPV vaccine, as is the case in Australia, the frequency of pathological changes in the cervix has been reduced, and the same is expected when it comes to the occurrence of carcinoma (23,24). In its report for 2022, the WHO states that 38 of 53 countries in the European region, including Serbia, introduced the HPV vaccine by the end of 2021. With this result, over half of the middle-income countries in the region have access to this vaccine (25). In Serbia, active recommended immunization for diseases caused by HPV is being carried out for persons of certain age, which is more precisely determined by the Rulebook on the program of mandatory and recommended immunization of the population against certain infectious diseases (26,27). According to the professional, methodological guidelines of the Institute of Public Health of Serbia, this immunization is recommended for children over nine years old, before the first sexual intercourse, primarily for children in the sixth grade of elementary school, in two or three doses, depending on the age and type of vaccine (28).

Our cross-sectional study has a few limitations related to the type of study itself, subjective self-assessment of students' knowledge that can be

interpreted differently and affect the quality of answers, as well as the possibility of obtaining socially desirable answers when it comes to lifestyles and habits. The strengths of this study are presented in the representativeness and size of the sample.

## Conclusion

Education of young people about the ways of transmission of HPV infection and the possibilities of prevention (with an emphasis on the HPV vaccine) is a priority. A multidisciplinary approach and the involvement of relevant social, health and educational institutions are needed, which, with their well-planned and organized actions, would continuously work to improve reproductive health. Thus, the importance of this public health problem would be indicated and the space for raising the level of knowledge about the importance of HPV immunization with the HPV vaccine would be expanded in the near future.

## Competing interests

The author declares no competing interests.

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## HRONIČNA BOLEST BUBREGA I SMRTNI ISHODI KOD PACIJENATA HOSPITALIZOVANIH ZBOG TIPO 2 DIJABETESA U BEOGRADU TOKOM 2019. GODINE

Nemanja Stefanović<sup>1\*</sup>

<sup>1</sup> Gradski zavod za javno zdravlje Beograd, Beograd, Republika Srbija

\* Korespondencija: Nemanja Stefanović, Gradski zavod za javno zdravlje Beograd, Bulevar despota Stefana 54a, 11000 Beograd, Republika Srbija; e-mail: nemanja.stefanovic@zdravlje.org.rs

### SAŽETAK

**Uvod/Cilj:** Hronična bolest bubrega (HBB) predstavlja važnu komplikaciju tipa 2 dijabetesa (T2D), koja može biti činilac pogoršanja zdravstvenog stanja pacijenata sa T2D. Cilj ove studije je bio da se ispita da li postoji značajna razlika u umiranju, kao i u odnosu na starost i pol, između pacijenata sa i bez hronične bolesti bubrega (šifre: N18.1 -N18.9) hospitalizovanih zbog T2D.

**Metode:** Iz baze individualnih izveštaja o hospitalizaciji Gradskog zavoda za javno zdravlje Beograd za 2019. godinu, izdvojeno je 1983 epizode bolničkog lečenja sa T2D kao osnovnim uzrokom hospitalizacije. Priprema i statistička obrada baze podataka izvršena je uz pomoć softverskog paketa programa *IBM SPSS Statistics for Windows, version 26* (*IBM Corp., Armonk, N.Y., USA*).

**Rezultati:** Smrtni ishodi su statistički značajno češći ( $p = 0,038$ ) u grupi sa bar jednom od pratećih dijagnoza N18.1-N18.9 u odnosu na grupu bez ovih dijagnoza (4,8% vs. 2,1%). Pacijenti iz epizoda bolničkog lečenja u grupi sa bar jednom od pratećih dijagnoza N18.1-N18.9 su u proseku 7,42 godine stariji u odnosu na grupu bez ovih dijagnoza ( $p < 0,001$ ). Zastupljenost epizoda bolničkog lečenja sa bar jednom od pratećih dijagnoza N18.1-N18.9 je statistički značajno češća ( $p = 0,006$ ) među muškim nego ženskim polom (5,5% vs. 4,0%).

**Zaključak:** Neophodna su dalja istraživanja u ovoj oblasti koja mogu doprineti umanjenju posledica koje ova stanja prouzrokuju – kako onih koji se neposredno odražavaju po zdravlje pacijenata, tako i ukupnog opterećenja zdravstvenog sistema, koje se ogleda u utvrđenim većim troškovima i dužem trajanju bolničkog lečenja pacijenata sa T2D, ukoliko ovi pacijenti boluju i od HBB.

**Ključne reči:** hronična bolest bubrega, tip 2 dijabetesa, hospitalizacija, smrtni ishodi

### Uvod

Hronična bolest bubrega (HBB) predstavlja stanje koje se definiše kao poremećaj strukture ili funkcije bubrega koji traje preko tri meseca i daje posledice po zdravlje (1,2). Kriterijumi za postavljanje dijagnoze HBB, izneti u *Kidney Disease: Improving Global Outcome* - KDIGO vodiču za dijagnostiku i klasifikaciju HBB, zahtevaju da jedna ili više od sledećih pojava bude prisutna kod pacijenta duže od tri meseca: markeri poremećaja bubrega (npr. albuminurija, poremećaji u sedimentu urina i sl.) i/ili smanjenje jačine glomerulske filtracije (JGF) ispod 60 ml/min/1,73m<sup>2</sup> (1,2). Povišen rizik za razvoj HBB zapaža se kod osoba sa šećernom bolešću, hipertenzijom, bolestima srca i krvnih sudova, multisistemskim bolestima (npr.

sistemski eritemski lupus), naslednim poremećajima bubrega, zabeleženim javljanjem bubrežnih bolesti u porodici, kod osoba koje koriste nefrotoksične lekove, kao i u populaciji starijih (1-3).

*Diabetes mellitus* (šećerna bolest), a posebno tip 2 dijabetesa - T2D (insulin nezavisan oblik šećerne bolesti), predstavljaju neke od najznačajnijih faktora rizika za razvoj HBB (4-6). Procene govore da je HBB zastupljena kod oko 50% pacijenata sa T2D u svetu, što je od posebne važnosti uzimajući u obzir podatak da je prema procenama na nivou sveta u 2017. godini, 462 miliona ljudi živilo sa T2D (6059/100.000) (7,8). Pokazano je da su različite komplikacije koje mogu nastupiti u sklopu T2D, povezane sa značajno većom učestalošću

## CHRONIC KIDNEY DISEASE AND FATAL OUTCOMES IN PATIENTS HOSPITALIZED DUE TO TYPE 2 DIABETES IN BELGRADE DURING 2019

Nemanja Stefanovic<sup>1\*</sup>

<sup>1</sup> City Institute for Public Health Belgrade, Belgrade, Republic of Serbia

\* Correspondence: Nemanja Stefanovic, City Institute for Public Health Belgrade, Despota Stefana Boulevard 54a, 11000 Belgrade, Republic of Serbia; e-mail: nemanja.stefanovic@zdravlje.org.rs

### SUMMARY

**Introduction/Aim:** Chronic kidney disease (CKD) is an important complication of type 2 diabetes (T2D), which can lead to further deterioration of health in T2D patients. The aim of this study was to examine whether there is a significant difference in dying, as well as in relation to age and gender, between patients with and without chronic kidney disease (codes: N18.1 -N18.9) hospitalized because of T2D.

**Methods:** The total of 1983 hospital admission episodes that occurred in 2019 in Belgrade, and met the designated selection criteria, were selected from the database maintained by the Institute of Public Health of Belgrade. The preparation and statistical analysis of database was done with the help of software package IBM SPSS Statistics for Windows version 26 (IBM Corp., Armonk, N.Y., USA).

**Results:** Fatal outcomes were significantly more frequent ( $p = 0.038$ ) in the group with at least one of diagnoses N18.1-N18.9, compared to the comparison group (4.8% vs. 2.1%). The patients in group with at least one of diagnoses N18.1-N18.9 were on average 7.42 years older ( $p < 0.001$ ), compared to the comparison group. The occurrence of hospital admission episodes with at least one of diagnoses N18.1-N18.9, was significantly more frequent ( $p = 0.006$ ) in males compared to females (5.5% vs. 4.0%).

**Conclusion:** Further research in this area is necessary, which can contribute to reducing the consequences caused by these conditions - both those that directly affect the health of patients, and the overall burden on the health system, which is reflected in the determined higher costs and longer duration of hospital treatment of patients with T2D if these patients also suffer from CKD.

**Keywords:** type 2 diabetes, chronic kidney disease, hospitalization, mortality

### Introduction

Chronic kidney disease is defined as abnormalities of kidney structure or function, present for more than three months, with implications for health (1,2). Criteria for chronic kidney disease presented in "Kidney Disease: Improving Global Outcome (KDIGO)" guidelines for the evaluation and classification of chronic kidney disease include either of the following markers present in patients for more than three months: recorded markers of kidney damage (e.g. albuminuria, urine sediment abnormalities etc.) and/or decreased glomerular filtration rate (GFR) below 60 ml/min/1.73 m<sup>2</sup> (1, 2). The increased risk of chronic kidney disease is noted in persons with diabetes mellitus, hypertension, cardiovascular diseases, multisystem diseases (e.g. systemic lupus erythematosus), inherited kidney

disorders, a family history of kidney diseases, in persons who use nephrotoxic medications, as well as in the elderly population (1-3).

Diabetes mellitus and especially type 2 diabetes (non-insulin-dependent form of diabetes) are some of the most important risk factors for chronic kidney disease (4-6). It is estimated that chronic kidney disease is present in about 50% of patients with type 2 diabetes in the world, which is of great importance considering the fact that according to the estimates in 2017, there were 462 million people who lived with type 2 diabetes worldwide (6059/100,000) (7,8). It has been shown that different complications that may appear in type 2 diabetes mellitus are associated with significantly greater frequency of hospitalizations

hospitalizacija i smrtnih ishoda ovih pacijenata (9), dok je umiranje tokom bolničkog lečenja kod pacijenata sa T2D veće u poređenju sa hospitalizovanim pacijentima bez T2D (10). Pogoršanje HBB kod bolnički lečenih pacijenata sa T2D može povećati smrtnost u toku bolničkog lečenja (11). Slično, opažena je i povećana smrtnost kod bolnički lečenih pacijenata sa T2D kod kojih se u toku bolničkog lečenja javе bubrežne komplikacije (12). Uočena je i češća hospitalizacija pacijenata sa HBB u odnosu na opštu populaciju (13). Pacijenati sa HBB su stariji, sa većim sistolnim krvnim pritiskom, pozitivnom porodičnom istorijom za dijabetes, kao i sa lošijim pokazateljima bubrežne funkcije (veća proteinurija i manja vrednost jačine glomerulske filtracije), češćom hospitalizacijom zbog svih uzroka, kao i zbog kardiovaskularnih poremećaja (13). Takođe, druge studije pokazuju da je pojava HBB kod pacijenata sa T2D povezana sa većim rizikom od smrtnog ishoda, kao i da je HBB jedna od najčešćih komplikacija kod ovih pacijenata koja nije bila prisutna na početku posmatranja (14).

Postojanje HBB kod pacijenata sa T2D povezano je i sa povećanom smrtnošću od kardiovaskularnih bolesti u poređenju sa pacijentima koji boluju od T2D, ali bez HBB (14,15). U studiji Qiroga i sar. češći smrtni ishodi usled kardiovaskularnih bolesti su prikazani kod mušaraca sa HBB, dok je dosadašnja istorija dijabetesa nezavisna od fatalnih ishoda usled kardiovaskularnih bolesti kod pacijenata sa HBB (16). Rezultati druge studije govore o većoj prisutnosti hronične bubrežne bolesti kod muškaraca sa T2D, kao i kod starijih (17). S druge strane, rezultati jedne meta-analize ukazuju da ne postoji razlika između muškaraca i žena u pogledu incidencije HBB koja je povezana sa dijabetes melitusom, ali da je rizik od kasnog stadijuma bolesti bubrega nešto veći kod žena sa dijabetesom u poređenju sa

muškarcima sa dijabetesom (18). Troškovi i trajanje bolničkog lečenja pacijenata sa T2D je veće ako pacijenti boluju i od HBB u poređenju sa pacijentima koji imaju T2D, ali bez HBB (19,20).

Cilj ove studije je bio da se ispita da li postoje značajna razlike u umiranju, kao i u odnosu na starost i pol, između pacijenata sa i bez hronične bolesti bubrega (šifre: N18.1 -N18.9) hospitalizovanih zbog T2D.

## Metode

Izvor podataka za istraživanje predstavlja baza individualnih izveštaja o hospitalizaciji Gradskog zavoda za javno zdravlje Beograd. Individualni izveštaj o hospitalizaciji predstavlja statistički izveštaj koji se popunjava i vodi za svakog pacijenta koji se prima na bolničko lečenje, tj. za pacijente koji su zbog epizode bolničkog lečenja ostali u bolnici duže od 24 časa, dok se takođe popunjava i za pacijente koji se zbrinjavaju u okviru dnevne bolnice (u trajanju kraćem od 24 časa) (21-23). Epizodu bolničkog lečenja čini period od dana prijema u bolnicu do dana otpusta (23).

Tromesne i četvoromesne šifre dijagnoza objavljene u Međunarodnoj statističkoj klasifikaciji bolesti i srodnih zdravstvenih problema - deseta revizija (MKB-10) (24), se prema Uputstvu za popunjavanje izveštaja o hospitalizaciji (23), unose u obrazac individualnog izveštaja o hospitalizaciji. Šifre, koje se prema MKB-10 klasifikaciji odnose na dijagnoze različitih oblika šećerne bolesti i HBB, predstavljeni su u tabeli 1 (pod a, b i c). Usled etioloških specifičnosti, iz ovog posmatranja isključena je dijagnoza „O24 - šećerna bolest u trudnoći“.

Prema KDIGO vodiču za dijagnostiku i klasifikaciju HBB, preporučuje se klasifikacija HBB prema uzroku, jačini glomerulske filtracije i stepenu albu-minurije, što kombinovanjem informacija, omo-

**Tabela 1.** Klasifikacija dijabetesa melitusa i hronične bolesti bubrega

<b>a. Tromesne MKB-10 dijagnoze - šećerna bolest</b>		
<b>Tromesna šifra prema MKB-10</b>	<b>MKB-10 dijagnoza, srpski</b>	<b>MKB-10 dijagnoza, latinski</b>
<b>E10</b>	Šećerna bolest, insulinozavisan oblik	Diabetes mellitus ab insulino dependens
<b>E11</b>	Šećerna bolest, insulinonezavisan oblik	Diabetes mellitus ad insulino independens
<b>E12</b>	Šećerna bolest kod pothranjenosti	Diabetes mellitus malnutritionalis
<b>E13</b>	Druga označena šećerna bolest	Diabetes mellitus alias, specificatus
<b>E14</b>	Šećerna bolest, neoznačena	Diabetes mellitus, non specificatus

and in-hospital deaths of these patients, while dying during hospital treatment in patients with type 2 diabetes mellitus are higher in comparison to hospitalized patients without type 2 diabetes mellitus (10). Worsening of chronic kidney disease in hospitalized patients with type 2 diabetes mellitus may increase dying during the course of hospital treatment (11). Similarly, increased mortality has been noticed in hospitalized patients with type 2 diabetes mellitus, in whom kidney complications appear during hospital treatment (12). One study has reported more frequent hospitalizations of patients with chronic kidney disease in comparison to general population (13). Patients with chronic kidney disease are older, with higher systolic blood pressure, a history of diabetes, as well as with worse indicators of kidney function (higher proteinuria, and lower level of glomerular filtration rate), with greater frequency of hospitalizations due to all causes, as well as hospitalizations due to cardiovascular disorders (13). Also, other studies show which included patients that were selected from medical records, it has been shown that the occurrence of chronic kidney disease in patients with type 2 diabetes mellitus is associated with a higher risk of fatal outcome, as well as that chronic kidney disease is at the same time one of the most frequent complications in these patients, which was not present at the beginning of observation (14).

The presence of chronic kidney disease in patients with type 2 diabetes mellitus is associated with the increased mortality due to cardiovascular diseases in comparison to patients with type 2 diabetes mellitus, and without chronic kidney disease (14,15). In the study by Qiroga et al. more frequent fatal outcomes due to cardiovascular diseases have been shown in male patients with

chronic kidney disease, while the previous history of diabetes was independent of fatal outcomes due to cardiovascular diseases in patients with chronic kidney disease (16). The results of one study report greater presence of chronic kidney disease in male patients with type 2 diabetes mellitus, as well as in the elderly (17). On the other hand, the results of one meta-analysis indicate that there is no difference between men and women regarding the incidence of chronic kidney disease that is associated with diabetes mellitus, but that the risk of late stage kidney disease is a bit higher in women with diabetes in comparison to men with diabetes (18). The costs and duration of hospital treatment of patients with type 2 diabetes mellitus are greater if patients have chronic kidney disease in comparison to patients who have type 2 diabetes, without chronic kidney disease (19,20).

The aim of this study was to examine whether there is a significant difference in dying, as well as in relation to age and gender, between patients with and without chronic kidney disease (codes: N18.1 -N18.9) hospitalized because of type 2 diabetes mellitus.

## Methods

The source of data used for the research is the database of individual reports on hospitalization of the City Institute of Public Health in Belgrade. An individual report on hospitalization is a statistical report which is completed and kept for each patient, who is admitted to hospital, that is, for patients who stay in the hospital longer than 24 hours due to an episode of hospital treatment, as well as for patients who are treated in a day hospital (lasting less than 24 hours) (21-23). An episode of hospital treatment is the period lasting from the day of admission till the day of discharge (23).

**Table 1.** Classification of diabetes mellitus and chronic kidney disease

<b>a. Three-digit ICD-10 codes – diabetes mellitus</b>		
<b>Three-digit code according to ICD-10</b>	<b>ICD-10 diagnosis, English</b>	<b>ICD-10 diagnosis, Latin</b>
<b>E10</b>	Insulin-dependent diabetes mellitus	Diabetes mellitus ab insulino dependens
<b>E11</b>	Non-insulin-dependent diabetes mellitus	Diabetes mellitus ad insulino independens
<b>E12</b>	Malnutrition-related diabetes mellitus	Diabetes mellitus malnutritionalis
<b>E13</b>	Other specified diabetes mellitus	Diabetes mellitus alias, specificatus
<b>E14</b>	Unspecified diabetes mellitus	Diabetes mellitus, non specificatus

**Tabela 1.** Klasifikacija dijabetesa melitusa i hronične bolesti bubrega (nastavak)

<b>b. Opis dodatnih brojeva u okviru četvoromesnih dijagnoza za šećernu bolest</b>		
<b>Broj</b>	<b>Značenje u MKB-10 dijagnozi, srpski</b>	<b>Značenje u MKB-10 dijagnozi, latinski</b>
.0	Sa diabetičnom komom bez ketoacidoze	Cum comato diabetico et sine ketoacidosis
.1	Sa ketoacidozom	Cum ketoacidosis
.2	Sa bubrežnim komplikacijama	Cum complicationibus renalibus
.3	Sa očnim komplikacijama	Cum complicationibus ophthalmicis
.4	Sa neurološkim komplikacijama	Cum complicationibus neurologicis
.5	Sa komplikacijama periferne cirkulacije	Cum complicationibus systematis circularis peripherici
.6	Sa drugim označenim komplikacijama	Cum complicationibus aliis specificatis
.7	Sa višestrukim komplikacijama	Cum complicationibus multiplicibus
.8	Sa neoznačenim komplikacijama	Cum complicationibus, non specificatis
.9	Bez komplikacija	Sine complicationibus

<b>c. Tromesne i četvoromesne MKB-10 dijagnoze koje se odnose na hroničnu bolest bubrega - značenja</b>		
<b>Šifra prema MKB-10</b>	<b>MKB-10 dijagnoza</b>	<b>Opis oštećenja bubrega i vrednosti jačine glomerulske filtracije (JGF)</b>
<b>N18</b>	Hronična bolest bubrega	Hronična bolest bubrega
<b>N18.1</b>	Hronična bolest bubrega 1. stepena	Normalna ili povećana JGF (>90 mL/min)
<b>N18.2</b>	Hronična bolest bubrega 2. stepena	Blago smanjenje JGF (60-89 mL/min)
<b>N18.3</b>	Hronična bolest bubrega 3. stepena	Umereno smanjenje JGF (30-59 mL/min)
<b>N18.4</b>	Hronična bolest bubrega 4. stepena	Teško smanjenje JGF (15-29 mL/min)
<b>N18.5</b>	Hronična bolest bubrega 5. stepena	Krajnji stadijum bolesti bubrega
<b>N18.9</b>	Hronična bolest bubrega, neoznačena	Hronična bolest bubrega, neoznačena

<b>d. Kategorije jačine glomerulske filtracije (JGF) u hroničnoj bolesti bubrega prema KDIGO vodiču</b>		
<b>Kategorija</b>	<b>JGF, mL/min/1.73m<sup>2</sup></b>	<b>Opis</b>
<b>G1</b>	≥ 90	Oštećenje bubrega sa normalnom ili povećanom JGF
<b>G2</b>	60-89	Oštećenje bubrega sa blagim smanjenjem JGF
<b>G3a</b>	45-59	Oštećenje bubrega sa umerenim smanjenjem JGF
<b>G3b</b>	30-44	
<b>G4</b>	15-29	Teško smanjenje JGF
<b>G5</b>	< 15	Terminalna insuficijencija bubrega

gućava i ocenu prognoze bolesti (1). KDIGO vodič prepoznaje opadajući raspon od šest kategorija jačine glomerulske filtracije u hroničnoj bolesti bubrega – G1, G2, G3a, G3b, G4, G5, gde G1 označava oštećenje bubrega sa normalnom ili povećanom jačinom glomerulske filtracije, dok G5 označava terminalnu insuficijenciju bubrega (Tabela 1 pod d)

(1,2). Sa druge strane, deseta revizija Međunarodne statističke klasifikacije bolesti i srodnih zdravstvenih problema (MKB-10) prepoznaje pet stadijuma HBB, koji prema referentnim vrednostima jačine glomerulske filtracije odgovaraju kategorijama iz KDIGO vodiča, s tim što treći stepen HBB prema MKB-10 obuhvata celokupan raspon vrednosti

**Table 1.** Classification of diabetes mellitus and chronic kidney disease

<b>b. Description of additional numbers in four-digit diagnostic codes for diabetes mellitus</b>		
<b>Number</b>	<b>Meaning in ICD-10 diagnosis, English</b>	<b>Meaning in ICD-10 diagnosis, Latin</b>
.0	With coma without ketoacidosis	Cum comato diabetico et sine ketoacidosi
.1	With ketoacidosis	Cum ketoacidosis
.2	With renal complications	Cum complicationibus renalibus
.3	With ophthalmic complications	Cum complicationibus ophthalmicis
.4	With neurological complications	Cum complicationibus neurologicis
.5	With peripheral circulatory complications	Cum complicationibus systematis circularis peripherici
.6	With other specified complications	Cum complicationibus aliis specificatis
.7	With multiple complications	Cum complicationibus multiplicibus
.8	With unspecified complications	Cum complicationibus, non specificatis
.9	Without complications	Sine complicationibus

<b>c. Three-digit and four-digit ICD-10 diagnoses relating to chronic kidney disease - meaning</b>		
<b>Code according to ICD-10</b>	<b>ICD-10 diagnosis</b>	<b>Description of kidney damage and values of glomerular filtration rate (GFR)</b>
N18	Chronic kidney disease	Chronic kidney disease
N18.1	Chronic kidney disease stage 1	Normal or high GFR (> 90 mL/min)
N18.2	Chronic kidney disease stage 2	Mildly decreased GFR (60-89 mL/min)
N18.3	Chronic kidney disease stage 3	Moderately decreased GFR (30-59 mL/min)
N18.4	Chronic kidney disease stage 4	Severely decreased GFR (15-29 mL/min)
N18.5	Chronic kidney disease stage 3	Kidney failure
N18.9	Chronic kidney disease, unspecified	Chronic kidney disease, unspecified

<b>d. Categories of glomerular filtration rate(GFR) in chronic kidney disease according to KDIGO Guidelines</b>		
<b>Category</b>	<b>GFR, ml/min/1.73m<sup>2</sup></b>	<b>Description</b>
G1	≥90	Chronic kidney disease with normal or high GFR
G2	60-89	Chronic kidney disease with mildly decreased GFR
G3a	45-59	Chronic kidney disease with moderately decreased GFR
G3b	30-44	
G4	15-29	Severely decreased GFR
G5	< 15	Kidney failure

Three-digit and four-digit diagnostic codes published in the International Statistical Classification of Diseases and Related Health Problems – 10<sup>th</sup> Revision (ICD-10) (24) are entered into the form of individual report on hospitalization according to the Guidelines for completing the report on hospitalization (23). Codes which,

according to the ICD-10, refer to different types of diabetes and chronic kidney disease are presented in Table 1 (a, b, c). Due to its etiological specificity, diagnosis O-24 – Diabetes in pregnancy has been excluded from this study.

According to the recommendations of KDIGO Guidelines for the evaluation and classification

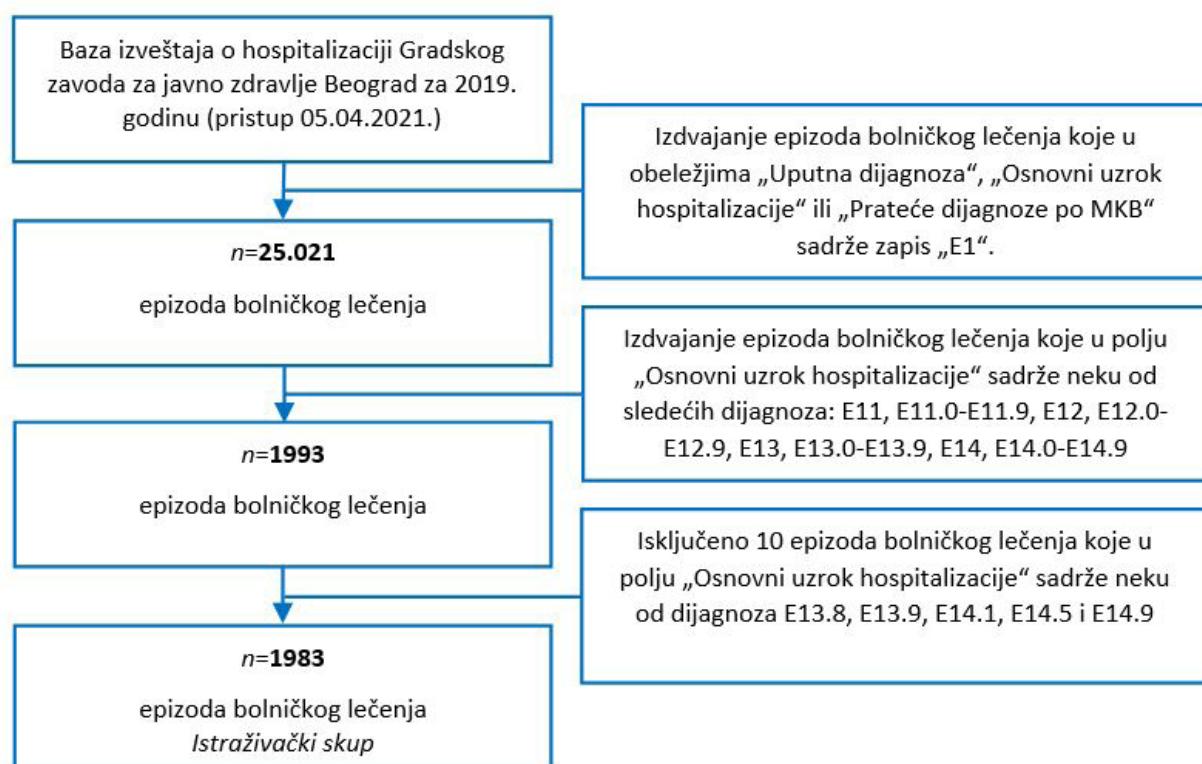
jačine glomerulske filtracije koji je u KDIGO vodiču predstavljen kao G3a i G3b (1,2,24). U ovom radu će za označavanje zdravstvenih stanja biti korišćena nomenklatura iz desete revizije Međunarodne statističke klasifikacije bolesti i srodnih zdravstvenih problema (MKB-10) (24).

Iz baze individualnih izveštaja o hospitalizaciji za teritoriju Beograda u 2019. godini, koju vodi Gradski zavod za javno zdravlje Beograd, pristupom na dan 05.04.2021. godine, izvršeno je izdvajanje epizoda bolničkog lečenja u kojima je u bar jednom od polja pod nazivima „Uputna dijagnoza“, „Osnovni uzrok hospitalizacije“ ili „Prateće dijagnoze po MKB“ zabeležen zapis „E1“, kako bi u pretrazi bile izdvojene šifre sledećih dijagnoza iz MKB-10 klasifikacije: E10, E10.0-E10.9, E11, E11.0-E11.9, E12, E12.0-E12.9, E13, E13.0-E13.9, E14, E14.0-E14.9, E15, E16, E16.0-E16.4, E16.8, E16.9 (ukupno su 64 dijagnoze ušle u pretragu) (Grafikon 1). Iz baze je ovim postupkom izdvojeno ukupno 25.021 epizoda bolničkog lečenja. Sledeći korak bio je izdvajanje epizoda bolničkog lečenja čiji je „Osnovni uzrok hospitalizacije“ pripadao nekoj od 44 dijagnoze koje se odnose na različite oblike šećerne bolesti, isključujući insulin-zavisni oblik (Grafikon 1), što je dalo ukupno 1993 epizoda bolničkog lečenja za dalju analizu. Dodatnih 10 epizoda bolničkog lečen-

ja (0,5%) za koje su kao osnovni uzrok hospitalizacije zabeležene dijagnoze E13.8, E13.9, E14.1, E14.5 i E14.9, isključeno je iz dalje obrade, jer stanja koja opisuju ne uključuju T2D prema MKB-10 klasifikaciji (24), i stoga je za istraživački skup preostalo ukupno 1983 epizode bolničkog lečenja.

U okviru 15 polja namenjenih unosu obeležja „Prateće dijagnoze po MKB“, maksimalan mogući broj unosa u istraživačkom uzorku ( $n=1983$ ), iznosi 29.745 (15 za svaku od 1983 epizode bolničkog lečenja). U 57 epizoda bolničkog lečenja u istraživačkom uzorku otkriveni su višestruki unosi istovetnih dijagnoza (navodimo primer slučaja jedne epizode bolničkog lečenja gde je dijagnoza E11.4 upisana u svako od mogućih 15 polja), što je smatrano tehničkim propustom, te je vršeno njihovo sažimanje u okviru baze istraživačkog uzorka, gde su u svakoj od opisanih 57 epizoda bolničkog lečenja odstranjeni svi višestruki unosi dijagnoza u okviru obeležja „Prateće dijagnoze po MKB“. Na ovaj način, ukupno je isključeno 504 ponavaljajuća unosa.

Za potrebe deskriptivnog predstavljanja podataka korišćeni su distribucija frekvencija (apsolutni i relativni brojevi), procenti, srednja vrednost, kvartili, standardna devijacija i medijana. Analiza postojanja statistički značajnih razlika numeričkih podataka, temeljila se na upotrebi neparametarskog



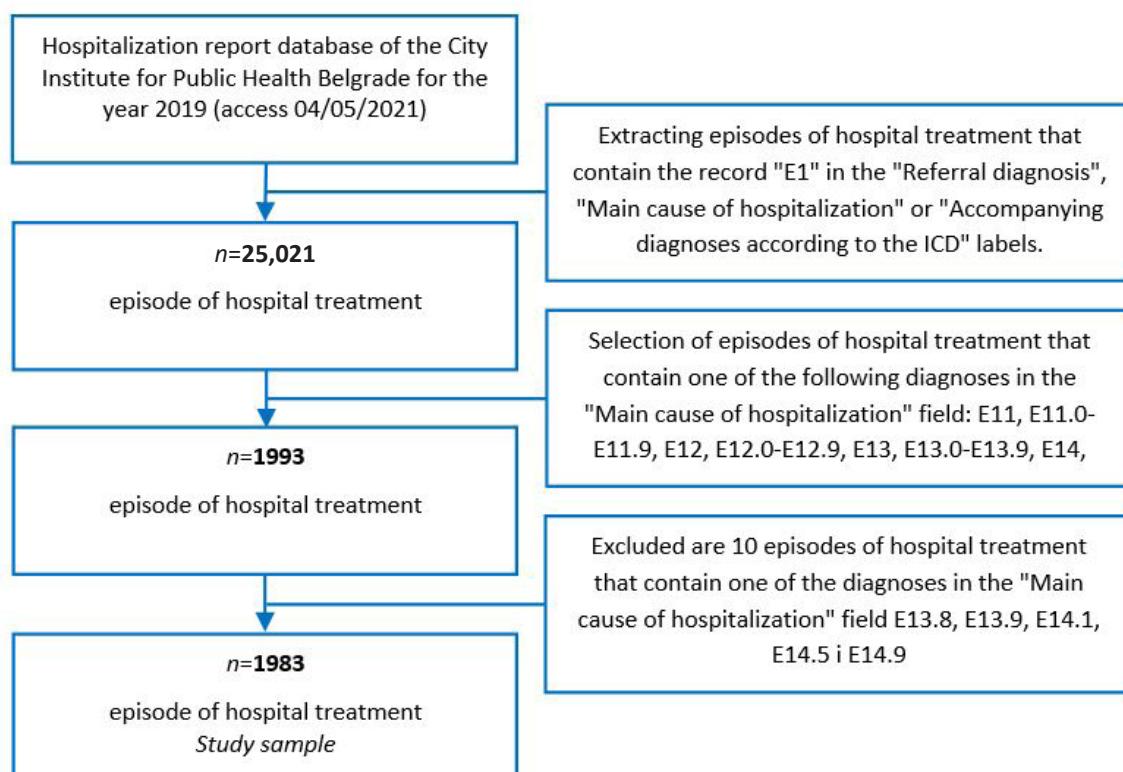
Grafikon 1. Formiranje istraživačkog skupa

of chronic kidney disease, chronic kidney disease is classified based on cause, GFR category, and albuminuria category, which by combining the information enables the assessment of disease prognosis (1). KDIGO Guidelines recognizes six GFR categories in chronic kidney disease – G1, G2, G3a, G3b, G4, G5, where G1 refers to kidney damage with normal or high glomerular filtration rate, whereas G5 refers to kidney failure (Table 1d) (1,2). On the other hand, the tenth revision of the International statistical classification of diseases and related health problems (ICD-10) recognizes five stages of chronic kidney disease, which according to reference values of GFR respond to the categories from KDIGO Guidelines, while the third stage of chronic kidney disease according to ICD-10 includes a whole range of values of GFR, which is presented as G3a and G3b in KDIGO Guidelines (1,2,24). The nomenclature from the tenth revision of the International Statistical Classification of Diseases and Related Health Problems will be used to identify health conditions in this study (24).

The database of individual reports on hospitalizations in Belgrade in 2019, which is maintained by the City Institute of Public Health in Belgrade, was accessed on 5 April, 2021 to select episodes of hospital treatment, where at least

one of five fields named “Referral diagnosis”, “The main reason of hospitalization” or “Concomitant diagnoses according to ICD” contained code “E1”, in order to single out codes of the following diagnoses during the search: E10, E10.0-E10.9, E11, E11.0-E11.9, E12, E12.0-E12.9, E13, E13.0-E13.9, E14, E14.0-E14.9, E15, E16, E16.0-E16.4, E16.8, E16.9 (the total of 64 diagnoses were included in the search) (Graph 1). The total of 25021 hospital admission episodes was selected from the database. The next step was the selection of hospital treatment episodes whose “Main cause of hospitalization” belonged to one of 44 diagnoses relating to different types of diabetes, excluding insulin-dependent type (Graph 1), which gave 1993 episodes of hospital treatments for further analysis. Additional 10 episodes of hospitalization (0.5%), whose main causes were diagnoses E13.8, E13.9, E14.1, E14.5 and E14.9, were excluded from further analysis because these conditions did not include type 2 diabetes mellitus according to ICD-10 classification (24), and therefore, the study sample included the total of 1983 episodes of hospital treatment.

The maximal possible number of entries in the study sample (n=1983) amounts to 29745 within 15 fields which were intended for entering



**Graph 1.** Formation of study sample

Vilkoksonovog testa sume rangova (*Mann-Whitney U Test*). Za proveru statističke značajnosti razlike u slučajevima kategoričkih podataka korišćen je Hi kvadrat test (*Chi-squared test*), ili po potrebi Fišerov test tačne verovatnoće (*Fisher's exact test*).

Provera ispunjenosti uslova za primenu odgovarajućeg statističkog testa, obavljena je ispitivanjem oblika raspodele vrednosti obeležja od interesa. Za ove potrebe, korišćeni su pokazatelji oblika raspodele (*Skewness, Kurtosis*), kao i posebni statistički testovi (*Kolmogorov-Smirnov test, Shapiro-Wilk test*). U slučaju obeležja „Starost“, raspodela vrednosti odstupala je od normalne raspodele, po obliku negativne iskošenosti, u nešto manjem stepenu (*Skewness=-0.96; Kurtosis=2.24; Kolmogorov-Smirnov Test Statistic=0.096, p=0.00; Shapiro-Wilk Test Statistic=0.954, p=0.00*). Kako bi se postigla normalizacija raspodele, pokušano je sa transformacijom putem kvadriranja vrednosti obeležja, ali značajniji rezultati nisu postignuti, što je opravdalo izbor neparametarskih metoda statističke analize.

Priprema i statistička obrada baze podataka izvršena je uz pomoć softverskog paketa programa *IBM SPSS Statistics for Windows, version 26* (*IBM Corp., Armonk, N.Y., USA*).

## Rezultati

Prosečna starost pacijenata zastupljenih u skupu od 1983 odabrane epizode bolničkog lečenja, iznosila je 64,6 godina ( $SD=11,7$ ), mediana 66,0 (minimalno 59,0, a maksimalno 72,0 godine). Najzastupljeniji uzrast je bio 68 godina, što je zabeleženo u 110 (5,5%) epizoda bolničkog lečenja.

Za 51,5% (n=1022) epizoda bolničkog lečenja zabeležen je ženski pol pacijenta, a muški u preostalih 48,5% (n=961) epizoda bolničkog lečenja.

Pojava bar jedne od pratećih dijagnoza koje označavaju HBB (N18-N18.9) zabeležena je u 188 (9,5%) epizoda bolničkog lečenja. Sa druge strane, ukupan broj zabeleženih unosa ovih pratećih dijagnoza iznosio je 209 (Tabela 2). Utvrđeno je da je u 168 (8,5%) epizoda bolničkog lečenja prisutna samo jedna od pratećih dijagnoza koje označavaju HBB (N18-N18.9), u 19 (0,9%) epizoda bolničkog lečenja prisutne su dve različite prateće dijagnoze N18-N18.9, dok su u samo jednom slučaju zabeležene tri različite prateće dijagnoze N18-N18.9 u okviru jedne epizode bolničkog lečenja. U okviru skupa od 20 epizoda bolničkog lečenja sa više od jedne prateće dijagnoze iz grupe N18-N18.9, najčešće se javljaju N18.3 – u 14 epizoda bolničkog lečenja, N18.9 u 13 epizoda bolničkog lečenja, potom N18.4 u 5, N18.1 u 4, N18.2 u 3 i N18.5 u 2 epizode bolničkog lečenja.

Broj epizoda bolničkog lečenja koje su se završile smrtnim ishodom iznosio je 47 (2,4%) od 1983. Od ovih 47 epizoda bolničkog lečenja, njih 9 (19%) imalo je zabeleženu bar jednu prateću dijagnozu koja se odnosila na HBB. Svi smrtni ishodi zabeleženi su u grupi epizoda bolničkog lečenja (n=168) u kojoj je prisutna samo jedna od pratećih dijagnoza koje označavaju hroničnu bolest bubrega (Tabela 2).

Smrtnih ishodi bili su statistički značajno učestaliji u grupi sa bar jednom od pratećih dijagnoza hronične bolesti bubrega u odnosu na grupu bez ovih pratećih dijagnoza (4,8% vs. 2,1%) (Tabela 3).

**Tabela 2.** Pregled broja pratećih dijagnoza koje označavaju hroničnu bolest bubrega (HBB) i broj smrtnih ishoda u grupama definisanim ovim dijagnozama (n=1983)

Šifra prema MKB-10	Broj epizoda bolničkog lečenja u kojima je zabeležena dijagnoza HBB (%)	Broj smrtnih ishoda u grupi (%)
N18	0 (0,0)	0 (0,0)
N18.1	9 (0,5)	0 (0,0)
N18.2	16 (0,8)	1 (0,05)
N18.3	79 (4,0)	0 (0,0)
N18.4	13 (0,7)	3 (0,15)
N18.5	10 (0,5)	1 (0,05)
N18.9	82 (4,1)	4 (0,2)
<b>Ukupno</b>	<b>209 (10,6)</b>	<b>9 (0,45)</b>

"Concomitant diagnoses according to ICD" (15 for each of 1983 episodes of hospital treatment). In the study sample, in 57 episodes of hospital treatment, the same diagnosis was reported more than once (there is an example of one episode of hospital treatment where diagnosis E11.4 was written in each of 15 possible fields), which was considered to be a technical error, and therefore, these entries were abridged within the database of the study sample, where all multiple entries of diagnoses were removed from each of 57 episodes of hospital treatment within the field "Concomitant diagnoses according to ICD. Thus, 504 duplicate entries were removed.

The distribution of frequency (absolute and relative numbers), percentages, mean value, quartiles, standard deviation and median were used for the descriptive analysis of data. The analysis of statistically significant data was based on the usage of non-parameter Mann-Whitney Test. A chi-squared test or Fisher's exact test were used in case of categorical data to check the statistical significance of differences.

Distribution of values was investigated in order to check whether the conditions for the application of appropriate statistical test were met. Thus, the indices of the shape of distribution were used (Skewness, Kurtosis), as well as specific statistical tests (The Kolmogorov-Smirnov test, Shapiro-Wilk test). As far as "age" marker is concerned, the distribution of values deviated from the normal distribution, and it was a negatively skewed distribution to a lesser extent (Skewness=-0.96; Kurtosis=2.24; Kolmogorov-

Smirnov Test Statistic=0.096, p=0.00; Shapiro-Wilk Test Statistic=0.954, p=0.00). In order to reach normal distribution, the values were transformed with the help of squaring, but significant results were not achieved, which justified the use of nonparametric methods of statistical analysis.

The preparation and statistical analysis of database was done with the help of software package IBM SPSS Statistics for Windows version 26 (IBM Corp., Armonk, N.Y., USA).

## Results

The average age of patients from 1983 selected episodes of hospital treatment amounted to 64.6 years (SD=11.7), media 66.0, (minimal 59.0 and maximal 72.0). The most frequent age was 68 years, which was recorded in 110 (5.5%) episodes of hospital treatment. For 51.5% (n=1022) episodes of hospital treatment, patients were women, while in 48.5% (n=961) episodes of hospital treatment, patients were men.

The occurrence of at least one concomitant diagnosis related to chronic kidney disease (N18-N18.9) was recorded in 188 (9.5%) episodes of hospital treatment. On the other hand, the total number of recorded entries of concomitant diagnoses amounted to 209 (Table 2). It was found that only one concomitant diagnosis relating to chronic kidney disease (N18-N18.9) was present in 168 (8.5%) episodes of hospital treatment, two different concomitant diagnoses N18-N18.9 were present in 19 (0.9%) episodes of hospital treatment, while three different concomitant diagnoses N18-N18.9 were recorded in one case

**Table 2.** Review of number of concomitant diagnoses relating to chronic kidney disease and number of fatal outcomes in groups defined by these diagnoses (n=1983)

Codes according to ICD-10	Number of episodes of hospital treatment in which diagnosis was recorded	Number of fatal outcomes in the group (%)
<b>N18</b>	0 (0.0)	0 (0.0)
<b>N18.1</b>	9 (0.5)	0 (0.0)
<b>N18.2</b>	16 (0.8)	1 (0.05)
<b>N18.3</b>	79 (4.0)	0 (0.0)
<b>N18.4</b>	13 (0.7)	3 (0.15)
<b>N18.5</b>	10 (0.5)	1 (0.05)
<b>N18.9</b>	82 (4.1)	4 (0.2)
<b>Total</b>	209 (10.6)	9 (0.45)

**Tabela 3.** Smrtni ishodi i hronična bolest bubrega (n=1983)

Bar jedna od dijagnoza (N18.1-N18.9)	Smrtni ishodi (% po redovima)		Ukupno (%)	p vrednost*
	Ne	Da		
Ne	1757 (97,9)	38 (2,1)	1795 (90,5)	
Da	179 (95,2)	9 (4,8)	188 (9,5)	0,038
<b>Ukupno (%)</b>	<b>1936 (97,6)</b>	<b>47 (2,4)</b>	<b>1983 (100)</b>	

\* p vrednost za Hi kvadrat test

Utvrđena je statistički značajna razlika u učestalosti pojave smrtnih ishoda između grupe epizoda bolničkog lečenja u kojima je zabeležena prateća dijagnoza N18.4 i grupe u kojoj su sve preostale epizode bolničkog lečenja bez pomenute prateće dijagnoze ( $p=0,003$ ) (Tabela 4). Ostale upoređivane grupe nisu pokazale statistički značajnu razliku u sličnim poređenjima. Smrtni ishodi bili su statistički značajno učestaliji u grupi epizoda bolničkog lečenja u kojima je zabeležena prateća dijagnoza N18.4 u poređenju sa grupom bez ove prateće dijagnoze (23,1% vs. 2,2%).

Utvrđeno je postojanje statistički značajne razlike ( $p < 0,001$ ) u odnosu na starost između grupe sa bar jednom od pratećih dijagnoza N18.1-N18.9 u odnosu na grupu bez ovih pratećih dijagnoza (Tabela 5). Pokazano je i da postoji statistički značajna razlika u odnosu na starost između grupe epizoda bolničkog lečenja definisanih pratećim dijagnozama N18.3, N18.4, N18.9 i njihovih uporednih grupa (Tabela 6). Nije utvrđeno postojanje statistički značajne razlike u starosti između grupe epizoda bolničkog lečenja definisanih pratećim dijagnozama N18.1, N18.2, N18.5 i njihovih uporednih grupa.

**Tabela 4.** Učestalost smrtnih ishoda između različitih grupa definisanih određenom dijagnozom hronične bolesti bubrega (n=1983)

Dijagnoza hronične bolesti bubrega	Smrtni ishodi (% po redovima)		p vrednost*
	Ne	Da	
N18.1	9 (100,0)	0 (0,0)	
Ostali bez N18.1	1927 (97,6)	47 (2,4)	1,000
N18.2	79 (100,0)	1 (6,3)	
Ostali bez N18.2	1857 (97,5)	46 (2,3)	0,320
N18.3	79 (100,0)	0 (0,0)	
Ostali bez N18.3	1857 (97,5)	47 (2,5)	0,259
N18.4	10 (76,9)	3 (23,1)	
Ostali bez N18.4	1926 (97,8)	44 (2,2)	0,003
N18.5	9 (90,0)	1 (10,0)	
Ostali bez N18.5	1927 (97,7)	46 (2,3)	0,214
N18.9	9 (90,0)	4 (4,9)	
Ostali bez N18.9	1927 (97,7)	43 (2,3)	0,127

\* p vrednost Fišerovog testa tačne verovatnoće

**Tabela 5.** Razlike u odnosu na starost u zavisnosti od prisustva bar jedne od dijagnoza hronične bolesti bubrega

Bar jedna od dijagnoza (N18.1-N18.9)	Uzrast (godine)		p vrednost*
	Ȑ	SD	
Ne	63,93	11,75	
Da	71,36	9,33	p < 0,001

Ȑ - aritmetička sredina, SD - standardna devijacija, \* p vrednost za Vilkoksonov test sume rangova

**Table 3.** Fatal outcomes and chronic kidney disease (n=1983)

At least one of diagnoses (N18.1-N18.9)	Fatal outcomes (% in rows)		Total (%)	p value*
	No	Yes		
No	1757 (97.9)	38 (2.1)	1795 (90.5)	
Yes	179 (95.2)	9 (4.8)	188 (9.5)	0.038
<b>Total (%)</b>	<b>1936 (97.6)</b>	<b>47 (2.4)</b>	<b>1983 (100)</b>	

\* p value for Chi squared test

within one episode of hospital treatment. Within the set of 20 episodes of hospital treatment with more than one concomitant diagnosis from the group N18-N18.9, N18.3 appeared most frequently – in 14 episodes of hospital treatment, N18.9 in 13 episodes of hospital treatment, followed by N18.4 in 5 episodes, N18.1 in 4, N18.2 in 3, N18.5 in 2 episodes of hospital treatment.

The number of episodes of hospital treatment that ended in fatal outcome amounted to 47 (2.4%) of 1983. Of 47 episodes of hospital treatment, 9 (19%) had at least one concomitant

diagnosis relating to chronic kidney disease. All fatal outcomes were recorded in the group of episodes of hospital treatment (n=168), in which only one concomitant disease relating to chronic kidney disease was present (Table 2).

Fatal outcomes were more frequent in the group of patients with at least one concomitant diagnosis of chronic kidney disease and this difference was significant in comparison to the group of patients without concomitant diagnoses (4.8% vs. 2.1%) (Table 3).

**Table 4.** Frequency of fatal outcomes between different groups defined by specified diagnosis of chronic kidney disease (n=1983)

Diagnosis of chronic kidney disease	Fatal outcomes (% in rows)		p value*
	No	Yes	
N18.1	9 (100.0)	0 (0.0)	
Others without N18.1	1927 (97.6)	47 (2.4)	1.000
N18.2	79 (100.0)	1 (6.3)	
Others without N18.2	1857 (97.5)	46 (2.3)	0.320
N18.3	79 (100.0)	0 (0.0)	
Others without N18.3	1857 (97.5)	47 (2.5)	0.259
N18.4	10 (76.9)	3 (23.1)	
Others without N18.4	1926 (97.8)	44 (2.2)	0.003
N18.5	9 (90.0)	1 (10.0)	
Others without N18.5	1927 (97.7)	46 (2.3)	0.214
N18.9	9 (90.0)	4 (4.9)	
Others without N18.9	1927 (97.7)	43 (2.3)	0.127

\*p value of Fisher's exact test

**Table 5.** Difference in age depending on the presence of at least one of diagnoses of chronic kidney disease

At least one of diagnoses (N18.1-N18.9)	Age		p value*
	$\bar{x}$	SD	
No	63.93	11.75	
Yes	71.36	9.33	p < 0.001

$\bar{x}$  - arithmetic mean, SD - standard deviation, \*p value for Wilcoxon rank-sum test

**Tabela 6.** Razlike u odnosu na starost između ispitivanih grupa definisanih određenom dijagnozom hronične bolesti bubrega

Dijagnoza hronične bolesti bubrega	Uzrast (godine)		p vrednost*
	Ȑ	SD	
N18.1	70,78	11,83	
Ostali bez N18.1	64,61	11,74	0,103
N18.2	69,00	6,75	
Ostali bez N18.2	64,60	11,77	0,121
N18.3	72,01	8,37	
Ostali bez N18.3	64,33	11,77	0,001
N18.4	71,62	11,56	
Ostali bez N18.4	64,59	11,73	0,013
N18.5	66,90	13,77	
Ostali bez N18.5	64,63	11,74	0,391
N18.9	71,52	9,74	
Ostali bez N18.9	64,34	11,73	< 0,001

Ȑ - aritmetička sredina, SD - standardna devijacija, \* p vrednost za Vilkoksonov test sume rangova

Osobe koje su pripadale grupi epizoda bolničkog lečenja koje su imale zabeleženu bar jednu prateću dijagnozu N18.1-N18.9 u proseku su bile 7,42 godine starije od svih ostalih osoba iz uporednih epizoda bolničkog lečenja. Osobe koje su pripadale grupi epizoda bolničkog lečenja koje su imale zabeleženu prateću dijagnozu N18.3 u proseku su bile 7,68 godina starije od svih ostalih osoba iz epizoda bolničkog lečenja bez ove prateće dijagnoze. Osobe koje su pripadale grupi epizoda bolničkog lečenja koje su imale zabeleženu prateću dijagnozu N18.4 u proseku su bile 7,02 godine starije od svih ostalih osoba iz epizoda bolničkog lečenja bez ove prateće dijagnoze. Osobe koje su pripadale grupi epizoda bolničkog lečenja koje su imale zabeleženu prateću dijagnozu N18.9 u proseku su bile 7,18 godina starije od svih ostalih osoba iz epizoda bolničkog lečenja bez ove prateće dijagnoze.

Ispitivano je postojanje razlika u zastupljenosti grupe definisane prisustvom bar jedne od pratećih

dijagnoza za oznaku hronične bolesti bubrega N18.1-N18.9 između muškaraca i žena (Tabela 7), kao i zastupljenost grupa definisanih pojedinačnim dijagozama N18.1-N18.9 između polova (Tabela 8). Epizode bolničkog lečenja sa bar jednom od pratećih dijagnoza N18.1-N18.9 statistički značajno ( $p = 0,006$ ) češće se javljaju među epizodama bolničkog lečenja sa zabeleženim muškim polom (5,5% vs. 4,0%). Epizode bolničkog lečenja sa pratećim dijagozama N18.4 i N18.9, statistički značajno češće se javljaju ( $p_{N18.4} = 0,039$ ) ( $p_{N18.9} = 0,001$ ) među epizodama bolničkog lečenja sa zabeleženim muškim polom (N18.4 - 0,5% vs. 0,1%) (N18.9 - 2,8% vs. 1,4%).

## Diskusija

Nedovoljno istraživanja koja bi upotpunila shvatanje uticaja HBB na učestalost pojave smrtnih ishoda kod pacijenata bolnički lečenih zbog T2D u našoj sredini, usmerilo je ovo istraživanje

**Tabela 7.** Pol i hronična bolest bubrega (n=1983)

Bar jedna od dijagnoza (N18.1-N18.9)	Pol (%)		Ukupno (%)	p vrednost*
	Muški	Ženski		
Ne	852 (43,0)	943 (47,5)	1795 (90,5)	
Da	109 (5,5)	79 (4,0)	188 (9,5)	0,006
<b>Ukupno (%)</b>	<b>961 (48,5)</b>		<b>47 (51,5)</b>	<b>1983 (100)</b>

\* p vrednost za Hi kvadrat test

**Table 6.** Differences in age between the examined groups defined by specific diagnosis of chronic kidney disease

Diagnosis of chronic kidney disease	Age		p value*
	$\bar{x}$	SD	
N18.1	70.78	11.83	
Others without N18.1	64.61	11.74	0.103
N18.2	69.00	6.75	
Others without N18.2	64.60	11.77	0.121
N18.3	72.01	8.37	
Others without N18.3	64.33	11.77	< 0.001
N18.4	71.62	11.56	
Others without N18.4	64.59	11.73	0.013
N18.5	66.90	13.77	
Others without N18.5	64.63	11.74	0.391
N18.9	71.52	9.74	
Others without N18.9	64.34	11.73	< 0.001

$\bar{x}$  - arithmetic mean, SD - standard deviation, \* p value for Wilcoxon rank-sum test

Statistically significant difference regarding the frequency of fatal outcomes was found between the group of hospital treatment episodes, in which the concomitant diagnosis N18.4 was recorded, and the group in which all remaining episodes of hospital treatment were without the above-mentioned concomitant diagnosis ( $p = 0.003$ ) (Table 4). Other compared groups did not show statistically significant difference in similar comparisons. Fatal outcomes were more frequent and this difference was statistically significant in groups of hospital treatment episodes, in which concomitant diagnosis N18.4 was recorded, in comparison to the group without this concomitant diagnosis (23.1% vs. 2.2%).

The statistically significant difference regarding age was found ( $p < 0.001$ ) between the group with at least one of concomitant diagnoses N18.1-N18.9 compared to the comparison group (Table 5).

The statistically significant difference regarding age was found between groups of hospital treatment

episodes defined by concomitant diagnoses N18.3, N18.4, N18.9 and the comparison groups (Table 6). The statistically significant difference regarding age was not found between hospital treatment episodes defined by concomitant diagnoses N18.1, N18.2, N18.5 and the comparison groups.

Persons who belonged to the group of hospital treatment episodes with at least one concomitant diagnosis N18.1-N18.9 were, on average, 7.42 years older than all other persons from comparison groups of hospital treatment episodes. Persons who belonged to hospital treatment episodes with concomitant diagnosis N18.3 were on average 7.68 years older than all the other persons without this concomitant diagnosis. Persons who belonged to the group of hospital treatment episodes with the concomitant diagnosis N18.4 were on average 7.02 years older than all the other persons from the group of hospital treatment episodes without this concomitant diagnosis. Persons who belonged

**Table 7.** Sex and chronic kidney disease (n=1983)

At least one of diagnoses (N18.1-N18.9)	Sex (%)		Total (%)	p value*
	Male	Female		
No	852 (43.0)	943 (47.5)	1795 (90.5)	
Yes	109 (5.5)	79 (4.0)	188 (9.5)	0.006
<b>Total (%)</b>	<b>961 (48.5)</b>		<b>47 (51.5)</b>	<b>1983 (100)</b>

\* p value of Chi-squared test

**Tabela 8.** Učestalost muškog i ženskog pola između različitih grupa definisanih određenom dijagnozom hronične bolesti bubrega (n=1983)

Dijagnoza hronične bolesti bubrega	Pol (%)		p vrednost*
	Muški	Ženski	
N18.1	5 (0,3)	4 (0,2)	
Ostali bez N18.1	956 (48,2)	1018 (51,3)	0,747**
N18.2	5 (0,3)	11 (0,5)	
Ostali bez N18.2	956 (48,2)	1011 (51,0)	0,167*
N18.3	38 (1,9)	41 (2,0)	
Ostali bez N18.3	923 (46,5)	981 (49,6)	0,948*
N18.4	10 (0,5)	3 (0,1)	
Ostali bez N18.4	951 (48,0)	1019 (51,4)	0,039*
N18.5	8 (0,4)	2 (0,1)	
Ostali bez N18.5	953 (48,0)	1020 (51,5)	0,058**
N18.9	55 (2,8)	27 (1,4)	
Ostali bez N18.9	906 (45,8)	995 (50,2)	0,001*

\*p vrednost prema Hi kvadrat testu; \*\*p vrednost prema Fišerovom testu tačne verovatnoće

prvenstveno ka ispitivanju razlika u pojavi smrtnih ishoda između različitih grupa definisanih prisustvom bilo koje ili pak određene prateće dijagnoze HBB (N18.1-N18.9).

Statistički značajno češća pojava smrtnih ishoda u grupi sa bar jednom od pratećih dijagnoza N18.1-N18.9, a u odnosu na grupu bez ovih dijagnoza, odgovara nalazima iz literature koji povezuju HBB sa višim rizikom za smrtni ishod kod pacijenata sa tipom 2 dijabetesa (11,12,14,15). Razvoj HBB može se kretati u smeru visokog rizika za nastupanje komplikovanih zdravstvenih stanja, dovodeći do pojave hronične bubrežne slabosti, terminalne bubrežne slabosti, kardiovaskularnih bolesti i uvećane smrtnosti ovih pacijenata (1,2,25). Utvrđena razlika u učestalostima smrtnih ishoda se stoga može tumačiti kao deo mogućih i očekivanih ishoda u kliničkom toku HBB kod pacijenata bolnički lečenih zbog T2D. Nisu utvrđene značajne razlike u odnosu na starost ( $p = 0,725$ ) i pol ( $p = 0,142$ ) između grupe preminulih sa bar jednom od pratećih dijagnoza N18.1-N18.9 i uporedne grupe preminulih bez ovih dijagnoza.

Posmatrajući razlike u učestalosti smrtnih ishoda između grupa definisanih prisustvom bar jedne od pratećih dijagnoza HBB (N18.1-N18.9) i njihovih uporednih grupa, pokazano je da značajna razlika postoji jedino u slučaju posmatranja grupe definisane dijagnozom N18.4, koja odgovara hroničnoj bolesti bubrega 4. stepena prema

MKB-10 klasifikaciji, čiji je ekvivalent G4 kategorija jačine glomerulske filtracije (JGF) u HBB prema KDIGO vodiču (1,24). Kategorija G4 karakteriše se teškim smanjenjem jačine glomerulske filtracije (JGF) ( $15-29 \text{ ml/min}/1.73\text{m}^2$ ), i smatra se stanjem visokog rizika za dalju progresiju HBB prema KDIGO vodiču (1). U literaturi postoje izveštaji koji povezuju smanjenje jačine glomerulske filtracije sa većim rizikom za razvoj infarkta miokarda ili moždanog udara kod pacijenata sa T2D (26), a pokazan je i uvećan rizik od smrtnog ishoda kod pacijenata sa dijabetesom koji imaju HBB udruženu sa bolestima srca ili moždanim udarom (27), što može pružiti objašnjenje za opaženi rezultat. Sa druge strane, za objašnjenje nalaza nepostojanja statistički značajne razlike u učestalosti smrtnih ishoda između preostalih ispitivanih grupa (posebno u kategorijama koje se prema KDIGO vodiču smatraju visoko rizičnim), potrebno je više usmerenih istraživanja kako bi se opažena pojava adekvatno tumačila.

Zabeležena statistički značajna razlika u odnosu na starost u epizodama bolničkog lečenja u kojima je zastupljena bar jedna od pratećih dijagnoza N18.1-N18.9, odgovara nalazima iz literature (17,18,28) koji povezuju zastupljenost HBB sa starijim uzrastom, a može se tumačiti i u kontekstu fiziološkog opadanja vrednosti jačine glomerulske filtracije sa starenjem (1). Daljom analizom, pokazano je da se opaženi rezultat prvenstveno može

**Tabela 8.** Frequency of male and female sex between different groups defined by specific diagnosis of chronic kidney disease – contingency table chi-squared test (n=1983)

Diagnosis of chronic kidney disease	Sex (%)		p value*
	Male	Female	
N18.1	5 (0.3)	4 (0.2)	
<b>Others without N18.1</b>	956 (48.2)	1018 (51.3)	0.747**
N18.2	5 (0.3)	11 (0.5)	
<b>Others without N18.2</b>	956 (48.2)	1011 (51.0)	0.167*
N18.3	38 (1.9)	41 (2.0)	
<b>Others without N18.3</b>	923 (46.5)	981 (49.6)	0.948*
N18.4	10 (0.5)	3 (0.1)	
<b>Others without N18.4</b>	951 (48.0)	1019 (51.4)	0.039*
N18.5	8 (0.4)	2 (0.1)	
<b>Others without N18.5</b>	953 (48.0)	1020 (51.5)	0.058**
N18.9	55 (2.8)	27 (1.4)	
<b>Others without N18.9</b>	906 (45.8)	995 (50.2)	0.001*

\*p value of Chi-squared test; \*\*p value of Fisher's exact test

to the group of hospital treatment episodes with the concomitant diagnosis N18.9 were on average 7.18 years older than all the other persons from the group of hospital treatment episodes without this concomitant diagnosis.

The existence of differences between men and women was investigated in the group defined by the presence of at least one concomitant disease N18.1-N18.8 (Table 7), as well as differences between men and women in the group defined by the presence of individual diagnoses N18.1-N18.9 (Table 8). The episodes of hospital treatment with at least one of concomitant diagnoses N18.1-N18.9 occur significantly more often ( $p = 0.006$ ) in males (5.5% vs. 4%). The episodes of hospital treatment with concomitant diagnoses N18.4 and N18.9 occur significantly more often ( $p_{N18.4} = 0.039$ ) ( $p_{N18.9} = 0.009$ ) in males (N18.4 = 0.5% vs. 0.1%) (N18.9 – 2.8% vs. 1.4%).

## Discussion

The insufficient number of studies, which would complement understanding of the influence of chronic kidney disease on the frequency of occurrence of fatal outcomes in patients hospitalized due to type 2 diabetes mellitus in our country, has directed this research primarily towards the investigation of differences in the occurrence of fatal outcomes between different groups defined by the presence of either of the concomitant diagnoses or certain diagnoses

relating to chronic kidney disease (N18.1-N18.9).

The more frequent occurrence of fatal outcomes was statistically significant in the group with at least one of concomitant diagnoses N18.1-N18.9 in comparison to groups without these diagnoses, which corresponds to the findings from the literature that associate chronic kidney disease with the higher risk of fatal outcome in patients with type 2 diabetes mellitus (11,12,14,15). The development of chronic kidney disease may contribute to the high risk of complicated health conditions, thus leading to the chronic kidney failure, end-stage kidney failure, cardiovascular diseases and increased mortality rates of these patients (1,2,25). The found difference in the frequency of fatal outcomes may be interpreted as part of possible and expected outcomes in the clinical course of chronic kidney disease in patients hospitalized due to type 2 diabetes mellitus. There was no statistically significant difference regarding age ( $p = 0.725$ ) and sex ( $p = 0.142$ ) between deceased patients with at least one of concomitant diagnoses N18.1-N18.9 and the comparison group of deceased patients without these diagnoses.

By observing the difference regarding the frequency of fatal outcomes between groups defined by the presence of at least one concomitant diagnosis designating chronic kidney disease (N18.1-N18.9) and comparison groups, it has been shown that statistically significant difference exists

pripisati razlikama u starosti između grupa epizoda bolničkog lečenja definisanih pratećim dijagnozama N18.3, N18.4 i N18.9 i njihovih uporednih grupa.

Statistički značajno veća zastupljenost epizoda bolničkog lečenja sa bar jednom od pratećih dijagnoza N18.1-N18.9 među epizodama bolničkog lečenja sa zabeleženim muškim polom, a u odnosu na epizode bolničkog lečenja sa zabeleženim ženskim polom, što je rezultat koji se javio i u poređenju grupa koje su imale zabeležene prateće dijagnoze N18.4 ili N18.9, u saglasnosti je sa delom navoda iz literature (17). Sa druge strane, postoje istraživanja koja nisu potvrdila razlike u riziku za pojavu HBB kod pacijenata sa dijabetesom, između osoba muškog i ženskog pola (18). Ograničen broj izvora koji se bavio ovim pitanjem, nalaže sprovođenje dodatnih istraživanja kako bi se adekvatno interpretirali dobijeni rezultati.

Neka od ograničenja ovog istraživanja mogu umanjiti mogućnost generalizacije zaključaka, pa je za potpunije sagledavanje rezultata ove studije, potrebno naglasiti i sledeće aspekte: nije postojala mogućnost utvrđivanja potencijalno ponovnih epizoda bolničkog lečenja za iste osobe; kriterijumi za unos uputne i pratećih dijagnoza, kao i osnovnog uzroka hospitalizacije, nisu dovoljno precizni, što se može odraziti na razumevanje vremenskog sleda pojave određenih pratećih dijagnoza, kao i ukupnu tačnost informacija u dijagnostičkom smislu.

**Prednosti istraživanja.** Izvor podataka predstavljaju baze zvanične statistike iz oblasti zdravstvene zaštite, što pruža mogućnost i za poređenje dobijenih rezultata sa podacima iz ranijeg perioda. Rezultati istraživanja mogu doprineti adekvatnjem sagledavanju problema HBB kod bolnički lečenih pacijenata sa T2D, a sa ciljem umanjenja posledica koje ova stanja prouzrokuju – kako onih koji se neposredno odražavaju po zdravlje pacijenata, tako i ukupnog opterećenja zdravstvenog sistema, koje se ogleda u utvrđenim većim troškovima i dužem trajanju bolničkog lečenja pacijenata sa T2D, ukoliko ovi pacijenti boluju i od HBB (19,20).

## Zaključak

Epizode bolničkog lečenja zabeležene u 2019. godini u Beogradu, čiji je osnovni uzrok hospitalizacije bio T2D, a koje su imale zabeleženu bar jednu od pratećih dijagnoza N18.1-N18.9, odlikovale su se većom učestalošću smrtnih ishoda u poređenju sa epizodama bolničkog lečenja bez ovih dijag-

noza. Pacijenti iz grupe epizoda bolničkog lečenja koju definiše prisustvo bar jedne od pratećih dijagnoza N18.1-N18.9 odlikuju se većom prosečnom starošću i većom zastupljenosti muškog pola.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

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only in the group defined by diagnosis N18.4, which corresponds to the fourth stage of chronic kidney disease according to ICD-10, whose equivalent is G4 category of glomerular filtration rate (GFR) in chronic kidney disease according to KDIGO Guidelines (1,24). The category G4 is characterized by severely decreased glomerular filtration rate (GFR) (15-29 ml/min/1.73m<sup>2</sup>) and it is considered the condition related to the high risk of further progression of chronic kidney disease according to KDIGO Guidelines (1). In the literature, one may find reports that associate the decreased GFR with the increased risk of myocardial infarction or stroke in patients with type 2 diabetes mellitus (26), while the increased risk of fatal outcome has been shown in patients with type 2 diabetes mellitus who have chronic kidney disease coexistent with heart disease or stroke (27), which may explain the observed result. On the other hand, in order to explain the absence of statistically significant difference regarding the frequency of fatal outcomes between the remaining examined groups (especially in categories, which are considered to be at the increased risk according to KDIGO categories), more targeted research is necessary in order to interpret adequately the observed occurrence.

The statistically significant difference regarding age in episodes of hospital treatment, in which at least one of concomitant diagnoses N18.1-N18.9 is present, corresponds to the literature findings (17,18,28) that associate chronic kidney disease with older age, while it can also be interpreted in the context of physiological decrease of glomerular filtration rate in older age (1). Further analysis has shown that the observed findings may be attributed to the difference in age between groups of hospital treatment episodes defined by concomitant diagnoses N18.3, N18.4 and N18.9 and the comparison groups.

Greater presence of episodes of hospital treatment with at least one concomitant diagnosis N18.1-N18.9 was statistically significant among episodes of hospital treatment that included males in comparison to episodes of hospital treatment that included females, which is the result of comparison of groups with concomitant diagnoses N18.4 or N18.9, and which is in accordance with some literature findings (17). On the other hand, there are studies which have not confirmed differences regarding the risk of chronic kidney disease in patients with diabetes between male

and female patients (18). The limited number of sources dealing with this subject topic demands further research in order to interpret the obtained results adequately.

Some of the limitations of this research may reduce the possibility of generalizations when making conclusions, and therefore, in order to perceive the results of this study more completely, the following aspects should be emphasized: there was no possibility of establishing the repeated episodes of hospital treatment for the same persons; criteria for the referral and concomitant diagnoses, as well as for the main cause of hospitalization are not sufficiently precise, which can have influence on understanding the temporal sequence of occurrence of certain concomitant diagnoses, as well as the accuracy of information regarding diagnostics.

The advantages of research. The source of data is the database of official statistics in the field of healthcare, which gives the possibility to compare the obtained results with the data from the previous periods. The results of research may contribute to perceive more adequately the problem of chronic kidney disease in hospitalized patients with type 2 diabetes mellitus, aimed at reducing the consequences of these conditions – those that have a direct influence on patients' health, as well as the total burden of the healthcare system, which is reflected in higher costs and longer hospital treatment of patients with type 2 diabetes mellitus coexistent with chronic kidney disease (19,20).

## Conclusion

The episodes of hospital treatment recorded in Belgrade in 2019, whose main cause of hospitalization was type 2 diabetes mellitus, with at least one of the concomitant diagnoses N18.1-N18.9, were characterized by greater frequency of fatal outcomes in comparison to episodes of hospital treatment without these diagnoses. Patients from the group of episodes of hospital treatment defined by at least one of the concomitant diagnoses were characterized by older average age and greater distribution of males.

## Competing interests

Authors declare no competing interests.

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## IZLOŽENOST UČENIKA SREDNJE ELEKTROTEHNIČKE ŠKOLE „NIKOLA TESLA“ BEŽIČNOM ELEKTROMAGNETNOM ZRAČENJU

Radoje Jevtić<sup>1\*</sup>, Ivana Janković<sup>1</sup>

<sup>1</sup> Elektrotehnička škola „Nikola Tesla“, Niš, Republika Srbija

\* Korespondencija: Radoje Jevtić, Elektrotehnička škola „Nikola Tesla“, Aleksandra Medvedeva 18, 18000 Niš, Republika Srbija; e-mail: milan.jvtc@gmail.com

### SAŽETAK

**Uvod/Cilj:** Bežično elektromagnetno zračenje rutera je svakodnevna pojava u životu i radu savremenog čoveka. Oni se široko primenjuju u mnogim profesionalnim, javnim i domaćim objektima, što znači da ljudi svih uzrasta mogu stalno biti izloženi elektromagnetnom zračenju ovog uređaja. Cilj istraživanja je bio da se utvrdi jačina električnog polja, jačina magnetnog polja i elektromagnetna izloženost učenika u različitim laboratorijama srednje škole „Nikola Tesla“, u zavisnosti od vrste ruteru koji su u njima postavljeni i da se neki od dobijenih rezultata provere odgovarajućim softverskim programom visokih frekvencija (engl. *High Frequency Simulation Software - HFSS*) za simulaciju elektromagnetnog zračenja kroz različite sredine.

**Metode:** Merenja jačine električnog i magnetnog polja, kao i elektromagnetno izlaganje, su realizovana, korišćenjem mernog instrumenta Spectran HF 60105, na četiri različita tipa ruteru instaliranih u četiri laboratorijske srednje škole „Nikola Tesla“ u Nišu. Merenja su realizovana na svakom ruteru, kroz pet položaja po horizontali i po vertikali, sa razmakom od 45° u odnosu na horizontalnu i normalnu osu ruteru, a u razmacima od 1 cm, što daje ukupan broj od hiljadu merenja.

**Rezultati:** Ostvareni mereni rezultati na četiri različita ruteru koji su radili na frekvenciji od 2,4 GHz za jačinu električnog polja (reda milivolta po metru), jačinu magnetnog polja (reda mikroampera po metru) i elektromagnetnu izloženost (reda mikrovati po kvadratnom centimetru) bili su ispod graničnih vrednosti definisanih standardima. Provera ostvarenih rezultata je realizovana samo za ruter TL-WR841HP pomoću HFSS za simulaciju elektromagnetnog zračenja kroz različite sredine. Rezultat provere simulacijom praktično potvrđuje verodostojnost izmerenih rezultata za ruter TL-WR841HP.

**Zaključak:** Merenje i praćenje elektromagnetnog zračenja predstavlja veoma važan zadatak u cilju očuvanja i unapređenja kvaliteta radne i životne sredine i kvaliteta života i zdravlja ljudi i dece. Softverski programi za simulaciju elektromagnetnog zračenja mogu da se koriste ukoliko zbog tehničkih problema nije moguće sprovesti eksperimentalno merenje zbog otežanog pristupa uređaju, opasnosti od prevelikog zračenja ili nekog drugog razloga.

**Ključne reči:** ruter, elektromagnetno zračenje, učenici

### Uvod

Savremeno društvo i savremeni način života podrazumevaju intenzivnu komunikaciju i stalni pristup velikoj grupi elektronskih podataka u realnom vremenu. Promet i promena elektronskih informacija ušli su u svaku poru savremenog društva. Ova činjenica govori o upotrebi savremenih uređaja, kao što su računari, laptopovi, mobilni telefoni, tableti, itd. Tehnologija je omogućila da se prenos elektronskih informacija između uređaja i korisnika može realizovati odgovarajućim kablovskim

(žičnim, optičkim, itd.) i bežičnim putem (1). Bežična komunikacija predstavlja jedan od najčešćih vi-dova saobraćaja (1). Ona služi za prenos informacija između dva ili više korisnika bez direktnе fizičke veze. Primeri bežičnog prenosa informacija su različiti: ruteri, *bluetooth* uređaji, mobilni uređaji, uređaji koji koriste satelitski sistem za precizno određivanje bilo koje geografske pozicije na zemlj - GPS (globalni položajni sistem; engl. *Global Positioning System*) uređaji, bežični miševi, bežične

## EXPOSURE OF THE STUDENTS OF THE SECONDARY SCHOOL OF ELECTRICAL ENGINEERING "NIKOLA TESLA" TO WIRELESS ELECTROMAGNETIC RADIATION

Radoje Jevtic<sup>1\*</sup>, Ivana Jankovic<sup>1</sup>

<sup>1</sup>Secondary School of Electrical Engineering „Nikola Tesla”, Niš, Republic of Serbia

Correspondence: Radoje Jevtic, Secondary School of Electrical Engineering „Nikola Tesla“, Aleksandra Medvedeva 18, 18000 Niš, Republic of Serbia: e-mail: milan.jvtc@gmail.com

### SUMMARY

**Introduction/Aim:** Wireless electromagnetic radiation from routers is an everyday occurrence in the life and work of modern man. They are widely used in many professional, public and domestic facilities, which means that people of all ages can be constantly exposed to electromagnetic radiation from these devices. The aim of this study was to determine the electric field strength, the magnetic field strength, and the electromagnetic exposure of students in different laboratories of the Secondary School “Nikola Tesla”, depending on the type of routers installed in them, as well as to check some of the obtained results with the help of the appropriate software program of high-frequency (High-Frequency Simulation Software – HFFSS) for the simulation of electromagnetic radiation through different environments.

**Methods:** Measurements of electric and magnetic field strength, as well as electromagnetic exposure, were carried out using the measuring instrument Spectran HF 60105, on four different types of routers installed in four laboratories of the Secondary School of Electrical Engineering “Nikola Tesla” in Niš. Measurements were realized on each router, through five horizontal and five vertical positions, with a distance of 45° in relation to the horizontal and normal axis of the router, and with spaces of 1 cm, which gives a total number of one thousand measurements.

**Results:** The measured results obtained on four different routers that operated at a frequency of 2.4 GHz for the electric field strength (measured in millivolts per meter), magnetic field strength (measured in microampere per meter) and electromagnetic exposure (in microWatts per square centimeter) were below the limit values defined by standards. The achieved results were verified only for the router TL-WR841HP with the help of HFSS for the simulation of electromagnetic radiation through different environments. The result of the simulation check practically confirms the reliability of the measured results for TL-WR841HP router.

**Conclusion:** Measuring and monitoring electromagnetic radiation is a very important task aimed at preserving and improving the quality of the working and living environment, as well as the quality of life and health of people and children. Software programs for the simulation of electromagnetic radiation can be used when it is not possible to carry out experimental measurements due to technical problems, hindered access to the device, danger of excessive radiation or some other reasons.

**Keywords:** router, electromagnetic radiation, students

### Introduction

Modern society and the modern way of life imply intensive communication and constant access to a large group of electronic data in real time. The circulation and change of electronic information have entered every pore of modern society. This fact speaks of the use of modern devices such as computers, laptops, mobile phones, tablets, etc. Technology has enabled

the transmission of electronic information between the device and the user to be realized via appropriate cables (wired, optical, etc.) and wirelessly (1). Wireless communication is one of the most common types of traffic (1). It serves to transfer information between two or more users without a direct physical connection. Examples of wireless transmission of information are various:

tastature, uređaji za daljinsko upravljanje, saobraćajni sistemi, računarske mreže i mnogi drugi (1). Udaljenost između bežičnih uređaja može biti od nekoliko metara do nekoliko hiljada kilometara. Potreba za bežičnom komunikacijom ima logične i praktične razloge: fizička ograničenja kada se koriste kablovi, povezivanje mobilnih uređaja, finansijske prednosti povezane sa žičnim i kablovskim prenosom, i drugo (1).

Ruter je jedan od najkorisnijih bežičnih uređaja (1). On omogućava povezivanje računarskih mreža na različitim frekvencijama, najčešće od nekoliko gigaherca. Generalno, ruteri mogu biti hardverski i softverski (1). Svaki hardverski ruter predstavlja računar sa softverom, dok softverski ruter predstavlja softver instaliran na serverima sa operativnim sistemima.

Zbog mnogih potencijala i učestalosti upotrebe, javljaju se logična pitanja o bezbednosti bežične tehnologije za zdravlje ljudi. Ovo se posebno odnosi na upotrebu bežičnih uređaja u objektima sa puno ljudi i dece, gde više korisnika može istovremeno da koristi jednu mrežu, kao što je Internet. Korisnici su stalno izloženi elektromagnetnom zračenju ruta (2). Jedan od tipičnih objekata gde se ruteri veoma često koriste za bežično povezivanje je škola u kojoj deca tj. đaci provode mnogo vremena u toku dana pa je samim tim njihova izloženost elektromagnetnom zračenju velika i skoro kontinuirana. Dakle, za ugradnju ruta u školama u kojima će ovi ruteri biti instalirani, veoma je važna njihova snaga i minimalno rastojanje između ruta i korisnika-učenika (3).

Elektromagnetno zračenje različitih uređaja može biti štetno po decu i odrasle. Brojna istraživanja pokazuju i dokazuju da štete koje mogu nastati mogu biti trenutnog i dugotrajnog karaktera (4-8). Trenutne smetnje se ogledaju u nedostatku koncentracije, povećanoj anksioznosti, peckanju i svrabu kože, problemima sa vidom, dok trajne

mogu biti veoma teške u vidu pojave određenih maligniteta (4-8). Neki naučnici smatraju da je elektromagnetno zračenje štetno, ali ima i onih koji tvrde i dokazuju da štetnosti nema. Posebno interesantnu grupu predstavljaju deca školskog uzrasta, čija je izloženost elektromagnetnom zračenju različitih uređaja, prvenstveno mobilnog telefona, rutera i drugih uređaja, znatno povećana. Iako postoje i uputstva i pravila o bezbednosti upotrebe mobilnih telefona, ona se veoma malo ili skoro uopšte ne poštuju od strane korisnika (4-8).

Postoji nekoliko standarda (Internacionalna komisija za zaštitu od nejonizujućeg zračenja, engl. *International Commission on Non-ionizing Radiation Protection – ICNIRP*; Institut elektronskih i elektrotehničkih inženjera, engl. *Institute of Electrical and Electronics Engineers - IEEE*, jugoslovenski univerzalni standard - JUS) koji se bave elektromagnetnim zračenjem (9). Ovi standardi se koriste za merenje utvrđenih vrednosti koje karakterišu elektromagnetno zračenje i određivanje graničnih vrednosti. Karakteristične elektromagnetne vrednosti su električno polje [V/m], magnetno polje [A/m] i elektromagnetna izloženost izražena kao [ $\text{mW/cm}^2$ ] ili [ $\text{W/m}^2$ ]. Izloženost elektromagnetnom zračenju se obično određuje za vreme od 6 minuta, u slučaju kontrolisanog izlaganja, odnosno 30 minuta, u slučaju nekontrolisanog izlaganja (9). Dozvoljene vrednosti izlaganja električnom i magnetnom polju za različite frekvencije, za neprofesionalnu i profesionalnu izloženost u vezi sa ICNIRP-om prikazane se u Tabeli 1, dok su dozvoljene vrednosti za elektromagnetnu izloženost u odnosu na IEEE C95.1 prikazane u Tabeli 2 (9).

Elektromagnetno zračenje se može podeliti na nisko i visokofrekventno. Realna je činjenica da savremeni čovek živi u elektromagnetnom smogu koji se sastoji iz mnogo različitih frekvencija iz mnogo različitih izvora. Ova podela elektomag-

**Tabela 1.** Dozvoljene vrednosti izlaganja električnom i magnetnom polju za različite frekvencije za neprofesionalnu i profesionalnu izloženost u odnosu na ICNIRP (9)

f [MHz]	E [V/m]	H [A/m]
10-400	28 61	0,0173 0,160
400-2000	$1.375\sqrt{f}$ $3.000\sqrt{f}$	$0.0037\sqrt{f}$ $0.0080\sqrt{f}$
2000-300000	61 137	0,160 0,360

routers, Bluetooth devices, mobile devices, devices that use a satellite system to accurately determine any geographic position on earth – GPS (Global Positioning System) devices, wireless mice, wireless keyboards, remote control devices, traffic systems, computer networks and many others (1). The distance between wireless devices can be from a few meters to several thousand kilometers. The need for wireless communication has logical and practical reasons: physical limitations when cables are used, connecting mobile devices, financial advantages connected with wired and cable transmission, etc. (1).

A router is one of the most useful wireless devices (1). It enables the connection of computer networks at different frequencies, usually of several gigahertz. In general, routers can be hardware and software. Each hardware router represents a computer with software, while a software router represents software installed on servers with operating systems.

Due to its many potentials and frequency of use, logical questions arise about the safety of wireless technology for human health. This especially applies to the use of wireless devices in facilities with a lot of people and children, where multiple users can simultaneously use a single network, such as the Internet. Users are constantly exposed to the electromagnetic radiation from the router (2). One of the very characteristic facilities where routers are frequently used for wireless connection is a school, where children, that is, students spend a lot of time during the day, and therefore, their exposure to electromagnetic radiation is high and almost continuous. Thus, for the installation of routers in schools, where these routers will be installed, their strength and minimal distance between the router and the user-student are very important (3).

Electromagnetic radiation from various devices can be harmful to children and adults. Numerous studies show and prove that the damage that can occur can be of an immediate or long-term nature (4-8). Instantaneous disturbances are reflected in the lack of concentration, increased anxiety, burning and itching of skin, problems with eyesight, while permanent ones can be very severe in the form of the appearance of some malignancies (4-8). Some scientists believe that electromagnetic radiation is harmful, but there are also those who claim and prove that it is not harmful. A particularly interesting group is school children, whose exposure to electromagnetic radiation from various devices, primarily mobile phones, routers and other devices has increased significantly. Although there are instructions and rules about safety of using mobile phones, they are respected by users very little or not at all (4-8).

There are several standards (International Commission on Non-ionizing Radiation Protection – ICNIRP; Institute of Electrical and Electronics Engineers – IEEE; Yugoslav Universal Standard – YUS) that deal with the electromagnetic radiation (9). These standards are used to measure the established values that characterize the electromagnetic radiation and determine the reference values. The characteristic electromagnetic values are the electric field [V/m], magnetic field [A/m], and electromagnetic exposure expressed as [ $\text{mW/cm}^2$ ] or [ $\text{W/m}^2$ ]. The exposure to electromagnetic radiation is usually determined for the time of six minutes, in the case of controlled exposure, or 30 minutes, in the case of uncontrolled exposure (9). The allowed values of exposure to electric and magnetic fields for different frequencies, for professional and non-professional exposure in relation to ICNIRP are shown in Table 1, while the allowed values for electromagnetic exposure in relation to IEEE C95.1 are shown in Table 2 (9).

**Table 1.** Allowed values of exposure to electric and magnetic field for different frequencies for non-professional and professional exposure in relation to ICNIRP (9)

f [MHz]	E [V/m]	H [A/m]
<b>10-400</b>	28	0.0173
	61	0.160
<b>400-2000</b>	$1.375\sqrt{f}$	$3.000\sqrt{f}$
		$0.0037\sqrt{f}$
<b>2000-300000</b>	61	0.160
	137	0.360

**Tabela 2.** Dozvoljene vrednosti za elektromagnetnu izloženost u odnosu na IEEE C95.1 standard (9)

Frekvencija [MHz]	Kontrolisana izloženost [mW/cm <sup>2</sup> ]	Nekontrolisana izloženost [mW/cm <sup>2</sup> ]
30-300	1,0	0,2
300-1500	f/300	f/1500
1500-100000	5	1,0

netnog zračenja je gruba, ali je najčešće korišćena, dok su razlozi za ovu vrstu podele uglavnom bili istorijski. Kada je ova podela u pitanju, niskofrekventno elektromagnetno zračenje podrazumeva širok opseg frekvencija, ali su najdominantnije frekvencije od 50 Hz ili 60 Hz i talasne dužine  $\lambda \sim 6000$  km ( $\lambda=c/v$ ). S druge strane, visokofrekventno elektromagnetno zračenje predstavlja frekvencije reda megaherca i gigaherca. Postoje neke razlike između niske i visoke frekvencije elektromagnetskog zračenja u reakciji, distribuciji, efektima i uticaju na ljudski organizam. Ljudsko telo predstavlja poluprovodni, nehomogen i disperzivni medijum za niskofrekventno elektromagnetno zračenje (9,10). Takođe, za niskofrekventno elektromagnetno zračenje, ljudsko telo se nalazi u tzv. „zoni indukcije“ i faktor oštećenja za niske frekvencije se može definisati u vezi sa formiranim gustinom struje, zbog normiranja rizika (9,10). Moguće je izračunati gustinu struje  $J$  za niske frekvencije povezane sa jednačinom  $J = \sigma E$ , gde je  $\sigma$  provodnost, a  $E$  jačina električnog polja.

Kada je u pitanju faktor oštećenja, moguće je izračunati ograničene vrednosti jačine električnog polja u različitim delovima ljudskog organizma. Važno je napomenuti da loši efekti elektromagnetičnih polja industrijskih frekvencija još nisu dovoljno proučeni. Faktor oštećenja, gustina struje i odgovarajući opis reakcija tkiva, organa i organizama prikazani su u Tabeli 3.

Visokofrekventno elektromagnetno zračenje u smislu pomenute podele podrazumeva tzv. RF-radio frekvencijsko zračenje. Ovo zračenje obuhvata širok opseg frekvencija, od frekvencija dugih talasa do frekvencija mikrotalasa. Visokofrekventno elektromagnetno zračenje prodire u okolinu kao što je ljudsko telo tako da za visoke frekvencije mora biti definisana dubina prodora označena kao  $\delta$  [m], u vezi sa jednačinom 1 (9).

$$\delta = \frac{1}{\omega} \cdot \left( \frac{\epsilon \mu}{2} \left( \sqrt{1 + \frac{\sigma^2}{\omega^2 \epsilon^2}} - 1 \right) \right)^{-1/2} \quad (1)$$

Ova vrednost nije ista za različite organe (mozak, jetra, organi za varenje itd.). Ona, naravno, nije dovoljna da detaljno opiše elektromagnetna polja koja su prodrla u ljudsko telo. Poznato je da lokalna distribucija visokofrekventnih elektromagnetnih polja u živim tkivima dovodi do termičkih i netermičkih efekata. Netermički efekti još nisu detaljno i dovoljno proučeni. To je činjenica jer se najčešće govorio o termičkim efektima. Za ove efekte korišćena je posebna veličina. Ova veličina je nazvana specifična stopa apsorpcije (eng. *Specific Absorption Rate - SAR*) i predstavljena je u jednačini 2 (9).

$$SAR = \frac{d}{dt} \left( \frac{dW}{dm} \right) \left[ \frac{W}{kg} \right] \quad (2)$$

**Tabela 3.** Faktor oštećenja za niske frekvencije (9)

Faktor oštećenja	Gustina struje J [mA/m <sup>2</sup> ]	Opis
A	1-10	Beznačajan biološki odgovor tkiva.
B	10-100	Lakši poremećaji vida i nervnog sistema.
C	100-1000	Stimulansi tkiva koji izazivaju nevoljne pokrete. Poremećaji srčanog ritma i centralnog nervnog sistema.
D	>1000	Termičko oštećenje tkiva. Poremećaji i otkazivanje nervnog sistema. Stanja koja dovode do smrtnog ishoda.

**Table 2.** Allowed values for electromagnetic exposure in relation to IEEE C95.1 standard (9)

Frequency [MHz]	Controlled exposure [mW/cm <sup>2</sup> ]	Uncontrolled exposure [mW/cm <sup>2</sup> ]
30-300	1.0	0.2
300-1500	f/300	f/1500
1500-100000	5	1.0

Electromagnetic radiation can be divided into low and high frequency electromagnetic radiation. It is a real fact that modern man lives in the electromagnetic smog that consists of many different frequencies from many different sources. This classification of electromagnetic radiation is rough, but it is the most commonly used, while the reasons for this type of classification were mostly historical. When it comes to this classification, low-frequency electromagnetic radiation includes a wide range of frequencies, but the most dominant frequencies are 50 Hz or 60 Hz and wave lengths  $\lambda \sim 6000$  ( $\lambda=c/v$ ). On the other hand, high frequency electromagnetic radiation represents frequencies measured in megahertz and gigahertz. There are some differences between low and high frequency electromagnetic radiation in the reaction, distribution, effects and impact on the human body. The human body is a semiconducting, inhomogeneous and dispersive medium for low frequency electromagnetic radiation (9,10). Also, for low-frequency electromagnetic radiation, the human body is in the so-called "zone of induction" and the damage factor for low frequencies can be defined in connection with the formed current density, due to risk norming (9,10). It is possible to calculate current density  $J$  for low frequencies related to the equation  $J=\sigma E$ , where  $\sigma$  is conductivity, while  $E$  is the electric field strength.

When it comes to damage factor, it is possible to calculate the limited values of the electric field strength in different parts of the human body. It is important to note that the bad effects of electromagnetic fields of industrial frequencies have not yet been sufficiently studied. The damage factor, current density and corresponding description of reactions of tissues, organs, and organisms are shown in Table 3.

High-frequency electromagnetic radiation in the sense of the aforementioned classification implies the so-called RF-radio frequency radiation. This radiation includes a wide range of frequencies, from long-wave frequencies to micro-wave frequencies. High-frequency electromagnetic radiation penetrates the environment such as the human body, and therefore, for high frequencies the penetration depth denoted as  $\delta$  [m], must be defined in relation to equation 1 (9).

$$\delta = \frac{1}{\omega} \cdot \left( \frac{\epsilon \mu}{2} \left( \sqrt{1 + \frac{\sigma^2}{\omega^2 \epsilon^2}} - 1 \right) \right)^{-1/2} \quad (1)$$

This value is not the same for different organs (brain, liver, digestive organs, etc.). This value, of course, is not enough to describe in detail the electromagnetic fields that have penetrated the human body. It is known that the local distribution

**Table 3.** Damage factor for low frequencies (9)

Damage factor	Current density J [mA/m <sup>2</sup> ]	Description
A	1-10	Insignificant biological tissue response.
B	10-100	Lighter vision and nervous system disorders.
C	100-1000	Tissue stimuli that lead to involuntary movements. Heart rhythm and central nervous system disorders.
D	>1000	Thermal tissue damage. Disorders and failure of the nervous system. Conditions that lead to death.

Ova veličina se može definisati i na druge načine, ali je važno napomenuti da je često nezavisna. Vrednosti za SAR su različite za profesionalne radnike i neprofesionalce (9). Efekti apsorbovane elektromagnetne energije se akumuliraju. Međutim, još uvek nije utvrđeno kada se pojavljuju nepovratni efekti. Ovo je posebno važno za mobilne telefone i rutere, jer ovi uređaji omogućavaju kratko i dugotrajno izlaganje visokofrekventnom elektromagnetnom zračenju. Dakle, neophodno je meriti visokofrekventno elektromagnetno zračenje mobilnih telefona i rutera, posebno kod mlađe populacije, kako bi se pronašla najmanja količina zračenja sa odgovarajućim kvalitetom signala (9,10).

Cilj ovog istraživanja je bio da se utvrdi jačina električnog polja, jačina magnetnog polja i elektromagnetna izloženost dece u različitim laboratorijama srednje škole „Nikola Tesla”, u zavisnosti od vrste rutera koji su u njima postavljeni i da se neki od dobijenih rezultata provere odgovarajućim simulacionim programom HFSS.

## Metode

U cilju merenja parametara visokofrekventnog elektromagnetnog zračenja u srednjoj elektrotehničkoj školi „Nikola Tesla” korišćena je metoda direktnog merenja u realnom vremenu korišćenjem Spectran HF 60105 instrumenta. Ovaj instrument je namenjen za merenje visokofrekventnog elektromagnetnog zračenja i njegovih parametara na frekvencijama od 1,0 MHz do 9,4 GHz. U cilju višestrukih merenja izloženosti visokofrekventnom elektromagnetnom zračenju korišćen je Spectran HF 60105 sa odgovarajućim softverom instaliranim na



Slika 1. Instrument Spectran HF 60105 za merenje parametara visokofrekventnog elektromagnetnog zračenja

laptopu. Instrument Spectran HF 60105 sa kompletom dodatnom opremom prikazan je na slici 1.

Merenja visokofrekventnog elektromagnetnog zračenja su realizovana u četiri najčešće korišćene laboratorije u Elektrotehničkoj školi „Nikola Tesla” u Nišu: laboratoriji broj 106 i 109 u prizemlju, 110 na prvom spratu, i 2 na drugom spratu. Višestruka merenja u trajanju od minimalno 6 minuta realizovana su horizontalno i vertikalno u odnosu na ose rutera, u opsegu od 0 do 100 cm, u koracima od 1 cm. Elektromagnetno zračenje je mereno na četiri različita tipa rutera u zavisnosti od laboratorije gde je sprovedeno istraživanje. Ruter koji se nalazio u laboratoriji 106 bio je TL-WR841N (slika 2a), u laboratoriji 2 TL-WR841HP (slika 2b), u laboratoriji 109 Mi AloT AC 2350 (slika 2c), a u laboratoriji 110 TL-WR740N (slika 2d).



Slika 2a. Ruteri u različitim laboratorijama, TL-WR841N u laboratoriji 106



Slika 2b. Ruteri u različitim laboratorijama, WR841HP u laboratoriji 2

of high frequency electromagnetic fields in living tissues leads to thermal and non-thermal effects. Non-thermal effects have not yet been studied in detail and sufficiently. This is a fact because thermal effects are the most common. A special measure was used for these effects. This measure was called the Specific Absorption Rate (SAR) and it is presented in equation 2 (9).

$$SAR = \frac{d}{dt} \left( \frac{dW}{dm} \right) \left[ \frac{W}{kg} \right] \quad (2)$$

This measure can be defined in other ways, but it is important to note that it is often dependent. The values for SAR are different for professional workers and non-professionals (9). The effects of the absorbed electromagnetic energy accumulate. However, it has not yet been established when irreversible effects appear. This is especially important for mobile phones and routers, because these devices enable short and long-time exposure to high frequency electromagnetic radiation. Thus, high frequency electromagnetic radiation of mobile phones and routers should necessarily be measured, especially in the younger population, in order to find the smallest radiation quantity with the appropriate signal quality (9,10).

The aim of this study was to determine the electric field strength, the magnetic field strength and the electromagnetic exposure of students in different laboratories of the Secondary School "Nikola Tesla", depending on the type of routers installed in them, as well as to check some of the



**Picture 1.** Instrument Spectran HF 60105 for measuring the parameters of high frequency electromagnetic radiation

obtained results with the help of the appropriate simulation program HFSS.

### Method

In order to measure the parameters of high frequency electromagnetic radiation in the Secondary School of Electrical Engineering "Nikola Tesla", the method of direct measurement in real time with the help of the Spectran HF 60105 instrument was used. This instrument is intended for measuring high frequency electromagnetic radiation and its parameters at frequencies from 1.0 MHz to 9.4 GHz. For the purpose of multiple measurements of exposure to high frequency electromagnetic radiation, Spectran HF 60105 was used with the appropriate software installed on the laptop. Spectran HF 60105 instrument



**Picture 2a.** Routers in different laboratories,  
TL-WR841N in laboratory 106

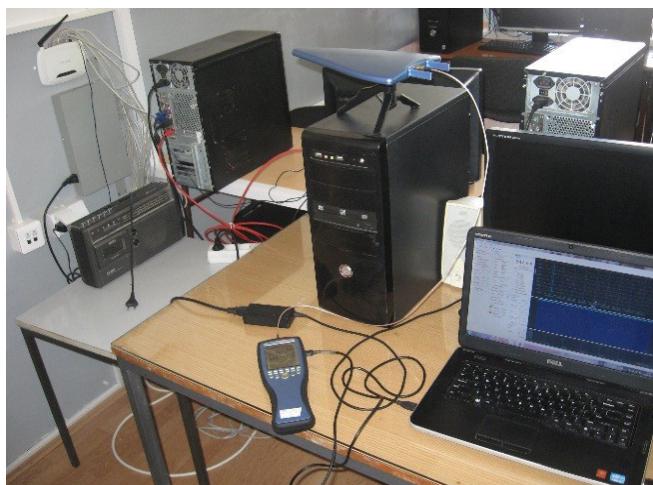


**Picture 2b.** Routers in different laboratories,  
TL-WR841HP in laboratory 2



Slika 2c. Ruteri u različitim laboratorijama,  
Mi AloT AC 1350 u laboratoriji 109

Svi ruteri na kojima su vršena merenja su radili na frekvenciji od 2,4 GHz. Sva merenja su realizovana u periodu od februara do septembra 2022. Minimalno trajanje svakog pojedinačnog merenja je bilo 6 minuta, u skladu sa standardima. Merenja su obuhvatala merenje jačine električnog polja, jačine magnetnog polja i elektromagnetne izloženosti. Ukupan broj realizovanih merenja po svakom ruteru je bio deset, pet po horizontali i pet po vertikali, sa razmakom od  $45^\circ$  u odnosu na horizontalnu i normalnu osu rutera. Merenja jačine električnog polja, jačine magnetnog polja i elektromagnetne izloženosti su realizovana tako što bi se instrument postavio u neki od navedenih položaja, na rastojanjima od po 1 cm, od 0 cm pa sve do 100 cm. Ukupan broj merenja za sve položaje je bio hiljadu. Ovo je urađeno čisto provere radi, iako su rezultati pokazali da su merene vrednosti na različitim rasto-



Slika 2d. Ruteri u različitim laboratorijama,  
TL-WR740N u laboratoriji 110

janjima vezano za različite položaje bili skoro identični. Sva meranja jačine električnog polja i jačine magnetnog polja uz pomoć instrumenta Spectran HF 60105 prikazani su na slikama 3a i 3b, a realizovana su prema uputstvu za upravljanje i merenje instrumentom, kao i korišćenjem softvera HFSS za proveru rezultata putem simulacije (11-14).

Karakteristična pozicija rutera u Elektrotehničkoj školi „Nikola Tesla“ u Nišu prikazana je na slici 4. Generalno, ruteri se postavljaju u prostorijama u tačkama gde će prijem signala biti najbolji ili gde uslovi instaliranja dozvoljavaju, a to su uglavnom lokacije ispod samog plafona ili uglovi plafona.

### Rezultati i diskusija

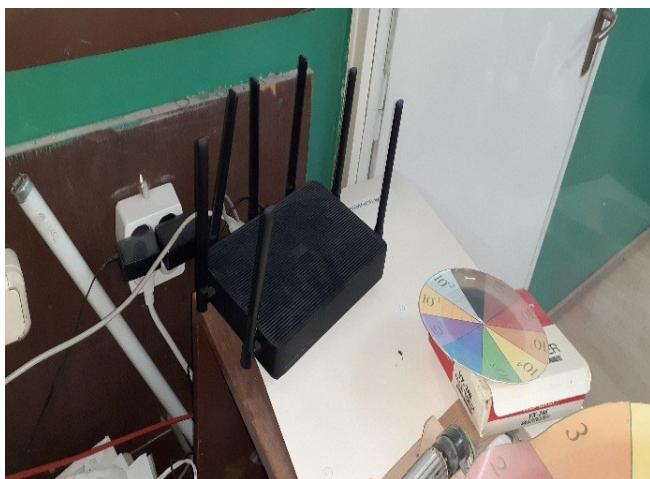
Primeri merenja jačine električnog polja i jačine magnetnog polja uz pomoć instrumenta Spectran HF 60105 prikazani su na slikama 3a i 3b,



Slika 3a. Primer merenja jačine električnog polja  
uz pomoć instrumenta Spectran HF 60105



Slika 3b. Primer merenja jačine električnog polja  
uz pomoć instrumenta Spectran HF 60105



**Picture 2c.** Routers in different laboratories, Mi AloT AC 1350 in laboratory 109



**Picture 2d.** Routers in different laboratories, TL-WR740N u in laboratory 110

with complete additional equipment is shown in Picture 1.

The measurements of high frequency electromagnetic radiation were carried out in four laboratories that were used most frequently at the Secondary School of Electrical Engineering "Nikola Tesla" in Niš: laboratories number 106 and 109 on the ground floor, laboratory number 110 on the first floor and laboratory number 2 on the second floor. Multiple measurements lasting at least 6 minutes were made horizontally and vertically from the router axis, in the range from 0 to 100 cm, in steps of 1 cm. Electromagnetic radiation was measured on four different types of routers depending on the laboratory where the research was conducted. The router located in laboratory 106 was TL-WR841N (Picture 2a), in laboratory 2 TL-WR841HP (Picture 2b), in laboratory 109 Mi

AloT AC 2350 (Picture 2c), and in laboratory 110 TL-WR740N (Picture 2d).

All the routers, on which the measurements were made, operated at a frequency of 2.4 GHz. All measurements were carried out from February to September 2022. The minimum duration of each individual measurement was 6 minutes, in accordance with the standards. The measurements included the measurements of the electric field strength, magnetic field strength and electromagnetic exposure. The total number of realized measurements for each router was ten, five horizontally and five vertically, with a distance of 45° in relation to the horizontal and normal axis of the router. The measurements of the electric field strength, magnetic field strength and electromagnetic exposure were realized by placing the instrument in one of these positions, at



**Picture 3a.** Example of measuring the electric field strength using the instrument Spectran HF 60105



**Picture 3b.** Example of measuring the electric field strength using the instrument Spectran HF 60105

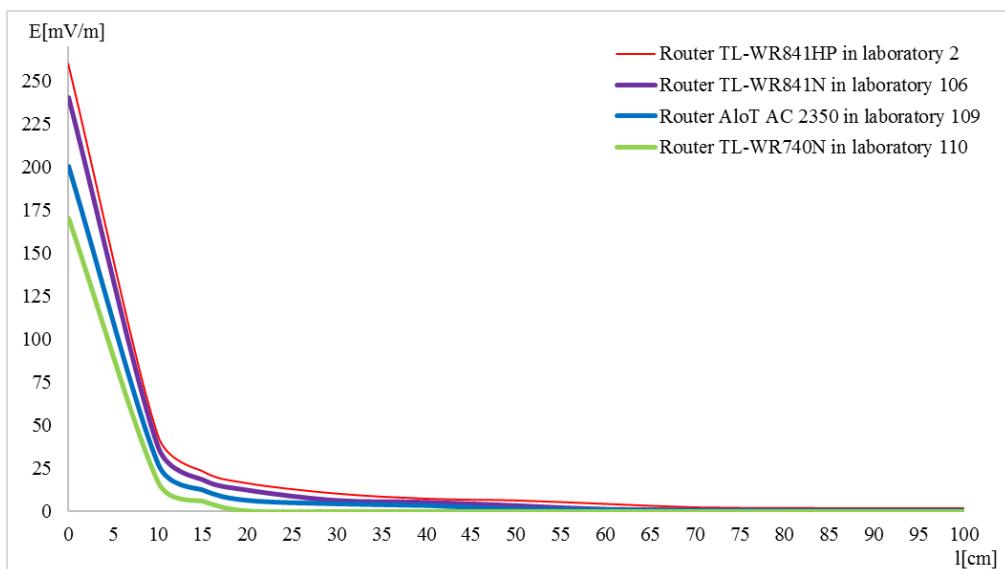


**Slika 4.** Karakteristična pozicija rutera (označena strelicom) na prvom spratu Elektrotehničke škole "Nikola Tesla" u Nišu

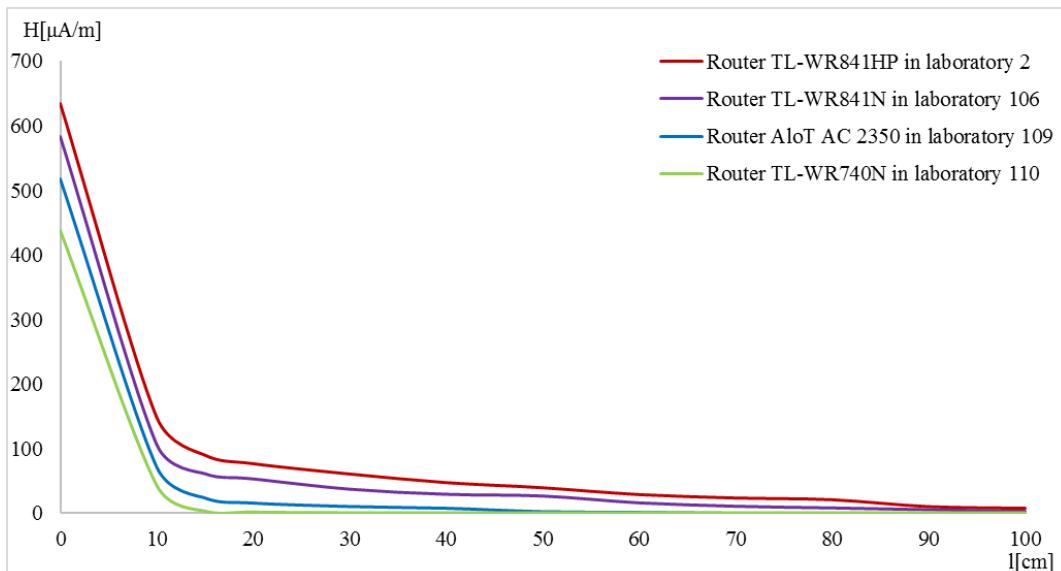
dok su kompletni rezultati jačine električnog polja, jačine magnetnog polja i elektromagnetne izloženosti prikazani na slikama 5-8.

Kada je u pitanju jačina električnog polja, rezultati prikazani na slici 5 su pokazali da su izmerene jačine električnog polja bile daleko ispod granične vrednosti za jačinu električnog polja u skladu sa važećim standardima ( $E = 61 \text{ V/m}$  za frekvencije veće od 2000 MHz, u skladu sa ICNIRP). Važno je napomenuti da je najmanja udaljenost od rutera (za sva četiri rutera) bila 1,2 metra, tako da je izračunata izloženost bila svega nekoliko mV/m, što je više od dvesta puta manja vrednost u odnosu na graničnu vrednost.

Kada je u pitanju jačina magnetnog polja, rezultati prikazani na slici 6 su pokazali da su izmerene



**Slika 5.** Kompletni rezultati merenja jačine električnog polja za sve rutere



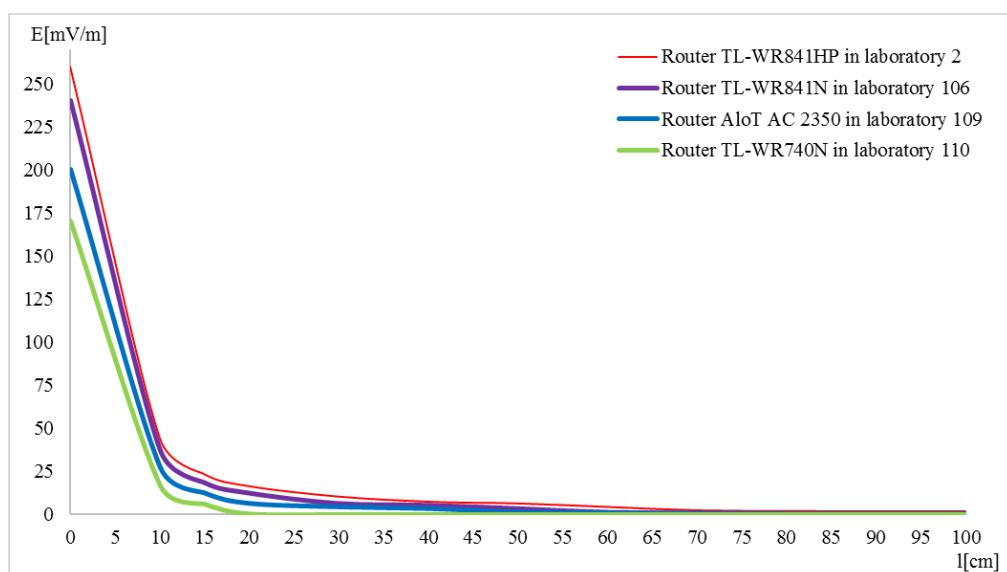
**Slika 6.** Kompletni rezultati merenja jačine magnetnog polja za sve rutere



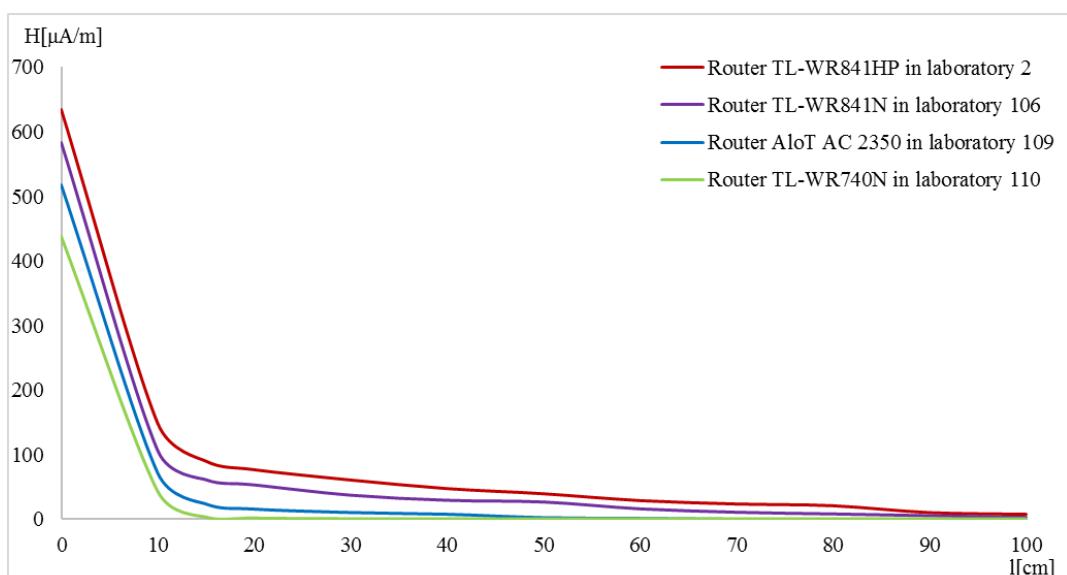
**Picture 4.** Characteristic position of router (marked with an arrow) on the first floor of the Secondary School of Electrical Engineering "Nikola Tesla" in Niš

distances of 1 cm, from 0 cm to 100 cm. The total number of measurements for all positions was one thousand. This was done purely for verification, although the results showed that the measured results at different distances for different positions were almost identical. All measurements of the electric field strength and magnetic field strength with the help of the Spectran HF 60105 instrument were shown in Pictures 3a and 3b, and they were realized according to the instructions for operating and measuring with the instrument, as well as using the HFSS software for checking the results with the help of simulation (11-14).

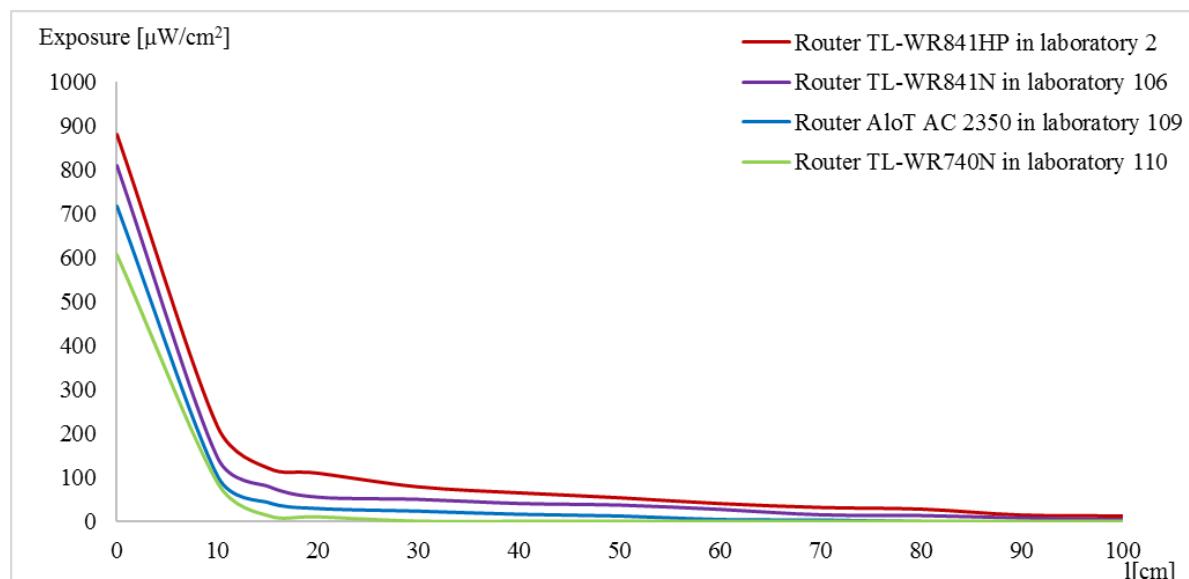
The characteristic position of router at the Secondary School of Electrical Engineering "Nikola Tesla" in Niš was shown in Picture 4. Generally,



**Picture 5.** Complete results of measurements of the electric field strength for all routers



**Picture 6.** Complete results of measurements of the magnetic field strength for all routers



Slika 7. Kompletni rezultati merenja elektromagnetske izloženosti za sve ruter.

jačine magnetnog polja bile daleko ispod graničnih vrednosti za jačinu električnog polja u skladu sa važećim standardima ( $H = 0,16 \text{ A/m}$  za frekvencije veće od 2000 MHz, u skladu sa ICNIRP). Najveća izmerena vrednost bila je više od dvesta puta manja u odnosu na graničnu vrednost.

Kada je u pitanju elektromagnetska izloženost, rezultati prikazani na slici 7 su pokazali da su izmerene jačine magnetnog polja bile daleko ispod granične vrednosti za jačinu električnog polja u skladu sa važećim standardima (elektromagnetska izloženost je  $5 \text{ mW/cm}^2$  za frekvencije veće od 1500 MHz u skladu sa IEEE C95.1). Najveća izmerena vrednost je bila daleko manja u odnosu na graničnu vrednost za vreme izlaganja od 6 minuta.

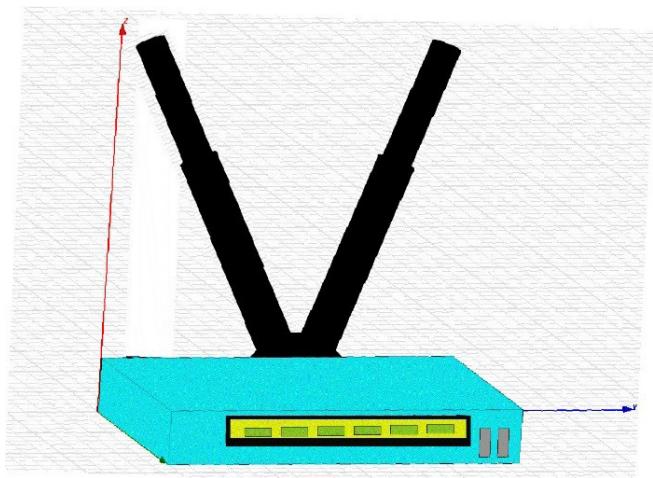
U cilju provere ostvarenih rezultata, urađena je simulacija jačine električnog polja i jačine magnetnog polja u softveru HFSS 10 za ruter TL-WR841HP. HFSS 10 je softver koji se koristi za proračun prođora visokofrekventnog elektromagnetskog zračenja kroz višeslojna okruženja. Ovaj softver omogućava simulaciju različitih elektronskih proizvoda, kao što su antene, komponente, konektori itd. Na tržištu je bilo nekoliko verzija ovog softvera. Zbog složenosti softvera za simulaciju i ograničenja papira, samo je simulacioni model ruteru TL-WR841HP korišćen kao primer za proveru. Simulacioni model ruteru TL-WR841HP u HFSS 10 prikazan je na slici 8, dok su uporedni rezultati za izmerene simulacije jačine električnog polja i jačine magnetnog polja prikazani na slikama 9a i 9b.

Simulacije su pokazale da su ostvareni rezultati simulacije za jačinu električnog polja i jačinu mag-

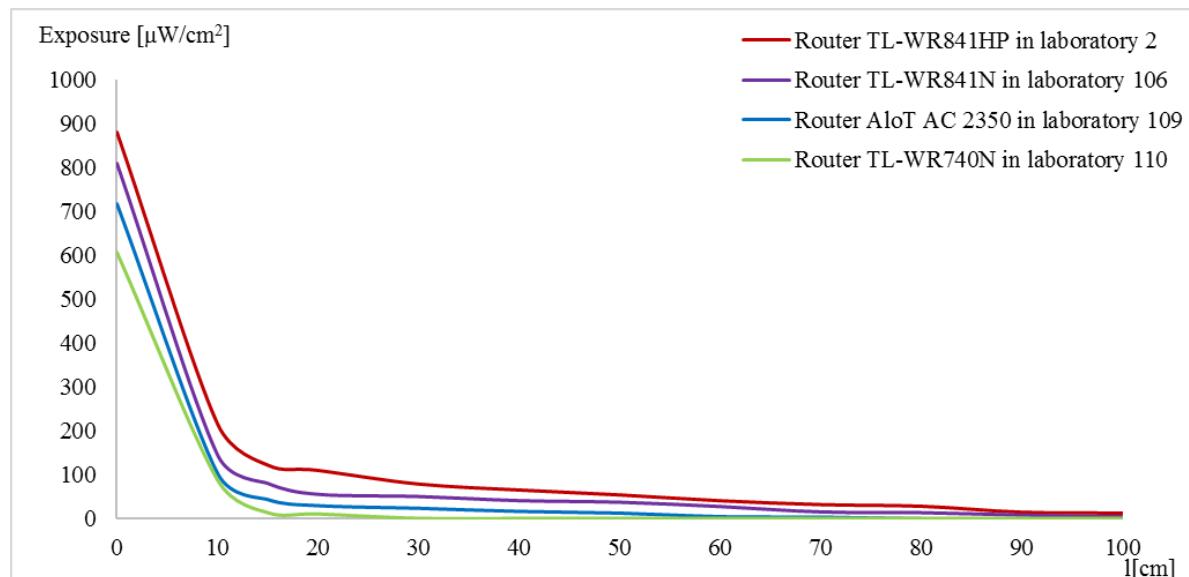
netnog polja nešto niži od rezultata dobijenih direktnim merenjem. Ovo je bilo očekivano zato što simulacija nije podrazumevala dodatno zračenje koje potiče od razvodne kutije, računara u učionici i drugih vrsta zračenja.

Slična ranija merenja realizovana na ruterima u školama su pokazala slične rezultate sa neznatnim razlikama (2,18). To znači da elektromagnetsko zračenje ruteru u učionicama u kojima su ruteri smešteni ne predstavlja opasnost za učenike kada su u pitanju izmerene vrednosti u poređenju sa odgovarajućim standardima.

Značaj ovakvog merenja je veoma veliki. Zbog činjenice da se nivo zračenja stalno povećava, važno je imati u vidu zračenje u smislu jačine zračenja, njegove učestalosti i izloženosti u radnoj i životnoj



Slika 8. Simulacioni model ruteru TL-WR841HP u HFSS softveru



**Picture 7.** Complete results of measurements of electromagnetic exposure for all routers

routers are placed in rooms at points where the signal reception will be the best and where the installation conditions allow, and these are generally locations under the ceiling or in the corners of the ceiling.

## Results and Discussion

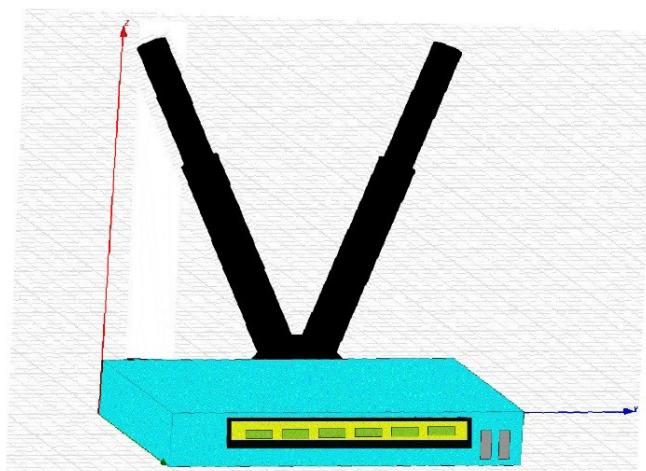
The examples of measurements of the electric field strength and magnetic field strength using the Spectran HF 60105 are shown in Pictures 3a and 3b, while the complete results of electric field strength, magnetic field strength and electromagnetic exposure are shown in Pictures 5-8.

When it comes to the electric field strength, the results shown in Picture 5 showed that the measured electric field strength was far below the limit value for the electric field strength in accordance with current standards ( $E = 61 \text{ V/m}$  for frequencies higher than 2000 MHz, in accordance with the ICNIRP). It is important to note that the smallest distance from the router (for all four routers) was 1.2 meters, so the calculated exposure was only a few mV/m, which is more than two hundred times lower than the limit value.

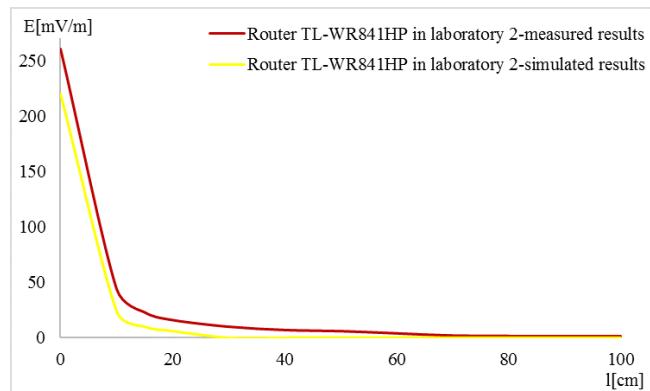
When it comes to the magnetic field strength, the results shown in Picture 6 showed that the measured magnetic field strength was far below the limit values for the electric field strength in accordance with the current standards ( $H = 0.16 \text{ A/m}$  for frequencies higher than 2000 MHz, in accordance with the ICNIRP). The highest measured value was more than two hundred times lower than the limit value.

When it comes to electromagnetic exposure, the results shown in Picture 7 showed that the measured magnetic field strength was far below the limit value for electric field strength in accordance with current standards (electromagnetic exposure is  $5 \text{ mW/cm}^2$  for frequencies higher than than 1500 MHz in accordance with IEEE C95.1). The highest measured value was far lower than the limit value for the exposure time of 6 minutes.

In order to verify the achieved results, the simulation of the electric field strength and magnetic field strength was conducted with the help of the software HFSS 10 for the TL-WR841HP router. HFSS is software used to calculate the penetration of high frequency electromagnetic radiation through multilayered environments.



**Picture 8.** Simulation model of router TL-WR841HP in HFSS software



**Slika 9a.** Uporedni rezultati za jačinu električnog polja rutera TL-WR841HP

sredini. Na primer, 5G mreža za mobilne telefone će omogućiti mnogo brži protok informacija na višim frekvencijama, ali će takođe značiti i veće zračenje. Dakle, veoma je važno imati u vidu kolичinu zračenja i izloženost ljudi, a posebno dece tom zračenju (16-18).

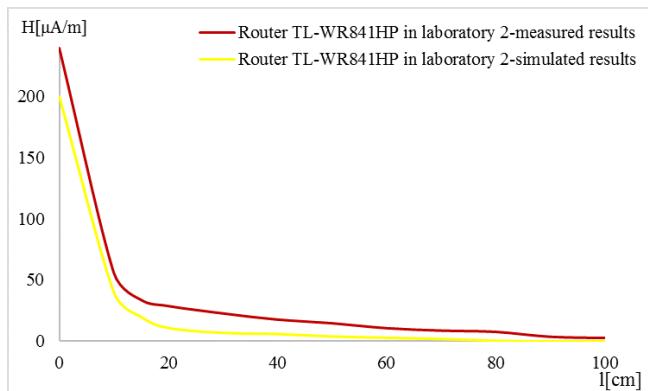
Buduća istraživanja bi trebalo da uključe stalno praćenje i merenje visokofrekventnog elektromagnetskog zračenja u cilju smanjenja zračenja, optimalne lokacije za antene, rutere i druge uređaje koji emituju zračenje. Takođe, trebalo bi da budu usmerena na poređenje elektromagnetnog zračenja na različitim frekvencijama. Na primer, u Elektrotehničkoj školi „Nikola Tesla“ u Nišu postavljena je još jedna mreža koja koristi frekvencije na 5 GHz. To podrazumeva korišćenje rutera na frekvencijama od 5 GHz. Postojanje dve mreže na različitim frekvencijama povećava nivo elektromagnetnog zračenja. Dakle, bilo bi veoma važno izmeriti iste vrednosti elektromagnetnog zračenja i uporediti ih sa izmerenim rezultatima, kao i sa važećim standardima. Takođe, buduća istraživanja bi morala da obuhvate merenje elektromagnetnog zračenja sistema koji koriste 5G tehnologiju.

## Zaključak

Sve veće prisustvo elektromagnetnog zračenja u radnoj i životnoj sredini zahteva stalno merenje i praćenje nivoa elektromagnetnog zračenja. Ovo bi moglo značajno poboljšati kvalitet radne i životne sredine, kao i kvalitet života i zdravlja ljudi i dece.

## Konflikt interesa

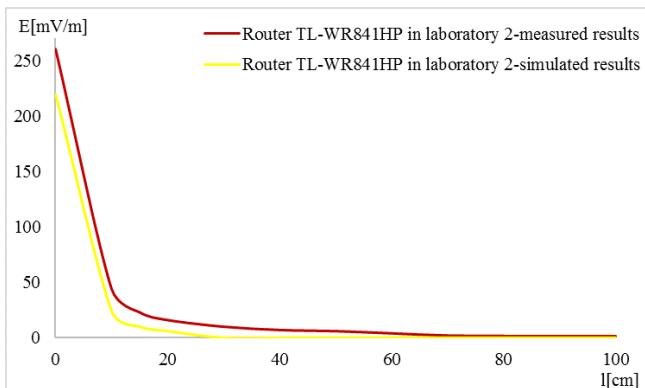
Autori su izjavili da nema konflikta interesa.



**Slika 9b.** Uporedni rezultati za jačinu električnog polja

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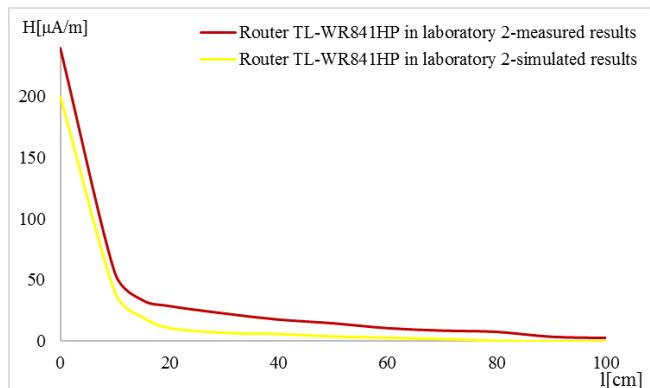
**Picture 9a.** Comparative results for the electric field strength of router TL-WR841HP

This software enables the simulation of various electronic products, such as antennas, components, connectors, etc. There were a few versions of this software on the market. Due to the complexity of the simulation software and paper limitations, only the simulation model of the TL-WR841HP router was used as a verification example. The simulation model of the TL-WR841HP router is shown in Picture 8, while the comparative results for the measured electric field strength and magnetic field strength simulations are shown in Pictures 9a and 9b.

The simulations showed that the simulation results for the electric field strength and magnetic field strength were slightly lower than the results obtained by direct measurement. This was expected because the simulation did not include additional radiation coming from the switch box, computers in the classroom and other types of radiation.

Similar earlier measurements that were carried out on routers in schools showed similar results with insignificant differences (2,18). This means that the electromagnetic radiation of the routers located in the classrooms does not pose a danger to the students when it comes to the measured values in comparison to the corresponding standards.

The significance of this measurement is very great. Due to the fact that the level of radiation is constantly increasing, it is important to consider radiation in terms of radiation strength, its frequency and exposure in the work and living environment. For example, 5G mobile phone network will enable much faster flow of information at higher frequencies, but it will also mean more radiation.



**Picture 9b.** Comparative results for the electric field strength

Therefore, it is very important to take into account the amount of radiation and the exposure of people, especially children, to that radiation (16-18).

Future research should include continuous monitoring and measurement of high frequency electromagnetic radiation in order to reduce radiation, as well as the optimal locations for antennas, routers and other radiation-emitting devices. Also, they should be aimed at comparing electromagnetic radiation at different frequencies. For example, at the Secondary School of Electrical Engineering "Nikola Tesla" in Niš, another network using 5 GHz frequencies has been installed. This implies the use of routers at 5 GHz frequencies. The existence of two networks at different frequencies increases the level of electromagnetic radiation. Therefore, it would be very important to measure the same values of electromagnetic radiation and compare them with the measured results, as well as with valid standards. Also, future research should include measuring the electromagnetic radiation of systems using 5G technology.

## Conclusion

The increasing presence of electromagnetic radiation in the working and living environment requires the constant measurement and monitoring of the level of electromagnetic radiation. This could significantly improve the quality of the working and living environment, as well as the quality of life and health of people and children.

## Competing interests

Authors declare no competing interests.

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