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

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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^2 (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 živelo sa T2D (6059/100.000) (7,8). Pokazano je da su različite komplikacije koje mogu nastupiti u sklopu T2D, povezane sa značajno većom učestalošću

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

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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^2 (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 jave 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 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

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 albuminurije, što kombinovanjem informacija, omo-

Tabela 1. Klasifikacija dijabetesa melitusa i hronične bolesti bubrega

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

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

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

b. Opis dodatnih brojeva u okviru četvoromesnih dijagnoza za šećernu bolest		
Broj	**Značenje u MKB-10 dijagnozi, srpski**	**Značenje u MKB-10 dijagnozi, latinski**
.0	Sa dijabetičnom komom bez ketoacidoze	Cum comato diabetico et sine ketoacidosi
.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

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

d. Kategorije jačine glomerulske filtracije (JGF) u hroničnoj bolesti bubrega prema KDIGO vodiču		
Kategorija	**JGF, ml/min/1.73m²**	**Opis**
G1	≥ 90	Oštećenje bubrega sa normalnom ili povećanom JGF
G2	60-89	Oštećenje bubrega sa blagim smanjenjem JGF
G3a	45-59	Oštećenje bubrega sa umerenim smanjenjem JGF
G3b	30-44	
G4	15-29	Teško smanjenje JGF
G5	< 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. Description of additional numbers in four-digit diagnostic codes for diabetes mellitus		
Number	**Meaning in ICD-10 diagnosis, English**	**Meaning in ICD-10 diagnosis, Latin**
.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

c. Three-digit and four-digit ICD-10 diagnoses relating to chronic kidney disease - meaning		
Code according to ICD-10	**ICD-10 diagnosis**	**Description of kidney damage and values of glomerular filtration rate (GFR)**
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

d. Categories of glomerular filtration rate(GFR) in chronic kidney disease according to KDIGO Guidelines		
Category	**GFR, ml/min/1.73m²**	**Description**
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 – 10th 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.

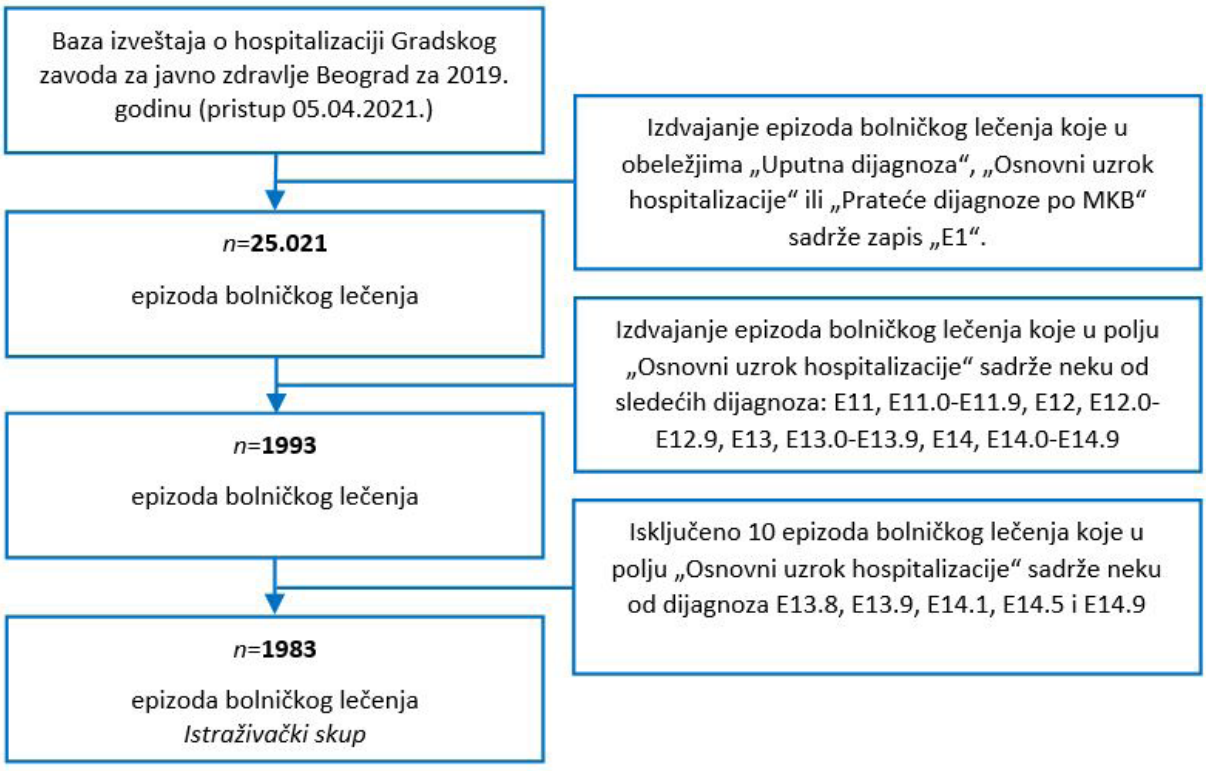
According to the recommendations of KDIGO Guidelines for the evaluation and classification

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 lečenja (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

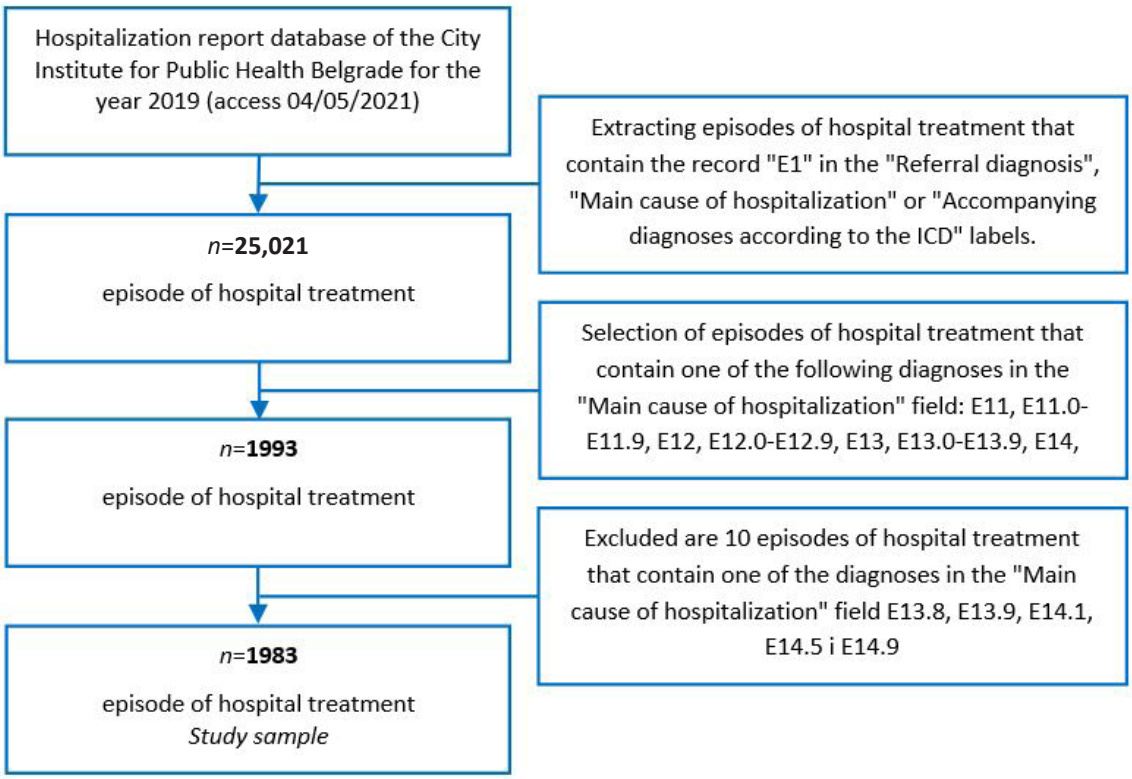


Grafikon 1. Formiranje istraživačkog skupa

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 razlika 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), medijana 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)
Ukupno	209 (10,6)	9 (0,45)

"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 (%)
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)
Total	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
Ukupno (%)	1936 (97,6)	47 (2,4)	1983 (100)	

*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 grupa 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 grupa 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)	1,000
Ostali bez N18.1	1927 (97,6)	47 (2,4)	
N18.2	79 (100,0)	1 (6,3)	0,320
Ostali bez N18.2	1857 (97,5)	46 (2,3)	
N18.3	79 (100,0)	0 (0,0)	0,259
Ostali bez N18.3	1857 (97,5)	47 (2,5)	
N18.4	10 (76,9)	3 (23,1)	0,003
Ostali bez N18.4	1926 (97,8)	44 (2,2)	
N18.5	9 (90,0)	1 (10,0)	0,214
Ostali bez N18.5	1927 (97,7)	46 (2,3)	
N18.9	9 (90,0)	4 (4,9)	0,127
Ostali bez N18.9	1927 (97,7)	43 (2,3)	

*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*
	$\bar{x}$	SD	
Ne	63,93	11,75	
Da	71,36	9,33	p < 0,001

$\bar{x}$ - 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
Total (%)	1936 (97.6)	47 (2.4)	1983 (100)	

*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)	1.000
Others without N18.1	1927 (97.6)	47 (2.4)	
N18.2	79 (100.0)	1 (6.3)	0.320
Others without N18.2	1857 (97.5)	46 (2.3)	
N18.3	79 (100.0)	0 (0.0)	0.259
Others without N18.3	1857 (97.5)	47 (2.5)	
N18.4	10 (76.9)	3 (23.1)	0.003
Others without N18.4	1926 (97.8)	44 (2.2)	
N18.5	9 (90.0)	1 (10.0)	0.214
Others without N18.5	1927 (97.7)	46 (2.3)	
N18.9	9 (90.0)	4 (4.9)	0.127
Others without N18.9	1927 (97.7)	43 (2.3)	

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

x̄ - 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 dijagnozama 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
Ukupno (%)	961 (48,5)	47 (51,5)	1983 (100)	

*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*
	x̄	SD	
N18.1	70.78	11.83	0.103
Others without N18.1	64.61	11.74	
N18.2	69.00	6.75	0.121
Others without N18.2	64.60	11.77	
N18.3	72.01	8.37	< 0.001
Others without N18.3	64.33	11.77	
N18.4	71.62	11.56	0.013
Others without N18.4	64.59	11.73	
N18.5	66.90	13.77	0.391
Others without N18.5	64.63	11.74	
N18.9	71.52	9.74	< 0.001
Others without N18.9	64.34	11.73	

x̄ - 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
Total (%)	961 (48.5)	47 (51.5)	1983 (100)	

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

*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 ml/min/1.73m^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 objašenjenje 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)	0.747**
Others without N18.1	956 (48.2)	1018 (51.3)	
N18.2	5 (0.3)	11 (0.5)	0.167*
Others without N18.2	956 (48.2)	1011 (51.0)	
N18.3	38 (1.9)	41 (2.0)	0.948*
Others without N18.3	923 (46.5)	981 (49.6)	
N18.4	10 (0.5)	3 (0.1)	0.039*
Others without N18.4	951 (48.0)	1019 (51.4)	
N18.5	8 (0.4)	2 (0.1)	0.058**
Others without N18.5	953 (48.0)	1020 (51.5)	
N18.9	55 (2.8)	27 (1.4)	0.001*
Others without N18.9	906 (45.8)	995 (50.2)	

*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 adekvatnijem 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 dijagnoza. 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 zastupljenošću muškog pola.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

Literatura

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter. Suppl. 2013; 3:1–150. doi:10.1038/kisup.2012.77 Dostupno na: https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf Poslednji pristup stranici: 05.06.2022.
2. Republička stručna komisija za izradu i implementaciju vodiča dobre kliničke prakse.Nacionalni vodič dobre kliničke prakse za prevenciju, dijagnostikovanje i lečenje hronične bolesti bubrega. Beograd: Agencija za akreditaciju zdravstvenih ustanova Srbije; 2013. Dostupno na: https://www.zdravlje.gov.rs/view_file.php?file_id=536&cache=srPoslednji pristup stranici: 05.06.2022.
3. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet 2017; 389(10075):1238-1252. doi: 10.1016/S0140-6736(16)32064-5.
4. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. Am J Kidney Dis 2012; 60(5):850-886. doi: 10.1053/j.ajkd.2012.07.005.
5. Afkarian M, Zelnick LR, Hall YN, Heagerty PJ, Tuttle K, Weiss NS, de Boer IH. Clinical Manifestations of Kidney Disease Among US Adults With Diabetes, 1988-2014. JAMA 2016; 316(6):602-10. doi: 10.1001/jama.2016.10924.
6. Doshi SM, Friedman AN. Diagnosis and Management of Type 2 Diabetic Kidney Disease. Clin J Am Soc Nephrol 2017; 12(8):1366-1373. doi: 10.2215/CJN.11111016.
7. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrol 2016; 12(2):73-81. doi: 10.1038/nrneph.2015.173.
8. Basith Khan MA, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends.J Epidemiol Glob Health 2020; 10(1):107-111. doi:10.2991/jegh.k.191028.001.
9. Yoo H, Choo E, Lee S. Study of hospitalization and mortality in Korean diabetic patients using the diabetes complications severity index. BMC Endocr Disord 2020; 20(1):122. doi: 10.1186/s12902-020-00605-5.
10. Papazafiropoulou A, Tentolouris N, Bousboulas S, Sotiropoulos A, Tamvakos E, Peppas T, Kardara M, Pappas S. In-hospital mortality in a tertiary referral hospital: causes of death and comparison between patients with and without diabetes. Exp Clin Endocrinol Diabetes 2010; 118(5):315-9. doi: 10.1055/s-0029-1241215.

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^2) 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.

11. Zelada H, Bernabe-Ortiz A, Manrique H. Inhospital Mortality in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study in Lima, Peru. J Diabetes Res 2016; 2016:7287215. doi: 10.1155/2016/7287215.
12. Atamari-Anahui N, Martinez-Ninanqui FW, Paucar-Tito L, Morales-Concha L, Miranda-Chirau A, Gamarra-Contreras MA et al. Factors associated to inpatient mortality rates in type-2-diabetic patients: a cross-sectional analytical study in three Peruvian hospitals. Medwave 2017; 17(9):e7097. doi:10.5867/medwave.2017.09.7097.
13. Schrauben SJ , Chen HY, Lin E, Jepson C, Yang W, Scialla JJ et al. Hospitalizations among adults with chronic kidney disease in the United States: A cohort study. PLoS Med 2020; 17(12):e1003470. doi: 10.1371/journal.pmed.1003470.
14. Birkeland KI, Bodegard J, Eriksson JW, Norhammar A, Haller H, Linssen GCM et al. Heart failure and chronic kidney disease manifestation and mortality risk associations in type 2 diabetes: A large multinational cohort study. Diabetes Obes Metab 2020; 22(9):1607-1618. doi: 10.1111/dom.14074.
15. Calvo-Hueros JI, Martín-Hidalgo-Barquero MV, Morales-Gabardino JA, Buitrago F. Chronic kidney disease prevalence and cardiovascular risk in a cohort of patients with type 2 diabetes followed for 10 years in Badajoz (Spain). An observational study. Prim Care Diabetes 2021; 15(2):391-396. doi: 10.1016/j.pcd.2020.11.015.
16. Quiroga B, Verdalles U, Reque J, García de Vinuesa S, Goicoechea M, Luño J. Cardiovascular events and mortality in chronic kidney disease (stages I-IV). Nefrologia. 2013;33(4):539-45. doi: 10.3265/Nefrologia.pre2013.May.11895.
17. Migdalis IN, Papanas N, Raptis AE, Ioannidis IM, Sotiropoulos AE, Dimitriadis GD, Hellenic Diabetic Nephropathy Study (HDNS) Group. The prevalence of diabetic chronic kidney disease in adult Greek subjects with type 2 diabetes mellitus: A series from hospital-based diabetes clinics. Diabetes Res Clin Pract 2020; 166:108243.,doi: 10.1016/j.diabres.2020.108243.
18. hen Y, Cai R, Sun J, Dong X, Huang R, Tian S et al. Diabetes mellitus as a risk factor for incident chronic kidney disease and end-stage renal disease in women compared with men: a systematic review and meta-analysis. Endocrine 2017; 55(1):66-76. doi: 10.1007/s12020-016-1014-6.
19. Satyavani K, Kothandan H, Jayaraman M, Viswanathan V. Direct costs associated with chronic kidney disease among type 2 diabetic patients in India. Indian J Nephrol 2014; 24(3):141-7. doi: 10.4103/0971-4065.132000.
20. Gülümsek E, Keşkek SO. Direct medical cost of nephropathy in patients with type 2 diabetes. Int Urol Nephrol 2022; 54(6):1383-1389. doi: 10.1007/s11255-021-03012-4.
21. Zakon o zdravstvenoj dokumentaciji i evidencijama u oblasti zdravstva, „Službeni glasnik RS“, br. 123/2014-2, 106/2015-65, 105/2017-32, 25/2019-3.
22. Pravilnik o obrascima i sadržaju obrazaca za vođenje zdravstvene dokumentacije, evidencija, izveštaja, registara i elektronskog medicinskog dosijea, „Službeni glasnik RS“109/2016-35, 20/2019-205.
23. Uputstvo za popunjavanje izveštaja o hospitalizaciji (Obrazac br. 3-21-61/62/65-Sr.), Institut za javno zdravlje Srbije „Dr Milan Jovanovć Batut“, Beograd, 17.06.2019.
24. Svetska zdravstvena organizacija (SZO). Međunarodna statistička klasifikacija bolesti i srodnih zdravstvenih problema, deseta revizija, srpsko izdanje 2010.Beograd: IZJZS „Dr Milan Jovanović Batut“, 2010. Poslednji pristup stranici: 05.06.2022.
25. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. JAMA. 2019; 322(13):1294-1304. doi: 10.1001/jama.2019.14745.
26. Currie CJ, Berni ER, Berni TR, Jenkins-Jones S, Sinsakul M, Jermutus L et al. Major adverse cardiovascular events in people with chronic kidney disease in relation to disease severity and diabetes status. PLoS One 2019; 14(8):e0221044. doi: 10.1371/journal.pone.0221044.
27. Wan EYF, Chin WY, Yu EYT, Wong ICK, Chan EWY, Li SX, Cheung NKL, Wang Y, Lam CLK. The Impact of Cardiovascular Disease and Chronic Kidney Disease on Life Expectancy and Direct Medical Cost in a 10-Year Diabetes Cohort Study. Diabetes Care 2020; 43(8):1750-1758. doi: 10.2337/dc19-2137.
28. Low SK, Sum CF, Yeoh LY, Tavintharan S, Ng XW, Lee SB, Tang WE, Lim SC. Prevalence of Chronic Kidney Disease in Adults with Type 2 Diabetes Mellitus. Ann Acad Med Singap. 2015; 44(5):164-71.

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Literature

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter., Suppl. 2013; 3:1–150. doi:10.1038/kisup.2012.77 Dostupno na: https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf Poslednji pristup stranici: 05.06.2022.
2. Republička stručna komisija za izradu i implementaciju vodiča dobre kliničke prakse.Nacionalni vodič dobre kliničke prakse za prevenciju, dijagnostikovanje i lečenje hronične bolesti bubrega. Beograd: Agencija za akreditaciju zdravstvenih ustanova Srbije; 2013. Dostupno na: https://www.zdravlje.gov.rs/view_file.php?file_id=536&cache=srPoslednji pristup stranici: 05.06.2022.
3. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet. 2017; 389(10075):1238-1252. doi: 10.1016/S0140-6736(16)32064-5.
4. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. Am J Kidney Dis 2012; 60(5):850-886. doi: 10.1053/j.ajkd.2012.07.005.
5. Afkarian M, Zelnick LR, Hall YN, Heagerty PJ, Tuttle K, Weiss NS, de Boer IH. Clinical Manifestations of Kidney Disease Among US Adults With Diabetes, 1988-2014. JAMA 2016; 316(6):602-10. doi: 10.1001/jama.2016.10924.
6. Doshi SM, Friedman AN. Diagnosis and Management of Type 2 Diabetic Kidney Disease. Clin J Am Soc Nephrol 2017; 12(8):1366-1373. doi: 10.2215/CJN.11111016.
7. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrols 2016; 12(2):73-81. doi: 10.1038/nrneph.2015.173.
8. Basith Khan MA, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global Burden of Disease and Forecasted Trends.J Epidemiol Glob Health 2020; 10(1):107-111. doi:10.2991/jegh.k.191028.001.
9. Yoo H, Choo E, Lee S. Study of hospitalization and mortality in Korean diabetic patients using the diabetes complications severity index. BMC Endocr Disord 2020; 20(1):122. doi: 10.1186/s12902-020-00605-5.
10. Papazafiropoulou A, Tentolouris N, Bousboulas S, Sotiropoulos A, Tamvakos E, Peppas T, Kardara M, Pappas S. In-hospital mortality in a tertiary referral hospital: causes of death and comparison between patients with and without diabetes. Exp Clin Endocrinol Diabetes 2010; 118(5):315-9. doi: 10.1055/s-0029-1241215.
11. Zelada H, Bernabe-Ortiz A, Manrique H. Inhospital Mortality in Patients with Type 2 Diabetes Mellitus: A Prospective Cohort Study in Lima, Peru. J Diabetes Res 2016; 2016:7287215. doi: 10.1155/2016/7287215.
12. Atamari-Anahui N, Martinez-Ninanqui FW, Paucar-Tito L, Morales-Concha L, Miranda-Chirau A, Gamarra-Contreras MA et al. Factors associated to inpatient mortality rates in type-2-diabetic patients: a cross-sectional analytical study in three Peruvian hospitals. Medwave 2017; 17(9):e7097. doi:10.5867/medwave.2017.09.7097.
13. Schrauben SJ , Chen HY, Lin E, Jepson C, Yang W, Scialla JJ et al. Hospitalizations among adults with chronic kidney disease in the United States: A cohort study. PLoS Med 2020;17(12):e1003470. doi: 10.1371/journal.pmed.1003470.
14. Birkeland KI, Bodegard J, Eriksson JW, Norhammar A, Haller H, Linssen GCM et al. Heart failure and chronic kidney disease manifestation and mortality risk associations in type 2 diabetes: A large multinational cohort study. Diabetes Obes Metab 2020; 22(9):1607-1618. doi: 10.1111/dom.14074.
15. Calvo-Hueros JI, Martín-Hidalgo-Barquero MV, Morales-Gabardino JA, Buitrago F. Chronic kidney disease prevalence and cardiovascular risk in a cohort of patients with type 2 diabetes followed for 10 years in Badajoz (Spain). An observational study. Prim Care Diabetes 2021; 15(2):391-396. doi: 10.1016/j.pcd.2020.11.015.
16. Quiroga B, Verdalles U, Reque J, García de Vinuesa S, Goicoechea M, Luño J. Cardiovascular events and mortality in chronic kidney disease (stages I-IV). Nefrologia 2013; 33(4):539-45. doi: 10.3265/Nefrologia.pre2013.May.11895.
17. Migdalis IN, Papanas N, Raptis AE, Ioannidis IM, Sotiropoulos AE, Dimitriadis GD, Hellenic Diabetic Nephropathy Study (HDNS) Group. The prevalence of diabetic chronic kidney disease in adult Greek subjects with type 2 diabetes mellitus: A series from hospital-based diabetes clinics. Diabetes Res Clin Pract 2020; 166:108243. doi: 10.1016/j.diabres.2020.108243.
18. hen Y, Cai R, Sun J, Dong X, Huang R, Tian S et al. Diabetes mellitus as a risk factor for incident chronic kidney disease and end-stage renal disease in women compared with men: a systematic review and meta-analysis. Endocrine. 2017; 55(1):66-76. doi: 10.1007/s12020-016-1014-6.
19. Satyavani K, Kothandan H, Jayaraman M, Viswanathan V. Direct costs associated with chronic kidney disease among type 2 diabetic patients in India. Indian J Nephrol. 2014; 24(3):141-7. doi: 10.4103/0971-4065.132000.
20. Gülümsek E, Keşkek SO. Direct medical cost of nephropathy in patients with type 2 diabetes. Int Urol Nephrol 2022; 54(6):1383-1389. doi: 10.1007/s11255-021-03012-4.
21. Zakon o zdravstvenoj dokumentaciji i evidencijama u oblasti zdravstva, „Službeni glasnik RS“, br. 123/2014-2, 106/2015-65, 105/2017-32, 25/2019-3.
22. Pravilnik o obrascima i sadržaju obrazaca za vođenje zdravstvene dokumentacije, evidencija, izveštaja, registara i elektronskog medicinskog dosijea, „Službeni glasnik RS“109/2016-35, 20/2019-205.
23. Uputstvo za popunjavanje izveštaja o hospitalizaciji (Obrazac br. 3-21-61/62/65-Sr.), Institut za javno zdravlje Srbije „Dr Milan Jovanovć Batut“, Beograd, 17.06.2019.
24. Svetska zdravstvena organizacija (SZO). Međunarodna statistička klasifikacija bolesti i srodnih zdravstvenih problema, deseta revizija, srpsko izdanje 2010.Beograd: IZJZS „Dr Milan Jovanović Batut“, 2010. Poslednji pristup stranici05.06.2022.

25. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. JAMA 2019; 322(13):1294-1304. doi: 10.1001/jama.2019.14745.

26. Currie CJ, Berni ER, Berni TR, Jenkins-Jones S, Sinsakul M, Jermutus L et al. Major adverse cardiovascular events in people with chronic kidney disease in relation to disease severity and diabetes status. PLoS One 2019; 14(8):e0221044. doi: 10.1371/journal.pone.0221044.

27. Wan EYF, Chin WY, Yu EYT, Wong ICK, Chan EWY, Li SX, Cheung NKL, Wang Y, Lam CLK. The Impact of Cardiovascular Disease and Chronic Kidney Disease on Life Expectancy and Direct Medical Cost in a 10-Year Diabetes Cohort Study. Diabetes Care 2020; 43(8):1750-1758. doi: 10.2337/dc19-2137.

28. Low SK, Sum CF, Yeoh LY, Tavintharan S, Ng XW, Lee SB, Tang WE, Lim SC. Prevalence of Chronic Kidney Disease in Adults with Type 2 Diabetes Mellitus. Ann Acad Med Singap 2015; 44(5):164-71.

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