

Epidemija malih boginja u Kraljevu, Srbija, 2017/2018

Snežana B. Knežević¹, Ljiljana P. Đurović¹,
Vladan D. Šaponjić², Verica D. Đukić², Nadica P. Radonjić²

¹Dom zdravlja Kraljevo

²Zavod za javno zdravlje, Kraljevo, Srbija

Measles outbreak in Kraljevo, Serbia 2017/2018

Snežana B. Knežević¹, Ljiljana P. Djurovic¹,
Vladan D. Šaponjić², Verica D. Djukic², Nadica P. Radonjić²

¹Primary Health care Center, Kraljevo

²Public health institute, Kraljevo, Serbia

Sažetak

Uvod. Male boginje su visokokontagiozna bolest koja širom sveta predstavlja značajan problem javnog zdravlja. U 14 evropskih zemalja su endemska bolest, uključujući i Srbiju.

Cilj rada. Prikaz epidemioloških karakteristika epidemije malih boginja, u odnosu na starost, pol, vakcinalni status, komplikacije i hospitalizaciju obolelih na teritoriji Kraljeva.

Metod. Retrospektivna epidemiološka studija pojedinačnih prijava malih boginja, zvaničnih izveštaja Zavoda za javno zdravlje i Doma zdravlja Kraljevo.

Rezultati. U periodu 30.10.2017.- 27.03.2018. godine obolelo je 243 od malih boginja, 135 (56%) žena i 108 (44%) muškaraca, ($p=0,127$). Prva dva slučaja su prijavljena 30.10.2017. nakon što su ostvarila kontakt sa obolelima u Prištini. Vrh epidemije je bio u decembru 2017. godine. Najviše je bilo obolelih od 30 do 49 godina, 147 (60,5%). Bolest je laboratorijski potvrđena kod 15 osoba. Dve doze vakcine je primilo 30 (12,3%) pacijenata, ostali su nepotpuno vakcinisani ili nepoznatog vakcinalnog statusa. Komplikacije je imalo 48 obolelih, statistički značajno više u grupi 1-4 godine ($p=0,0004$); pneumonije 12,3%, dijareju 6,6%, upalu srednjeg uha 1,6%. Smrtni slučajevi nisu prijavljeni tokom epidemije malih boginja u Kraljevu. Obolelo je 40 (16,5%) zdravstvenih radnika i drugi zaposleni u zdravstvenim ustanovama.

Zaključak. Imunizacija sa dve doze vakcine sa obuhvatom najmanje 95% opšte populacije, jedina je efikasna preventivna mera protiv malih boginja. U primarnoj zdravstvenoj zaštiti sve sumnjive slučajeve treba prepoznati, otkriti, prijaviti i istražiti kako bi se, što je pre moguće, prekinuli lanci prenosa virusa. Neophodno je sprovođenje propisanih protivepidemijskih mera i saradnja izabranih lekara i specijalista epidemiologije.

Ključne reči: epidemija, imunizacija, eliminacija, preporuke

Abstract

Introduction: Measles is a very contagious, infectious disease. It is a humongous health problem all over the world. It is an endemic disease in 14 European countries, including Serbia.

Objective: Review of epidemiologic characteristics of a measles epidemic in relation to age, gender, vaccination status, complications and hospitalizations of the diseased in Kraljevo area.

Method: Retrospective epidemiologic study of the individual illness reports, official reports of the Public health institute and Primary Health care Center, Kraljevo.

Results: During the period from October, 30th 2017 to March 27th, 2017, 243 persons fell ill with measles of whom 135 (56%) were women, and 108 (44%) were men ($p=0,127$). The first two cases were reported on October, 30th 2017. after they've been in contact with the diseased persons in Priština. The outbreak peak was in Decembre, 2017. The majority of the diseased were aged 30-49, 147 (60.5%). The illness was confirmed in the lab, in 15 persons. 30 (12.3%) people received two vaccine doses, while the rest were either incompletely vaccinated or of the unknown vaccination status. Complications appeared in 48 patients, and it was statistically significant in the age group 1-4 ($p=0.0004$). Complications were pneumonia 12.3%, diarrhea 6.6%, otitis media 1.6%. There were no death outcomes during the measles outbreak in Kraljevo. There were 40 (16.5%) diseased health workers and other health personnel.

Conclusion: Immunization with two vaccine doses, which would include at least 95% of the general population, is the only effective preventive measure against measles. All the suspicious disease cases should be recognized, detected, reported and investigated in order to disrupt the viral breach, as soon as possible. It is necessary to undertake the anti-epidemic measures and enable adequate cooperation between general physicians (GPs) and epidemiologists.

Keywords: disease outbreak, immunization, elimination, recommendations

Correspondence to:

Snežana B. Knežević
Dom zdravlja Kraljevo
lesta59@yahoo.com

Увод

Male boginje su visokokontagiozna bolest uzrokovana virusom malih boginja (rod *Morbillivirus*, porodica *Paramyxoviridae*). Virus je prečnika 150 nm-300 nm, jezgro virusa sadrži jednolančanu RNA. Postoji samo jedan antigenski tip virusa malih boginja. Poreklo reči male boginje verovatno potiče od srednjovekovne latinske reči *miser*, što znači jedno (engl. *measles*). Istorijski, epidemije malih boginja su često bile *ubice* dece i poznato je da su promenile tok istorije. Većina smrtnih slučajeva se još uvek javlja kod novorođenčadi i male dece koja žive u zemljama u razvoju¹.

Smatra se da je virus malih boginja evoluirao od predaka kao zoonoza, praistorijski domaćin je bio pas u zajednicama u kojima su stoka i ljudi živeli u neposrednoj blizini. Virus je počeo da cirkuliše među ljudima pre 5.000-10.000 godina, kada se ljudska populacija omasovila duž dolina reka na Srednjem istoku. Ne postoje latentne ili perzistentne infekcije virusom malih boginja koje dovode do produžene zaraznosti i nema rezervoara kod životinja. Virus se može održavati u ljudskim populacijama samo neprekinutim lancem akutnih infekcija¹.

Pre rasprostranjene primene vakcina protiv malih boginja, skoro svi su bili inficirani u ranom detinjstvu i stekli doživotni imunitet (95% do petnaeste godine života). Tada je bilo više od dva miliona smrtnih ishoda kao posledica malih boginja godišnje u svetu².

Virus je prvi izolovao John Enders 1954. godine. Vakcinacija u svetu je započela 1963. godine, živom atenuisanim Edmonston-Enders vakcinom. Kombinovana antitela se razvijaju kod oko 95% dece koja su vakcinu primila sa 12 meseci života i kod 98% dece koja su primila dve doze vakcine. Kombinovana živa vakcina protiv malih boginja, zaušaka i rubele - MMR je licencirana 1971. godine. Imunizacija sa dve doze vakcine sprovodi se od 1989. godine, kod nas se druga doza vakcine protiv malih boginja primenjuje od 1993. godine. Kombinovana živa vakcina protiv malih boginja, zaušaka, rubele i varičele - MMRV licencirana je 2005. godine i kod nas se, za sada, ne primenjuje³.

Značajan napredak u smanjenju globalne incidencije i mortaliteta ostvaren je sprovođenjem vakcinacije. Efikasnost zaštite jednom dozom vakcine koja se primeni nakon 12 meseci života je 84%. Među decom koja ne odgovore na prvu dozu, njih oko 95% razvije imunitet nakon druge doze. Jedna doza ispravno primenjene vakcine, koja dovodi do serokonverzije, omogućava doživotnu zaštitu za većinu zdravih osoba. Iako se sekundarni neuspesi mogu pojaviti povremeno zbog opadanja imuniteta, taj faktor nema značajnu ulogu u prenošenju virusa⁴.

Vakcinacija protiv malih boginja se u Republici Srbiji sprovodi od 1971. godine. Od 1981. se sprovodila bivalentnom vakcinom (male boginje, zauške). Vakcinacija sa dve doze MMR vakcinom primenjuje se od 1993. god. U periodu

Introduction

Measles is a highly contagious infectious disease caused by the measles virus, of the genus *Morbillivirus*, within the family of *Paramyxoviridae*. The virus is 150-300 nm in diameter and its nucleus contains single-stranded RNA. There is only one antigenic type of the measles virus. Measles word origin probably derives from the medieval Latin word *miser*, meaning miserable. In the past, measles outbreaks were often child killers and they were known to change the history course. Majority of the death cases, even nowadays, occur in newborns and small children, in developing countries.¹

It is considered that the virus evolved from the zoonosis ancestor. The prehistoric host was a dog, in communities where livestock and people lived in close proximity. The virus started circulating among people 5.000-10.000 years ago when the human population grew bigger in river valleys in the Middle East. There are no latent or persistent measles infections which would lead to prolonged contagiousness and there are no virus reservoirs in animals. The virus can survive in the human population only through an unbroken chain of acute infections.¹

Before the widespread use of the measles vaccine, the majority of people were infected in early childhood and thus gained life long immunity (95% of people until the age of 15). More than two million people died of measles worldwide, back then.²

The virus was first successfully isolated by John Enders in 1954. The vaccination started in 1963, with live attenuated Edmonstone-Enders strain vaccine. Combined antibodies develop in approximately 95% of children vaccinated at 12 months and in 98% of children vaccinated with two doses of the vaccine. MMR (combined live vaccine against measles, mumps, and rubella) was firstly licensed in 1971. Immunization with two doses of the vaccine started in 1989. and in our country since 1993. MMRV (combined live vaccine against measles, mumps, rubella, and varicella) was licensed in 2005. but is not used in our country.³

Substantial progress in global incidence and mortality decrease has been made through vaccination. The protection efficacy with one dose of the vaccine given at 12 months of age is 84%. Among the children who do not respond to the first dose of the vaccine, 95% develop immunity after the second dose. One dose of the properly given vaccine ensures life long immunity for the majority of healthy persons. Although secondary failures may occur from time to time, due to the immunity decline, it doesn't play a major role in the viral spread.⁴

The vaccination against measles started in 1971 in the Republic of Serbia. Since 1981 it was performed with a bivalent vaccine (measles, mumps). Vaccination with MMR vaccine started in 1993, with two doses of the vaccine. From 1994-2006, the second dose of the vaccine was given at 12

od 1994. do 2006. godine druga doza vakcine davala se deci sa navršenih 12. godina, u šestom razredu osnovne škole. Nakon tog perioda, prva doza se daje sa navršenih 12 meseci a druga pre polaska u školu. Ako se iz bilo kog razloga (osim trajnih kontraindikacija) aktivna imunizacija ne sprovede u preporučenom vremenu, dete treba vakcinisati primenom dve doze u razmaku ne kraćem od 4 nedelje, do navršenih 18 godina života^{5,6}.

Nakon uvođenja vakcine protiv malih boginja 1971. godine, epidemije su se javljale svakih 3–5 godina, sa višestruko manjim brojem obolelih. Broj obolelih u Srbiji se smanjivao sa 37.441 slučajeva obolelih 1980. godine na 4.692 i 7 smrtnih ishoda tokom poslednje velike epidemije 1997. godine. U oktobru 2017. počinje velika epidemija malih boginja u Srbiji, sa 693 obolela, da bi se nastavila u 2018. sa ukupno 5.783 obolela i 15 smrtnih ishoda, od kojih su 2.933 laboratorijski potvrđena u Institutu za virusologiju, vakcine i serume „Torlak” u Beogradu. Srbija je država u kojoj male boginje nastavljaju da se endemski održavaju^{5,7,8}.

Pojava malih boginja registrovana je na teritoriji svih okruga u Republici Srbiji, pri čemu je većina obolelih (88%) registrovana na teritoriji Beograda, Nišavskog, Pčinjskog, Raškog i Jablaničkog okruga. Na teritoriji Raškog okruga prijavljena su 252 slučaja, od čega 243 kod pacijenata sa prebivalištem na teritoriji Kraljeva.

Zajedničkim i koordinisanim delovanjem Primarne zdravstvene zaštite Doma zdravlja (DZ) Kraljevo, Zavoda za javno zdravlje (ZJZ) Kraljevo (Centar za kontrolu i prevenciju bolesti), Službe hitne medicinske pomoći DZ Kraljevo, Odeljenja pedijatrije i Odeljenja za infektivne i tropске bolesti Opšte bolnice „Studenica” Kraljevo, u skladu sa stručno-metodološkim uputstvima - suzbijeno je prenošenje bolesti.

Inkubacija i klinička slika

Inkubacioni period od vremena ekspozicije do početka groznice i ospe traje 10-14 (najduže 7-21) dana. Oboleli su najzarazniji 1-3 dana pre izbijanja ospica, a kada se one pojave postoji značajno smanjenje virulentnosti virusa. Stopa sekundarnog obolevanja prijemčivih ukućana je viša od 80%³. Bolest počinje sa prvim simptomom koji karakteriše groznica, slabost, kašalj, koriza i konjunktivitis. Pacijent ima grub, neproduktivan kašalj tokom febrilnog perioda, traje 1-2 nedelje kod nekomplikovanih slučajeva i obično je poslednji simptom koji prestaje. Mlađa deca često imaju limfadenopatiju a starija fotofobiju i artralgiu. Koplikove mrlje, male bele lezije na bukalnoj mukozi, pojavljuju se pre osipa. Karakteristična eritematozna i makulopapulозна ospa se pojavljuje prvo na licu i iza ušiju 2-4 dana nakon prodromalnih simptoma, zatim se širi na trup i ekstremitete. Ospa je najintenzivnija od drugog do trećeg dana i traje 3-7 dana. Nakon toga sledi fina deskvamacija kože^{9,10}.

years of age, in the sixth grade. After 2006, the first dose was being given at twelve months and the second just before the school starting age. If for some reason (except for permanent contraindications) active immunization isn't performed in the recommended period, a child should be vaccinated with two doses of the vaccine, no less than four weeks apart, before 19 years of age.^{5,6}

After the introduction of the measles vaccine in 1971, the outbreaks appeared every 3-5 years, with significantly less diseased persons. The number of the diseased in Serbia declined from 37441 in 1980 to 4692 and 7 death cases during the last great outbreak in 1997. There was a great measles outbreak in October 2017, with 693 measles cases and it continued in 2018, with a total of 5783 measles cases and 15 deaths due to measles. Out of the total number, 2933 cases were confirmed in laboratories of the Institute for virology, vaccines and serums 'Torlak', Belgrade. Measles keeps being an endemic disease in Serbia.^{5,7,8}

Measles cases were registered in all Serbian counties. The highest percentage was registered in Belgrade (88%), followed by Nisavski, Pećinski, Raski and Jablanicki county. In Raska county, there were 252 registered disease cases, of whom 243 were the citizens of Kraljevo.

Joint and coordinated activity of the Primary Health care Center Kraljevo, the Public health institute, Kraljevo (Center for prevention and disease control), Emergency department, Kraljevo, Pediatrics department and Infectious disease department of 'Studenica' hospital, Kraljevo, stopped the disease spreading, using expert instructions.

Incubation and clinical features

The incubation period, from the exposition to the onset of fever and rash lasts 10-14 days (the least 7 and the longest 21 days). The diseased is the most contagious 1-3 days before the rash occurrence and when it does appear there is a significant decline in virulence. The risk of secondary disease contraction among the susceptible family members is higher than 80%.³

The disease starts with prodromal symptoms, such as fever, weakness, cough, coryza, and conjunctivitis. A patient has rough, unproductive cough during the febrile period, which lasts 1-2 weeks, in uncomplicated cases, and is usually the symptom that ceases last. Younger children usually have lymphadenopathy and older photophobia and arthralgia. Koplik's spots, seen inside the mouth, appear before the rash. The red maculopapular rash appears on the face and behind the ears first, 2-4 days after prodromal symptoms, spreading afterward on the body and extremities. The rash is the most intense between the second and the third day and it lasts 3-7 days. Fine skin desquamation appears afterward.^{9,10}

Komplikacije vidimo kod 30% slučajeva i najčešće su to pneumonija, dijareja, upala srednjeg uha, slepilo, dehidracija, encefalitis, postinfektivna encefalopatija, febrilne konvulzije i krup. Teška klinička slika se javlja kod nedovoljno uhranjene dece, posebno one koja imaju nedostatak vitamina A, kao i prisutnih komorbiditeta poput *HIV/AIDS* infekcije^{1,9}. Pneumonije izazivaju značajan morbiditet i mortalitet. Virus malih boginja može biti uzročnik upale pluća, ali je češće u pitanju sekundarna infekcija drugim virusnim agensima ili bakterijama¹⁰.

Cilj rada

Cilj rada je bio da se prikažu epidemiološke karakteristike epidemije malih boginja u odnosu na vreme javljanja, dužinu trajanja, starost, pol i vakcinalni status obolelih, komplikacije bolesti, učestalost hospitalizacija i obolevanje zdravstvenih radnika u Domu zdravlja Kraljevo, tokom njenog trajanja u periodu 2017/2018. godine.

Metod

Sprovedena je otvorena retrospektivna epidemiološka studija nakon epidemije malih boginja na teritoriji za koju Dom zdravlja Kraljevo obezbeđuje zdravstvenu zaštitu, u periodu 30.10.2017. – 27.03.2018. god. Svi pacijenti oboleli od malih boginja sa prebivalištem na teritoriji grada, uključeni su u studiju. Osnovni kriterijumi su: dijagnoza malih boginja (klinička, laboratorijska ili epidemiološka povezanost slučaja), oba pola i sve starosne grupe. Korišćeni su opšti principi za definisanje slučajeva po preporuci Evropskog centra za sprečavanje i suzbijanje bolesti iz 2017. godine i Zakona o zaštiti stanovnika od zaraznih bolesti^{11,12}.

Za prikupljanje podataka upotrebljeni su: službeni podaci o broju i kretanju malih boginja u Domu zdravlja Kraljevo u periodu 30.10.2017.- 27.03.2018. godine, pojedinačne prijave ZJZ Kraljevo (Centar za kontrolu i prevenciju bolesti), koje se redovno isporučuju nadležnom Institutu za javno zdravlje Republike Srbije (IJZ) „Dr Milan Jovanović Batut” u Beogradu, kao i njihovi zvanični izveštaji^{12,13}.

Pored demografskih, ovi obrasci sadrže i epidemiološke podatke (broj obolelih, incidenciju, vakcinalni status) i kliničke (komplikacije, smrtni ishod) podatke. Uzorci za laboratorijsku potvrdu malih boginja su prikupljeni u Službi epidemiologije ZJZ Kraljevo. Prva četiri dana bolesti uzimani su bris grla i nosa za detekciju virusa lančanom polimeraza reakcijom (PCR), a nakon tog perioda analiza imunoenzimskim ELISA testom (3-28 dana), ukupno 15 uzoraka. Uzorci su analizirani u referentnoj laboratoriji Instituta za virusologiju, vakcine i serume „Torlak” u Beogradu. Njihova preporuka je bila da se kod najmanje 10-15 ispitanika na početku epidemi-

The complications are found in 30% of the measles cases and the most frequent are pneumonia, diarrhea, otitis media, blindness, dehydration, encephalitis, post-infective encephalopathy, febrile convulsions, and croup. Very difficult clinical features appear in malnourished children, especially the ones with vitamin A deficiency, as well as those with concomitant comorbidities, such as AIDS.^{1,9} Pneumonia causes significant mortality and morbidity. Measles virus may cause pneumonia, but more often the cause of pneumonia is the secondary infection caused by other viruses or bacteria.¹⁰

Objective

Review of epidemiologic characteristics of a measles outbreak in relation to onset, duration, age, gender, vaccination status, complications, hospitalization incidence and the number of the diseased health workers in Primary Health care Center, Kraljevo during the outbreak in 2017/2018.

Method

An open retrospective epidemiological study was performed, after the measles outbreak, in the area covered by Primary Health care Center, Kraljevo, from October 30th, 2017 to March 27th, 2018. All the diseased patients from the territory were included in the study. Inclusion criteria were: measles diagnosis (clinical features, lab results, and epidemiological features), both genders and all ages. General principals were used for case defining, according to European CDC recommendations from 2017 and the Act on the protection of the population from infectious diseases.^{11,12}

Data gathering was achieved using: official data on the number and distribution of the measles cases in Primary Health care Center, Kraljevo, from October 30th, 2017 to March 27th, 2018, individual disease reports from the Public health institute, Kraljevo (Center for prevention and disease control). These reports are regularly forwarded to the Public health institute of the Republic of Serbia “Dr. Milan Jovanovic Batut”, in Belgrade, so we used their official reports as well.^{12,13}

The data contain demographic, epidemiological (the number of the diseased, the incidence, vaccination status), and clinical (complications, death outcomes) information. The samples for lab analysis were gathered in the Public health institute, Kraljevo (Epidemiology department). During the first four days of the disease duration, throat and nose swab were taken and processed with PCR, and after this period ELISA test (3.-28. day) was used. In total, there were 15 samples. These samples were analyzed in the reference laboratory of the Institute for virology, vaccines and serums-Torlak, Belgrade. The Institute’s recommendation was to confirm the diagnosis in at least 10-15 patients, at the begin-

je izvrši potvrda dijagnoze malih boginja imunoenzimskim testom (*IgG*, *IgM* antitela), što je i učinjeno.

Izabrane lekare i pedijatre Doma zdravlja o početku epidemije informisali su epidemiolozi Centra za kontrolu i prevenciju bolesti ZJZ Kraljevo. Preciziran je, prema stručno-metodološkom uputstvu i pooštrenom nadzoru, način prijavljivanja sumnje i definisani su slučajevi malih boginja^{11,12}.

Uspostavljena je komunikacija mobilnim telefonima. Podaci koje su izabrani lekari odmah prosledivali kod sumnje ili klinički potvrđenog slučaja malih boginja, bili su: pojedinačna prijava zarazne bolesti, a telefonom su slali potrebne podatke o pacijentima¹³.

Epidemiolozi su identifikovali puteve prenošenja bolesti i vršili epidemiološko ispitivanje. Preporučena je vakcinacija svih osetljivih zdravstvenih radnika. Vršena je revizija vakcinalnih kartona u kartotekama i imunizacija nevakcinisanih i nepotpuno vakcinisanih lica uzrasta od 12 meseci do navršanih 18 godina. Redovno je vršena analiza podataka, efekti mera na suzbijanju epidemije malih boginja i izveštavanje nadležne ustanove (IJZ „Dr Milan Jovanović Batut”)^{13,14,15}.

Uloga izabranih lekara sastojala se u otkrivanju slučajeva, preduzimanju propisanih mera za sprečavanje prenošenja i suzbijanja bolesti, kao i da pouče obolele i lica iz njihove okoline o načinu zaštite od bolesti. Bolesnika sa sumnjom na male boginje odvajali su od ostalih pacijenata u deo za izolaciju. Ukoliko je bolesnik zahtevao hospitalno lečenje, obavestavali su infektivno odeljenje, kako bi se pravovremeno pripremila soba za izolaciju. Delili su obolelima savete telefonom da bi se izbegli nepotrebni dolasci u ambulanu i ostvarivanje kontakta sa osetljivom populacijom u čekaonici i pružali su informacije putem medija.

Za istraživanje je pribavljena saglasnost Etičkog odbora Doma zdravlja Kraljevo. Podaci su uneti u tabelu *Excel* programa, verzija 2017. Za analiziranje rezultata korišćeni su metodi deskriptivne statistike: prebrojavanje, učestalost, minimalna i maksimalna vrednost i procenti. Za utvrđivanje značajnosti razlike između obeležja korišćen je χ^2 -test nezavisnosti. Nivo značajnosti je podešen na 95% interval poverenja.

Rezultati

Epidemija malih boginja je započela u Kraljevu 30.10.2017. godine sa dvoje obolelih - osobom ženskog pola starom 26 godina i bebom od 6 meseci, koje su bile u kontaktu sa obolelima tokom boravka u Prištini. To su prvi slučajevi morbila posle 20 godina u Kraljevu, koji su na Institutu za virusologiju, vakcine i serume „Torlak“ laboratorijski potvrđeni⁸. Zavod za javno zdravlje Kraljevo je nakon porodične, 10.11.2017. god. prijavio i epidemiju u romskom naselju sa četiri obolela, što je ukupno šest. Nakon toga, ZJZ Kraljevo 14.11.2017. godine prijavljuje epidemiju malih boginja⁸.

ning of the outbreak, using immunoenzyme technique (*IgM*, *IgG* antibodies), and we did as instructed.

The GPs and pediatricians from our clinic were informed of the measles outbreak start by the epidemiologists from the Center for prevention and disease control of the Public health institute, Kraljevo. The disease surveillance was intensified^{11,12}.

We communicated using cell phones. The GPs and pediatricians filled in the forms for individual infectious disease reports, if they suspected or confirmed the measles case, and they forwarded all the necessary data about the patient, by phone¹³.

The epidemiologists identified the ways of the measles virus transmission and did epidemiological research. The vaccination of all sensitive health workers was recommended. Vaccination charts were revised and all those aged 12 months to 18 years, who were not vaccinated or incompletely vaccinated got their vaccine shots. Data analysis was performed regularly, as well as effects of the undertaken measures and reports from the referral institute (Dr. Milan Jovanovic Batut)^{13,14,15}.

GP's role was to identify the disease, undertake necessary measures to stop the disease spreading and teach the diseased and the people from their surrounding how to protect themselves. The patients who were suspected of having measles were separated from other patients and taken to the isolation unit. If the patient's treatment required a hospital stay, the Infectious disease ward was notified, so they could prepare the isolation unit. The information was also given by phone and through media to avoid clinic visits and further disease transmission.

We got the approval of the Ethics committee of Primary Health care Center to perform the research. The data were processed using Excel 2017. For data analysis, we used descriptive statistics methods: counting, frequency, minimal and maximal values, and percentages. For the confirmation of the statistical significance, we used χ^2 -test. Significance level was set to 95% confidence interval.

Results

The measles outbreak started on October 30th, 2017, in Kraljevo. There were two cases: female, 26 years and baby, 6 months old, who had contact with the diseased persons during their stay in Priština. It was the first measles case in our town after 20 years. The cases were confirmed in the laboratories of the Institute for virology, vaccines and serums-Torlak.⁸ The Public health institute in Kraljevo firstly confirmed familial, and then general measles outbreak, on November 10th, 2017, in the Romani community, with four diseased persons, which made 6 persons in total. After that the Public health institute, Kraljevo announced the general measles outbreak, on November 14th, 2017.⁸

Epidemija je trajala do 27.03.2018. godine, kada su registrovana dva poslednja slučaja. Odjavljena je 21 dan nakon što je izbila ospa poslednjem prijavljenom pacijentu. Ukupno su obolele 243 osobe sa prebivalištem na teritoriji Kraljeva.

Klasifikaciju slučaja zarazne bolesti na sumnjive, verovatne i potvrđene, u skladu sa definicijom slučaja prema stručno-metodološkom uputstvu, vršili su epidemiolozi ZJZ Kraljeva, koja je podrazumevala sledeće simptome i znake

The epidemic lasted until March 27th, 2018 when the last two cases were registered. The outbreak was called off 21 days after the last person's measles rash appearance was confirmed. In total, there were 243 people from our town who suffered from measles. The cases classification - suspected, probable and confirmed was performed by the epidemiologists from the Public health institute, Kraljevo. It included these symptoms and signs of the disease: rash, fever ($>38^{\circ}\text{C}$),



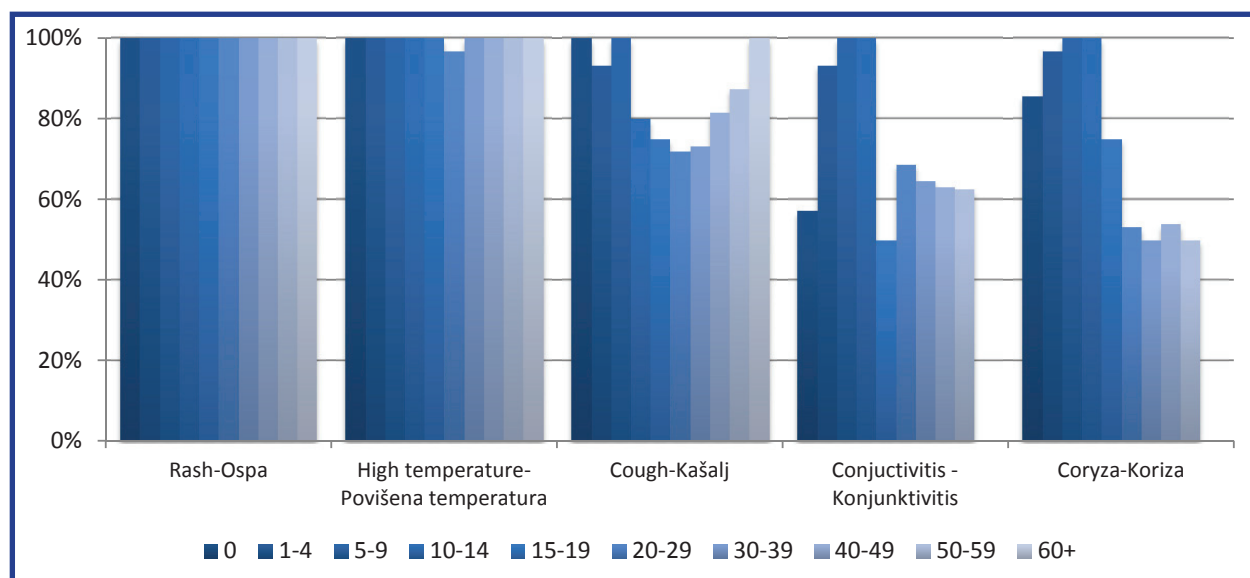
Picture 1. Maculopapulose rash
Slika 1. Makulopapulозна ospa

bolesti: ospe: povišenu telesnu temperaturu ($>38^{\circ}\text{C}$), kašalj, konjunktivitis, korizu^{6,12} (Slika 1).

Najučestaliji simptomi kod obolelih od malih boginja u ordinacijama izabranih lekara kao i prilikom epidemioloških nadzora, bili su ospa, povišena telesna temperatura, kašalj i opšta slabost. Učestalost simptoma i znakova prema godinama starosti prikazana je na Grafikonu 1.

cough, conjunctivitis, coryza.^{6,12} (Picture 1)

The most frequent measles symptoms in GP offices were rash, fever, cough and generalized weakness. The frequency of the disease symptoms and signs according to age is shown in Graph 1.

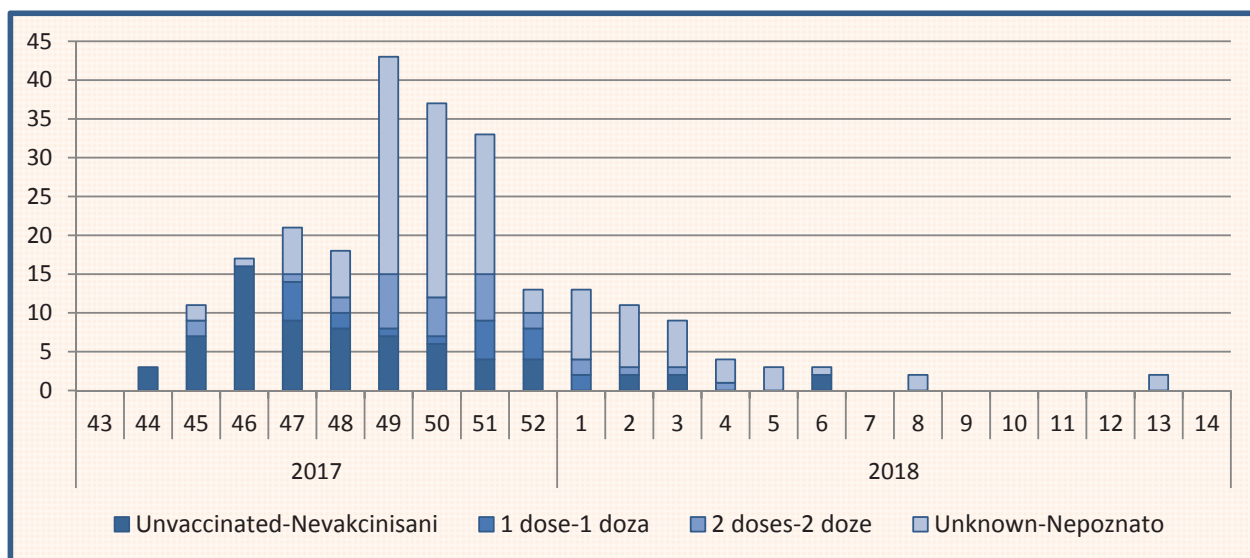


Graph 1. Frequency of measles symptoms and signs

Grafikon 1. Učestalost simptoma i znakova malih boginja

Na vrhu epidemijskog talasa, period 49-51 nedelja, statistički značajno su više obolevala lica nepoznatog vakcinalnog statusa ($p=0,001$), (Grafikon 2).

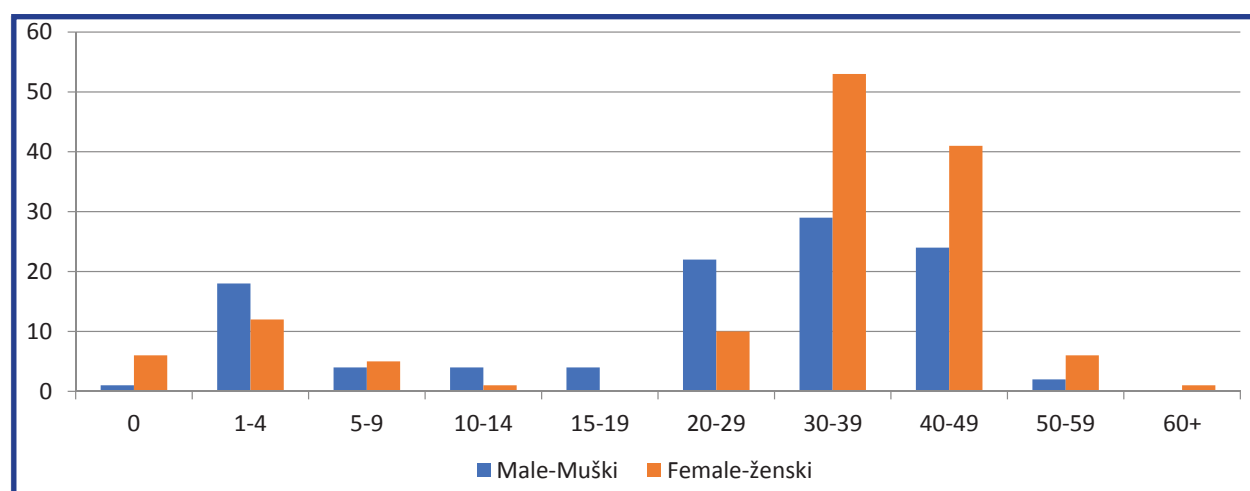
At the peak of the outbreak (49.-51. week), people with unknown vaccination status were the ones who got ill the most, and it was statistically significant ($p=0,001$). (Graph 2)



Graph 2. Number of disease cases by weeks and vaccination status
Grafikon 2. Broj obolelih po nedeljama i vakcinalnom statusu

Najmlađi oboleli pacijent je beba stara dva meseca a najstariji 60 godina. Najveći procenat (33,7%) obolelih je u grupi 30-39 godina, a najmanji (0,4%) u grupi pacijenata od 60 i više godina. Postoji veća učestalost obolevanja žena u grupama 30-39 i 40-49 godina, ali nije statistički značajna ($p=0,06$), (Grafikon 3).

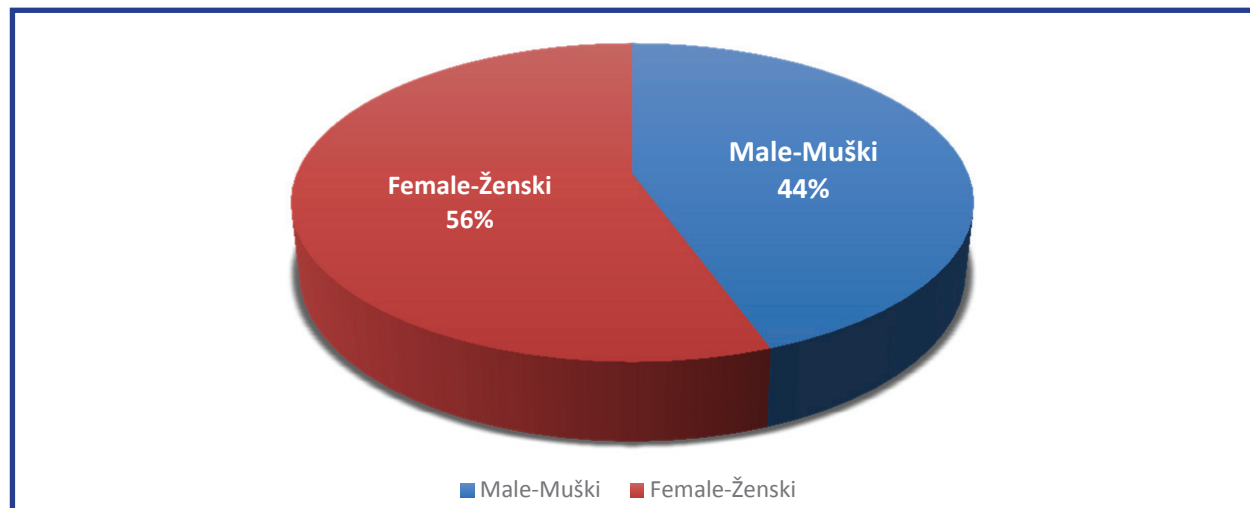
Youngest patient was a baby, 2 months old and the oldest 60 years of age. The highest percentage of the diseased (33.7%) was among those 30-39 years of age, and the lowest (0.4%) among those over 60. The frequency of the diseased was higher among females 30-39 and 40-49 years of age, but it wasn't statistically significant ($p=0.06$). (Graph 3)



Graph 3. Distribution of measles cases by age and gender
Grafikon 3. Distribucija malih boginja prema godinama starosti i polu

Bilo je 135 (56%) pacijenata ženskog pola i 108 (44%) muškog pola, nema statističke značajnosti u obolevanju prema polu ($p=0,127$), (Grafikon 4).

There were 135 diseased females (56%) and 108 males (44%), but there was no statistically significant difference in the number of diseased according to gender ($p=0.127$). (Graph 4)



Graph 4. Gender structure of the diseased
Grafikon 4. Polna struktura obolelih

Prema programu imunizacije, 7 obolele dece do 12 meseci starosti nisu bili predviđeni da prime prvu dozu *MMR vaccine*. Zaražena deca iz grupa 1-4 i 5-9 godina, ukupno 39 (16,1%), nisu primila nijednu dozu *MMR* (100%). Nisu imunizovani ni u grupama 50-59 i 60+ godina (u njihovom detinjstvu nije se primenjivala vakcina protiv malih boginja). Najveći broj obolelih - 82 (33,6%) je u grupi 30-39 godina (generacije kada se po pravilniku sprovodila imunizacija jednom dozom vaccine). U opisanoj epidemiji 87,6% pacijenata nije bilo vakcinisano sa dve doze vaccine ili je vakcinalni status nepoznat. Procenat osoba sa nepoznatim vakcinalnim statusom najveći je u grupi 30-39 godina (22,6%), (Tabela 1).

Diseased children, up to twelve months age (there were 7), weren't scheduled to get the *MMR vaccine*, according to the vaccination program. Infected children from group ages 1-4 and 5-9, the total of 39 children (16.1%) didn't receive a single dose of *MMR vaccine* (100%). Those in age groups 50-59 and over 60 also weren't vaccinated (because when they were young there was no *MMR vaccine*). The largest number of the diseased 82 (33.6%) was in age group 30-39 (those were the generations who received only one dose of the vaccine). In this outbreak, 87.6% of the diseased weren't vaccinated with two doses of the vaccine or had an unknown vaccination status. The percentage of patients with an unknown vaccination status was the highest in the age group 30-39 (22.6%). (Table 1)

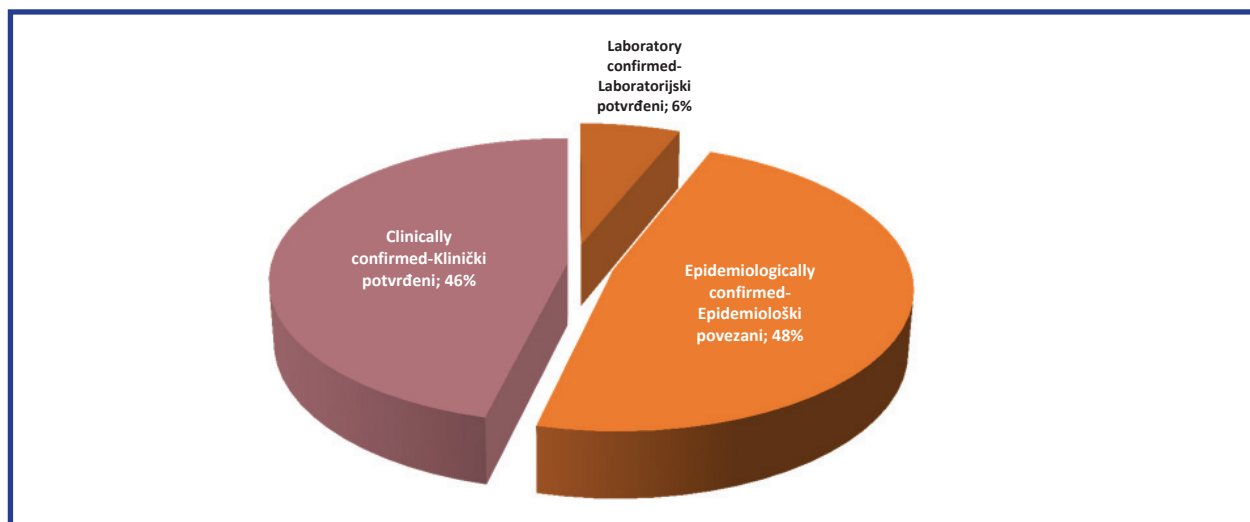
Table 1. Measles cases and their vaccination status by age group

Tabela 1. Slučajevi malih boginja i njihov vakcinalni status prema starosnim grupama

Number of vaccines	2	1	0	Unknown
Age	N (%)	N (%)	N (%)	N (%)
0	0 (0)	0 (0)	7 (2.9)	0 (0)
1-4	0 (0)	0 (0)	30 (12.4)	0 (0)
5-9	0 (0)	0 (0)	9 (3.7)	0 (0)
10-14	1 (0.4)	0 (0)	4 (1.6)	0 (0)
15-19	4 (1.6)	0 (0)	0 (0)	0 (0)
20-29	11 (4.5)	2 (0.8)	5 (2.1)	14 (5.9)
30-39	13 (5.3)	11 (4.5)	3 (1.2)	55 (22.6)
40-49	1 (0.4)	7 (2.9)	3 (1.2)	54 (22.2)
50-59	0 (0)	0 (0)	8 (3.3)	0 (0)
>60	0 (0)	0 (0)	1 (0.4)	0 (0)

Laboratorijski je potvrđeno 15 (6,2%) slučajeva malih boginja, koliko je i bila preporuka Instituta za virusologiju, vakcine i serume „Torlak” na početku epidemije. Definicije slučajeva prema kliničkoj dijagnozi - 112 (46,1%), prema epidemiološkim kriterijumima - 116 (47,7%), (Grafikon 5)

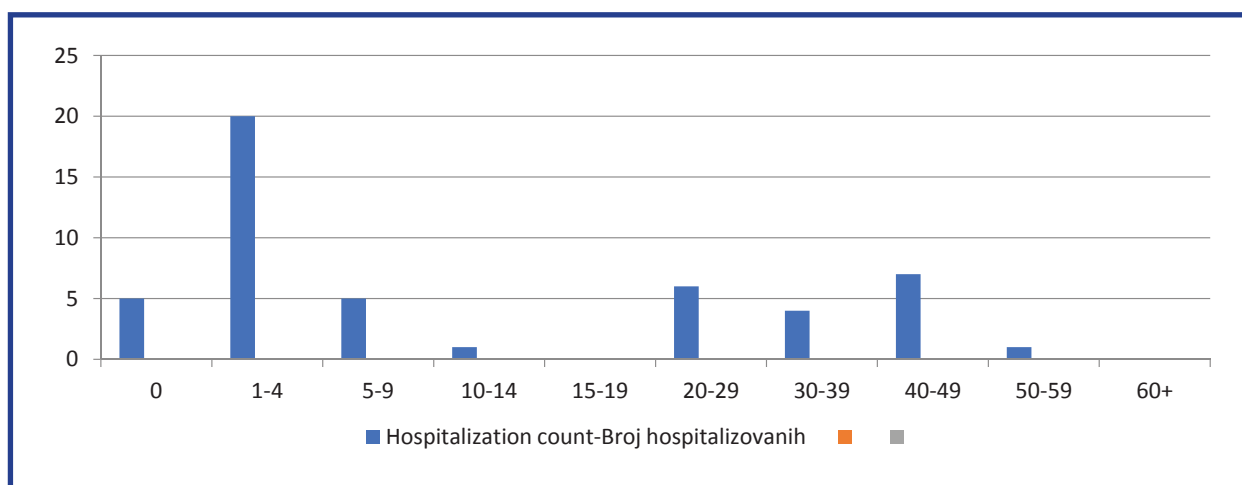
There were 15 (6,2%) lab confirmed measles cases. There were 112 (46.1%) measles cases according to clinical diagnosis and 116 (47.7%) according to epidemiologic criteria. (Graph 5)



Graph 5. Case definitions
Grafikon 5. Definicije slučajeva

Ukupno je hospitalizovano 49 (20,6%) pacijenata, statistički značajno više u grupi 1-4 godine starosti ($p=0,009$). U grupi 15-19 i 60+ godina niko nije hospitalizovan, (Grafikon 6).

The total number of hospitalized patients was 49 (20.6%) and it was statistically significantly highest in the 1-4 age group ($p=0.009$). In age groups 15-19 and over 60, no one was hospitalized. (Graph 6)



Graph 6. Number of hospitalized patients by age
Grafikon 6. Broj hospitalizovanih pacijenata prema starosti.

Posmatrano prema najčešćim komplikacijama malih boginja, u ispitivanoj populaciji je zabeleženo ukupno 50 (20,6%), u grupi 1-4 godine 21 (43,8%), što je statistički značajno ($p=0,0004$). U grupama 15-19 i 60+ godina nisu zabeležene komplikacije. Pneumonije su se razvile kod 30 (12,3%) pacijenata, dijareja kod 16 (6,6%), 4 (8%) slučajeva upale srednjeg uha, svi u grupi 1-4 godine. Smrtnih ishoda nije bilo tokom epidemije malih boginja u Kraljevu, (Tabela 2)

Table 2. Measles complications
Tabela 2. Komplikacije malih boginja

Complications	Pneumonia N (%)	Diarrhea N (%)	Otitis media N (%)
Age			
0	2 (4)	1 (2)	0 (0)
1-4	12 (24)	5 (10)	4 (8)
5-9	2 (4)	0 (0)	0 (0)
10-14	1 (2)	1 (2)	0 (0)
15-19	0 (0)	0 (0)	0 (0)
20-29	3 (6)	1 (2)	0 (0)
30-39	3 (6)	1 (2)	0 (0)
40-49	6 (12)	5 (10)	0 (0)
50-59	1 (2)	2 (4)	0 (0)
>60	0 (0)	0 (0)	0 (0)

Obolelo je kupno 40 (16,5%) zdravstvenih radnika i drugih zaposlenih u zdravstvenim ustanovama.

The total of 40 (16.5%) health workers and other medical personnel fell ill.

Diskusija

Male boginje izaziva jedan od najinfektivnijih virusa poznat čoveku. Virus je antigenski stabilan, do sada su poznata 23 genotipa a jedan serotip. Osetljiv je na ultraljubičastu svetlost, toplotu, kiseline, etar i tripsin. Nema asimptomatskog vironoštva kod čoveka. Virus ostaje aktivan u vazduhu ili na zaraženim predmetima tokom dva sata. Prenosi se putem vazduha kapljicama, koje se izbacuju kašljanjem i kihanjem obolelih ili direktnim kontaktom sa sekretom nosa i ždrela inficiranih osoba^{3,9}.

U zemljama sa umerenom klimom, prenos malih boginja se povećava krajem zime i tokom proleća a u tropskim zemljama nakon kišne sezone. Pre vakcinacije protiv malih boginja, epidemije su se javljale svake 2-3 godine, a u periodu vakcinacije u zemljama gde je obuhvat vakcinom zadovoljavajući, nešto ređe (5-7 godina). Kako se broj osetljivih pojedinaca vremenom povećavao, epidemije su nastajale i u zemljama sa visokim obuhvatom vakcinom. Trajanje epidemije varira u zavisnosti od veličine populacije, naseljenosti i imuniteta stanovništva. Epidemije su prijavljene i u populacijama u kojima je samo 3%-7% osoba osetljivo¹⁶.

Discussion

Measles is caused by one of the most infectious viruses known to mankind. The virus displays antigenic stability and there are 23 genotypes and 1 serotype, that we know of today. It is sensitive to ultraviolet light, heat, acid, ether and trypsin. There are no asymptomatic virus carriers in humans. The virus stays active in the air and on the infected objects for two hours. It is an airborne disease, which spreads through coughs and sneezes of the diseased persons or in direct contact with the mouth or nasal secretions.^{3,9}

In the countries with a temperate climate, the measles transmission increases by the end of winter and the beginning of spring, and in the countries with tropical climate after the rain season. Before the measles vaccine, the outbreaks appeared every 2-3 years, and after, in the countries where vaccination coverage is satisfactory every 5-7 years. As the number of sensitive individuals increased over time, the outbreaks started appearing even in the countries with high vaccination coverage. The outbreak duration varies depending on the population size, density, and immunity. They were also reported in the populations with only 3-7% of sensitive people.¹⁶

Tokom 2017. godine globalno registrovano je 173.330 slučajeva malih boginja, a 2018. godine 229.068. U evropskom regionu SZO tokom 2017. godine prijavljeno je 25.465 slučajeva u 15 od 53 zemlje, sa najmanje 37 smrtnih ishoda, od toga čak 15 u Srbiji tokom 2017. i 2018. godine⁸. U 2018. godini bilo je 59.578 obolelih, dvostruko više, sa 35 smrtnih ishoda. Najveći broj slučajeva registrovan je u Ukrajini i Rumuniji, zatim u Italiji, Grčkoj, Nemačkoj, Tadžikistanu, Francuskoj, Srbiji, Ruskoj Federaciji i Belgiji¹⁷. Boginje se šire Evropom jer je pokrivenost vakcinom u mnogim zemljama suboptimalna. Samo u Mađarskoj, Portugaliji, Slovačkoj i Švedskoj u 2017. godini postignut je 95% i veći obuhvat stanovništva sa obe doze vakcine^{17,18,19}. Tokom 2018. godine u svim regionima SZO male boginje su ponovo endemične^{20,21}.

Od ukupnog broja obolelih tokom 2017. godine u Srbiji, 28,7% je registrovano u Kraljevu, da bi, potom, kako se širila epidemija 2018. godine taj procenat iznosio 0,9%. Na teritoriji našeg Doma zdravlja najviše je bilo obolelih u grupi 30-39 (33,7%) godina, slično kao na nivou cele Srbije (30,3%)⁸. U Kraljevu je obolelo 12,3% dece uzrasta 1-4 godine, što je niže nego u ostalom delu zemlje (16,6%), u sličnom istraživanju u Italiji (35%)²², Niškom i Topličkom okrugu tokom epidemije 2015. (22,9%)²³, u Bosni 2014-2015 (17%)²⁴. Na globalnom nivou, bebe ispod godinu dana i mala deca (1-4 godine) su najviše zastupljeni uzrast u obolevanju (2/3 svih slučajeva), na evropskom nivou u istom periodu zastupljene su sa 30%, dok je u Kraljevu bilo 15,2% obolelih u tom uzrastu^{17,21}.

Svi oboleli u Kraljevu su imali karakterističnu ospu (100%), 99,7% je imalo povišenu temperaturu, 66% konjunktivitis i 66,5% korizu.

Kod naših pacijenata je zabeležena niža učestalost komplikacija (20,6%) nego što je to na globalnom nivou (30%)⁵, u Bosni²⁴ (24%), tokom epidemije u Niškom i Topličkom okrugu (33,1%)²³, a viša nego u Italiji (16%)²².

Tokom epidemije u Kraljevu učestalost pneumonija je bila 12,3%, najzastupljenija u grupi 1-4 godine (24%), više nego na teritoriji Srbije (10,1%), Bosne 5,1%²⁴, u Italiji 3,5%²², a manje nego u Niškom i Topličkom okrugu (14,1%)³². U zemljama u razvoju dijareja je komplikacija koja negativno doprinosi nutritivnom statusu dece zbog slabosti i smanjenog unosa hrane, a zahtevi metabolizma se povećavaju. U Kraljevu je dijareja kao komplikacija prijavljena u 6,6% slučajeva, manje nego u sličnim istraživanjima^{23,24}. Febrilne konvulzije su najčešća neurološka komplikacija, zatim encefalitis, postinfektivna encefalopatija i subakutni sklerozirajući panencefalitis (retko hronično, degenerativno oboljenje povezano sa perzistentnom infekcijom centralnog nervnog sistema, koje se manifestuje nekoliko godina nakon infekcije)^{3,10}. Nisu prijavljene neurološke komplikacije.

U Kraljevu je 20,6% obolelih hospitalizovano, manje u odnosu na ostali deo Srbije (33%)⁸ a u okvirima izveštaja Globalnog akcionog plana vakcinacije SZO 2012-2020, godine, gde se kreće u rasponu 10%-30%²¹.

There were 173330 measles cases worldwide in 2017., and 2018. 229068. In the European region, WHO reported 25465 cases in 2017. Out of 53 countries, 15 were affected, and there were 37 death outcomes, of which even 15 were in Serbia, during 2017 and 2018.⁸ In 2018 the number was doubled 59578, with 35 deaths. The highest number of the diseased was registered in Ukraine and Romania, followed by Italy, Greece, Germany, Tadzekistan, France, Serbia, Russian Federation, and Belgium.⁸ The measles is spreading throughout Europe due to the suboptimal vaccination coverage. Only Hungary, Portugal, Slovakia and Sweden achieved 95% and higher vaccination coverage with both doses of the vaccine, in 2017.^{17,18,19} In 2018, all WHO regions became endemic again.^{20,21}

Out of the total number of the diseased in Serbia, in 2017, 28.7% were registered in Kraljevo, but as the outbreak was spreading further, this number came to 0.9% in 2018. Among our patients, the highest number of the diseased was in the age group 30-39 (33.7%), which was similar to the rest of Serbia (30.3%).⁸ In the age group 1-4, the percentage of the diseased was 12.3%, which was lower than in the rest of the country (16.6%), or similar research in Italy (35%)²², Niski and Toplicki county during the epidemic in 2015. (22.9%)²³, in Bosnia 2014-2015 (17%)²⁴. On a global level, babies (under the age of 1) and small children (ages 1-4) are the ones with the highest number of the diseased (2/3 of all cases). In Europe, this number was 30% and in Kraljevo 15.2%.^{17,21}

All the diseased in Kraljevo had a distinctive rash (100%), 99.7% had a fever, 66% conjunctivitis, and 66.5% coryza.

The incidence of complications was lower in our patients (20.6%) compared to the global situation (30%)⁵, Bosnia²⁴ (24%), during the outbreak in Niski and Toplicki county (33,1%)²³, and higher than Italy (16%)²².

During the outbreak in Kraljevo, the incidence of pneumonia was 12.3%, the highest in the age group 1-4 (24%), which was higher than in the rest of Serbia (10.1%), Bosnia 5.1%²⁴, 3.5% Italy²², and lower than in Niski and Toplicki county²³ (14.1%). Diarrhea is especially dangerous in the developing countries, because it deteriorates already bad nutritional status, while the metabolic demands are on the rise. Diarrhea, as a measles complication, was registered in 6.6% of cases in Kraljevo, which was lower compared to similar researches.^{23,24} Febrile convulsions are the most common neurologic complication, followed by encephalitis, post-infective encephalopathy, and subacute sclerosing panencephalitis (rare chronic, degenerative disease connected with persistent central nervous system infection which may appear several years after the measles).^{3,10} There were no registered neurologic complications.

There were 20.6% hospitalized patients in Kraljevo, which was less than in the rest of Serbia (33%)⁸, but in the range of Global action plan on vaccination report from WHO (2010-2020) which is 10%-30%.

Kod postavljanja kliničke dijagnoze, diferencijalno-dijagnostički dolaze u obzir sva oboljenja sa ospom i povišenom temperaturom: šarlah, rubela, *exanthema subitum*, enterovirusne infekcije, adenovirusne infekcije, infektivna mononukleoza, infekcija alfavirusima, herpes virusima tip 6 i 7, parvo virusima B19, denga, meningokokcemija, toksični šok sindrom, Kawasakijeva bolest^{9,25}.

Ne postoji specifična terapija, već se primenjuju suportivne mere i prevencija komplikacija i sekundarnih infekcija, nadoknada tečnosti i rehidracija, antibiotici kod razvoja komplikacija. Vitamin A se primenjuje u svim slučajevima malih boginja u zemljama u razvoju, gde su deca pothranjena, jer sprežava nastanak slepila i smanjuje smrtni ishod za 50%. Preporuka je dati dve doze, po 50-200.000 IU vitamina A^{9,10}.

Male boginje globalno i dalje predstavljaju vodeći uzrok smrti kod dece, koji se može sprečiti, zahvaljujući dostupnoj, bezbednoj, efikasnoj i jeftinoj vakcini, kao i značajnom progresu u kontroli bolesti^{2,18,20,26}.

Svetska pokrivenost vakcinom protiv malih boginja 2016. godine iznosila je 85% za jednu dozu i 61% za obe doze. Iste godine zabeleženo je 89.780 smrtnih slučajeva zbog malih boginja (većinu čine deca do 5 godina starosti), prvi put u istoriji ispod 100.000, što predstavlja 84% manje nego 2000. godine²¹. Procenjuje se da je sprečeno 20,4 miliona smrtnih slučajeva primenom vakcine 2000-2016²¹ godine. Svih 6 regiona SZO kroz Globalni akcioni plan vakcinacije²¹ imaju za cilj eliminaciju malih boginja do 2020. godine, što je teško dostići¹⁷. Globalna pokrivenost prvom dozom vakcine ima plato od 2010. (84%) do 2017. (85%), ali je značajno povećana pokrivenost drugom dozom vakcine, 2000. je bila 39% a 2017. 67%²⁰.

Tokom epidemije u Kraljevu, evidentirano je da 87,6% obolelih nije bilo vakcinisano ili je vakcinalni status nepoznat, dok je u celoj Srbiji 94%⁸ a u evropskom regionu SZO 98%²⁰.

Kod 123 (50,6%) obolelih nije poznat vakcinalni status, više nego na evropskom nivou u istom periodu (10%)¹⁷. Nepotpuno je vakcinisano njih 90 (37%), manje nego u sličnom istraživanju (53%)²³ a više nego u evropskim zemljama (11%)¹⁷ i Bosni (3,3%)²⁴.

Nijednu vakcinu protiv malih boginja nije primilo 70 (28,8%) lica, manje nego u Bosni (68,4%)²⁴ i Italiji (95%)²². Ovde su računata i obolela deca do 12 meseci starosti, koja nisu bila u programu imunizacije. Dve doze vakcine je primilo 30 (12,3%), više nego u Bosni (4,7%)²⁴ i Niškom i Topličkom okrugu (3%)²³. Vakcinisani sa obe doze imali su primarni ili sekundarni neuspeh vakcinacije²⁷.

Prema izveštaju IJZ Batut⁸, 13% zaposlenih u zdravstvenim ustanovama je imalo učešće u ukupnom obolevanju. U Kraljevu je registrovan veći procenat obolevanja kod zaposlenih u zdravstvenim ustanovama (16%). Aktivna imunizacija zdravstvenih radnika ne samo da ih štiti od profesionalne izloženosti, već sprečava širenje malih boginja na

Differential diagnosis may include diseases with rash and fever: scarlet fever, rubella, exanthema subitum, Enterovirus infections, Adenovirus infections, infectious mononucleosis, Alphavirus infections, infections with Herpes virus type 6 and 7, Parvovirus B19, dengue, meningococemia, toxic shock syndrome, Kawasaki disease.^{9,25}

There is no specific treatment for measles, and it's usually supportive treatment and prevention of complications and secondary infections, maintaining good hydration, antibiotics in the case of complications. Vitamin A is used in measles cases, in all developing countries, due to child malnutrition, because it prevents blindness and reduces death outcomes for 50%. The recommended dose of vitamin A is 50-200.000IU.^{9,10}

Measles are still the leading cause of death in children, all over the world, and it is preventable thanks to the measles vaccine which is available, safe, effective and cheap.^{2,18,20,26}

Worldwide coverage with measles vaccine in 2016 was 85% with one dose and 61% with two doses of the vaccine. There were 89780 death outcomes due to measles in 2016 (the majority in children under the age of 5) and for the first time in history under 100.000 measles deaths. This number was 84% lower than in 2000.²¹ It is estimated that the vaccination prevented 20.4 million deaths in the 2000-2016 period.²¹ All six WHO regions are aiming at measles elimination, by the year 2020, through their Global action plan on vaccination²¹, but it will be difficult to achieve.¹⁷ Global vaccine coverage, with the first dose, reached its plateau in 2010 (84%) to 2017 (85%), but there was a significant rise in the coverage with the second dose (in 2000. 39%, and 2017. above 67%).²⁰

There were 87.6% of the diseased who were not vaccinated or their vaccination status was unknown, during the measles outbreak in Kraljevo. In the rest of Serbia this number was 94%⁸ and in the European WHO region 98%²⁰. In 123 (50.6%) patients, vaccination status was unknown, which is higher than in Europe, in the same period (10%).¹⁷ Out of this number, 90 (37%) had been incompletely vaccinated, which was less than in the similar research (53%)²³, and more than in European countries (11%)¹⁷ and Bosnia (3.3%)²⁴.

There were 70 (28.8%) patients who didn't receive a single dose of the measles vaccine, which is less than in Bosnia (68.4%)²⁴ and Italy (95%)²². This number includes the children under the age of twelve months, who are not included in the vaccination plan. There were 30 (12.3%) patients who received 2 doses of the vaccine, which is more than in Bosnia 4.7%²⁴ and Niski and Toplicki county (3%)²³. There were those who received both doses of the vaccine and had a primary or secondary vaccination failure.²⁷

According to the Public health institute-Batut⁸ report, among the diseased, there were 13% of health workers. In Kraljevo this percent was even higher 16%. Active immunization of health workers protects not only them but prevents measles spread to sensitive patients, who visit health

osetljive pacijente tokom njihovog dolaska u domove zdravlja¹⁸. Zdravstveni radnici koji nemaju dokumentaciju da su primili dve doze vakcine, ili nemaju laboratorijsku potvrdu imuniteta (nalaz specifičnih *IgG* antitela), treba da budu vakcinisani sa dve doze *MMR* vakcine¹⁴.

Imunizacija je jedina efikasna preventivna mera protiv malih boginja. Pokrivenost vakcinacijom sa dve doze od najmanje 95% opšte populacije na nacionalnom i subnacionalnom nivou je neophodna da bi se osigurao prekid cirkulacije virusa. Jačanje i obezbeđenje visokokvalitetnog nadzora, uključujući praćenje promena u epidemiologiji malih boginja, pomaže u koordinaciji javnih zdravstvenih aktivnosti. U primarnoj zdravstvenoj zaštiti sve sumnjive slučajeve treba otkriti, prijaviti i istražiti, kako bi se što je pre moguće prekinuli lanci prenosa bolesti. Izabrani lekari kroz stalnu edukaciju pacijenata o ulozi i koristi imunizacije kao najefikasnije mere u prevenciji širenja zaraznih bolesti i pružanje informacija zasnovanih na naučnim činjenicama, treba da povrate poverenje građana činjenicom da je vakcinacija kao nijedna druga medicinska intervencija spasila najveći broj života. Potrebno je povećanje aktivnosti na većem obuhvatu rutinskom imunizacijom, kao i formiranje baza podataka u vidu elektronskih registara za dokumentovanje vakcinalnog statusa pojedinaca.

Zaključak

Epidemija malih boginja u Kraljevu trajala je pet meseci. Obbolele su 243 osobe. Najučestaliji simptomi bili su ospa, povišena telesna temperatura, kašalj i opšta slabost. Značajno su više obolevale osobe nepoznatog vakcinalnog statusa. Najveći procenat obolelih je u grupi 30-39 godina. Sva obolela deca do devet godina starosti nisu primila nijednu dozu vakcine protiv malih boginja. Hospitalizacije i komplikacije su bile najčešće kod dece do četiri godine starosti. Najzastupljenije komplikacije su bile pneumonije, dijareja i upale srednjeg uha. Ukupno četrdeset zdravstvenih radnika i drugih zaposlenih u zdravstvenim ustanovama je obolelo tokom epidemije. Smrtnih ishoda nije bilo.

care facilities¹⁸. Health workers who have no medical records of receiving two doses of the vaccine or no lab confirmation of their immunity (specific *IgG* antibodies) should be vaccinated with two doses of the *MMR* vaccine.¹⁴

Immunization is the only effective, preventive measure against measles. Two dose vaccine coverage, of at least 95%, of the general population, would be necessary to stop virus circulation. Ensuring and strengthening high quality surveillance, including monitoring the changes in measles epidemiology helps in coordinating the activity of public health care services. All the suspicious disease cases should be recognized, detected, reported and investigated in order to disrupt the viral breach, as soon as possible. GPs should educate their patients on the importance of immunization, as the most efficient preventive measure. The information should be evidence based and convincing enough to restore people's trust in the vaccines. Vaccination, as no other medical intervention, saved millions of lives worldwide. Routine vaccine coverage should be increased, as well as forming database (electronic records on an individual's vaccination status).

Conclusion

Measles outbreak in Kraljevo lasted for 5 months. There were 243 diseased persons. The most frequent symptoms were rash, fever, cough, and general weakness. There were significantly more diseased persons among those with the unknown vaccination status. The majority of the diseased were in the 30-39 age group. All the diseased children, up to 9 years of age, didn't receive a single dose of the measles vaccine. Hospitalizations and complications were the most frequent among the children up to 4 years. The most frequent complications were pneumonia, diarrhea, and otitis media. There were a total of 40 health workers and other health personnel who fell ill. There were no death outcomes.

Literatura / References

1. Moss WJ. *Measles*. The Lancet. 2017; 390(10111): 2490–2502.
2. World Health Organization. *Eliminating measles and rubella* - Framework for the verification process in the WHO European Region 2014. Copenhagen, WHO Regional Office for Europe; 2014 [accessed 28 January 2019]
3. World Health Organization. *Vaccine-induced immunity appears to be long-term, and is probably lifelong in most individuals*. Available from: <https://measlesrubellainitiative.org/wp-content/uploads/2017/01/Surv-guidelines-measles-CR-infection.pdf> [accessed 2019 January 27]
4. European Centre for Disease Prevention and Control. *Risk of measles transmission in the EU/EEA, 21 March 2018*. Stockholm, ECDC. 2018. Available from: <https://ecdc.europa.eu/en/publications-data/rapid-riskassessment-risk-measles-transmission-eueea> [accessed 2019 January 27].
5. World Health Organization. *WHO vaccine-preventable diseases: monitoring system. 2018 global summary. estimated vaccination coverage and VPD by country*. Available from: http://apps.who.int/immunization_monitoring/globalsummary/countries?countrycriteria%5bcountry%5d%5b%5d=SRB [accessed 2019 January 27]
6. Ministarstvo zdravlja Republike Srbije. *Pravilnik o imunizaciji i načinu zaštite lekovima* (Službeni glasnik RS, br. 88/17, 11/18, 14/18).
7. World Health Organization. *Immunization, Vaccines and Biologicals*. Available from: <https://www.who.int/immunization/diseases/measles/en/> [accessed 2019 January 25]
8. Institute of Public Health of Serbia. *The current epidemiological situation of measles in the Republic of Serbia*. 2018. Available from: <http://www.batut.org.rs/index.php?content=1629> [accessed 2019 January 25]
9. Božić M, Dokić Lj, Nikolić S, Pavlović M, Šašić M. *Infektivne bolesti*. Udžbenik za studente medicine. Medicinski fakultet Univerziteta u Beogradu. Beograd: CIBID. 2009.
10. Naim YH. *Measles virus A pathogen, vaccine, and a vector*. Hum Vaccin Immunother. 2015; 11(1): 21–26.
11. European Centre for Disease Prevention and Control (ECDC). EUVAC net. Case Definition. Measles. Stockholm: ECDC. Available from: <https://ecdc.europa.eu/en/surveillance-and-disease-data/eu-case-definition> [accessed 2019 January 27].
12. Ministarstvo zdravlja Republike Srbije. *Zakon o zaštiti stanovnika od zaraznih bolesti* (Sl. glasnik RS, br 15/16).
13. Ministarstvo zdravlja Republike Srbije. *Pravilnik o prijavljivanju zaraznih bolesti i posebnih zdravstvenih pitanja* (Sl. glasnik RS, br 44/17).
14. *Mere sprečavanja širenja virusa morbila u zdravstvenim ustanovama*. Available from: <http://www.batut.org.rs/download/reZaSprecavanjeSirenjaVirusaMorbilaUZU.pdf> [accessed 2019 January 27].
15. Ministarstvo zdravlja Republike Srbije. *Uredba o programu zdravstvene zaštite stanovništva od zaraznih bolesti*. „Sl. glasnik PC”, br. 22/16.
16. Coughlin MM, Beck AS, Bankamp B, Rota PA. *Perspective on Global Measles Epidemiology and Control and the Role of Novel Vaccination Strategies*. Viruses. 2017;9(1):1-17.
17. European Centre for Disease Prevention and Control. *Monthly measles and rubella monitoring report, January 2019*. Stockholm, ECDC. 2018. Available from: <https://ecdc.europa.eu/en/measles> [accessed 2019 January 27]
18. O'Connor P, Jankovic D, Muscat M, Ben-Mamou M, Reef S, Papania M et al. *Measles and rubella elimination in the WHO Region for Europe: progress and challenges*. Clin Microbiol Infect. 2017; 23(8): 504–510.
19. World Health Organization. *Measles-containing vaccine 2nd dose – reported estimates of MCV2 coverage* [Internet]. Geneva: WHO; 2018. Available from: http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tscoveragemcv2.html. [accessed 28 January 2019].
20. World Health Organization. *2018 Assessment report of the strategic global vaccine action plan*. [accessed 28 January 2019]
21. *Global measles and rubella strategic plan 2012–2020*. Geneva: World Health Organization; 2012. (http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396_eng.pdf [accessed 28 January 2019])
22. Palamara MA, Visalli G, Picerno I, Di Pietro A, Puglisi G, Marano F. Measles outbreak from February to August 2017 in Messina, Italy. J Prev Med Hyg 2018; 59: E8-E13.
23. Veličković Z, Ilić M, Nataša Rančić N. *Measles outbreak in the Nišava and Toplica districts*. Acta Medica Medianae 2016; 55(2): 71-75.
24. Čalkić L, Skomorac M, Tandir S, Sivić S, Bajramović-Omeragić L. *Public health significance of immunization and epidemic occurrence of measles*. Med Glas (Zenica) 2018; 15(1): 46-51.
25. Đurić-Petković D, Ristanović E, Kuljić-Kapulica N. *Virus malih boginja*. MD-Medical Data 2017; 9(3): 181-184.
26. Simons E, Ferrari M, Fricks J, Wannemuehler K, Anand A, Burton A, et al. *Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data*. Lancet 2012; 9;379(9832):2173-78.
27. M-M-R® II. *Measles, mumps, and rubella virus vaccine live*. Kenilworth, NJ: Merck & Co.; revised October 2015.

Primljen * Received 02.04.2019.
Ispravljen * Corrected 28.07.2019.
Prihvaćen * Accepted 01.08.2019.