

# UZROK PREVREMENOG POROĐAJA KAO PROGNOŠTIČKI FAKTOR NEONATALNOG ISHODA I NAČINA ZAVRŠAVANJA POROĐAJA

ORIGINALNI RAD

ORIGINAL ARTICLE

## CAUSE OF PREMATURE BIRTH AS A PROGNOSTIC FACTOR OF NEONATAL OUTCOME AND TYPE OF DELIVERY

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### SAŽETAK

**Uvod:** Prevremeni porođaj je porođaj pre 37. nedelje gestacije. Prevremeni porođaji su najčešće uzrokovani pojavom regularnih uterinskih kontrakcija, prevremenim prsnućem plodovih ovojaka ili abrupcijom posteljice. U 20% – 30% slučajeva kada postoje maternalne ili fetalne komplikacije, prevremeni porođaj može biti indukovano. Najčešći razlog za to su preeklampsija, zastoj u rastu ploda, te teška srčana oboljenja majke.

**Cilj rada:** Cilj rada jeste utvrđivanje povezanosti uzroka i vremena nastanka prevremenog porođaja sa neonatalnim ishodom.

**Materijali i metode:** Retrospektivnom studijom smo analizirali prevremeno porođene pacijentkinje u Ginekološko-akušerskoj klinici „Narodni front“ tokom 2020. kao i uzrok njihovog prevremenog porođaja, stanje ploda nakon porođaja. Komparirali smo neonatalni ishod kod spontanog i indukovano prevremenog porođaja.

**Rezultati:** Od ukupnog broja porođaja ( $n = 4.211$ ), od jula do decembra 2020. godine, 498 je bilo pretermijskih, što čini 11,83%. Na osnovu podataka o vitalnom statusu prematurusa, procenat mrtvih nedonoščadi iznosio je 8,9%, dok je procenat živih iznosio 91,1%. Apgar skor je bio najviši kod novorođenčadi iz vaginalnog porođaja, nakon 34. nedelje gestacije, sa intaktnim plodovima opnama i spontanom uspostavljanjem kontrakcija. Prema datoj studiji, 54,1%, pretermijskih porođaja je završeno carskim rezom, što je uzrokovano gestacijskom starošću trudnoće mlađom od 28 nedelja gestacije i dominantno karličnom prezentacijom ploda.

**Zaključak:** Značajna učestalost prevremenog porođaja, u odnosu na ukupan broj porođaja, ukazuje na ozbiljnost problema i dalju tendenciju rasta broja prevremenih porođaja i pored primenjenih svih preventivnih mera. Bolji ishod trudnoća se uočava kod porođaja u kasnijoj gestaciji, nakon 34. nedelje, sa intaktnim plodovima opnama, bez znakova infekcije. Viši Apgar skor kod dece iz spontanog u odnosu na indukovani prevremeni porođaj govori o boljem neonatalnom ishodu.

**Ključne reči:** prevremeni porođaj, prematurus, Apgar skor

### ABSTRACT

**Introduction:** Premature birth, occurring before the 37<sup>th</sup> gestational week, is commonly attributed to uterine contractions, premature rupture of the amniotic sac, or placental abruption. In 20% – 30% cases involving maternal or fetal complications, premature birth may be induced, often due to conditions such as preeclampsia, fetal growth retardation, or severe maternal heart disease.

**Aim:** The study aims to determine whether the cause and time of preterm birth affect the neonatal outcome.

**Material and methods:** This retrospective study analyzes patients prematurely born at the Obstetrics and Gynecology Clinic *Narodni Front* in 2020, the cause of their premature birth, as well as the status of the fetus after birth. In the study, we compared the neonatal outcome in spontaneously induced preterm birth.

**Results:** Among all the births ( $n = 4,211$ ), in the period between July and December 2020, there were 498 preterm births, i.e., 11.83%. Based on the data on the status of the premature infants' vital signs, the percentage of stillborn preterm infants was 8.9% while the percentage of live births was 91.1%. The Apgar score was the highest in neonates born by vaginal birth after the 34<sup>th</sup> week of gestation, with intact fetal membranes and spontaneous contractions. According to the study, 54.1% of preterm births ended in cesarean section due to gestational age younger than 28 weeks and with a predominantly pelvic presentation of the fetus.

**Conclusion:** The high rate of premature births highlights a serious problem and suggests a continued rising trend, despite preventive efforts. Improved outcomes are seen in pregnancies reaching later gestational weeks, particularly after the 34<sup>th</sup> week of gestation, with intact fetal membranes and no signs of infection. Spontaneously born premature infants tend to have higher Apgar scores and better neonatal outcomes, as compared to induced births.

**Keywords:** preterm birth, premature infant, Apgar score

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## UVOD

Pretermijski porođaj je jedan od najaktuelnijih problema perinatalne medicine danas. Predstavlja potencijalno vrlo opasan perinatalni događaj, prvenstveno sa stanovišta perinatalnog morbiditeta i mortaliteta. Po definiciji, to je porođaj koji nastupi pre 37. gestacijske nedelje [1]. Prema podacima Svetske zdravstvene organizacije (SZO), na osnovu gestacijske starosti, prevremeni porođaj može biti ekstremno rani – pre 28. nedelje gestacije, rani – između 28. i 32. nedelje gestacije, umereno rani – između 32. i 34. nedelje gestacije, te kasni – između 34. i 37. nedelje gestacije. Novorođenče iz pretermijskog porođaja se naziva nedonoščetom ili prematurusom. Dugo se definicija pretermijskog porođaja vezivala za telesnu masu novorođenčeta, ali danas se zna da je za preživljavanje mnogo značajnija gestacijska starost trudnoće i zrelost prematurusa nego sama telesna masa na rođenju [1].

Prematuritet je najvažniji pojedinačni faktor neonatalnog morbiditeta, mortaliteta i kasnih posledica na preživelim. Ishod i tok prevremenog porođaja zavise i od ekonomske razvijenosti zemlje. Na našim prostorima učestalost pretermijskog porođaja iznosi oko 8% [1].

Prematurusi su ugroženi nezrelošću svih organskih sistema, ali pluća i centralni nervni sistem su posebno osetljivi. Komplikacije kod prevremeno rođene dece mogu se javiti neposredno nakon rođenja. Najčešće i najozbiljnije su: intraventrikularna hemoragija, respiratorni distres sindrom, sepsa i nekrotizirajući enterokolitis. Kasne komplikacije se uočavaju tokom odrastanja i predstavljaju trajne sekvele: retinopatija, cerebralna paraliza, psihomotorni i kognitivni poremećaji. Prematurusi predstavljaju veliki problem, ne samo za pojedince i porodicu, već i za društvo uopšte [1].

Etiologija prevremenog porođaja je multifaktorijalna, neretko ne možemo utvrditi tačan uzrok njegovog nastanka. Uzroke možemo podeliti na promenljive i nepromenljive, kao i na uzroke maternalnog ili fetalnog porekla. Najčešći uzroci su infekcija, multiparitet, anomalije materice, kratak vremenski period između dve trudnoće, te raniji prevremeni porođaji u anamnezi. Na povećanje rizika utiču stil života, pušenje, loša ishrana, konzumiranje lekova, alkohola i droga (posebno kokaina), stres, loši socioekonomski uslovi. Uopšteno posmatrajući etiološke faktore, jedna trećina pretermijskih porođaja je uzrokovana infekcijom i prevremenim prsnućem plodovih ovojaka (engl. *preterm premature rupture of membranes -PPROM*), druga trećina je posledica maternalnih i fetalnih faktora, a kod preostale trećine, koja je po nekim podacima i do 50% nepoznate etiologije, govorimo o idiopatskom prevremenom porođaju. Najznačajniji faktori rizika koji su u vezi sa majkom su

## INTRODUCTION

Preterm birth is one of the most relevant problems of perinatal medicine today. It represents a potentially very dangerous perinatal event, primarily from the point of view of perinatal morbidity and mortality. By definition, it is a birth that occurs before the 37<sup>th</sup> week of gestation [1]. According to World Health Organization (WHO) data, based on gestational age, premature birth can be extremely preterm – before the 28<sup>th</sup> week of gestation, very preterm – between the 28<sup>th</sup> and 32<sup>nd</sup> weeks of gestation, moderate preterm – between the 32<sup>nd</sup> and 34<sup>th</sup> weeks of gestation, and late preterm – between the 34<sup>th</sup> and 37<sup>th</sup> weeks of gestation. A newborn baby born prematurely is called a premature or preterm infant. For a long time, the definition of preterm delivery was linked to the body weight of the newborn, but today it is known that the gestational age of the pregnancy and the maturity of the preterm infant are much more important for survival than the body weight at birth [1].

Prematurity is the single most important factor in neonatal morbidity, mortality, and subsequent effects on surviving infants. The outcome and course of premature birth also depend on the economic development of the country. In our region, the frequency of preterm birth is about 8% [1].

Premature babies are threatened by the immaturity of all organ systems, but the lungs and central nervous system are particularly sensitive. Complications in premature babies can occur immediately after birth. The most common and most serious are the following: intraventricular hemorrhage, respiratory distress syndrome, sepsis, and necrotizing enterocolitis. Late complications are observed during adulthood and represent permanent sequelae: retinopathy, cerebral palsy, and psychomotor and cognitive disorders. Premature babies are a significant problem, not only for individuals and families but also for society in general [1].

The etiology of premature birth is multifactorial, and we often cannot determine the exact cause of its occurrence. The causes can be categorized as variable and non-variable, as well as causes of maternal or fetal origin. The most common causes are infection, multiparity, uterine anomalies, a short period between two pregnancies, and previous premature births in the anamnesis. Lifestyle, smoking, poor diet, consumption of medicines, alcohol and drugs (especially cocaine), stress, and poor socioeconomic conditions increase the risk of premature birth. Looking at the etiological factors in general, one third of preterm births are caused by infection and premature rupture of membranes (PPROM), another third is the result of maternal and fetal factors, and the remaining third, which ac-

sledeći: pozitivna prethodna anamneza preterminskog porođaja, životno doba trudnice (ispod 20 ili preko 35 godina), višerotke, rađanje dece male telesne mase, hipertenzivna bolest u trudnoći, urinarnе infekcije, infektivne bolesti, febrilna stanja majke, maligna oboljenja, anemija, *diabetes mellitus*, razvojne anomalije uterusa, inkompetentan i insuficijentan donji uterušni segment, povećana količina plodove vode, krvarenja iz uterusa (abrupcija placente, *placenta previa*, placentalna insuficijencija), kao i druga hronična oboljenja majke [1].

Kod intaktnih plodovih ovojaka, preterminski porođaj može biti uzrokovan ascendentnim širenjem infekcije iz vagine i cerviksa. To je stanje neme infekcije, kada postoji intrauterina infekcija, ali nema kliničkih znakova koji ukazuju na njeno prisustvo. Od fetalnih faktora na prvom mestu su višeploidne trudnoće, zatim fetalne anomalije, intrauterini zastoj u rastu, intrauterino uginuće ploda, anomalije položaja i prezentacije [1].

Cilj rada je da se utvrdi da li uzrok i vreme nastanka prevremenog porođaja utiče na neonatalni ishod.

## MATERIJALI I METODE

Iz baze podataka porođaja obavljenih tokom 2020. godine u Ginekološko-akušerskoj klinici „Narodni front“, u studiju su uključeni samo preterminski porođaji u vremenskom periodu od 1. 07. 2020. do 31. 12. 2020. godine. Iz studije su isključene sve višeploidne trudnoće, kao i prevremeni porođaji indukovani zbog anomalija ploda. Metodama deskriptivne statistike opisali smo makroskopski izgled plodove vode, pol, vitalni status novorođenčeta, način završetka porođaja, intaktnost plodovih opni, položaj ploda, Apgar ocenu u prvom i petom minutu, te prepartalno primenjenu terapiju deksametazonom kod trudnica.

### Statistička analiza

Podaci su uneti u bazu podataka i obrađeni korišćenjem programa *IBM SPSS 25*. U radu su korišćene metode deskriptivne i analitičke statistike. Od metoda deskriptivne statistike korišćene su: mere centralne tendencije, mere varijabiliteta i relativni brojevi. Od metoda analitičke statistike korišćene su metode za procenu značajnosti razlike, hi-kvadratni test i Men Vitnijev test, kao i metode za procenu značajnosti povezanosti, Spirmanov koeficijent korelacije ranga. Vrednost  $p < 0,05$  je smatrana statistički značajnom.

## REZULTATI

Od ukupnog broja porođaja ( $n = 4.211$ ), od jula do decembra 2020. godine, bilo je 498 preterminskih, što čini 11,83% (Grafikon 1). Na osnovu podataka o vitalnom statusu prematurusa, procenat mrtvih nedonoščadi iznosio je 8,9%, a živih 91,1%.

According to some data is up to 50% of unknown etiology, is idiopathic premature birth. The most significant risk factors related to the mother are the following: positive previous history of preterm birth, age of the pregnant woman (below 20 or over 35 years), multiple births, birth of children with low body weight, hypertensive disease in pregnancy, urinary infections, infectious diseases, febrile maternal conditions, malignant diseases, anemia, diabetes mellitus, developmental anomalies of the uterus, incompetent and insufficient lower uterine segment, increased amount of amniotic fluid, bleeding from the uterus (abruption of the placenta, placenta previa, placental insufficiency), as well as other chronic maternal diseases [1].

In the case of intact fetal membranes, preterm delivery can be caused by an ascending infection from the vagina and cervix. It is a state of silent infection, when there is an intrauterine infection, but there are no clinical signs indicating its presence. Of the fetal factors, multiple pregnancies are the most common cause of premature birth, followed by fetal anomalies, intrauterine growth retardation, intrauterine death of the fetus, and anomalies of position and presentation [1].

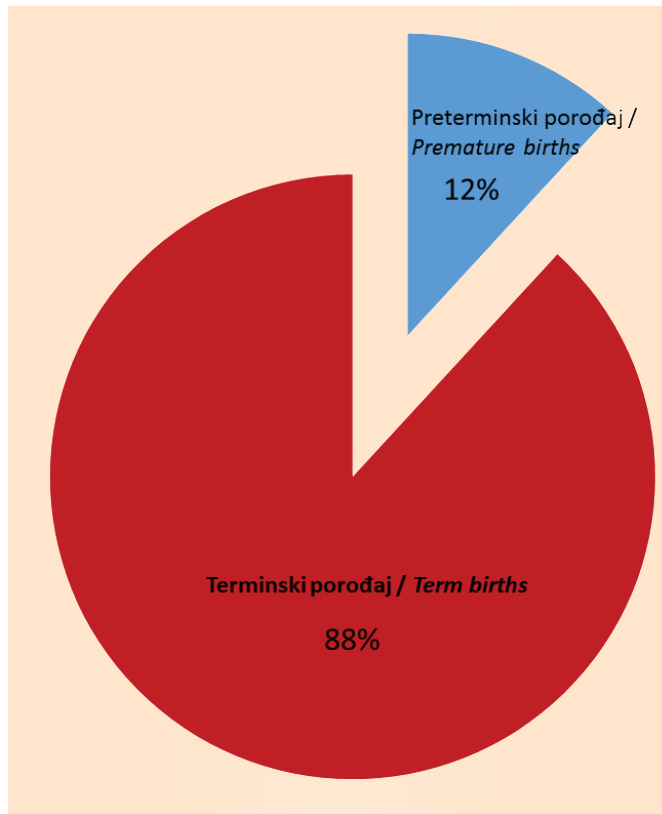
The study aims to determine whether the cause and time of premature birth affect the neonatal outcome.

## MATERIALS AND METHODS

From the database of deliveries performed during 2020 at the Obstetrics and Gynecology Clinic *Narodni Front*, only preterm births occurring in the period between July 1, 2020, and December 31, 2020, were included in the study. All multiple pregnancies, as well as premature births induced due to fetal anomalies, were excluded from the study. Using the methods of descriptive statistics, we described the macroscopic appearance of the amniotic fluid, the sex, the status of the newborn's vitals, the way the delivery was completed, the structural integrity of the fetal membranes, the position of the fetus, the Apgar score at one and five minutes after birth, and noted prepartum dexamethasone therapy administered in the expectant mothers.

### Statistical analysis

The data were entered into the database and processed using the *IBM SPSS 25* software. Methods of descriptive and analytical statistics were applied in the study. The following methods of descriptive statistics were used: measures of central tendency, measures of variability, and relative numbers. The following methods of analytical statistics were used: methods for assessing the significance of difference, the Chi-square test, and the Mann-Whitney test, as well as methods for assessing



**Grafikon 1.** Prikaz odnosa pretermijskih porođaja u odnosu na sve porođaje u Ginekološko-akušerskoj klinici „Narodni front“ u vremenskom periodu od 1. 07. 2020. do 31. 12. 2020. godine

**Figure 1.** Overview of preterm births compared to all births at the Obstetrics and Gynecology Clinic Narodni Front in the period between July 1, 2020 and December 31, 2020

Prema datoj studiji, 54,1%, pretermijskih porođaja je završeno carskim rezom, što je uzrokovano gestacijskom starošću trudnoće mlađom od 28 nedelja gestacije i dominantno karličnom prezentacijom ploda. Vaginalnim putem je bilo završeno 46% porođaja.

Najčešće je plod bio u prezentaciji glavom (41,9%), dok je prezentacija zatkom bila prisutna u 3,4% slučajeva. Akušerske intervencije, vakum i unutrašnji okret, urađene su u samo 0,6% slučajeva. Spontano prsnuće vodenjaka, kao uzrok prevremenog porođaja, zabeleženo je u 39,7% slučajeva, dok su plodove opne bile intaktne kod 60,3% svih prevremenih porođaja. Metodama analitičke statistike ( $p = 0,075$ ) uočeno je da ne postoji značajna diskrepancija između načina ruptur vodenjaka i vitalnog statusa prematurusa.

Plod, kao porođajni objekat, utiče na tok i ishod porođaja svojim položajem [1]. U našoj studiji, podaci u vezi sa položajem ploda (385) govore da je bilo 313 (79,2%) uzdužnih položaja glavom, 41 (10,4%) uzdužni karlični, 19 (4,8%) nožnih, 11 (2,8%) poprečnih, 8 (2%) karličnih, dva (0,5%) zadnja potiljačna, te jedan (0,3%) kosi.

the significance of association, Spearman's rank correlation coefficient. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

Of the total number of births ( $n = 4,211$ ), in the period between July and December 2020, there were 498 preterm births, which is 11.83% (Figure 1). Based on the data on the status of the premature infants' vital signs, the percentage of stillborn preterm infants was 8.9% while the percentage of live births was 91.1%.

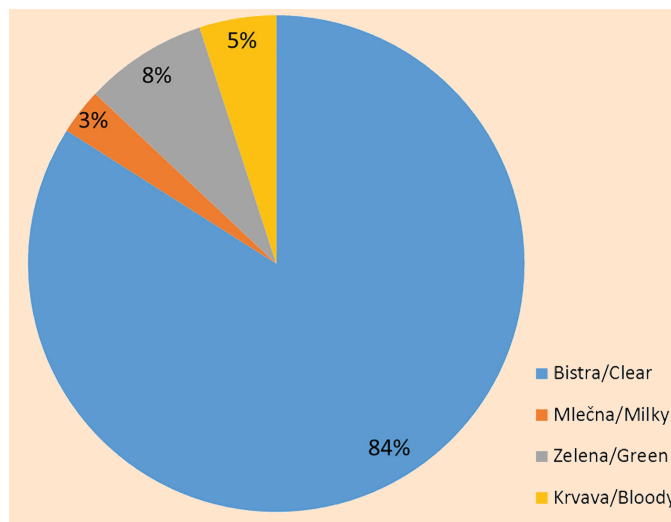
According to the study, 54.1% of preterm births ended in cesarean section due to gestational age younger than 28 weeks and with a predominantly pelvic presentation of the fetus. A total of 46% of births were completed vaginally.

Most often, the fetal presentation was cephalic (41.9%), while the pelvic presentation was present in 3.4% of cases. Obstetric interventions, vacuum and internal rotation, were performed in only 0.6% of cases. Spontaneous rupture of the amniotic sac, as a cause of premature birth, was recorded in 39.7% of cases, while the amniotic sac was intact in 60.3% of all premature births. Methods of analytical statistics ( $p = 0.075$ ) revealed no significant discrepancy between the mechanism of amniotic sac rupture and the status of the preterm infants' vital signs.

The fetus, as the object of the delivery, affects the course and outcome of childbirth with its position [1]. In our study, data related to fetal position (385) indicate that there were 313 (79.2%) cases of longitudinal cephalic position, 41 (10.4%) cases of longitudinal pelvic position, 19 (4.8%) cases of breech presentation, 11 (2.8%) cases of transverse lie, 8 (2%) cases of pelvic presentation, two (0.5%) cases of occiput posterior position, and one case of (0.3%) oblique position.

First-time mothers included in the study made up 61.5% (294) of the sample, 24.9% (119) of the subjects were second-time mothers, 8.6% (41) had delivered their third baby, 3.6% (17) of the mothers had given birth for the fourth time, 1% (5) had delivered a baby for the fifth time, while for 0.4% of the subjects this was their sixth or seventh delivery.

Amniotic fluid is an incredibly complex and dynamic milieu that changes as pregnancy progresses. It contains nutrients and growth factors, which facilitate the growth of the fetus, it provides mechanical movements of the fetus and antimicrobial effects that protect the fetus, and it allows assessment of fetal maturity and disease [2]. Of the available data for 390 preterm births, 327 (83.8%) had clear amniotic fluid, in 18 (4.6%) cases it was bloody, in 12 (3.1%) instances it was milky, and in 33 (8.5%) it had green discoloration (Figure 2).



**Grafikon 2.** Učestalost različitog makroskopskog izgleda plodove vode kod pretermijskih porođaja (bistra, zelena, krvava, mlečna)

**Figure 2.** The frequency of different forms of amniotic fluid macroscopic appearance in preterm births (clear, green, bloody, milky)

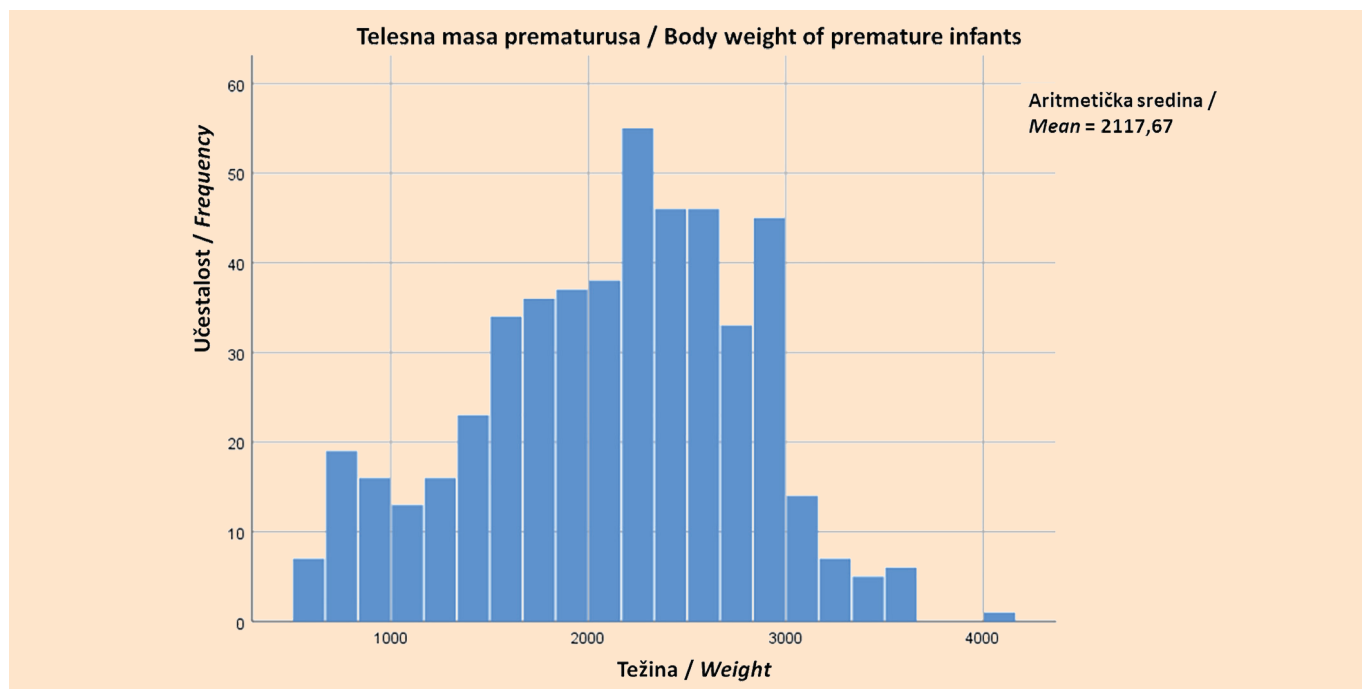
Prvorotke uključene u istraživanje su činile 61,5% (294), drugorotki je bilo 24,9% (119), trećerotki 8,6% (41), četvorotki 3,6% (17), petorotki 1% (5), dok je šestorotki i sedmorotki bilo 0,4%.

Plodova voda je neverovatno složen i dinamičan milje koji se menja kako trudnoća napreduje. Sadrži hranjive materije i faktore rasta, koji olakšavaju rast fetusa, obezbeđuje mehaničke pokrete fetusa i antimikrobne efekte koji štite fetus, te omogućava procenu zrelosti i bolesti fetusa [2]. Od postojećih podataka za

Despite technological progress and efforts made by doctors to preserve the health of newborns in recent years, extremely preterm infants (born before the 28<sup>th</sup> week of gestation) or with an extremely low birth weight (< 1,000 g) remain at high risk of death and disability, while female preterm infants, on average, have a better survival rate, as compared to the male sex [3]. Based on the data for 397 preterm births, 200 (50.4%) preterm males and 197 (49.6%) females were born. Using the chi-square test ( $p = 0.617$ ), no statistically significant difference in the vital status of newborns was found between the male and female sex. The average weight of the total number of premature babies was  $2117.67 \pm 684.22$  g, the average length was  $44.17 \pm 5.47$  cm, and the mean value of head circumference was  $31.05 \pm 3.44$  cm (Figure III). The highest frequency of premature births was in the 33<sup>rd</sup> week of gestation.

The Apgar score is a clinical assessment of the newborn's ability to survive based on vital parameters such as skin color, heart rate, breathing, muscle tone, and reflex response. It is determined at one and five minutes after childbirth. The score can range from 0 to 10. An Apgar score of 8 – 10 is considered normal, a score of 4 – 7 indicates moderate, and a score of 0 – 3 indicates severe neuromuscular depression, which most often occurs as the result of perinatal asphyxia [1,4].

The total number of available data regarding the Apgar score at one minute after birth is for 474 preterm infants. Of the given number, 39 (8.2%) preterm infants had a score of 0, 2 (0.4%) preterm infants had a score of 1, a score of 2 was found in 7 (1, 5%) premature babies,



**Grafikon 3.** Prikaz telesne mase prematurusa uključenih u studiju, u gramima

**Figure 3.** Body weight of premature infants included in the study, in grams

390 pretermijskih porođaja, 327 (83,8%) je imalo bistru plodovu vodu, 18 (4,6%) krvavu, 12 (3,1%) mlečnu i 33 (8,5%) zelenu prebojenost (Grafikon II).

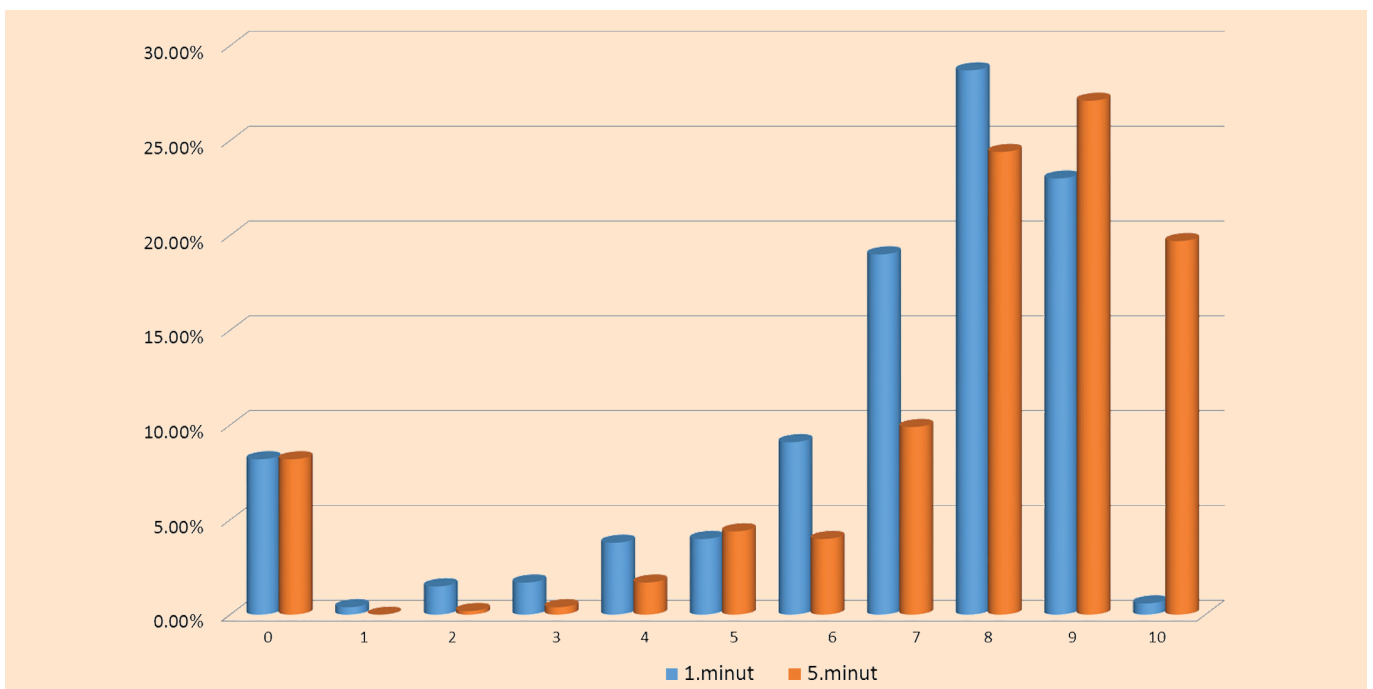
Uprkos tehnološkom napretku i naporima lekara da očuvaju zdravlje novorođenčadi tokom poslednjih godina, ekstremni prematurusi (rođeni pre 28. nedelje gestacije) ili sa ekstremno malom porođajnom težinom (< 1.000 g) ostaju pod visokim rizikom od smrti i invaliditeta, dok ženska nedonoščad, u proseku, imaju bolju stopu preživljavanja u odnosu na muški pol [3]. Na osnovu podataka za 397 pretermijskih porođaja, rođeno je 200 (50,4%) prematurusa muškog pola i 197 (49,6%) ženskog pola. Korišćenjem hi-kvadratnog testa ( $p = 0,617$ ) nije pronađena statistički značajna razlika vitalnog statusa novorođenčadi između muškog i ženskog pola. Prosečna težina totalnog broja prematurusa je bila  $2117,67 \pm 684,22$  g, dužina  $44,17 \pm 5,47$  cm, dok je srednja vrednost obima glave iznosila  $31,05 \pm 3,44$  cm (Grafikon III). Najveća frekvencija prevremenih porođaja bila je u 33. nedelji gestacije.

Apgar skor predstavlja kliničku procenu životne sposobnosti novorođenčeta na osnovu vitalnih parametara kao što su boja kože, srčana radnja, disanje, mišićni tonus, refleksni odgovor. Određuje se u prvom i petom minutu nakon porođaja. Skor se može kretati u rasponu od 0 do 10. Normalnim se smatra Apgar skor 8 – 10, skor 4 – 7 ukazuje na umerenu, a skor od 0 – 3 na tešku neuromišićnu depresiju, do koje najčešće dolazi usled perinatalne asfiksije [1,4].

Ukupan broj podataka o Apgar skoru u prvom minutu iznosi 474. Od datog broja, zbir 0 je imalo 39

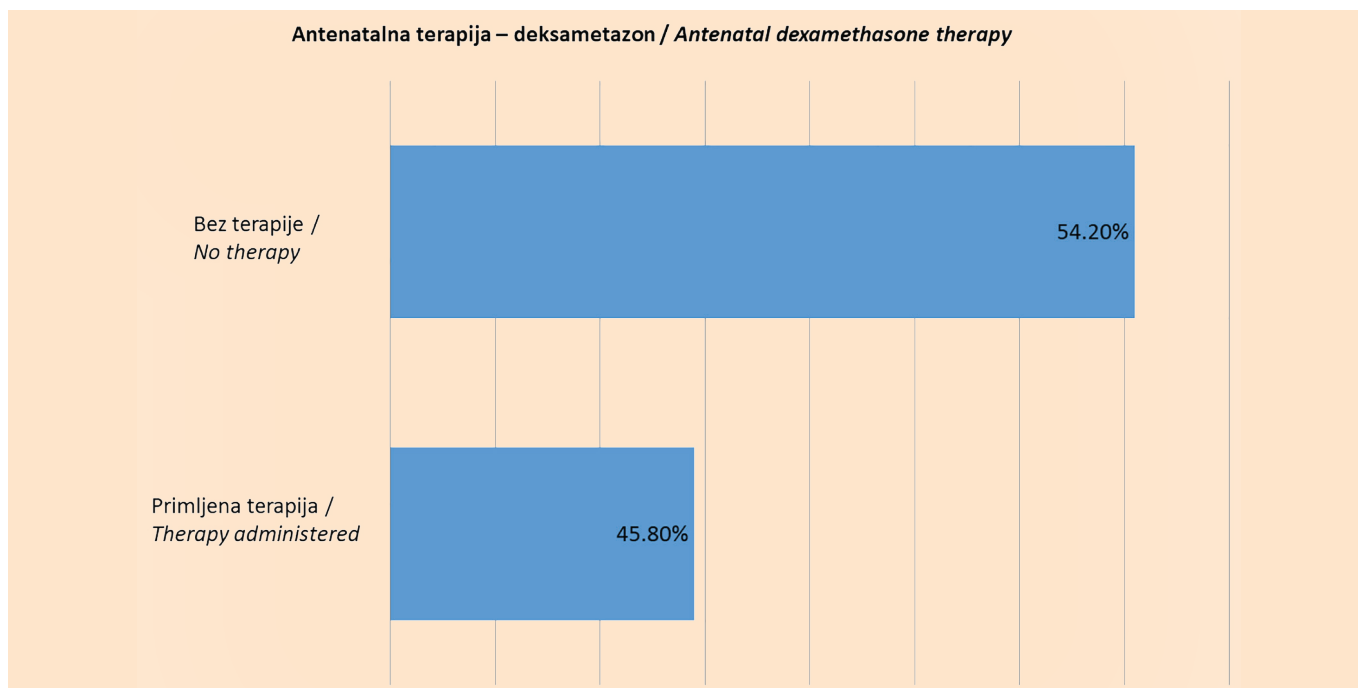
a score of 3 was registered in 8 (1.7%) preterm infants, 18 (3.8%) premature babies had a score of 4, a score of 5 was found in 19 (4%) premature newborns, a score of 6 was registered in 43 (9.1%) premature babies, a total of 90 (19.0%) preterm infants had a score of 7, 136 (28.7%) preterm newborns had a score of 8, 109 (23.0%) of them had a total of 9, while 3 (0.6%) premature babies scored a 10.

Today, greater importance is attached to the score at five minutes after birth, as it indicates the speed of adaptation of a healthy newborn, or the dynamics of recovery of an asphyxiated one [4]. From the database of 476 Apgar scores at five minutes after birth, a score of 0 was found in 39 (8.2%) premature babies, a score of 1 does not exist in the database, a score of 2 was recorded in one (0.2%) premature baby, a sum of 3 was found in 2 (0.4%) preterm infants, a score of 4 was determined in 8 of them (1.7%), a score of 5 was registered in 21 (4.4%) premature babies, a score of 6 was found in 19 (4.0%) premature infants, a score of 7 was registered in 47 (9.9%) cases, 116 (24.4%) premature babies had a score of 8, 129 (27.1%) of them had a score of 9, while 94 (19.7%) preterm infants scored a 10 (Figure IV). The Apgar score was the highest in newborns delivered vaginally, after the 34<sup>th</sup> week of gestation, with intact fetal membranes, and spontaneous onset of contractions. This data shows that the outcome of pregnancy is better in childbirth occurring later in gestation, after the 34<sup>th</sup> week, with intact fetal membranes and without signs of infection. A higher Apgar score in children from spontaneous



Grafikon 4. Vrednost Apgar skora u prvom i petom minutu, u rasponu od 0 do 10

Figure 4. The value of Apgar scores at one and five minutes after birth, ranging from 0 to 10



**Grafikon 5.** Učestalost porodilja koje nisu primale deksametazon i onih koje jesu primale deksametazon

**Figure 5.** The frequency of mothers who did not receive dexamethasone therapy and those who did receive dexamethasone therapy

(8,2%) prematurusa, zbir 1 je imalo 2 (0,4%) prematurusa, zbir 2 je imalo 7 (1,5%) prevremeno rođenih beba, zbir 3 je imalo 8 (1,7%) njih, zbir 4 je imalo 18 (3,8%) beba, zbir 5 je imalo 19 (4%) novorođenčadi, zbir 6 je imalo 43 (9,1%) prematurusa, zbir 7 je imalo 90 (19,0%) beba, zbir 8 je imalo 136 (28,7%) novorođenčadi, zbir 9 je imalo 109 (23,0%) njih, dok je zbir 10 ocenjeno 3 (0,6%) prematurusa.

Danas se veći značaj pridaje skor u petom minutu, koji označava brzinu adaptacije zdravog, odnosno dinamiku oporavka asfiktičnog novorođenčeta [4]. Iz baze 476 podataka o Apgar skor u petom minutu rođenja imamo zbir 0 kod 39 (8,2%) prematurusa, zbir 1 ne postoji u bazi, zbir 2 je zabeležen kod jednog (0,2%) prematurusa, zbir 3 je dobilo 2 (0,4%) novorođenčeta, zbir 4 je utvrđen kod njih 8 (1,7%), zbir 5 kod 21 (4,4%) prematurusa, zbir 6 kod njih 19 (4,0%), zbir 7 kod njih 47 (9,9%), zbir 8 kod 116 (24,4%) beba, zbir 9 kod njih 129 (27,1%), dok je zbir 10 imalo njih 94 (19,7%), (Grafikon IV). Apgar skor je bio najviši kod novorođenčadi iz vaginalnog porođaja, nakon 34. nedelje gestacije, sa intaktnim plodovim opnama i spontanijem uspostavljanjem kontrakcija. Ovaj podatak nam ukazuje da je bolji ishod trudnoća kod porođaja u kasnijoj gestaciji, nakon 34. nedelje, sa intaktnim plodovim opnama, bez znakova infekcije. Viši Apgar skor kod dece iz spontanog u odnosu na indukovani prevremeni porođaj govori i o boljem neonatalnom ishodu.

Kortikosteroidi se upotrebljavaju u cilju povećanja produkcije surfaktanta i ubrzanja fetalne plućne maturacije kod pretećeg prevremenog porođaja [1]. U

versus induced premature birth also indicates a better neonatal outcome.

Corticosteroids are administered in order to increase the production of surfactant and accelerate fetal lung maturation in case of threat of premature birth [1]. It has been proven in numerous studies that antenatal dexamethasone treatment of parturients results in a significantly lower risk of neonatal death, without any evidence of harm to the patient or the newborn [5]. A total of 228 (45.8%) parturients included in the study received dexamethasone, while 270 (54.2%) did not (Figure V). A statistically significant difference was observed in the status of the vitals in preterm infants whose mothers received dexamethasone, as compared to those who did not receive this treatment, using the chi-square test ( $p < 0.001$ ). According to our study, premature babies whose mothers received antenatal therapy had higher Apgar scores at one minute ( $p = 0.004$ ) and five minutes ( $p = 0.046$ ) after birth.

## DISCUSSION

A study conducted by Goldenberg et al., in 2008, in the United States of America (USA), indicates that the frequency of preterm births is about 12% - 13% in the United States and 5% - 9% in many other developed countries. However, the rate of premature birth also depends on the geographical location, mainly due to increased risk factors, as well as due to premature births resulting from multiple IVFs [6]. Common causes of preterm delivery include preeclampsia or eclampsia

brojnim studijama je dokazano da antenatalna terapija porodilja deksametazonom rezultira značajno manjim rizikom od neonatalne smrti, bez ikakvih dokaza o šteti po pacijentkinje ili novorođenčad [5]. Ukupno 228 (45,8%) porodilja uključenih u studiju je primilo deksametazon, dok 270 (54,2%) nije (Grafikon V). Uočena je statistički značajna razlika u vitalnom statusu prematurusa čije su majke primile deksametazon u odnosu na one koje nisu, primenom hi-kvadratnog testa ( $p < 0,001$ ). Prema našoj studiji, viši Apgar skor u prvom ( $p = 0,004$ ) i petom minutu ( $p = 0,046$ ) su imali prematurusi čije su majke primile antenatalnu terapiju.

## DISKUSIJA

Istraživanje, koje su sproveli Goldenberg i saradnici u Sjedinjenim Američkim Državama (SAD) 2008. godine ukazuje na to da je učestalost prevremenih porođaja oko 12% – 13% u Sjedinjenim Američkim Državama i 5% – 9% u mnogim drugim razvijenim zemljama, međutim stopa prevremenog porođaja zavisi i od geografske lokacije, uglavnom zbog povećanja faktora rizika i zbog prevremenih porođaja usled višeplođnih vantelesnih oplodnji [6]. Česti razlozi uključuju preeklampsiju ili eklampsiju i intrauterini zastoj rasta ploda. Od ukupnog broja pretermijskih porođaja, učestalost indukovanih porođaja iznosi 30 – 35%, spontani prevremeni porođaj ima učestalost 40% – 45%, dok je učestalost PPROM-a 25% – 30% [6]. Spontani porođaj i PPROM su zajedno označeni kao spontani prevremeni porođaji [6]. U našoj studiji je učestalost pretermijskih porođaja, tokom posmatranog perioda od šest kalendarskih meseci, iznosila 11,83%, dok se spontano započeti porođaj uočava kod 39,7% a indukovani porođaj kod 60,3% slučajeva.

Rizici se smanjuju sa porastom gestacijskog doba [1]. Pre 34. nedelje više od polovine pretermijskih neonatusa ima neku komplikaciju, dok se nakon 36. nedelje komplikacije sreću kod oko 16% njih.

Prema studiji koju su sproveli Mejo i saradnici 2017. godine u Sjedinjenim Američkim Državama, izuzetno mlade nulipare su u većem riziku od prevremenog porođaja, ali mehanizam nije jasno utvrđen [7]. Retrospektivnom kohortnom studijom su obuhvaćene nulipare starosti od 13 do 20 godina kod kojih je prevremeno završena pojedinačna trudnoća, u vremenskom periodu od 2007. do 2011. godine [7]. Rezultati govore da je najveća prevalencija, odnosno 14,5% pretermijskih porođaja kod najmlađih nulipara starosti 13 godina, a najniža upravo kod najstarijih, iz posmatrane grupe, odnosno kod dvadesetogodišnjakinja (6,7%) [7]. Naime, značajno je povećan rizik od spontanog prevremenog porođaja kod subjekata mlađih od 16 godina [7].

Naše istraživanje korelira sa dokazima koji upućuju na povećani rizik od prevremenog porođaja kod

and intrauterine growth retardation. Of the total number of preterm births, the frequency of induced births is 30% - 35%, the frequency of spontaneous preterm births is 40% - 45%, and the frequency of PPROM is 25% - 30% [6]. Spontaneous labor and PPROM are collectively referred to as spontaneous preterm labor [6]. In our study, the frequency of preterm births, during the observed period of six calendar months, was 11.83%, while spontaneous births were observed in 39.7%, and induced births in 60.3% of cases.

The risks decrease with increasing gestational age [1]. Before the 34<sup>th</sup> week, more than half of preterm neonates have some complication, while after the 36<sup>th</sup> week, complications occur in about 16% of preterm infants.

According to a study conducted by Mayo et al., in 2017, in the United States of America, extremely young nulliparous women are at higher risk of preterm birth, but the mechanism has not been clearly established [7]. A retrospective cohort study included nulliparae aged 13 to 20 years who had a single pregnancy terminated prematurely, in the period between 2007 and 2011 [7]. The results show that the highest prevalence, i.e. 14.5% of preterm births, is among the youngest nulliparae, aged 13, while the lowest prevalence of preterm deliveries was among the oldest in the observed group, i.e. among twenty-year-old women (6.7%) [7]. Namely, the risk of spontaneous preterm birth is significantly higher in subjects younger than 16 years [7].

Our study correlates with the evidence pointing to an increased risk of premature delivery in nulliparous women, who account for as many as 61.5% (294) cases, while women giving birth for the second time make up 24.9% (119) of the cases, women delivering their third child account for 8.6% (41) of preterm deliveries, those delivering their fourth child make up 3.6% (17) of cases, women having their fifth child constitute 1% (5) of all cases, and those delivering their sixth or seventh child contribute with only 0.4%, but we do not have data on the age of the mothers.

A 2017 UK study by Roberts et al. supports evidence that antenatal corticosteroids accelerate fetal lung development in case of the threat of premature birth [5]. The study included 7,774 parturients and 8,158 preterm infants [5]. Antenatal corticosteroid therapy, as compared to placebo or no treatment, clearly reduces some of the most serious complications in preterm infants, such as perinatal mortality, neonatal mortality, respiratory distress syndrome, intravascular hemorrhage, necrotizing enterocolitis, the need for mechanical ventilation, and systemic infection in the first 48 hours of life [5]. Based on the available data, we compared the status of the vitals of neonates with the use



nulipara, koje čine čak 61,5% (294) slučajeva, dok drugorotke čine 24,9% (119), trećerotke 8,6% (41), četvorrotke 3,6% (17), petorotke 1% (5), a šestorotke i sedmorotke samo 0,4% prevremenih porođaja, ali ne posedujemo podatke o starosti porodilja.

Studija koju su sproveli Roberts i saradnici 2017. godine u Velikoj Britaniji podržava dokaze da primena antenatalnih kortikosteroida ubrzava razvoj fetalnih pluća kod pretećih pretermijskih porođaja [5]. U studiju je uključeno 7.774 porodilje i 8.158 prematurusa [5]. Terapija antenatalnim kortikosteroidima, u poređenju sa placebo ili bez tretmana, jasno redukuje neke od najozbiljnijih komplikacija kod nedonoščadi, kao što su perinatalni mortalitet, neonatalni mortalitet, respiratorni distres sindrom, intravaskularna hemoragija, nekrotizirajući enterokolitis, potreba za mehaničkom ventilacijom i sistemska infekcija u prvih 48 sati života [5]. Prema dostupnim informacijama, uporedili smo vitalni status neonatusa sa primenom deksametazona kod porodilja u 394 slučajeva. U grupi pacijentkinja koje su primile terapiju deksametazonom (172), smrtnost je zabeležena kod samo 1 neonatusa što čini 0,6%, dok je 171 (99,4%) neonatus ostao živ. Sa druge strane, u grupi pacijentkinja koje nisu primile terapiju (222), bilo je 34 (15,3%) preminulih neonatusa i 188 (84,7%) živih.

U studiji koju su sproveli Li i saradnici 2013. godine u Kini dokazano je da sistem Apgar skora ima kontinuiranu, značajnu vrednost za predviđanje neonatalnih ishoda, kako za terminsku novorođenčad tako i za pretermijsku [8]. Prevremeni porođaji su imali oko 10 do 20 puta veću incidenciju niskog Apgar skora tokom petog minuta (< 7) nego terminski porođaji, iako je velika većina prevremenih porođaja imala rezultat veći od 7 [8]. Neonatalna stopa mortaliteta se smanjivala sa povećanjem Apgar skora. Analizirani su pretermijski porođaji od 24. do 36. gestacijske nedelje [8]. Vrednosti Apgar skora u petom minutu bile su: 1 kod 0,43 % prematurusa sa stopom neonatalnog mortaliteta od 581,86; 2 kod 0,293% prematurusa sa stopom mortaliteta koja je iznosila 334,68; 3 kod 0,38% prematurusa sa stopom mortaliteta od 192,42; 4 kod 0,57% prematurusa kod kojih je stopa mortaliteta bila 121,28; 5 kod 1% prematurusa sa stopom mortaliteta od 74,58; 6 kod 2,31% prematurusa koji su imali stopu mortaliteta od 43,47; 7 kod 5,2% prematurusa sa stopom mortaliteta od 18,91; 8 kod 16% prematurusa kod kojih je stopa mortaliteta iznosila 4,39; 9 kod 69,60% prematurusa sa stopom mortaliteta od 0,59; te 10 kod 4,23% prematurusa koji su imali stopu neonatalnog mortaliteta od 0,37 [8].

Međutim, Apgar skor ima svoja ograničenja [8]. Brojni faktori mogu uticati na Apgar rezultat kao što su

of dexamethasone in parturients, in 394 cases. In the group of patients who received dexamethasone therapy (172), mortality was recorded in only 1 neonate, which is 0.6%, while 171 (99.4%) neonates survived. On the other hand, in the group of female patients who did not receive this treatment (222), there were 34 (15.3%) deceased neonates while 188 (84.7%) survived.

In a study conducted by Li et al., in 2013, in China, it was demonstrated that the Apgar score system has a continuous, significant value for predicting neonatal outcomes, both for term and preterm infants [8]. Preterm births had about a 10 to 20 times higher incidence of low 5-minute Apgar scores (< 7) than term births, although a vast majority of preterm births had a score greater than 7 [8]. The neonatal mortality rate decreased with the increase of the Apgar score. The analysis included preterm births occurring between the 24<sup>th</sup> and the 36<sup>th</sup> gestational week [8]. Apgar score values at five minutes after birth were as follows: a score of 1 in 0.43% of premature infants with a neonatal mortality rate of 581.86; a score of 2 in 0.293% of premature babies with a mortality rate of 334.68; a score of 3 in 0.38% of premature babies with a mortality rate of 192.42; a score of 4 in 0.57% of premature infants, whose mortality rate was 121.28; a score of 5 in 1% of premature babies with a mortality rate of 74.58; a score of 6 in 2.31% of premature babies who had a mortality rate of 43.47; a score of 7 in 5.2% of premature babies with a mortality rate of 18.91; a score of 8 in 16% of premature babies with the mortality rate of 4.39; a score of 9 in 69.60% of premature babies with a mortality rate of 0.59; and a score of 10 in 4.23% of premature infants who had a neonatal mortality rate of 0.37 [8].

However, the Apgar score has its limitations [8]. Numerous factors can affect the Apgar score, such as drugs, trauma, congenital anomalies, infections, hypoxia, and hypovolemia, especially in premature births [8]. To date, there are but several consistent data on the significance of the Apgar score in preterm infants [8]. Because score components such as tone, color, and reflex excitability depend in part on the physiological maturity of infants, this situation may cause a healthy preterm infant without evidence of asphyxia to score lower, simply because of its current immaturity [8].

In our study, at five minutes after birth, we recorded an Apgar score of 0 in 8.2% of premature babies, a score of 1 does not exist in the database, a score of 2 was found in 0.2% of the cases, a score of 3 was recorded in 0.4% of premature babies, a score of 4 was registered in 1.7% of preterm infants, a score of 5 was recorded in 4.4% of the babies, a score of 6 occurred in 4.0% of cases, a score of 7 was observed in 9.9% of preterm infants, a score of 8 occurred in 24.4 % of cas-

lekovi, traume, urođene anomalije, infekcije, hipoksija, hipovolemija, naročito kod prevremenih porođaja [8]. Do danas, postoji nekoliko konzistentnih podataka o značaju Apgar skora kod nedonoščadi [8]. Pošto elementi skora kao što su tonus, boja i refleksna razdražljivost delimično zavise od fiziološke zrelosti odojčadi, ova situacija može dovesti do toga da zdravo prevremeno rođeno dete bez dokaza o asfiksiji dobije niži rezultat samo zbog trenutne nezrelosti [8].

U našem istraživanju, u petom minutu rođenja, imamo Apgar zbir 0 kod 8,2% prematurusa, zbir 1 ne postoji u bazi, zbir 2 se javlja kod 0,2% prematurusa, zbir 3 je zabeležen kod 0,4% prematurusa, zbir 4 je utvrđen kod 1,7% prematurusa, zbir 5 je zabeležen kod 4,4% njih, zbir 6 se javlja kod 4,0% prematurusa, zbir 7 uočavamo kod 9,9% prematurusa, zbir 8 se javlja kod 24,4% prematurusa, zbir 9 je prisutan kod 27,1% njih, dok je zbir 10 zabeležen kod 19,7% preautrusa. Ograničenja istraživanja su nedovoljan broj ispitanika i kratak vremenski period posmatranja.

## ZAKLJUČAK

Značajna učestalost prevremenog porođaja (11,8%) u ukupnom broju porođaja, ukazuje na ozbiljnost problema i dalju tendenciju rasta broja prevremenih porođaja i pored primenjenih svih preventivnih mera. Visoka učestalost vitalne novorođenčadi (91%) ukazuje na to da se, uz adekvatnu i pravovremenu terapiju, kao i uz adekvatan izbor u načinu završavanja ranih prevremenih porođaja, poboljšava perinatalni ishod novorođenčeta.

Visoka zastupljenost carskog reza (54,1%) pretermijskih porođaja je uzrokovana gestacijskom starošću trudnoće mlađom od 28. nedelje gestacije i dominantno karličnom prezentacijom ploda.

Intaktne plodove opne u više od polovine prevremenih porođaja govore da je najčešći uzrok prevremenih porođaja spontano započeta uterusna aktivnost kod prvorođene, što nam sugeriše na potrebu bolje informisanosti, kao i rasprostranjenosti preventivnih mera.

Bistra plodova voda (83,8%) ukazuje na to da infekcija nije bila dominantni uzrok prevremenog porođaja u našoj studiji.

Apgar skor je bio najviši kod novorođenčadi iz vaginalnog porođaja, nakon 34. nedelje gestacije, sa intaktnim plodovim opnama i spontanim uspostavljanjem kontrakcija. Ovaj podatak nam ukazuje na to da je bolji ishod trudnoća kod porođaja u kasnijoj gestaciji, nakon 34. nedelje, sa intaktnim plodovim opnama i bez znakova infekcije. Viši Apgar skor kod dece iz spontanog, u odnosu na indukovani prevremeni porođaj, govori o boljem neonatalnom ishodu. Bolji Apgar skor kod novorođenčadi čije su majke primile deksameta-

es, a score of 9 was present in 27.1% of premature infants, while a score of 10 was recorded in 19.7% of cases. Limitations of the research include the insufficient number of subjects and the short observation period.

## CONCLUSION

A significant frequency of premature births (11.8%) in the total number of births indicates the seriousness of the problem and the further tendency of the number of premature births to increase despite the implementation of all preventive measures. The high frequency of vital newborn infants (91%) indicates that, with adequate and timely therapy, as well as with an appropriate choice in the way that early premature delivery is completed, the perinatal outcome of the newborn improves.

A high incidence of cesarean section (54.1%) in preterm births is caused by the gestational age of the pregnancy that is younger than the 28<sup>th</sup> week as well as the predominant pelvic presentation of the fetus.

Intact fetal membranes in more than half of premature births indicate that the most common cause of premature deliveries is spontaneously initiated uterine activity in primiparous mothers, which suggests the need for better information dissemination and wider implementation of preventive measures.

Clear amniotic fluid (83.8%) indicates that infection was not the dominant cause of preterm birth in our study.

The Apgar score was the highest in newborns delivered vaginally, after the 34<sup>th</sup> week of gestation, with intact fetal membranes and spontaneous onset of contractions. This data indicates that the pregnancy outcome is better in late gestation, after the 34<sup>th</sup> week, with intact fetal membranes and no signs of infection. A higher Apgar score in children from spontaneous, compared to induced premature birth, indicates a better neonatal outcome. A better Apgar score in newborns whose mothers received dexamethasone indicates that we significantly improve the perinatal outcome with its application.

The frequency of preterm births is still increasing and is therefore a challenge for perinatologists and neonatologists. We emphasize the importance of implementing preventive measures at the level of primary health care in order to establish control over premature births.

**Conflict of interest:** None declared.

zon ukazuje na to da njegovom primenom značajno poboljšavamo perinatalni ishod.

Učestalost prevremenih porođaja je i dalje u porastu i stoga predstavlja izazov za perinatologe i neonatologe. Napominjemo značaj implementacije preventivnih mera na nivou primarne zdravstvene zaštite kako bi se uspostavila kontrola nad prevremenim porođajima.

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