

The influence of maternal and foetal factors on the success of medically induced labour

Utjecaj majčinih i fetalnih faktora na uspješnost medikamentozne indukcije poroda

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Abstract. Labour induction is the process in which labour is induced mechanically or pharmacologically. The percentage of induced labours is between 1.4% and 32% of the total number of births in the world. The aim of this research is to present the number of medically induced labours from 2012 to 2019 at the Clinic for Gynaecology and Obstetrics of the Clinical Hospital Center in Osijek and to present the success rate of medically induced labour and factors, both maternal and/or foetal which may affect it. **Materials and methods:** In the study 2361 subjects were included whose births were induced by medication regardless of the indication for medically induced labour, gestational age or mother's age. χ^2 test, Mann Whitney U test, Fisher's exact test, Kruskal Wallis test (Pot Hoc Conover), and the univariate and multivariate logistic regression model were used. **Results:** The percentage of inductions was 13.8%. 81% of the child births was completed vaginally, while 19% was completed by the caesarean section. The univariate regression analysis found that meconium amniotic fluid increases the risk of the caesarean section after the labour has been induced. Factors decreasing the possibility of the caesarean section after induced labour include multiparity, women age between 25 and 35 years and women bearing female children. The multivariate statistical regression model found that women over the age of 36 are 1.58 times more likely to have the caesarean section. Women with meconium amniotic fluid are 1.47 times more likely to have the caesarean section. Multiparity in the mother and the female sex of the child reduce the probability of the caesarean section after induced labour (odds ratio (OR) 0.20, $P=0.02$ and OR 0.84, $P=0.09$, respectively). **Conclusion:** The study indicates that multiparity and female gender of child increase the probability of the vaginal birth after the induction, while the mother's age over 36 and meconium amniotic fluid after the induction increase the risk of the caesarean section.

Key words: caesarean section; induced labour; oxytocin; prostaglandins

Sažetak. Indukcija poroda postupak je kojim mehaničkim ili farmakološkim putem pokušavamo potaknuti porod. Postotak induciranih porođaja u svijetu mjeri se od 1,4 do čak 32 % od ukupnog broja poroda. Cilj je ovog preglednog rada prikazati broj medikamentozno induciranih poroda u razdoblju od 2012. do 2019. godine na Klinici za ginekologiju Kliničkog bolničkog centra u Osijeku, prikazati uspješnost medikamentozne indukcije poroda te koji od materničnih i/li fetalnih faktora mogu utjecati na uspjeh indukcije poroda. **Materijali i metode:** Koristili smo podatke iz rađaonskog protokola Klinike za ginekologiju i porodništvo Kliničkog bolničkog centra u Osijeku. U istraživanje smo uključili 2361 ispitanicu čiji su porodi inducirani medikamentozno. Statistički smo obradili podatke o vrsti indukcije poroda, indikacijama za indukciju poroda te načinu poroda nakon indukcije. Koristili smo χ^2 test, Mann Whitney U test, Fisherov egzaktni test, Kruskal Wallis test (Pot Hoc Conover) te model univarijantne i multivarijantne logističke regresije. **Rezultati:** Postotak indukcija bio je 13,8%. U 81% slučajeva porod je dovršen vaginalnim putem, dok je u 19% slučajeva dovršen carskim rezom. Utvrdili smo da je čimbenik rizika za carski rez nakon indukcije poroda dijagnoza mekonijске plodove vode, dok su čimbenici koji smanjuju vjerojatnost carskog reza – dob majke od 25 do 35 godina, trudnice koje su rodile žensko dijete te trudnice koje su do sada već rađale. Modelom multivarijantne statističke

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regresije utvrdilo se da žene u dobi iznad 36 godina imaju 1,58 puta veću šansu za carski rez u odnosu na mlađe, a one s prisutnom dijagnozom mekonijske plodove vode 1,47 puta veću šansu za carski rez u odnosu na one koje nemaju navedenu dijagnozu. Multiparitet u majke te ženski spol djeteta smanjuju vjerojatnost carskog reza nakon indukcije poroda (redom OR 0.20, $P = 0.02$ te OR 0.84, $P = 0.09$). **Zaključak:** Studija je pokazala da su multiparitet i ženski spol djeteta protektivni faktori za vaginalni porod, dok su dob majke iznad 36 godina te zelena plodna voda nakon indukcije poroda rizični faktori za carski rez.

Ključne riječi: carski rez; inducirani porod; oksitocin; prostaglandini

Induction of labour is the process in which labour is induced mechanically or pharmacologically. The percentage of induced labour is increasing worldwide and is measured from 1.4% to as much as 32% of the total number of births.

INTRODUCTION

Induction of labour is the process in which labour is induced mechanically or pharmacologically. Indications for labour induction are diverse and related to the mothers' or child's condition. If the continuation of pregnancy threatens to harm the mother or the child, induced labour may have indication^{1,2}.

The percentage of induced labour is increasing worldwide³⁻⁵ and is measured from 1.4% to as much as 32% of the total number of births⁶. In 2/3 of cases, induced labour is completed vaginally⁷. For medically induced labour (MIL) are most commonly used prostaglandin preparation and/or oxytocin intravenously (I.V.). Labour induction bears its risks and complications. They include the increased use of uterotonics after the childbirth, the prolonged latent phase of labour, intrapartum haemorrhage, postpartum hysterectomy, more frequent use of analgesics, and delayed onset of breastfeeding⁷. The caesarean section is also one of the possible complications of induced labour. Research has shown that medically induced labour is not related to a higher percentage of the caesarean sections as mode of delivery⁶⁻⁹.

So far, the studies of the factors influencing the completion of induced labour included various

maternal, foetal, biochemical, and ultrasound variables⁸⁻¹³. The heterogeneity of topics presents a major obstacle in such research. The types of inductions and factors affecting it are not always comparable due to induction methods and different initial obstetric findings¹¹.

The aim of this paper is to present systematically the number of medically induced labours at the Clinic for Gynaecology and Obstetrics of the Clinical Hospital Centre in Osijek. The paper also aims to present the success rate of medically induced labours and factors, both maternal and/or foetal that may affect the success of induced labour. Success of labour is defined as vaginal delivery after induction. In addition, the aim is to research if there is a statistically significant difference in the percentage of caesarean sections between the group of medically induced labours and non-induced labours.

MATERIALS AND METHODS

This retrospective cohort study used data from the birth protocol of the Clinic for Gynaecology and Obstetrics of the Clinical Hospital Centre in Osijek from 1st January 2012 to 31st December 2019. The study included respondents whose births were medically induced (prostaglandin preparations or oxytocin I. V.) regardless of the indications, gestational age and mother's age. The total number of mothers included in this study is 2361. We studied eight variables related to mothers and new-borns. Variables observed in mothers include age, parity, type of labour induction and the mode of delivery. In new-borns, gestational age at birth, birth weight and foetal gender is observed. We also observed if meconium amniotic fluid showed after induction of labour. The data on the mode of induction, indications for induction and mode of delivery after the induction were statistically processed.

Statistics

In the study, χ^2 test, Mann Whitney U test, Fisher's exact test, Kruskal Wallis test (Pot Hoc Conover), and the univariate and multivariate logistic regression model is used. Multivariate logistic regression was applied to observe the negative outcome prediction model (caesarean

section). Stepwise logistic regression was used to choose the predictor, and the data were considered statistically significant if the value was higher than 0.10. As the criterion in the study, a cut-off value of 0.20 is selected. All *P* values were two-sided. The level of significance was set to Alpha = 0.05. The analysis was conducted using the MedCalc Statistical Software version 19.4.1 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2020) and the IBM SPSS Statistics 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.)

RESULTS

Median mothers' age was 30 (IQ 26-33 years). There were 17 103 births, 13.8% were induced. Regarding the method of labour induction, Prepidil gel was used in 62.9%, Prostin gel in 3.6%, and Syntocinon 33.5%. In the χ^2 test, some general gynaecological medical data were also analysed. Given the number of births, 59% were primiparous women, while 41% were multiparous women. With respect to the newborns' gender, 53% were male, while 47% were female. The largest

number of children (52%) weighed 2500-3500 g, followed by 41% of those heavier than 3500 g, while only 7% were under 2500 grams.

Table 1 presents the indications for induction of labour.

Of the total number of births, 81% were completed vaginally, while the remaining 19% were completed by caesarean section. The most common indication for the caesarean section after the induction was the threat of foetal asphyxia (33.1%), followed by dystocia (27.1%).

Logistic regression was used to evaluate the effect of several factors on the probability that induced labour would end up with caesarean section (dependent variable). In the case of the independent variables, we observed variables that proved to be significant or were mentioned as significant in the literature: maternal age, gestational age, mode of induction, parity, sex and weight of the child, and meconium amniotic fluid.

The univariate regression analysis indicated that factors increasing the risk of caesarean section after induced labour include the diagnosis of meconium amniotic fluid, while "protective fac-

Table 1. Indications for induction of labour

	Number (%)				<i>p</i> *
	Prepidil gel (n=1483)	Prostin gel (n=84)	Syntocinon (n=790)	Total (n=2357)	
RVP	410 (28)	3 (4)	137 (17)	550 (23)	<0.001
pRVP	71 (5)	1 (1)	15 (2)	87 (4)	0.001
IUGR	111 (7)	4 (5)	33 (4)	148 (6)	0.007
GDM	52 (4)	7 (8)	39 (5)	98 (4)	0.04
HTA	54 (4)	6 (7)	25 (3)	85 (4)	0.18
preeclampsia	43 (3)	6 (7)	16 (2)	65 (3)	0.02
Post term pregnancy	557 (38)	34 (40)	244 (31)	835 (35)	0.004
unknown	86 (6)	12 (14)	203 (26)	301 (13)	<0.001
oligohydramnios	64 (4)	2 (2)	17 (2)	83 (4)	0.02
foetal indications	9 (0.6)	2 (2.4)	23 (2.9)	34 (1.4)	<0.001
rh immunization	4 (0.3)	2 (2.4)	2 (0.3)	8 (0.3)	0.005
polyhydramnios	1 (0.1)	0	6 (0.8)	7 (0.3)	0.01
mors fetus in utero	13 (0.9)	3 (3.6)	20 (2.5)	36 (1.5)	0.003
Mother's diseases	8 (0.5)	2 (2.4)	8 (1)	18 (0.8)	0.10
St post IVF	0	0	2 (0.3)	2 (0.1)	0.14

*Fisher's exact test. Bold denotes statistical significance. Abbreviations: RVP – ruptura velamentosum precox, pRVP – premature ruptura velamentosum precox; IUGR – intrauterine growth restriction; GDM – gestational diabetes mellitus, HTA – hypertension arterialis in graviditatem.

Table 2. Predicting the possibility of a caesarean section – multivariate regression analysis

Predictor	β	Standard deviation	Wald	P	OR	95% CI
Mothers' age (36 years and more)	0,46	0,17	7,01	0,008	1,58	1,13 – 2,22
Induction (Prep)						
Prostin	-0,79	0,36	4,74	0,03	0,45	0,22 – 0,92
Syntocinon	-0,50	0,13	14,91	<0,001	0,36	0,47 – 0,78
Liquor amnii meconialis (yes)	0,38	0,17	5,26	0,02	1,47	1,06 – 2,04
Parity (multiparity)	-1,62	0,14	122,2	<0,001	0,19	0,15 – 0,22
New-borns' gender (female)	-0,24	0,11	4,9	0,03	0,78	0,63 – 0,97

β -Regression coefficient. Bold denotes statistical significance. Abbreviations: OR – odds ratio; CI – confidence interval.

tors", i.e. factors reducing the possibility of the caesarean section include mother's age 25 – 35 years, women who have previously given birth to a female child, and multiparous women.

Five independent predictors made a unique statistically significant contribution to the model (Hosmer–Lemeshow test, $P=0.81$). The model as a whole is statistically significant ($\chi^2=208.5$, $P<0.001$), and overall explains 8.5% (by Cox & Snell and by Nagelkerke) of the caesarean section variance, and accurately classifies 80.98% of cases. The results of multivariate statistic regression have been shown in Table 2.

The multivariate statistical regression model found that women aged 36 and more are 1.58 times more likely to have the caesarean section (OR 1.58, 95%CI 1.13 to 2.22). In addition, women with diagnosed meconium amniotic fluid have a 1.47-fold higher chance of the caesarean section (odds ratio (OR) 1.47, 95% confidence interval (CI) 1.06 to 2.04).

Furthermore, multiparity (OR 0.19, 95% CI 0.15 to 0.22) as well as a female child's gender (OR 0.78, 95% CI 0.63 to 0.97) have a "protective" effect, i.e. they reduce the probability of the caesarean section after induced labour.

DISCUSSION

This paper observed nine variables related to the mother and a newborn, as well as the effect of those variables on the success of medically induced labour. The paper also presented the prevalence and indications for medically induced labour. In our study, there are 13.8% medically induced labours, which is lower than the world average, which ranges from 10% to as much as 35.5% in

Sri Lanka². In developing countries, the percentage of medically induced labours is still slightly lower. Guerra et al. Reported 11.4% induced labours in Latin America⁸, Asghar et al. reported a 12.5% induction rate in their study¹⁴, while the average percentage in developed countries is about 20%^{5,13}.

Indications for induced labour in this study were as follows: post-term pregnancy in 34% of cases, premature rupture of membranes in 23% of cases, intrauterine growth restriction (IUGR) in 6% of cases, while the other indications were less common. A similar percentage and distribution of indications was shown in the works of Vogel et al., Mozurkewich et al., and Mishanina et al.²⁻⁴.

In 81% of cases, the delivery was completed vaginally, while in the remaining 19% the delivery was completed by the caesarean section, which is in line with the world standard. In the study by Batinelli et al., the percentage of caesarean sections was 19.3%, in Darney et al. it was 16%, in the study by Yawn et al. Only 7.1%, while in the study by Asghar et al., the percentage of caesarean sections was 28.5%¹³⁻¹⁶.

At the same time, in the group of the remaining pregnant women, from 2012 to 2019 (14742 pregnant women whose births were not induced), the childbirth was completed by the caesarean section in 4420 (29.9%) of them, which shows that the percentage of caesarean sections is significantly lower in group of induced labours. Mishanina et al. proved similarly in their 2012 meta-analysis, which showed that the percentage of caesarean sections in induced labours is significantly lower than in the case of the prospective procedure by as much as 12%⁴.

Our results of univariate and multivariate logistic regression showed that factors increasing the risk of caesarean section after induced labour include the diagnosis of meconium amniotic fluid, while “protective factors”, i.e. factors reducing the possibility of the caesarean section include mother’s age 25-35 years, women who have previously given birth to a female child, and multiparous women.

In the case of mother’s age, this study indicates that in pregnant women between 26 and 35 years of age there is a reduced possibility of the caesarean section in medically induced labour, while the possibility increases if the mother is older than 36 years of age, by 1.58 times.

Crane et al. concluded that younger mothers have a higher percentage of successful inductions and a lower percentage of the caesarean sections¹⁷. Grobman et al. stated that older women experience longer latent phase and are more likely to have the caesarean section¹⁸, while Nader et al. included maternal age, along with other factors, in the prediction score that successfully predicted the success of induced labour¹⁹. Perhaps the most comprehensive study was conducted by Dunn et al., who also showed that in women over 38 years of age the possibility of completing a birth by the caesarean section doubles in induced labour²⁰. Rane et al., Riboni et al., and Bueno et al., on the other hand, found no correlation between maternal age and the caesarean section²¹⁻²³. Several hypotheses could explain the correlation between maternal age and the caesarean section in induced labour. It is possible that somewhat lower uterine vascularization in older pregnant women may result in insufficient adaptation to the increased hemodynamic needs in pregnancy²¹. In relation to that, older pregnant women may be less tolerant of the increased hemodynamic requirements in both pregnancy and childbirth. Furthermore, a gradual decline in myometrium function with age could lead to less effective uterine contractions in pregnant women^{24,25}. Likewise, the presence of medical comorbidities in pregnant women could contribute to a decrease in the physiological tolerance of older mothers to childbirth, and lead to a slightly higher percentage of caesarean sections²⁶.

Another factor that affects the success of childbirth in induced labour is child’s sex. In our study, it was proven that mothers who gave birth to a female child have a lower percentage of caesarean sections after medically induced labour.

This result certainly coincides with the results of previous research on the influence of child’s sex on the outcome of childbirth in the medically induced labours. In the studies conducted by Eogan et al., Agarawal et al., Antonakou et al., and Toricelli et al. there was a statistically significant cor-

Our study found that mother’s age between 26 and 35, female child, and maternal parity positively correlate with the success of medically induced labour, while mother’s age above 35 and meconium amniotic fluid diagnosis are risk factors that lead to the caesarean section in medically induced labours.

relation between male children and higher percentage of caesarean sections in medically induced labours²⁷⁻³⁰. The whole range of smaller researches showed the same results³¹⁻³⁶. There is only one study that showed there was no correlation between child’s sex and a higher percentage of caesarean sections after medically induced labour³⁷.

There are a number of explanations as to why the percentage of the caesarean sections after medically induced labour is higher in male compared to female children.

Firstly, male infants are usually of higher birth weight, which more often leads to lack of progress in childbirth and the consequent caesarean section³⁶.

Secondly, during birth, foetal distress is more common in male new-borns, so the percentage of caesarean sections is more common. This could be the result of differences in response to hypoxia depending on child’s sex. An important item in the neonatal response to hypoxia is the level of catecholamines in the newborn, which is lower in male children. Thus, their response to hypoxia is consequently worse³⁸⁻⁴¹.

The third explanation is related to differences in growth curves in male and female new-borns. The growth curve in male new-borns is faster.

Male infants, given the growth curve, usually have a slightly smaller placenta with respect to their growth. This automatically leads to slightly less placental reserves for the time of the delivery, when the conditions are suboptimal, and they react more quickly to stress⁴²⁻⁴⁴. This result is consistent with the results in the world literature, confirmed by numerous studies.

In addition, there is a fourth possible explanation. There are different pathways of steroid hormones leading to the onset of induced labour in male and female new-borns and thus different foetoplacental responses to induced labour process in female and male new-borns, which may ultimately lead to a difference in the percentage of caesarean sections³⁰.

The third factor with the protective effect against the caesarean section in medically induced labour is maternal parity. In our study, mothers who have already given birth had a lower possibility of completing medically induced labour by the caesarean section.

Some of the researchers, such as Pevzner et al. and Chandra et al., believe that parity is the most important variable in predicting the type of delivery after medically induced labour^{45,46}. In these studies, the results indicate that women who have already given birth have a lower percentage of completed caesarean pregnancies than primiparous women^{1,23,46,47}. However, Cammu, Setyorini, and Yeast showed different results^{9,48,49}.

Such results could be the consequence of different criteria for including patients in research.

The theory that the percentage of the caesarean sections is lower after medically induced labour in women who have already given birth is that the primiparous cervix is still extremely immature as opposed to that in multiparous women, and it takes longer to stimulate it⁵⁰. Consequently, the result is a higher risk of the caesarean section.

LIMITATIONS OF THE STUDY

A limitation of our study is the size of our sample, more precisely, in the observed eight years we analysed 2361 medically induced labours. The stated number is in relation to the prevalence of medical induction of labour, on average there

were 2130 births per year in the observed period at our Clinic. Another limitation of this research is the lack of certain medical data, since the research is retrospective. The extension of the research to certain interesting features found in the literature was not possible due to lack of data in the available medical documentation (cervical latent phase length, Bishop Score, maternal body mass index (BMI)). Similar research in Eastern Croatia has not been conducted, but it would be helpful to compare it with this study.

CONCLUSION

Our study found that mother's age between 26 and 35, female child, and maternal parity positively correlated with the success of medically induced labour, while mother's age above 35 and meconium amniotic fluid diagnosis are risk factors that led to the caesarean section in medically induced labours.

Conflicts of interest: Authors declare no conflicts of interest.

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