PREVALENCE, RISK FACTORS AND PREGNANCY OUTCOMES OF LABOR INDUCTION IN CROATIA – A NATIONAL ONE-YEAR STUDY

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Objective: The aim of this study was to determine the prevalence of labor induction in Croatia, as well as the main risk factors and adverse pregnancy outcomes associated with labor induction. *Materials and methods:* A cross-sectional study was performed using data from medical birth certificates collected in 2019 in Croatia. *Results:* Among 36,603 deliveries in 2019, the prevalence of labor induction was 14.1%. Women whose labor was induced were older, had a higher body mass index (BMI), and more frequent gestational weight gain above recommendations compared to women with spontaneous onset of labor (p<0.001). Induced labors were more frequent in pregnancies with gestational diabetes, gestational hypertension, preeclampsia, and fetal growth restriction (p<0.001 all). Women with induced labor had a higher incidence of cesarean section, vacuum extraction, postpartum hemorrhage, shoulder dystocia, and more frequently delivered infants above 4000 g (p<0.05 all). Logistic regression showed that maternal age, pre-pregnancy BMI, gestational diabetes, gestational hypertension, preeclampsia, fetal growth restriction, and gestational age at delivery were significant predictors of labor induction (p<0.001 all). *Conclusions.* The prevalence of labor induction in Croatia is 14.1%. Labor induction is associated with important risk factors and adverse perinatal outcomes, which can partially be attributed to the mode of labor onset. All of these should be taken into account when performing this obstetric procedure.

Key words: labor induction, prevalence, risk factors, cesarean section, logistic regression analysis

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INTRODUCTION

Induction of labor refers to the initiation of labor before its spontaneous onset and, when performed for appropriate indications, can have significant benefits for both the mother and the child (1). This obstetric procedure is performed in circumstances when the risk of waiting for spontaneous onset of labor is considered to be greater than the risk of inducing labor, i.e., in prolonged pregnancies, pregnancies burdened with prelabor rupture of membranes, fetal compromise, or maternal complications such as hypertensive disorders of pregnancy, diabetes mellitus or gestational diabetes, cholestasis, fetal growth restriction (FGR), and others (2,3).

According to the World Health Organization (WHO) data, labor induction is of increasing prevalence worldwide and present in up to one in four deliveries in developed countries, whereas its prevalence is lower in developing countries (4). Namely, up to 32.6% of labors in England are induced as compared with 25.7% in the USA and 22% in France, while official national data for Croatia are lacking (5-7).

Studies have recognized certain risk factors and obstetric complications associated with labor induction. Older pregnant women (above 35 years of age), those with a higher pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) above recommendations are more likely to have their labor induced

(8-10). Maternal complications associated with labor induction include chorioamnionitis and postpartum hemorrhage from uterine atony (11,12), whereas studies regarding the mode of delivery following labor induction report conflicting results. Some observational studies indicate that induced labors have an increased risk of cesarean section (CS) (13,14), while others relate this association to various prepartum and intrapartum factors not directly linked with labor induction (15). These include certain pregnancy complications and nulliparity. Conversely, results of a 2015 literature review and 2014 meta-analysis suggest that the term labor induction may, in fact, be associated with a decreased risk of CS (16,17), while a study by Grobman *et al*. (18) suggests that induction of labor at 39 weeks of gestation in low-risk nulliparous women results in a significantly lower frequency of CS compared to expectant management.

The aim of this study was to determine the prevalence of labor induction in Croatia and to detect the main risk factors and adverse pregnancy outcomes associated with labor induction in our population.

MATERIALS AND METHODS

This was a cross-sectional study performed using data from medical birth certificates (MBC) collected in 2019 in Croatia as part of perinatal statistics data reporting to the Croatian Institute of Public Health (CIPH). Completing MBCs is mandatory for all doctors attending labor at all labor units in the country. The study included pregnant women who gave birth in 2019 in Croatia. Inclusion criteria were spontaneous or induced onset of labor, while women who delivered by elective CS were excluded from the study.

Registered and approved methods of labor induction in Croatia include mechanical methods, i.e., amniotomy and transcervical balloon catheter; and pharmacological methods, i.e., oxytocin infusion and prostaglandin E2 (2,3). Prostaglandin E1 (misoprostol) is neither registered nor approved for labor induction in Croatia.

The parameters assessed in this study were pre-pregnancy BMI and GWG. Based on the WHO classification system, women were assigned to 4 groups according to pre-pregnancy BMI, as follows: underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) and obese (≥30.0kg/m^2) (19). The optimal GWG for each pre-pregnancy BMI group was defined *per* Institute of Medicine (IOM) recommendations, as follows: 13-18 kg for underweight women, 11-16 kg for normal BMI women, 7-11 kg for overweight women, and 5-9 kg for obese women (20). Other parameters analyzed were the frequency of pregnancy complications (incidence of gestational diabetes, gestational hypertension, preeclampsia and FGR), labor complications (postpartum hemorrhage, retained placenta, shoulder dystocia and episiotomy rate), as well as neonatal complications (birth weight below 2500 g and above 4000 g, Apgar score <7 after 5 minutes, and NICU admission).

Statistical analyses were performed using SPSS ver. 21.0. Homogeneity of variance was tested using Levene's test. Continuous variables were presented as mean ± standard deviation (SD), while categorical data were presented as frequency and percentage. Differences between groups of independent continuous variables were analyzed using the t-test, while differences in the occurrence of individual conditions were compared using the χ^2-test.

Logistic regression was performed to ascertain the effects of maternal age, pre-pregnancy BMI, gestational age at delivery, and pregnancy complications such as gestational diabetes, gestational hypertension, preeclampsia and FGR on labor induction. In addition, logistic regression analysis was performed to ascertain the effects of maternal age, pre-pregnancy BMI, newborn weight, and induction of labor on three selected outcomes, i.e., likelihood of non-vaginal delivery, shoulder dystocia, and 5-min Apgar score <7. Statistical significance was defined as $p<0.05$. Ethical approval for the study was obtained from the CIPH Ethics Committee for Public Health Research, grant number 381-08-83-20-2.

RESULTS

A total of 36,632 deliveries in 2019 in Croatia were reported to CIPH using MBCs. Data regarding the onset of labor were missing in 29 (0.08%) MBCs and they were excluded from the study, leaving 36,603 deliveries for further analysis. Elective CS was performed in 4,576 cases and 253 labors were involved in perinatal death, excluding these cases from the analysis. Labor was induced in 5,153 (14.1%) deliveries, while the remaining 26,621 deliveries had a spontaneous onset.

General characteristics of women with spontaneous and induced onset of labor are presented in Table 1. Compared to women with spontaneous onset of labor, women with an induced onset were older, more frequently overweight before pregnancy, and were more frequent in the IOM GWG category above recommended. Differences in all these characteristics were statistically significant ($p<0.001$).

Table 1. *Characteristics of pregnant women with spontaneous and induced onset of labor in Croatia in 2019*

	Spontaneous onset	Induced onset	p-value
Age (years) (mean ± SD)	30.6±5.4	31.0±5.4	<0.001
<18	0.7%	0.3%	<0.001
18-35	82.3%	82.0%	
>35	17.0%	19.2%	
Pre-pregnancy BMI (kg/m2) (mean ± SD)	23.6±4.2	24.5±4.7	<0.001
<18.5	5.4%	3.6%	<0.001
18.5-24.9	66.9%	60.2%	
25.0-29.9	19.8%	24.1%	
≥30.0	7.9%	12.2%	
GWG; IOM category+ (kg) (mean ± SD)	13.8±5.4	14.1±5.5	<0.001
Below	21.3%	17.1%	<0.001
In range	35.5%	33.9%	
Above	43.2%	49.1%	
GA at delivery (weeks)++ (mean ± SD)	39.1±1.8	39.6±1.6	<0.001
<37	12.0%	8.10%	<0.001
37+0-38+6	13.3%	13.4%	
39+0-40+6	58.1%	46.5%	
41+0-41+6	13.8%	25.8%	
≥42	2.9%	6.2%	

SD = standard deviation; GWG = gestational weight gain; IOM = Institute of Medicine; GA = gestational age

+According to the Institute of Medicine weight gain recommendations. Available at: https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Weight-Gain-During-Pregnancy

++Classification of deliveries from 37 weeks into early term, full term, late-term and post-term according to recommendations from the Defining "Term" Pregnancy Workgroup (22)

Table 2. *Pregnancy outcomes of deliveries with spontaneous and induced onset in Croatia in 2019*

Pregnancy outcome	Spontaneous onset n (%)	Induced onset n (%)	p-value
Mode of delivery			<0.001
Vaginal	22304 (83.8)	3957 (76.7)	
Vacuum extraction	398 (1.5)	106 (2.1)	
Cesarean section	3918 (14.7)	1090 (21.2)	
Pregnancy complications			
Gestational diabetes	1311 (5.0)	534 (10.4)	<0.001
Gestational hypertension	308 (1.2)	190 (3.7)	<0.001
Preeclampsia	59 (0.2)	48 (0.9)	<0.001
FGR	253 (1.0)	199 (3.9)	<0.001
Labor complications			
Retained placenta	362 (1.4)	90 (1.7)	0.033
Postpartum hemorrhage	46 (0.2)	17 (0.3)	0.021
Shoulder dystocia	44 (0.2)	17 (0.3)	0.014
Episiotomy	7255 (27.3)	1240 (24.1)	<0.001
Neonatal complications			
BW <2500g	1134 (4.3)	200 (3.9)	0.215
BW >4000g	2903 (10.9)	731 (14.2)	<0.001
5-min Apgar <7	158 (0.6)	24 (0.5)	0.225
NICU admission	1234 (4.6)	214 (4.2)	0.118

FGR = fetal growth restriction; BW = birth weight; NICU = neonatal intensive care unit

Labor was induced more frequently in pregnancies with complications and this group had a higher incidence of CS and instrumental delivery (i.e., vacuum extraction). The induced labor group also had a higher incidence of all labor complications analyzed in this study. Women whose labor had been induced gave birth more frequently to infants with birth weight above 4000 g. All pregnancy complications and outcomes analyzed are presented in Table 2.

A logistic regression model with labor induction as outcome revealed that maternal age, maternal pre-pregnancy BMI, gestational age at delivery and pregnancy complications such as gestational diabetes, gestational hypertension, preeclampsia and FGR were significant predictors of induction of labor. This is presented as Model I in Table 3, R square was 6.3%.

Other logistic regression models analyzed the effects of maternal age, pre-pregnancy BMI, newborn weight and induction of labor on the likelihood of non-vaginal delivery, shoulder dystocia and 5-min Apgar score <7, and are presented in Table 3.

Although each of the variables in Model II (outcome of non-vaginal delivery) had a statistically significant effect on outcome (p<0.001), outcome prediction was highly limited due to the low R square (3.2%). Model III (outcome of shoulder dystocia) suggested that newborn weight was a significant predictor of shoulder dystocia [OR 1.002 (95% CI 1.001-1.002)], i.e., the odds of shoulder dystocia increase with birth weight increase. However, as in Model II, the R square in Model III was low (6.6%). Model IV (outcome of 5-min Apgar <7) suggested that newborn weight was a significant predictor of low 5-min Apgar score [OR 0.998 (95% CI 0.0997-0.998)], i.e., the odds of low 5-min Apgar decrease as birth weight increases. R square in Model IV was 25.6%. The models revealed that labor induction was not a significant predictor of either shoulder dystocia or low Apgar score.

Table 3. *Logistic regression models for Model I-IV, i.e., induction of labor, not delivering vaginally, shoulder dystocia, and 5-min Apgar <7 as outcomes*

Variable	Odds ratio	95% CI	p-value
Model I – outcome of induction of labor (R square 6.3%)			
Maternal age	1.020	1.013-1.026	<0.001
Maternal BMI	1.034	1.026-1.041	<0.001
Gestational diabetes	2.045	1.820-2.298	<0.001
Gestational hypertension	2.751	2.244-3.373	<0.001
Preeclampsia	4.022	2.617-6.181	<0.001
FGR	5.529	4.520- 6.763	<0.001
GA at delivery	1.269	1.238-1.301	<0.001
Model II – outcome of not delivering vaginally (R square 3.2%, $\chi 2$=505.629, p<0.001)			
Maternal age	0.983	0.977-0.989	<0.001
Maternal BMI	0.953	0.946-0.960	<0.001
Newborn weight	1.000	1.000-1.001	<0.001
Induction of labor	1.484	1.369-1.609	<0.001
Model III – outcome of shoulder dystocia (R square 6.6%, $\chi 2$=44.503, p<0.001)			
Maternal age	1.040	0.983-1.101	0.169
Maternal BMI	1.033	0.973-1.096	0.285
Newborn weight	1.002	1.001-1.002	<0.001
Induction of labor	0.686	0.353-1.333	0.266
Model IV – outcome of 5-min Apgar <7 (R square 25.6%, $\chi 2$=451.388, p<0.001)			
Maternal age	0.991	0.962-1.021	0.547
Maternal BMI	1.014	0.976-1.053	0.473
Newborn weight	0.998	0.997-0.998	<0.001
Induction of labor	1.070	0.657-1.741	0.787

BMI = body mass index; FGR = fetal growth restriction; CI = confidence interval

DISCUSSION

The prevalence of labor induction in Croatia of 14.1% is lower than in several other Western European countries where it is reported to be above 20% (5, 7), but similar to the prevalence of 13.8% in one clinical center in Croatia (21). Even though accurate comparison is difficult due to the lack of data on the modes of labor onset from the majority of European countries, it seems that the labor induction rate in Croatia is still below the European average. Several ideas might explain this. Obstetric practice possibly differs among countries where some national guidelines are more prone to labor induction compared to others. Also, there might be a difference in data collection; labor induction can be performed on a favorable and unfavorable cervix. It is possible that some analyses include both groups, whereas others only focus on labor induction with unfavorable cervices, without accentuating it in the Methods section.

Maternal overweight and high GWG, advanced maternal age, and prolonged pregnancy are factors previously found to be positively associated with labor induction (8-10). These observations were confirmed in this study accentuating the necessity of good preconceptional and antenatal care. Special emphasis should be given to educating women regarding weight management before and during pregnancy in order to keep the rates of labor induction within reasonable limits. A higher mean gestational age at delivery in the induced labor group was expected as the main indication for labor induction in prolonged pregnancy with the aim of avoiding post-term pregnancy risks (12).

Labor induction was performed more frequently in pregnancies with complications, and some of these complications were indications for labor induction. Our study also showed that pregnant women with gestational diabetes or gestational hypertension had a twofold greater risk of undergoing labor induction compared to pregnant women without these complications. These risks increase up to fourfold and fivefold for pregnancies burdened with preeclampsia or FGR. Therefore, in order to reduce the incidence of labor induction, additional preventive measures for reducing pregnancy complications should be implemented.

The association of labor induction with a higher incidence of CS found in this study is in concordance with some previously published studies (13,14) and contradictory to results from other studies (16,18). The higher incidence of CS in the induced labor group found in this study must be observed with caution as it might not be directly associated with labor induction but with various other antenatal factors. These include pregnancy complications, which necessitated labor induction in the first place, prolonged pregnancy, higher maternal age or BMI, neonatal weight above 4000 g, or others. Further studies are necessary to better evaluate these associations, possibly by comparing induction of labor with expectant management rather than spontaneous onset of labor. Regression analysis performed also suggests that the outcome of 'non-vaginal delivery' can be predicted with labor induction. However, due to the low explanatory power of the model used and a multitude of other risk factors unrelated to investigated variables, the results of this model should be interpreted with caution.

Other complications associated with labor induction identified in this study, such as instrumental delivery (i.e., vacuum extraction), shoulder dystocia, retained placenta and postpartum hemorrhage, are also im-

portant. These are partly linked to labor induction but also may arise from other antenatal and intrapartum factors. Nonetheless, all listed complications are significantly associated with the induced onset of labor, making such deliveries to fall in the high-risk category. Hence, the management of these labors requires additional attention, as well as careful and critical planning of labor induction. Increased neonatal weight represents a well-known risk factor for shoulder dystocia (23) but the association of neonatal weight with 5-min Apgar score values remains more complicated. Results of some studies disprove the negative effect of macrosomia on 5-min Apgar scores, while other studies corroborate it (24,25). The practice of labor induction has been shown by randomized controlled trials to benefit neonatal outcomes, reducing the incidence of fetal distress, stillbirth, and other postnatal complications (26,27). Further work and additional studies are necessary to better understand these associations.

Limitations of the study include the absence of data regarding the indications and methods of labor induction and the cervix status (favorable or unfavorable) prior to induction. Studies have concluded that these parameters significantly impact outcomes of labor induction and might influence the results. Also, it would have been interesting to have included data on the indications for CS in order to differentiate those directly related to labor induction from those that were not. The strength of this study is that it was a national-based study performed on the whole population of pregnant women and deliveries in Croatia in 2019. This large sample with no inclusion bias represents a valuable addition to understanding the risk factors and pregnancy outcomes associated with labor induction.

CONCLUSION

The prevalence of labor induction in Croatia in 2019 was 14.1%. Women whose labor was induced were older, had higher BMI, GWG above recommendations, and more frequent pregnancy complications. Induced labor was more often burdened with labor complications, which could partially be attributed to the mode of labor onset.

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SAŽETAK

UČESTALOST, RIZIČNI ČIMBENICI I ISHODI TRUDNOĆA KOD INDUKCIJE PORODAJA U HRVATSKOJ – NACIONALNO JEDNOGODIŠNJE ISTRAŽIVANJE

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Cilj: Indukcija poroda važan je opstetrički zahvat koji se provodi u sve većem broju poroda diljem svijeta s ciljem smanjenja perinatalnog pobola i smrtnosti. Cilj ovog istraživanja bio je utvrditi učestalost indukcije poroda u Hrvatskoj te glavne rizične čimbenike i nepoželjne ishode povezane s indukcijom poroda. ***Materijali i metode:*** Provedeno je presječno istraživanje pomoću podataka sakupljenih pri prijavi poroda u Hrvatskom zavodu za javno zdravstvo u 2019. godini u Republici Hrvatskoj. ***Rezultati:*** Na ukupno 36.603 poroda u 2019. godini u Republici Hrvatskoj učestalost indukcije poroda bila je 14,1 %. Trudnice kod kojih je porođaj bio induciran bile su starije, imale su veći indeks tjelesne mase i češće prirast tjelesne težine u trudnoći iznad preporučenog u usporedbi s trudnicama koje su imale spontani početak poroda (p<0,001 sve). Porođaj je češće induciran kod trudnoća s komplikacijama poput gestacijskog dijabetesa, gestacijske hipertenzije, preeklampsije i intrauterinog zastoja u rastu ploda (p<0,001 sve). Trudnice kojima je porođaj induciran češće su rodile carskim rezom, vakuum-ekstrakcijom, češće su imale postpartalno krvarenje, distociju fetalnih ramena te su češće rađale novorođenčad iznad 4000 g u usporedbi s trudnicama u kojih je porođaj započeo spontano (p<0,05). Logistička regresija pokazala je kako su dob trudnice i indeks tjelesne mase prije trudnoće, gestacijski dijabetes, gestacijska hipertenzija, preeklampsija, intrauterini zastoj u rastu ploda i gestacijska dob kod poroda značajni prediktori indukcije poroda (p<0,001 sve). ***Zaključak:*** Učestalost indukcije poroda u Hrvatskoj je 14,1%. Indukcija poroda povezana je s važnim rizičnim čimbenicima i nepoželjnim perinatalnim ishodima koji se djelomice mogu pripisati načinu početka poroda. O svemu navedenom treba voditi računa kada se savjetuje i planira navedeni opstetrički zahvat.

Ključne riječi: indukcija poroda, učestalost, rizični čimbenici, carski rez, logistička regresija