VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/GP.a2021.0168

Factors associated with caesarean section in women referred for preinduction — a nested case-control study in dinoprostone and misoprostol groups

Teresa Gornisiewicz[1], Katarzyna Kusmierska-Urban[2*], Hubert Huras[2], Aleksander Galas[3]

[1]Department of Obstetrics and Perinatology, University Hospital, Cracow, Poland
[2]Department of Obstetrics and Perinatology, Jagiellonian University Medical College, Cracow, Poland
[3]Chair of Epidemiology and Preventive Medicine, Jagiellonian University Medical College, Poland
**employed until 2019*

ABSTRACT

Objectives: Induction of labour is a beneficial perinatal procedure, but may be associated with some risks. The aim of this study was to identify factors associated with the need for Caesarean section in women referred for preinduction with dinoprostone and misoprostol.

Material and methods: It was a retrospective cohort study of 560 pregnant women who underwent labour induction for medical reasons. Analyses were performed separately in the dinoprostone and misoprostol group. Above other characteristics, the diameters of the pelvis and abdominal circumference of pregnant women were analysed.

Results: There were some mothers' characteristics like age, weight, BMI, presence of hypothyroidism or diabetes, which were not associated with Caesarean section deliveries.

Women in the misoprostol group with gestational age less than 38 weeks had an increased risk of Caesarean section (OR 2.189; p = 0.041). The analyses of combined effect of mothers age and parity history showed 6.7 (in dinoprostone group) and over 10 times (in misoprostol group) increased the risk of Caesarean section in nulliparous women over 35 years of age.

Conclusions: The increased risk of Caesarean delivery in the dinoprostone group was combined with the intertrochanteric dimensions such as the mother's height measuring less than 165 cm, nulliparity and hypertension. In the misoprostol group, strong risk factors for Caesarean delivery were mothers aged 35 years or more, gestational age less than 38 weeks and nulliparity and hypertension as in dinoprostone group. The oxytocin infusion had increased the risk of Caesarean section only in the combined dinoprostone and misoprostol group. Further high-quality studies are warranted.

Key words: misoprostol; dinoprostone; caesarean section risk factors

Ginekologia Polska

INTRODUCTION

The general aim of labour induction is to improve the perinatal outcome for both the newborn and mother. A successful induction of labour is achieved when it ends with a vaginal delivery within 24 hours minus maternal complications and delivering a healthy newborn in a good condition (e.g., with a high, ≥ 8 Apgar score). Among a variety of available methods, the pharmacological ones, mostly prostaglandins, are more common, but still being extensively investigated. The research tries to find the safest way to induce the delivery of the baby in the most appropriate time, and to identify the clinical parameters which can be used to predict the labor induction outcome [1]. The most common problem and concern for the obstetricians is the need for Caesarean section (C/S), especially an emergency situation, as a result of failed labor induction. Therefore, pregnant women who are at the greatest risk of C/S delivery should be identified to optimize the strategies of treatment. Although the studies showed a variety of possible factors affecting the labor progress, including mother's age, parity, body mass index [2], the use of epidural anesthesia, a method of labor induction [3], and the status of the cervix

Corresponding author:
Teresa Gornisiewicz
Department of Obstetrics and Perinatology, University Hospital, Cracow, Poland
e-mail: teresagornisiewicz@wp.pl

Received: 2.03.2021 Accepted: 19.07.2021 Early publication date: 1.10.2021

accessed by Bishop score, there is still an open question of which prostaglandin should be chosen and to whom to get the reduction of C/S risk and to improve perinatal outcomes.

The purpose of this study was to identify factors associated with the need for C/S procedures in daily clinical practice, when dinoprostone gel at a dose of 0.5 mg (Prepidil, Pfizer Polska Sp. z o.o.) or misoprostol vaginal insert at a dose of 0.2 mg (Misodel, Ferring Pharmaceuticals Poland sp. z o.o) were applied for labor induction. Besides the commonly used characteristic checks, the aim was to focus on the mother's anthropometric measurements including diameters of the pelvis as well as some related indexes, including proportions of different pelvic diameters to mother's height or estimated fetal birth weight (EFBW) in relation to pelvic diameters.

MATERIAL AND METHODS

The original research was a retrospective cohort study of 560 pregnant women who underwent labor induction for medical reasons at the Obstetric and Perinatology Department at the University Hospital in Cracow, between January 2015 and April 2019. The research was conducted to evaluate the effectiveness and safety of two delivery induction methods, being dinoprostone gel at a dose of 0.5 mg (Prepidil, Pfizer Polska Sp. z o.o.) or misoprostol vaginal insert at a dose of 0.2 mg (Misodel, Ferring Pharmaceuticals Poland sp. z o.o). The study details have been described elsewhere [4]. In brief, first, all women fulfilling the inclusion criteria were identified in the hospital database. Next, all available data was extracted from the hospital electronic database and available paper charts. The following information was recorded at the time of study enrollment: maternal age and body mass index (BMI), number of pregnancies, gestational age, Bishop's score, the mode of delivery - vaginal birth or C/S, selected comorbidities (hypertension, diabetes, hypothyroidism, Streptococcus agalactiae positive culture), ultrasound EFBW, as well as diameters of the pelvis, and abdominal circumference in some pregnant women. Additionally, other data was collected (the indication for induction of labour, time from drug administration to vaginal delivery or time to any (vaginal or by Caesarean section) delivery and time to the onset of labor, maternal complications such as episiotomy, the rupture of perineum, the placenta abruption or placenta arrest, and anaemia requiring blood transfusion), but the daunting analysis of those are the subject of different articles [4]. Neonatal outcomes, such as birth weight, birth length, gender and 1-minute Apgar score were also accessed.

The primary inclusion criteria were as follows: singleton gestation with cephalic presentation requiring labor induction for medical indications, with the cervical state described as ≤4 in the Bishop's score and with no active labor before administration of the drug. Women were excluded if the EFBW was > 4500 g, had any known contraindication to vaginal delivery, or any contraindication for prostaglandins usage.

As the purpose of the study was to identify risk factors associated with C/S, the nested case-control approach had been implemented. Meaning all the C/S deliveries had been identified in the included cohort (these were considered as cases) and they were compared with vaginal deliveries. Analyses were performed separately in the dinoprostone group and in the misoprostol group.

Statistical analysis

For the purpose of the presented study, as the first step we created two groups based on the delivery preinduction method, meaning the dinoprostone group (D group; 350 patients) or the misoprostol group (M group; 210 patients). We considered if the woman had been primarily referred to the dinoprostone group or the misoprostol group. In these groups, characteristics of pregnant women who had vaginal delivery and underwent C/S were compared. In the secondary analyses, which were intended to identify factors associated with the C/S, three groups were created. The basis for that was the identified presence of the third group of pregnant women who received two considered prostaglandins (meaning the leading doctor had decided to use the second drug sometime after the first one). Only a group of women who received dinoprostone first, and as a next step the misoprostol was found (D+M group; 100 patients). The significance of the difference between groups was determined by the parametric t-test or non-parametric the U-Mann-Whitney test, depending on whether the assumption of normal distribution, verified by the Shapiro-Wilk test, had been fulfilled. To identify factors associated with the C/S risk logistic regression models were calculated. In the first step, the mother's age, anthropometric characteristics including diameters of pelvis, parity history, diagnosis of concomitant disease, pre-ripening cervical characteristic and EFBW were analysed in the univariable analyses. Next, the factors showing significant impact were considered for multivariable analyses to identify those which independently were associated with C/S risk. Analyses were done separately in different treatment groups enabling to show determinants which might be different across treatment type. The pair-wise procedure was applied for missingness. The p-value below 0.05 was considered statistically significant. The IBM SPSS Statistics version 26 was used for calculations.

RESULTS

Characteristics of the study groups at admission are shown in Table 1. There were no significant differences in maternal age, weight or BMI at admission, presence of hy-

Table 1. Clinical characteristics of study participants across route of birth delivery status in the dinoprostone and misoprostol groups

	Dinoprostone			Misoprostol		
	Vaginal delivery [n = 242]	**Caesarean Section [n = 108]**	**p-value**	**Vaginal delivery [n = 125]**	**Caesarean Section [n = 85]**	**p-value**
Maternal age (years) Mean, (SD) Median (Q1–Q3)	 30.4 (4.6) 30.0 (27.0–34.0)	 30.8 (4.4) 30.0 (28.0–34.0)	 $p^{ett} = 0.382$	 30.5 (3.9)* 31.0 (28.0–33.0)	 31.5 (4.5)* 31.0 (28.0–35.0)	 $p^{MW} = 0.054$
Weight at admission (kg) Mean, (SD) Median (Q1–Q3)	[n = 102] 79.7 (13.4)* 78.0 (70.0–88.0)	[n = 94] 80.2 (14.5)* 78.0 (71.5–88.3)	 $p^{MW} = 0.933$	[n = 37] 78.8 (12.4)* 77.0 (69.5–84.0)	[n = 76] 82.2 (15.5)* 80.5 (70.0–91.8)	 $p^{MW} = 0.250$
Height (cm) Mean, (SD) Median (Q1–Q3)	[n = 207] 167.1 (5.7) 167.0 (164.0–171.0)	[n = 105] 164.5 (6.7) 164.0 (160.0–169.0)	 $p^{ett} < 0.001$	[n = 110] 166.8 (5.4) 167.0 (163.8–170.0)	[n = 84] 165.8 (6.1) 165.0 (162.0–170.0)	 $p^{ett} = 0.231$
Body mass index at admission (kg/m^2) Mean, (SD) Median (Q1–Q3)	[n = 102] 28.4 (4.3) 28.4 (24.9–31.2)	[n = 94] 29.6 (4.9)* 29.0 (25.5–32.1)	 $p^{MW} = 0.128$	[n = 36] 28.5 (3.5)* 27.4 (25.7–31.5)	[n = 76] 30.0 (5.3)* 29.4 (26.0–33.1)	 $p^{MW} = 0.202$
Hypertension	20 (8.3%)	23 (21.3%)	Df = 1 p = 0.001	12 (9.6%)	18 (21.2%)	Df = 1 p = 0.026
Diabetes	57 (23.6)	23 (21.3%)	Df = 1 p = 0.681	15 (12.0%)	11 (12.9%)	Df = 1 p = 0.999
Diabetes — insulin therapy	37 (15.3%)	18 (16.7%)	Df = 1 p = 0.752	9 (7.2%)	8 (9.4%)	Df = 1 p = 0.612
Hypothyroidism	90 (37.2%)	41 (38.0%)	Df = 1 p = 0.905	46 (36.8%)	35 (41.2%)	Df = 1 p = 0.565
GBS	67 (27.7%)	27 (25.0%)	Df = 1 p = 0.606	23 (18.4%)	16 (18.8%)	Df = 1 p = 0.999
Number of pregnancies [n (%)] 1 2 ≥ 3	 145 (59.9%) 57 (23.6%) 40 (16.5%)	 82 (75.9%) 17 (15.7%) 9 (8.3%)	 Df = 2 p = 0.013	 71 (57.6%) 24 (19.2%) 29 (23.2%)	 54 (63.5%) 19 (22.4%) 12 (14.1%)	 Df = 2 p = 0.265
Parity history (current delivery included) [n (%)] 1 2 ≥ 3	 171 (70.7%) 50 (20.7%) 21 (8.7%)	 96 (88.9%) 8 (7.4%) 4 (3.7%)	 Df = 2 p = 0.001	 85 (68.0%) 28 (22.4%) 12 (9.6%)	 74 (87.1%) 7 (8.2%) 4 (4.7%)	 Df = 2 p = 0.005
Nulliparous [n (%)]	168 (69.4%)	94 (87.0%)	Df = 1 p < 0.001	80 (64.0%)	70 (82.4%)	Df = 1 p = 0.005
Miscarriage history [n (%)] no yes	 196 (81.0%) 46 (19.0%)	 93 (86.1%) 15 (13.9%)	 Df = 1 p = 0.287	 96 (76.8%) 29 (23.2%)	 63 (74.1%) 22 (25.9%)	 Df = 1 p = 0.743
Pre-ripening cervical characteristics [n (%)] Dilatation ≤ 1 cm Effacement ≤ 50% Oxytocin use	 224 (92.6%) 230 (95.0%) 98 (40.5%)	 105 (97.2%) 105 (97.2%) 54 (50.0%)	 Df = 1 p = 0.141 Df = 1 p = 0.410 Df = 1 p = 0.103	 109 (87.2%) 112 (89.6%) 11 (8.8%)	 85 (100.0%) 85 (100.0%) 10 (11.8%)	 Df = 1 p = 0.001 Df = 1 p = 0.002 Df = 1 p = 0.640
Gestational age (weeks)# Mean, (SD) Median (Q1–Q3)	 39.8 (1.3)* 40.0 (39.0–41.0)	 39.8 (1.3)* 40.0 (39.0–41.0)	 $p^{MW} = 0.674$	 39.3 (1.7)* 40.0 (39.0–40.0)	 38.7 (2.2)* 39.0 (37.0–40.0)	 $p^{MW} = 0.025$
Estimated birth weight (g) Mean, (SD) Median (Q1–Q3)	[n = 65] 3497.2 (440.1)* 3600.5 (3265.0–3832.0)	[n = 43] 3608.1 (493.7)* 3700.0 (3300.0–3975.0)	 $p^{MW} = 0.099$	[n = 65] 3393.4 (530.7)* 3485.0 (3116.5–3748.5)	[n = 48] 3187.5 (627.0) 3225.0 (2850.5–3746.8)	 $p^{MW} = 0.086$

*–p < 0.05 by the Shapiro-Wilk test for normal distribution; ett — the t-test for equal variances; MW — the U-Mann-Whitney test, for categorical data p-value calculated by the chi-2 test; Df — degrees of freedom; # — at time of administration of the first dose of the drug

Table 2. Mother's anthropometric characteristics of the pelvis across route of birth delivery status in the dinoprostone and misoprostol groups

	Dinoprostone			Misoprostol		
	Vaginal delivery [n = 242]	Caesarean Section [n = 108]	p-value	Vaginal delivery [n = 125]	Caesarean Section [n = 85]	p-value
Diameters of the pelvis						
External conjugate (cm) Mean, (SD) Median (Q1–Q3)	[n = 152] 21.1 (1.6)* 21.0 (20.0–22.0)	[n = 75] 21.0 (1.7)* 21.0 (20.0–22.0)	$p^{MW} = 0.981$	[n = 109] 21.1 (1.7)* 21.0 (20.0–22.0)	[n = 74] 21.3 (1.6)* 21.0 (20.0–22.0)	$p^{MW} = 0.757$
Interspinal dimension (cm) Mean, (SD) Median (Q1–Q3)	[n = 154] 24.0 (1.7)* 24.0 (23.0–25.0)	[n = 75] 23.8 (1.4)* 24.0 (23.0–25.0)	$p^{MW} = 0.489$	[n = 109] 24.0 (1.4)* 24.0 (23.0–25.0)	[n = 74] 23.7 (1.5)* 24.0 (23.0–25.0)	$p^{MW} = 0.260$
Intercristal dimension (cm) Mean, (SD) Median (Q1–Q3)	[n = 154] 27.8 (1.9)* 28.0 (26.0–29.0)	[n = 75] 27.6 (1.6)* 28.0 (26.0–29.0)	$p^{MW} = 0.502$	[n = 109] 27.7 (1.6)* 28.0 (26.5–29.0)	[n = 74] 27.7 (2.1)* 27.0 (26.8–29.0)	$p^{MW} = 0.838$
Intertrochanteric dimension (cm) Mean, (SD) Median (Q1–Q3)	[n = 154] 33.3 (2.7)* 33.0 (32.0–35.0)	[n = 75] 32.3 (2.3)* 32.0 (31.0–34.0)	$p^{MW} = 0.002$	[n = 109] 32.6 (2.2)* 33.0 (31.0–34.0)	[n = 74] 33.0 (2.2)* 33.0 (31.0–34.0)	$p^{MW} = 0.408$

pothyroidism, diabetes or GBS between vaginal and C/S deliveries independently whether the D or M groups were investigated (Tab. I). A statistically significant difference was found in a mother's height, as women who delivered by the vaginal route were taller than the C/S group. The difference, however, was observed in the D group ($p < 0.01$) only. In both (D and M) groups, women in the C/S delivery groups were more frequently diagnosed with hypertension, or they were nulliparous. What was interesting were the differences in pre-ripening cervical characteristics and gestational age being noticed in the M group only (Tab. 1).

We have compared pelvis diameters, maternal abdominal circumference and some created indexes which included diameters of the pelvis in relation to mother's height, abdominal circumference to height, and additionally EFBW in relation to mother's height and EFBW to available pelvis diameters. The measurements which were found to be significantly different between vaginal delivery and C/S groups were the intertrochanteric dimensions, which were lower in the C/S deliveries observed in the D group, and the EFBW to height index which were higher in the C/S deliveries, also in the D group (Tab. 2 and 3).

Analysis of neonatal outcomes across the route of birth delivery status in the D and M groups show significant differences in Apgar scores. In both prostaglandin groups neonates delivered by C/S had on average, less points in Apgar scale (means: 9.5 *vs.* 9.8 points, and 9.1 *vs.* 9.8 points), while only the M group had lower birth weight (3229g in C/S *vs.* 3405 g in vaginal delivery group; $p = 0.038$) (Tab. 4). It is worth noting the gestational age was also significantly younger in the C/S as compared to the vaginal delivery group observed in the M group (38.7 *vs.* 39.3; $p = 0.025$), but not in the D group (Tab. 1).

The next step was the analysis of possible factors associated to the C/S risk in the three (D, M and D + M) preinduction groups. Among pregnant women, who were treated by dinoprostone, height (both, considered as categorical < 165 cm *vs.* ≥ 165 cm: OR: 2.1, or as continuous: for each 1 cm increase: OR: 0.9), and intertrochanteric dimension (continuous, for each 1 cm increase OR: 0.8), and additionally the number of pregnancies, nulliparity, and hypertension were significantly associated with C/S risk. In the M group, higher risk has been observed in mothers which were over 35 years of age (OR 2.5) and in their gestational age less than 38 weeks (OR 2.0). Nulliparity and hypertension were also risk factors identified in this group (Tab. 5). In the D + M group statistically significant clinical features were hypertension and treatment by oxytocin. After univariable analyses, the variables, which were identified as associated significantly with C/S risk, were put in the multivariable model to check whether some of them are independent risk factors for C/S delivery. Across different preinduction groups hypertension was identified as an independent risk factor for each treatment strategy. Additionally, nulliparity was associated with C/S delivery in both, the D group and the M group. Gestational age less than 38 weeks was a risk factor for women treated by misoprostol, and oxytocin use for those who received both preinduction drugs. Mothers over 35 years of age seemed to be a risk factor if the misoprostol was used, whereas height (being taller) decreased the risk if the dinoprostone was used.

Finally, we tried to look at the combined effect of parity history and the mother's age. The study showed 6.7 and more than 10 times the increased risk of Caesarean section in nulliparous women aged over 35 years in both D and M groups, respectively (Fig. 1).

Table 3. Mothers' anthropometric indexes across route of birth delivery status in the dinoprostone and misoprostol groups

	Dinoprostone			Misoprostol		
	Vaginal delivery [n = 242]	Caesarean Section [n = 108]	p-value	Vaginal delivery [n = 125]	Caesarean Section [n = 85]	p-value
External conjugate/height [%] Mean, (SD) Median (Q1–Q3)	[n = 134] 12.6 (0.9)* 12.5 (12.0–13.0)	[n = 72] 12.8 (1.0)* 12.7 (12.2–13.2)	$p^{MW} = 0.322$	[n = 96] 12.7 (1.2)* 12.7 (12.0–13.1)	[n = 73] 12.8 (0.9)* 12.6 (12.2–13.3)	$p^{MW} = 0.323$
Interspinal dimension/height [%] Mean, (SD) Median (Q1–Q3)	[n = 135] 14.4 (1.03)* 14.4 (13.6–15.1)	[n = 72] 14.5 (1.11) 14.5 (13.6–15.2)	$p^{MW} = 0.795$	[n = 96] 14.4 (0.84) 14.4 (13.8–14.9)	[n = 73] 14.3 (0.94) 14.3 (13.7–15.0)	$P^{tte} = 0.744$
Intercristal dimension/height [%] Mean, (SD) Median (Q1–Q3)	[n = 135] 16.7 (1.01) 16.7 (15.9–17.2)	[n = 72] 16.7 (1.11) 16.7 (16.1–17.5)	$p^{tte} = 0.682$	[n = 96] 16.5 (0.95) 16.7 (15.9–17.1	[n = 73] 16.7 (1.23)* 16.7 (16.0–17.3)	$p^{MW} = 0.479$
Intertrochanteric dimension/height [%] Mean, (SD) Median (Q1-Q3)	[n = 135] 20.0 (1.50)* 19.9 (18.9–20.8)	[n = 72] 19.6 (1.50) 19.4 (18.4–20.6)	$p^{MW} = 0.080$	[n = 96] 19.5 (1.43) 19.4 (18.6–20.6)	[n = 73] 19.9 (1.42) 20.0 (18.8–20.8)	$p^{tte} = 0.066$
Abdominal circumference (cm) Mean, (SD) Median (Q1–Q3)	[n = 143] 109.4 (8.9) 108.0 (103.0–114.0)	[n = 72] 109.7 (8.4) 109.5 (103.3–116.0)	$P^{tte} = 0.828$	[n = 104] 108.2 (8.0)* 107.0 (103.0–112.0)	[n = 71] 109.6 (9.6) 108.0 (103.0–115.0)	$p^{MW} = 0.226$
Abdominal circumference/height [%] Mean, (SD) Median (Q1–Q3)	[n = 127] 65.2 (5.1)* 64.7 (61.2–68.3)	[n = 69] 66.5 (5.6) 66.3 (62.4–69.7)	$p^{MW} = 0.124$	[n = 91] 64.8 (4.9)* 64.6 (60.9–68.5)	[n = 70] 66.3 (5.8) 66.0 (62.2–69.7)	$p^{MW} = 0.063$
EFBW/height [g/cm]	[n = 57] 21.0 (2.5)* 21.4 (19.3–22.9)	[n = 42] 21.8 (3.2) 22.0 (19.9–23.9)	$p^{MW} = 0.049$	[n = 58] 20.6 (2.9)* 21.2 (18.8–22.5)	[n = 48] 19.3 (3.9) 19.5 (17.1–22.3)	$p^{MW} = 0.083$
EFBW/abdominal circumference	[n = 46] 32.2 (3.9)* 32.5 (29.9–35.3)	[n = 31] 32.3 (5.0) 33.8 (28.2–36.2)	$p^{MW} = 0.729$	[n = 53] 31.7 (4.4)* 32.2 (29.3–34.4)	[n = 40] 30.2 (5.3) 30.5 (26.3–35.1)	$p^{MW} = 0.159$
EFBW/External conjugate	[n = 47] 264.9 (22.3) 166.1 (151.0–180.8)	[n = 33] 170.0 (27.1) 176.2 (155.0–184.4)	$p^{tte} = 0.362$	[n = 58] 161.3 (23.5)* 165.5 (145.5–178.9)	[n = 43] 155.0 (32.7) 160.0 (132.7–180.6)	$p^{MW} = 0.371$
EFBW/Interspinal dimension	[n = 48] 146.4 (17.8)* 150.0 (135.2–157.0)	[n = 33] 149.2 (24.2) 152.2 (132.7–168.1)	$p^{MW} = 0.328$	[n = 58] 141.1 (21.8)* 147.5 (130.5–154.4)	[n = 43] 138.3 (27.9) 142.9 (120.0–156.5)	$p^{MW} = 0.486$
EFBW/Intercristal dimension	[n = 48] 125.2 (15.9)* 131.1 (115.4–136.3)	[n = 33] 128.9 (19.9) 132.1 (117.4–143.7)	$p^{MW} = 0.291$	[n = 58] 122.1 (18.2)* 127.2 (110.3–135.6)	[n = 43] 117.9 (22.5) 120.0 (104.3–131.9)	$p^{MW} = 0.239$
EFBW/Intertrochanteric dimension	[n = 48] 104.5 (13.5) 105.7 (97.4–114.8)	[n = 33] 110.2 (17.6) 111.8 (101.6–124.6)	$p^{tte} = 0.104$	[n = 58] 104.5 (15.8)* 106.5 (93.2–118.4)	[n = 43] 99.0 (18.8)* 103.3 (85.9–111.8)	$p^{MW} = 0.178$

DISCUSSION

Labor induction is a perinatal intervention which is becoming more common worldwide and is of growing importance providing the opportunity to treat unfavorable cervixes. Although prostaglandin medications have been used for several years [5], there is still a need to get more knowledge about maternal and fetal characteristics which are associated with an increased risk of C/S. This issue was addressed by our study, through the investigation of the two prostaglandins, which are most often used in clinical practice, dinoprostone and misoprostol.

There are several clinical and anthropometric features which may cause the necessity of C/S delivery. First, a well-known determinant is nulliparity and cervical ripeness status at the beginning of the procedure. Although the preinduction with prostaglandins was introduced into clinical practice, the risk of vaginal labor failure is bigger when dealing with an unripe cervix, especially in nulliparous patients [6–7]. Similar effects have been observed in our study. Additionally, our study revealed nulliparity as an independent risk factor of C/S regardless of the type of preinduction method used. Maslow and Sweeny showed also an almost three-fold increased risk of C/S among nulliparas and a two-fold increase among parous women who underwent induction compared with nulliparas and multiparous women who did not [8]. Although the last study

Table 4. Neonatal outcomes across route of birth delivery status in the dinoprostone and misoprostol groups

	Dinoprostone			Misoprostol		
	Vaginal delivery [n = 242]	Caesarean Section [n = 108]	p-value	Vaginal delivery [n = 125]	Caesarean Section [n = 85]	p-value
Apgar score (points) Mean, (SD) Median (Q1–Q3)	9.8 (0.7)* 10 (10–10)	9.5 (1.3)* 10 (9–10)	$p^{MW} < 0.001$	9.8 (1.0)* 10 (10–10)	9.1 (1.7)* 10 (9–10)	$p^{MW} < 0.001$
Apgar score ≤ 6 points at the 1st min (n, %)	3 (1.2%)	5 (4.6%)		3 (2.4%)	9 (10.6%)	
Apgar score 7–8 points at the 1st min (n, %)	8 (3.3%)	6 (5.6%)		4 (3.2%)	9 (10.6%)	
Apgar score 9-10 points at the 1st min (n, %)	231 (95.5%)	97 (89.8%)	$p^{F} = 0.081$	118 (94.4%)	67 (78.8%)	$p^{F} = 0.003$
Birth weight (g) Mean, (SD) Median (Q1–Q3)	3507 (426)* 3545 (3242–3800)	[n = 107] 3573 (479)* 3580 (3230–3880)	$p^{MW} = 0.216$	3405 (487)* 3460 (3080–3735)	3229 (620) 3240 (2805–3695)	$p^{MW} = 0.038$
Birth length (cm) Mean, (SD) Median (Q1–Q3)	55.6 (2.8)* 56.0 (54.0–57.0)	[n=107] 55.5 (3.1) 56.0 (53.0–58.0)	$p^{MW} = 0.946$	54.9 (3.2)* 55.0 (53.0–57.0)	54.2 (3.5) 54.0 (52.0–56.0)	$p^{MW} = 0.103$
			Df = 1			Df = 1
Female (n, %)	125 (51.7%)	44 (40.7%)	$p^{chi2} = 0.065$	63 (50.4%)	46 (54.1%)	$p^{chi2} = 0.673$

* –p < 0.05 by the Shapiro-Wilk test for normal distribution; MW — the U Mann-Whitney test; chi2 — the chi-squared test with 1degree of freedom; F — the exact Fisher's test

is not unequivocally comparable with the present one, it shows a trend of higher risk depending on parity. Like in the other study with dinoprostone agents, although on a smaller study group where multiple logistic regression analysis also showed that the gravidity (OR = 0.61, 95% CI 0.408–0.892; p = 0.011) was an independent predictor of successful labor induction, with no statistically significant differences in maternal age, gestational age, body mass index, fetal sex or the Bishop score at the time of admission [9].

Among other parameters of possible importance in predicting likelihood of successful labor induction, Pevzner et al., was pointing out the maternal body mass index (BMI) less than 30 and height greater than 165 cm [10]. The analyses of those parameters in our database revealed some similarities, especially when considering parity and mother's height. In the dinoprostone group, the height of women who gave vaginal birth was 167 cm average compared to 164 cm in those who underwent C/S. Patients in the M and D groups, however, had no differences in body mass index and maternal weight at admission. Our study provided an opportunity to analyse pelvic dimensions and abdominal circumference of pregnant women. These features were of our special interest because they are seldom listed as an important parameter influencing labor induction outcome. We have checked whether pelvimetric measurements in conjunction with EFBW or with mother's height have any correlation with the mode of delivery. The majority of our results, however, were not statistically significant (Tab. 5). Only intratrochanteric diameter in the D group showed a difference, as a bigger dimension was observed in the vaginal delivery subgroup. It was associated, with high probability and maternal height, which was also statistically greater in that subgroup. When put together the obstetric pelvimetry with EFBW the risk of cephalopelvic disproportion should be reduced [11–12], which is also a basic rule of proper qualification of pregnant woman to labour induction procedures and these relationships have been confirmed by our study as well.

Pevzner showed that fetal weight over 4000 g may be a risk factor of induction failure [10]. Other research showed important differences in average birth weight of 3421.11 ± 368.14 in successful *vs.* 3566.36 ± 345.16 in the failed induction group (p = 0.033) [9]. Our study showed important differences in birth weight in the M group, but in an opposite way, as it turns out that smaller babies were born by C/S (3229 ± 620 vs 3405 ± 487; pMW = 0.038). Although the EFBW is routinely performed during the ultrasound testing at the admission to the hospital, it is not obligatory to introduce it into the electronic database in our hospital and therefore some of records were missing in the current analysis, making the groups smaller sizes. This may be a reason for not reaching the statistical significance of ultrasonographic fetal weight estimation, especially in the misoprostol group (Tab. 1). When we looked closer we saw that in the M group, the birth weight in the C/S subgroup might be an effect of gestational age, while as a possible C/S risk factor (OR 2.189; p = 0.041) the

Table 5. Analysis of possible factors associated with Caesarean section in the dinoprostone, and misoprostol, and dinoprostone with misoprostol groups

	Dinoprostone [n = 250]				Misoprostol [n = 210]				Dinoprostone+misoprostol [n = 100]			
	OR	95% CI		p-value	OR	95% CI		p-value	OR	95% CI		p-value
Mother's age (years)	1.008	0.951	1.069	0.778	1.067	0.997	1.142	0.062	1.082	0.968	1.208	0.164
Mother's age > 35 years	1.128	0.581	2.189	0.721	2.510	1.301	4.845	0.006	3.117	0.847	11.467	0.087
Weight at admission (kg)	0.994	0.971	1.019	0.657	1.018	0.989	1.048	0.215	1.019	0.976	1.063	0.393
Weight at admission > 78 kg$	0.977	0.499	1.912	0.946	1.267	0.578	2.778	0.555	0.920	0.304	2.790	0.884
Height (cm)	0.930	0.885	0.977	0.004	0.969	0.922	1.020	0.226	0.940	0.874	1.011	0.094
Height < 165cm	2.125	1.182	3.820	0.012	1.308	0.729	2.347	0.368	1.778	0.762	4.147	0.183
Body mass index at admission (kg/m^2)	1.032	0.958	1.112	0.405	1.075	0.980	1.178	0.125	1.100	0.965	1.253	0.153
BMI > 30 kg/m^2	0.958	0.477	1.923	0.904	1.996	0.863	4.616	0.106	1.687	0.551	5.171	0.360
Abdominal circumference [cm]	0.990	0.945	1.036	0.657	1.019	0.984	1.055	0.290	1.005	0.958	1.055	0.834
External conjugate (cm)	0.939	0.710	1.241	0.658	1.050	0.882	1.249	0.584	0.976	0.783	1.216	0.826
Interspinaldimention (cm)	0.878	0.695	1.109	0.276	.892	0.727	1.094	0.272	0.974	0.749	1.266	0.844
Intercristal dimension (cm)	0.876	0.707	1.086	0.228	1.020	0.868	1.200	0.807	1.016	0.805	1.282	0.897
Intertrochanteric dimension (cm)	0.796	0.670	0.944	0.009	1.014	0.922	1.114	0.775	0.850	0.696	1.038	0.111
External conjugate/height [%]	1.247	0.767	2.030	0.373	1.152	0.858	1.547	0.346	0.985	0.661	1.467	0.940
Interspinal dimension/height [%]	1.087	0.749	1.576	0.661	0.944	0.668	1.334	0.744	1.107	0.739	1.660	0.622
Intercristal dimension/height [%]	1.043	0.713	1.525	0.830	1.189	0.892	1.583	0.237	1.063	0.711	1.587	0.767
Intertrochanteric dimension/height [%]	0.790	0.599	1.041	0.094	1.241	0.995	1.548	0.055	0.836	0.603	1.160	0.283
abdominal circumference/height [%]	1.037	0.960	1.119	0.360	1.057	0.995	1.122	0.071	1.034	0.951	1.123	0.435
EFBW/height [g/cm]	1.227	0.988	1.524	0.065	0.895	0.797	1.005	0.062	1.031	0.818	1.298	0.797
EFBW/abdominal circumference	1.047	0.892	1.228	0.575	0.940	0.861	1.025	0.163	0.994	0.850	1.162	0.939
EFBW/External conjugate	1.018	0.988	1.049	0.233	0.992	0.978	1.006	0.272	1.006	0.980	1.034	0.647
EFBW/Interspinal dimension	1.016	0.984	1.048	0.333	0.995	0.979	1.011	0.555	1.000	0.967	1.033	0.988
EFBW/Intercristal dimension	1.028	0.986	1.072	0.190	0.990	0.971	1.010	0.328	1.002	0.967	1.039	0.895
EFBW/Intertrochanteric dimension	1.038	0.991	1.087	0.112	0.981	0.959	1.005	0.116	1.020	0.976	1.066	0.379
Number of pregnancies			For trend	0.014			For trend	0.220			For trend	0.255
1	1 (ref)				1 (ref)				1 (ref)			
2	0.458	0.219	0.959	0.038	1.041	0.518	2.092	0.910	0.958	0.310	2.958	0.941
≥ 3	0.412	0.171	0.994	0.049	0.589	0.280	1.240	0.164	0.240	0.028	2.087	0.196
Parity history (current delivery included)			For trend	0.005			For trend	0.013			For trend	0.135
1	1 (ref)				1 (ref)				1 (ref)			
2	0.284	0.114	0.705	0.007	0.284	0.117	0.688	0.005	0.402	0.079	2.043	0.272
≥ 3	0.321	0.091	1.129	0.077	0.473	0.159	1.405	0.178	---	---	---	#
Nulliparous	3.146	1.506	6.573	0.002	2.492	1.295	4.797	0.006	2.353	0.605	9.158	0.217
Miscarriage history	0.751	0.348	1.617	0.464	1.126	0.595	2.132	0.715	0.600	0.194	1.861	0.377
Pre-ripening cervical characteristics												
Dilatation ≤ 1 cm	3.622	0.817	16.048	0.090	—	—	—	#	—	—	—	#
Effacement ≤ 50%	2.123	0.458	9.835	0.336	—	—	—	#	0.633	0.038	10.430	0.749
Oxytocin use	1.117	0.638	1.956	0.698	1.352	0.547	3.339	0.514	2.947	1.282	6.774	0.011
Gestational age (weeks)	0.899	0.702	1.150	0.396	0.841	0.727	0.973	0.020	1.109	0.846	1.455	0.453
Gestational ageless than 38 weeks	2.781	0.676	11.449	0.157	2.024	1.009	4.060	0.047	0.764	0.180	3.251	0.715
Estimated birth weight (for change by 100g)	1.112	0.982	1.260	0.095	0.941	0.880	1.005	0.072	0.999	0.874	1.143	0.992
Hypertension	2.690	1.233	5.869	0.013	2.647	1.209	5.794	0.015	3.677	1.025	13.193	0.046
Diabetes	0.699	0.350	1.394	0.309	1.274	0.558	2.909	0.565	1.225	0.461	3.252	0.684
Diabetes — insulin therapy	0.910	0.417	1.984	0.812	1.487	0.536	4.129	0.446	1.491	0.521	4.266	0.456
Hypothyroidism	1.153	0.645	2.062	0.631	1.221	0.696	2.142	0.487	0.690	0.304	1.562	0.373
GBS	0.790	0.414	1.509	0.476	1.082	0.539	2.174	0.825	0.970	0.387	2.428	0.948

OR — odds ratio; CI — confidence interval; EFBW — estimated fetal birth weight; # — cannot estimate model parameters due to limited sample size; $ — the observed median in the vaginal delivery route group (total)

Table 6. Identified risk factors of Caesarean section across different preinduction groups — multivariable analysis

	Dinoprostone [n = 250]				Misoprostol [n = 210]				Dinoprostone + Misoprostol [n = 100]			
	OR	95% CI		p-value	OR	95% CI		p-value	OR	95% CI		p-value
Mother's age > 35 years	#				3.252	1.561	6.778	0.002	#			
Height (cm)	0.929	0.882	0.979	0.006	#				#			
Nulliparous	3.669	1.665	8.085	0.001	3.341	1.608	6.940	0.001	#			
Gestational age less than 38 weeks	#				2.189	1.032	4.642	0.041	#			
Hypertension	3.586	1.434	8.967	0.006	2.278	0.995	5.211	0.051	4.146	1.096	15.684	0.036
Oxytocin use	#				#				3.149	1.333	7.441	0.009

OR — odds ratio; CI — confidence interval; # — not considered for the model as a significant effect in the univariable analysis was not observed; additionally Intertrochanteric dimension was removed from the dinoprostone analysis due to too high number of missingness leading to no stable model estimates

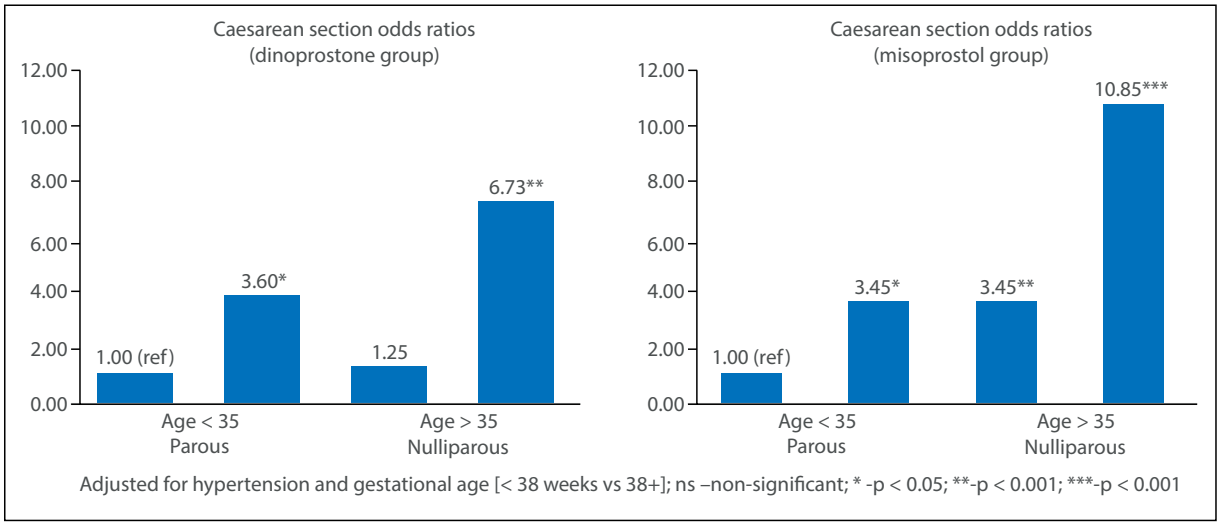

Figure 1. Combined effect of mother's age and parity history on the Caesarean section risk estimates

gestational age less than 38 weeks was found, which was not observed in dinoprostone group. Studies analysing preterm deliveries showed that vaginal live birth rates increased with gestational age [13], and, additionally, lower gestational age at delivery was a significant predictor of ripening failure [14].

In general, the aim of this study was to compare the two most used prostaglandins separately and if something happened, the two-drug group (group M + D). We also checked if oxytocin augmentation has any influence on the final results. What is interesting is that we have found that only in combination of D and M the oxytocin infusion had increased the risk of C/S. Misoprostol alone probably has not only cervical ripening capability, but also labor induction properties [15] and is more cost-effective than dinoprostone [16]. But there is still a group of patients irresponsive to any labour agents, which needs further studies.

No significant differences in maternal age and miscarriage history were found among the M and D groups, which stays in compliance with other studies [7, 10]. Multivariable analysis, however, showed that mothers aged over 35 years in the misoprostol group increased the risk of C/S 3.2 times with statistical significance (p = 0.002). The current results support the findings of previous studies on advanced maternal age [17–19]. Only ages > 35 years, and not the age itself, was a statistically significant predictor of caesarean delivery rate in the misoprostol group. When further analyzes were performed on the combined effects of mother's age and parity history on the caesarean section risk, adjusted for hypertension and gestational age, it revealed that nulliparous women over 35 years of age in the D and M groups had 6.73- and 10.85-times higher risk, respectively, for C/S than parous pregnant women below 35 years of age (Fig. 1). Another study showed that primigravidas induced with misoprostol had a higher C/S rate compared to multiparas (40.58% vs. 16.13%), and what is more, there were statistically important differences in average age of those women, as primigravidas and multiparas

were 27.71 ± 5.45 and 31.58 ± 5.68 years old, respectively (p = 0.0016) [20].

Other study also showed that maternal age over 35 years and nulliparity were significantly associated with caesarean delivery when induced with dinoprostone gel [2]. On the other hand, our study did not identify gestational diabetes mellitus as associated with the route of delivery, likewise it was published by Hawkins et al., study with misoprostol induction [21]. These results, however, differ from other observations [2], and in contrary to hypertension which came out in our work, to be very strong predictor of C/S and which stays in compliance with Sievert et al. [2, 22].

The presented study, however, has some limitations. First, was a surprising number of patients do not have available data on pelvic diameters, which decreased the power of our conclusions in this area, which requires further investigation. Next, our study was performed in a nested case-control design. The primary investigation, therefore, did not focus on risk groups, as one of underlying inclusion criteria. As a next step, it would be useful to perform some observations in well-defined risk groups, to check the prospective observation the C/S risk estimates across different preinduction methods. We would like to mention also that there are many more factors possibly contributing to C/S risk. The most important, however, as mother's age, parity history, increased BMI, extremes of neonatal birth weight or complicated pregnancy and others were controlled in our study by the inclusion criteria or by implementation of multivariable statistical analyses.

In summary, the main findings of the present study were that the increased risk of Caesarean delivery in dinoprostone group was combined with the mother's height less than 165 cm, nulliparity and hypertension. Subsequently in the misoprostol group, strong risk factors of Caesarean delivery were mother's aged 35 or more, gestational age less than 38 weeks and nulliparity and hypertension as in dinoprostone group. Although, in both M and D groups, nulliparous women aged 35 or more years had significantly bigger risk of Caesarean section than multiparous women. The risk was slightly bigger in misoprostol group. Therefore, in our opinion, the aforementioned features should be considered before the decision about the preinduction method. Further high-quality studies assessing the possible Caesarean section risk factors of misoprostol and dinoprostone in selected groups of patients are warranted.

Acknowledgments

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

Financial disclosure

The authors received no financial support for the study conduct.

REFERENCES

1. Rayburn WF, Zhang J. Rising rates of labor induction: present concerns and future strategies. Obstet Gynecol. 2002; 100(1): 164–167, doi: 10.1016/s0029-7844(02)02047-1, indexed in Pubmed: 12100818.
2. Mhaske N, Agarwal R, Wadhwa RD, et al. Study of the risk factors for cesarean delivery in induced labors at term. J Obstet Gynaecol India. 2015; 65(4): 236–240, doi: 10.1007/s13224-014-0596-2, indexed in Pubmed: 26243989.
3. Chaemsaithong P, Kwan AHW, Tse WT, et al. Factors that affect ultrasound-determined labor progress in women undergoing induction of labor. Am J Obstet Gynecol. 2019; 220(6): 592.e1–592.e15, doi: 10.1016/j.ajog.2019.01.236, indexed in Pubmed: 30735668.
4. Gornisiewicz T, Kusmierska-Urban K, Huras H, et al. Comparison of Misoprostol versus Dinoprostone for delivery induction among pregnant women without concomitant disease. Ginekol Pol. 2020; 91(12): 726–732, doi: 10.5603/GP.2020.0119, indexed in Pubmed: 33447991.
5. Bomba-Opoń D, Drews K, Huras H, et al. Polish Gynecological Society Recommendations for labor induction. Ginekol Pol. 2017; 88(4): 224–234, doi: 10.5603/GP.a2017.0043, indexed in Pubmed: 28509326.
6. Yeast JD, Jones A, Poskin M. Induction of labor and the relationship to cesarean delivery: A review of 7001 consecutive inductions. Am J Obstet Gynecol. 1999; 180(3 Pt 1): 628–633, doi: 10.1016/s0002-9378(99)70265-6, indexed in Pubmed: 10076139.
7. Vrouenraets FP, Roumen FJ, Dehing CJG, et al. Bishop score and risk of cesarean delivery after induction of labor in nulliparous women. Obstet Gynecol. 2005; 105(4): 690–697, doi: 10.1097/01.AOG.0000152338.76759.38, indexed in Pubmed: 15802392.
8. Maslow AS, Sweeny AL. Elective induction of labor as a risk factor for cesarean delivery among low-risk women at term. Obstet Gynecol. 2000; 95(6 Pt 1): 917–922, doi: 10.1016/s0029-7844(00)00794-8, indexed in Pubmed: 10831992.
9. Hou L, Zhu Yu, Ma X, et al. Clinical parameters for prediction of successful labor induction after application of intravaginal dinoprostone in nulliparous Chinese women. Med Sci Monit. 2012; 18(8): CR518–CR522, doi: 10.12659/msm.883273, indexed in Pubmed: 22847202.
10. Pevzner L, Rayburn WF, Rumney P, et al. Factors predicting successful labor induction with dinoprostone and misoprostol vaginal inserts. Obstet Gynecol. 2009; 114(2 Pt 1): 261–267, doi: 10.1097/AOG.0b013e3181ad9377, indexed in Pubmed: 19622986.
11. Spörri S, Gyr T, Schollerer A, et al. [Methods, techniques and assessment criteria in obstetric pelvimetry]. Z Geburtshilfe Perinatol. 1994; 198(2): 37–46, indexed in Pubmed: 8023529.
12. Korhonen U, Taipale P, Heinonen S. The diagnostic accuracy of pelvic measurements: threshold values and fetal size. Arch Gynecol Obstet. 2014; 290(4): 643–648, doi: 10.1007/s00404-014-3271-z, indexed in Pubmed: 24816688.
13. Feghali M, Timofeev J, Huang CC, et al. Preterm induction of labor: predictors of vaginal delivery and labor curves. Am J Obstet Gynecol. 2015; 212(1): 91.e1–91.e7, doi: 10.1016/j.ajog.2014.07.035, indexed in Pubmed: 25068566.
14. Melamed N, Yogev Y, Hadar E, et al. Preinduction cervical ripening with prostaglandin E2 at preterm. Acta Obstet Gynecol Scand. 2008; 87(1): 63–67, doi: 10.1080/00016340701778773, indexed in Pubmed: 18158629.
15. Ramsey PS, Ramin KD, Ramin SM. Labor induction. Curr Opin Obstet Gynecol. 2000; 12(6): 463–473, doi: 10.1097/00001703-200012000-00002, indexed in Pubmed: 11128407.
16. Ramsey PS, Harris DY, Ogburn PL, et al. Comparative cost analysis of prostaglandin analogues dinoprostone and misoprostol as labor preinduction agents. Prim Care Update Ob Gyns. 1998; 5(4): 182–565, doi: 10.1016/s1068-607x(98)00095-x, indexed in Pubmed: 10838340.
17. Pinheiro RL, Areia AL, Mota Pinto A, et al. Advanced maternal age: adverse outcomes of pregnancy, a meta-analysis. Acta Med Port. 2019; 32(3): 219–226, doi: 10.20344/amp.11057, indexed in Pubmed: 30946794.
18. Hansen JP. Older maternal age and pregnancy outcome: a review of the literature. Obstet Gynecol Surv. 1986; 41(11): 726–742, doi: 10.1097/00006254-198611000-00024, indexed in Pubmed: 2950347.

19. Jacobsson Bo, Ladfors L, Milsom I. Advanced maternal age and adverse perinatal outcome. Obstet Gynecol. 2004; 104(4): 727–733, doi: 10.1097/01.AOG.0000140682.63746.be, indexed in Pubmed: 15458893.
20. Jagielska I, Kazdepka-Ziemińska A, Tyloch M, et al. Obstetric outcomes of pre-induction of labor with a 200 µg misoprostol vaginal insert. Ginekol Pol. 2017; 88(11): 606–612, doi: 10.5603/GP.a2017.0109, indexed in Pubmed: 29303214.
21. Hawkins JS, Stephenson M, Powers B, et al. Diabetes mellitus: an independent predictor of duration of prostaglandin labor induction. J Perinatol. 2017; 37(5): 488–491, doi: 10.1038/jp.2016.270, indexed in Pubmed: 28125096.
22. Sievert RA, Kuper SG, Jauk VC, et al. Predictors of vaginal delivery in medically indicated early preterm induction of labor. Am J Obstet Gynecol. 2017; 217(3): 375.e1–375.e7, doi: 10.1016/j.ajog.2017.05.025, indexed in Pubmed: 28526449.