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Indications for induction of labour and mode of delivery in nulliparous term women with an unfavourable cervix

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Objectives: To determine the association between indications for induction of labour (IOL) and mode of delivery in nulliparous women with unfavourable cervix.
Methods: We identified nulliparous singleton term women with an unfavourable cervix who underwent IOL between 1 January 2013 and 31 December 2017 in an obstetrics unit. Clinical data of patients and their neonates were collected. The primary outcome was the mode of delivery (vaginal vs caesarean). Secondary outcomes were the instrumental delivery rate, indications for caesarean section, and maternal and neonatal complication stratified by indications of IOL.
Results: 1156 women were included for analysis. The IOL success (vaginal delivery) rate was 66.4%, the instrumental delivery rate was 19.2%, and the caesarean delivery rate was 33.6%. After controlling the confounding factors (maternal age, stature, weight gain during pregnancy, and Bishop score), indications for IOL independently associated with the mode of delivery were post-date pregnancy (adjusted odds ratio [OR_{adj}]=2.30, p<0.001), diabetes mellitus diseases (OR_{adj}=1.67, p=0.015), hypertensive disorders (OR_{adj}=1.72, p=0.015), and large-for-gestational-age fetus (OR_{adj}=2.32, p=0.001). Maternal age ≥35 years, body mass index ≥25 kg/m^2, more weight gain during pregnancy were associated with caesarean section, whereas taller stature and a more favourable Bishop score were associated with vaginal delivery.
Conclusion: Different indications for IOL affect the mode of delivery differently. Post-date pregnancy, diabetes mellitus diseases, hypertensive disorders, and large-for-gestational-age fetus are independent risk factors for caesarean delivery.

Keywords: Cervix uteri; Delivery, obstetric; Labor, induced

Introduction

Induction of labour (IOL) is commonly performed for various indications[1]. From 2004 to 2014, the incidence of IOL in all hospitals in Hong Kong had increased from 18.4% to 22.3%[2]. According to the Cochrane Review 2020, IOL after 37 weeks of gestation reduces the stillbirth rate, perinatal morbidity, and mortality[3].

Failed IOL results in caesarean section, which may result in maternal morbidity and adverse maternal experience in childbirth. The failure rate is higher in nulliparous women with an unfavourable cervix[4]. Predictors for IOL success (vaginal delivery) include multiparity, taller maternal statures, lower maternal body mass index (BMI), lower estimated fetal weight, and a favourable Bishop score[5-7]. There are limited studies on whether indications of IOL predict mode of delivery[8-11]. This study aims to determine the association between indications for IOL and mode of delivery in nulliparous women with unfavourable cervix.

Methods

This retrospective cohort study was approved by the Kowloon West Cluster Research Ethics Committee (reference: KW/EX-19-042(134-04)). Through the Clinical Data Analysis and Reporting System, we identified nulliparous women with a singleton pregnancy who underwent IOL at term for an unfavourable cervix (modified Bishops score of <7) and were prescribed with prostaglandin E2 (PGE2) vaginal tablet (3 mg) for pre-induction cervical priming between 1 January 2013 and 31 December 2017 in the obstetrics unit of Princess Margaret Hospital, Hong Kong. Individual patient records were reviewed, and demographic and clinical data of patients and their neonates were collected.

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Cases excluded were stillbirth before cervical priming, major fetal anomalies, allergy to PGE2, prelabour rupture of membranes (PROM) before cervical priming, and contraindications to vaginal delivery such as non-vertex presentation and placenta previa. Women who were prescribed with other doses or formulations of PGE2 under different IOL protocols (eg, 10 mg slow-release pessary or 1.5 mg vaginal tablet) were also excluded, as were non-Chinese patients and patients with PROM and stillbirth before IOL.

The primary outcome was the mode of delivery (vaginal vs caesarean). Secondary outcomes were the instrumental delivery rate, indications for caesarean section, and maternal and neonatal complication stratified by indications of IOL.

Reasons for caesarean section were categorised as fetal wellbeing related (fetal distress and non-reassuring cardiotocogram) and progress related (labour dystocia). The latter were further sub-categorised as (1) failed cervix dilatation despite serial PGE2 for cervical priming and oxytocin for IOL, (2) failure to enter active phase of labour despite 1 to <5 cm cervix dilatation, and (3) failure to progress despite active labour achieved, with ≥5 cm cervix dilatation.

Elective IOL was not performed. Some women had more than one indication for IOL. Indications for IOL were categorised as (1) post-date pregnancy beyond 40 weeks, (2) diabetes mellitus (DM) including pre-existing DM and gestational DM (fasting plasma glucose of >5.1 mmol/l or 2-hour plasma glucose of >8.5 mmol/l[12]) on either diet or insulin control, (3) hypertensive disorder including pre-existing hypertension (≥140/90 mmHg pre-pregnancy or before 20 weeks of gestation), gestational hypertension (≥140/90 mmHg after 20 weeks), pre-eclampsia (gestational hypertension with proteinuria, maternal organ damage, or sign of uteroplacental dysfunction), gestational proteinuria (≥300 mg/day of urinary protein in the absence of hypertension after 20 weeks of gestation), eclampsia (seizure activity or unexplained coma during pregnancy or postpartum in women with pre-eclampsia), (4) small-for-gestational-age fetus (estimated fetal weight ≤10 percentile on ultrasonography), (5) large-for-gestational-age fetus (estimated fetal weight ≥90 percentile on ultrasonography), (6) polyhydramnios (single deepest pocket >8 cm or amniotic fluid index >95 percentile), (7) oligohydramnios (single deepest pocket <2 cm or amniotic fluid index <5 percentile), (8) reduced fetal movement (<10 discrete fetal movements in 2 hours by maternal counting), and (9) others including suboptimal cardiotocogram, antepartum haemorrhage, obstetrics cholestasis, and bad obstetrics history.

Dating ultrasonography was performed in most women in the first trimester or as part of first-trimester Down syndrome screening. For women with antenatal first visit beyond first trimester, ultrasonography was performed as soon as possible to confirm the gestation.

Patients with indication for IOL were admitted by obstetricians. The cervix was assessed digitally for Bishop score. Women with unfavourable cervix (Bishop score <7) were given 3 mg vaginal PGE2 tablet daily in posterior fornix until a favourable cervix (Bishop score ≥7) was achieved. Fetal heart was monitored immediately before and after each application of PGE2. The application of PGE2 was delayed during painful regular uterine contraction (>2 contractions in 10 minutes) until uterine contraction subsided. Once the cervix was ripened, patients were transferred to the delivery suite for artificial rupture

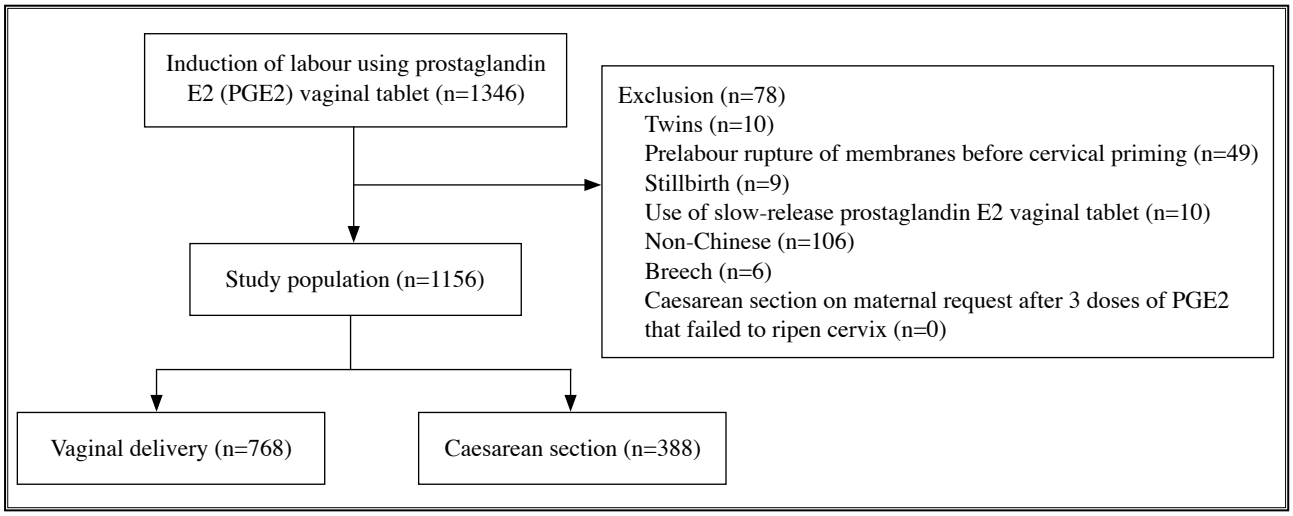

Figure. Recruitment flow diagram

of membranes and oxytocin infusion with continuous fetal heart monitoring. For patients with spontaneous PROM after application of PGE2 but without active labour, oxytocin infusion was initiated within 24 hours of PROM regardless of the Bishop score. Active labour is defined as cervical dilatation of ≥5 cm with regular uterine contraction[13]. If the cervix remained unfavourable after three consecutive applications of PGE2, the decision of further doses of PGE2 versus resting or elective caesarean section was made jointly with the patient. There was no upper limit on the number of PGE2 application.

The vaginal delivery group and the caesarean section group were compared using Pearson Chi-squared test or Fisher's exact test (for categorical variables) and independent *t*-test (for continuous variables). Univariate binary logistic regression analysis was used to identify the indications for IOL related to the mode of delivery (vaginal vs caesarean) and potential risk factors. Factors with a p value of <0.1 were included in the multivariate regression. Statistical analysis was performed using SPSS (Windows version 26; IBM Corp, Armonk [NY], US). A p value of <0.05 was considered statistically significant.

Results

Of 1346 nulliparous women who received PGE2 vaginal inserts, 92.1% were of Chinese ethnicity. Among them, 1156 met the inclusion criteria (Figure). The IOL success (vaginal delivery) rate was 66.4%, the instrumental delivery rate was 19.2%, and the caesarean delivery rate was 33.6%. Compared with women in the caesarean delivery group, those in the vaginal delivery group were younger and taller and more likely to have lower pre-pregnant BMI and less weight gain during pregnancy, deliver at earlier gestational age, and have a Bishop score of ≥4 prior to cervical priming (Table 1).

The caesarean delivery group had more indications for IOL (p for trend=0.002, Table 2). The most common indication for IOL was post-date pregnancy, followed by DM diseases and hypertensive disorders. Caesarean section was associated with post-date pregnancy (p=0.027), DM diseases (p=0.006), hypertensive disorders (p=0.017), large-for-gestational-age fetus (p=0.001), and polyhydramnios (p=0.036), whereas vaginal delivery was associated with small-for-gestational-age fetus (p<0.001) and reduced fetal movement (p=0.002).

Table 1. Characteristics of nulliparous women who received prostaglandin E2 vaginal tablet

Maternal characteristic	Mode of delivery		p Value
	Vaginal delivery (n=768)*	Caesarean section (n=388)*	
Maternal age, y	30.3±5.2	32.0±5.0	<0.001
≥35	158 (20.6)	124 (32.0)	<0.001
Body height, cm	159.8±5.6	157.8±5.6	<0.001
<150	19 (2.5)	28 (7.2)	
150-159.9	350 (45.9)	219 (56.4)	
160-169.9	355 (46.5)	130 (33.5)	
≥170	39 (5.1)	11 (2.8)	
Pre-pregnant body mass index (BMI)			<0.001
Underweight	141 (18.4)	39 (10.1)	
Normal	504 (65.6)	249 (64.2)	
Pre-obesity (BMI, 25.0-29.9)	89 (11.6)	71 (18.3)	
Obesity class I (BMI, 30.0-34.9)	26 (3.4)	22 (5.7)	
Obesity class II (BMI, 35.0-39.9)	3 (0.4)	7 (1.8)	
Obesity class III (BMI, >40)	0	0	
Weight gain during pregnancy, kg	14.2±5.6	15.2±5.7	0.008
Gestational age at delivery, wks	39.7±1.4	40.0±1.4	0.003
Bishop score ≥4	668 (87.0)	276 (71.1)	<0.001
Group B streptococcus positive	139 (18.1)	86 (22.2)	0.099
Epidural analgesia	76 (9.9)	52 (13.4)	0.073
Presence of fibroid	48 (6.3)	30 (7.7)	0.343

* Data are presented as mean±SD or No. (%) of cases

In multivariate logistic regression analysis, after controlling the confounding factors (maternal age, stature, weight gain during pregnancy, and Bishop score), indications for IOL independently associated with the mode of delivery were post-date pregnancy (adjusted odds ratio [OR_{adj}]=2.30, p<0.001), diabetes mellitus diseases

Table 2. Mode of delivery stratified by indications for induction of labour (IOL)

Indication for IOL	Mode of delivery		p Value
	Vaginal delivery (n=768)*	Caesarean section (n=388)*	
No. of indications			0.006
1	674 (87.8)	313 (80.7)	
2	84 (10.9)	67 (17.3)	
≥3	10 (1.3)	8 (2.0)	
Post-date pregnancy	258 (33.6)	156 (40.2)	0.027
Diabetes mellitus diseases	132 (17.2)	93 (24.0)	0.006
Hypertensive disorders	133 (17.3)	90 (23.2)	0.017
Small-for-gestational-age fetus	147 (19.1)	30 (7.7)	<0.001
Large-for-gestational-age fetus	51 (6.6)	48 (12.4)	0.001
Polyhydramnios	21 (2.7)	20 (5.2)	0.036
Oligohydramnios	32 (4.2)	9 (2.3)	0.109
Reduced fetal movement	53 (6.9)	10 (2.6)	0.002
Others	45 (5.9)	17 (4.4)	0.292

* Data are presented as No. (%) of cases

Table 3. Logistic regression analyses for predictors for caesarean section

Variable	Univariable		Multivariable	
	Odds ratio (95% confidence interval)	p Value	Adjusted odds ratio (95% confidence interval)	p Value
Maternal age ≥35 y	1.81 (1.38-2.39)	<0.001	1.54 (1.13-2.11)	0.007
Body height	0.94 (0.92-0.96)	<0.001	0.93 (0.91-0.95)	<0.001
Pre-pregnant body mass index (reference: normal)				
Underweight	0.56 (0.38-0.82)	0.003	0.74 (0.49-1.13)	0.166
Pre-obesity and obesity classes I-III	1.72 (1.26-2.33)	<0.001	1.66 (1.17-2.35)	0.005
Weight gain during pregnancy	1.03 (1.01-1.05)	0.008	1.04 (1.02-1.07)	0.001
Bishop score	0.65 (0.57-0.73)	<0.001	0.65 (0.57-0.75)	<0.001
Group B streptococcus positive	1.29 (0.95-1.74)	0.100	-	-
Epidural analgesia	1.41 (0.97-2.05)	0.074	1.21 (0.80-1.83)	0.375
Presence of fibroid	1.26 (0.78-2.02)	0.344	-	-
Indication for induction of labour				
Post-date pregnancy	1.33 (1.03-1.71)	0.027	2.30 (1.49-3.54)	<0.001
Diabetes mellitus diseases	1.52 (1.13-2.05)	0.006	1.67 (1.10-2.52)	0.015
Hypertensive disorders	1.44 (1.07-1.95)	0.017	1.72 (1.11-2.66)	0.015
Small-for-gestational-age fetus	0.35 (0.23-0.54)	<0.001	0.66 (0.39-1.14)	0.137
Large-for-gestational-age fetus	1.98 (1.31-3.00)	0.001	2.32 (1.39-3.87)	0.001
Polyhydramnios	1.93 (1.03-3.61)	0.039	1.45 (0.70-3.01)	0.318
Oligohydramnios	0.55 (0.26-1.16)	0.114	-	-
Reduced fetal movement	0.36 (0.18-0.71)	0.003	0.62 (0.29-1.31)	0.210

(OR_{adj}=1.67, p=0.015), hypertensive disorders (OR_{adj}=1.72, p=0.015), and large-for-gestational-age fetus (OR_{adj}=2.32, p=0.001) [Table 3].

Labour dystocia was the main reason for caesarean section. Fetal wellbeing was the main reason for caesarean section for small-for-gestational-age fetus (53.3%). There were six cases of second-stage caesarean section; three of which were due to DM diseases (Table 4).

There was no case of maternal death or hysterectomy. Four mothers who were induced for DM disease (n=3) and hypertensive disorder (n=1) required admission to the intensive care unit. The duration of IOL was >48 hours in at least half of cases of polyhydramnios and large-for-gestational-age fetus, and the postpartum haemorrhage was ≥1 L in over 5% for these two indications for IOL (Table 5). One baby induced for post-date pregnancy died from antepartum haemorrhage owing to undiagnosed vasa previa after application of PGE2. Meconium-stained amniotic fluid was observed in 24.6% of cases of post-date pregnancy.

Table 4. Operative delivery stratified by indications for induction of labour*

Indication for induction of labour	Mode of delivery			Reason for caesarean section					
	Vaginal delivery	Operative delivery		Progress related			Progress related total	Fetal wellbeing related	Others
		Instrumental delivery	Caesarean section	Failed cervical dilation	1 to <5cm dilatation	≥5cm dilatation			
Post-date pregnancy (n=414)	258 (62.3)	79 (19.1)	156 (37.7)	75 (48.1)	40 (25.6)	11 (7.1)	126 (80.8)	27 (17.3)	3 (1.9)
Diabetes mellitus diseases (n=225)	132 (58.7)	44 (19.6)	93 (41.3)	49 (52.7)	17 (18.3)	9 (9.7)	75 (80.6)	16 (17.2)	2 (2.2)
Hypertensive disorders (n=223)	133 (59.6)	39 (17.5)	90 (40.4)	50 (55.6)	9 (10)	6 (6.7)	65 (72.2)	16 (17.8)	9 (10)
Small-for-gestational-age fetus (n=177)	147 (83.1)	24 (13.6)	30 (16.9)	12 (40)	1 (3.3)	1 (3.3)	14 (46.7)	16 (53.3)	0
Large-for-gestational-age fetus (n=99)	51 (51.5)	21 (21.2)	48 (48.5)	26 (54.2)	6 (12.5)	7 (14.6)	39 (81.2)	7 (14.6)	2 (4.2)
Polyhydramnios (n=41)	21 (51.2)	6 (14.6)	20 (48.8)	12 (60)	2 (10)	1 (5)	15 (75)	3 (15)	2 (10)
Oligohydramnios (n=41)	32 (78.0)	8 (19.5)	9 (22.0)	7 (77.8)	0	0	7 (77.8)	2 (22.2)	0
Reduced fetal movement (n=63)	53 (84.1)	15 (23.8)	10 (15.9)	6 (60)	1 (10)	0	7 (70)	2 (20)	1 (10)
Others (n=62)	45 (72.6)	13 (21.0)	17 (27.4)	8 (47.1)	4 (23.5)	1 (5.9)	13 (76.5)	4 (23.5)	0

* Data are presented as No. (%) of cases

Table 5. Maternal and neonatal outcomes stratified by indications for induction of labour (IOL)*

Indication for IOL	Postpartum haemorrhage ≥1 L	Duration of IOL >48 hours	5-min Apgar <7	Meconium-stained amniotic fluid
Post-date pregnancy (n=414)	5 (1.2)	103 (24.9)	1 (0.2)	102 (24.6)
Diabetes mellitus diseases (n=225)	8 (3.6)	95 (42.2)	1 (0.4)	20 (8.9)
Hypertensive disorders (n=223)	6 (2.7)	86 (38.6)	1 (0.4)	22 (9.9)
Small-for-gestational-age fetus (n=177)	1 (0.6)	42 (23.7)	2 (1.1)	8 (4.5)
Large-for-gestational-age fetus (n=99)	5 (5.1)	49 (49.5)	0	7 (7.1)
Polyhydramnios (n=41)	3 (7.3)	23 (56.1)	0	2 (4.9)
Oligohydramnios (n=41)	0	18 (43.9)	0	4 (9.8)
Reduced fetal movement (n=63)	0	15 (23.8)	0	8 (12.7)
Others (n=62)	4 (6.5)	17 (27.4)	0	5 (8.1)

* Data are presented as No. (%) of cases

Discussion

Post-date pregnancy, hypertensive disorder, DM diseases, and large-for-gestational-age fetus were independent predictors of caesarean section, after adjusting for maternal age, stature, weight gain in pregnancy, and Bishop score. In the present study, patients may have multiple indications for IOL, and the independent effect of each indication on the mode of delivery was analysed. In contrast, previous studies arbitrarily assigned a single dominant indication for each case, and heterogenous indications for IOL were grouped into four categories: maternal, fetal, PROM, and hypertensive disorder[8,9]. Macrosomia and intrauterine growth restriction are contrasting indications but become indistinguishable under the fetal indication. Retrospectively deciding which indication is predominant in a particular case may introduce selection bias. Decision for IOL in some cases may be due to multiple indications, all similarly weighed, without one being predominant. In the present study, large-for-gestational-age fetus was associated with caesarean section, but small-for-gestational-age fetus was not.

Prolonged pregnancy ≥40 weeks is an independent risk factor for caesarean delivery (OR=2.028, p=0.016)[9]. Fetal compromise is associated with post-date pregnancy, and the caesarean section rate increases in those induced for post-date pregnancy[9]. In the present study, labour dystocia was the main reason (80.8%) for caesarean section in post-date pregnancy, whereas only 17.3% were for fetal distress. Although the proportion of cases of meconium-stained amniotic fluid in post-date pregnancy was relatively high, this was compatible with more advanced maturity in post-date babies, not necessarily reflecting impaired fetal wellbeing.

In the present study, hypertensive disorders were associated with a higher rate for caesarean section in nulliparous women; this may be due to a relatively larger sample size of 223. This association was demonstrated in multiparous women only but not in nulliparous women[8]. Although pre-eclampsia is the result of placental trigger, the present study failed to demonstrate any association between hypertensive disorders and caesarean for fetal wellbeing.

The caesarean section rate increases in women with gestational DM[14,15]. In the present study, a relatively higher proportion of women with DM had labour dystocia despite achieving active labour. This finding is consistent with that in a study that significantly more nulliparous women with gestational DM had caesarean section for cephalopelvic disproportion[14].

In the present study, several maternal factors were identified to predict the mode of delivery, consistent with those reported in previous studies[5-7,16-22]. The IOL success (vaginal delivery) rate was 66.4%, similar to the 63.7% reported in an epidemiological study[23].

In the present study, nulliparous women induced for small-for-gestational-age fetus had a high vaginal delivery rate of 83.1% and a low instrumental delivery rate of 13.6%. Similarly, women induced for reduced fetal movement and oligohydramnios had a high vaginal delivery rate of 84.1% and 78%, respectively, whereas caesarean section was performed in nearly 50% of the women induced for large-for-gestational-age fetus and polyhydramnios. These findings may guide clinicians on counselling patients for option of elective caesarean section when the chance of successful vaginal delivery is low.

Limitations of our study were its retrospective nature and the inter-rater variability in assessment of the Bishop score as well as the unavailability of more comprehensive outcome measures for babies such as arterial cord blood gas values, rates of admission to neonatal intensive care unit, and long-term baby outcome. Nonetheless, our study is the largest study that addresses the associations between indications for IOL and the mode of delivery in nulliparous Chinese women with unfavourable cervix. We used a unified IOL protocol. The original indications for IOL were retained to avoid the bias in retrospective re-interpretation and grouping. In addition, confounding factors were controlled. Studies with better case selection and stratification of gestation for IOL for each indication are warranted, especially for indications with lower success rate such as large-for-gestational-age fetus[24]. Indication-specific induction strategy may be the way forward.

Conclusion

Different indications for IOL affect the mode of delivery differently. Post-date pregnancy, DM diseases, hypertensive disorders, and large-for-gestational-age fetuses are independent risk factors for caesarean delivery.

Conflict of interest

The authors have no conflicts of interest to disclose.

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