







Effects of maternal age on the mode of delivery following induction of labor in nulliparous term pregnancies: A retrospective cohort study

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Abstract

Background and Aim: Increased maternal age at the time of pregnancy and labor is believed to have potential complications. To evaluate the effects of maternal age on the mode of delivery among nulliparous women with term pregnancies who underwent labor induction.

Methods: In this retrospective cohort study, 313 women with the gestational age of at least ≥ 37 weeks, were enrolled. They were divided based on their maternal ages as: Group A < 35 years old (y/o) and Group B ≥ 35 y/o patients. Demographic features and other variables (i.e., past medical history, social history, indications and methods of labor induction, causes of cesarean delivery) were recorded from patients' files. Final outcomes were categorized as: primary (i.e., rate of cesarean section: C/S) and (b) secondary (i.e., duration of labor, postpartum complications, neonatal variables). All data were analyzed by the SPSS ver.21 software.

Results: Median and interquartile ranges of gestational age were not significantly different, comparing the two groups ($p = 0.415$), although these variables were significantly different regarding maternal height among the two groups ($p = 0.007$). There was a significant relationship between the methods of labor induction among the two groups ($p = 0.005$). There was a prominent statistical relationship between (a) C/S deliveries and also (b) indications of C/S among the two groups ($p = 0.004$ and $p = 0.033$, respectively). Univariate logistic regression test revealed maternal age groups, neonatal weight, and history of underlying diseases had significant results ($p < 0.05$).

Conclusions: Increased maternal age is associated with higher rates of CS among nulliparous women with term pregnancies who underwent labor induction.

KEYWORDS

maternal age, nulliparous, labor induction

1 | INTRODUCTION

In the past decade, severe maternal complications of pregnancies have shown an upward trend among women of childbearing age, affecting more than 50,000 women annually in the United States.^{1,2} Furthermore, as the age of women at the time of pregnancy and labor is increasing rapidly among nations, increasing the complication rates could rise even more.^{1,3} Miscarriage, congenital or chromosomal abnormalities, hypertension, diabetes, placenta previa, preterm labor is some of the potential complications, mostly attributed to labor. These, could develop more chances of occurrence in the mothers, aged over 35 years old. In such age range, stillbirth is among the most important issues, as chances of these women for future pregnancies decrease.⁴⁻⁶

Statistics reveal that the rates of cesarean deliveries are higher among women over 35 years old, compared with younger mothers.^{1,6,7} It is also estimated that mothers' age could be accounted even as an independent risk factor for cesarean sections (C/S) or poor obstetric outcomes. Although, other factors like abnormal labor, underlying diseases, or patients' choices are also attributable to the final rates of C/S, records show that among nulliparous women aged 35-39 the rates of C/S is twice as normal and reaches up to three times more in the ones over 40 years old.^{2,4-6}

Considering that in recent years the age of childbearing in women has been increased for various reasons and the increase in maternal age has been reported as an independent risk factor for cesarean delivery and adverse obstetric outcomes,⁸ to prevent the increase in cesarean section and reduce maternal risks, fetal or delivery complications, labor induction in this age group of pregnant women has been considered. Induction of labor, in contrast to past studies, is now believed to be a helpful method during labor. During this process, physicians could decrease the maternal and fetal adverse outcomes of labor.^{6,9,10}

Evidence has recently shown that labor induction before 41 weeks or sooner is not only not related to the higher rates of C/S, but also could be cost-beneficial in terms of obstetric interventions.^{5,6,10,11} Also, in women between 40 and 44 years old, it is believed that, the process could lead to better prenatal outcomes.^{9,11-14} On the other hand, there are studies with conflicting results. In a study conducted on women under labor induction, it has been reported that with increasing maternal age and gestational age (GA), even in multiparous women, the chance of cesarean section increases,¹⁵ and there is a linear relationship between maternal age and cesarean delivery rate, that is, with increasing maternal age, cesarean section rate increases.¹⁶ However, there are limited studies on the effect of age on the type of delivery after induction of labor and their results are different.^{12,17-19} Although this information is useful, whether induction of labor is a risk factor for cesarean section women aged 35 and over is still an important and challenging question. Therefore, in the present study, we evaluated the effects of maternal age on the mode of delivery among nulliparous women with term pregnancies who underwent labor induction.

2 | PATIENTS AND METHODS

In this retrospective cohort study, we evaluated the nulliparous term pregnant women who underwent induction of labor in Al-Zahra University Hospital of Rasht, in the north of Iran. Inclusion criteria included: All nulliparous women with a singleton pregnancy with cephalic presentation admitted to the hospital for induction of labor with the GA of at least 37 weeks or more, who underwent routine prenatal care. Exclusion criteria included; complicated pregnancies (i.e., major fetal structural anomalies or aneuploidy, severe pre-eclampsia, insulin-dependent diabetes, severe intrauterine growth retardation (IUGR), and any underlying maternal comorbidities). Following proper confirmation of the ethical committee of Guilan University of Medical Sciences (IR.GUMS.REC.1399.176), the case files of subjects were reviewed and analyzed. Study group classifications: We divided our two groups of study based on their age as the ones less than 35 years old (Group A) versus 35 years old and older (Group B).

Sample size: Based on Walker et al.'s¹⁸ study, the sample size of the study with the test power of 75% and confidence interval (CI) of 95% was estimated at least 187 patients in each group. However, we could enroll 187 patients in group B and 206 individuals in Groups A, with a total number of 393 patients.

Study variables: Demographic maternal features (weight, height, history of smoking or drinking, or substance abuse), past medical history (pregestational diabetes, gestational diabetes, chronic hypertension, gestational hypertension, pre-eclampsia, and any other underlying comorbidities), past obstetric history (parity, number of abortions), indications of labor induction (postterm pregnancies, fetal heart rate (FHR) abnormalities, oligohydramnios, polyhydramnios, IUGR, elective induction of labor and any other possible causes of labor induction), GA at the time of labor, Bishop score (dilation, effacement, fetal station, consistency and position of cervix at the time of admission), method of cervical ripening (Foley catheter or misoprostol), mode of delivery (normal vaginal delivery or cesarean section: C/S). Causes of C/S (abnormal FHR, failure to progress, meconium passage).

The course of study: Following sample size definition, study group classification, and variables' identification, we categorized our ultimate outcomes into two major groups as primary and secondary results. Our basic primary outcome was the C/S rates, while the secondary ones include: duration of labor, perinatal complications (e.g., chorioamnionitis), duration of maternal hospitalization, postpartum complications (e.g., post-partum hemorrhage and anemia due to acute hemorrhage), neonatal variables (age, APGAR scores [at first and fifth minutes]), neonatal weight and neonatal intensive care units admissions.

2.1 | Statistical analysis

Following data collection, analysis was conducted using SPSS software version 21. After examining the normality of the data, the

Mann–Whitney test was used to compare the means for continuous variables, and χ^2 or Fisher's exact test was used for stratified variables. Logistics regression was used to examine the effect of maternal age over 35 years as an independent risk factor for cesarean section. Multivariate logistic regression were performed to control variables age, body mass index (BMI), neonatal weight, number of abortions, GA, past medical history, type of labor induction, in one-way analyses to calculate odds ratio (OR), with 95% CIs. The significance level of the data was considered less than 0.05.

2.2 | Ethical consideration

Ethical approval was obtained from the ethics committee of the Vice-Chancellor of Research at Guilan University of Medical Sciences (Code: IR.GUMS.REC.1399.176). All stages of this study have been performed according to the Helsinki declaration. All procedures of the study were explained clearly to the participants who had the eligible inclusion criterion. Moreover, all participants voluntarily filled out the written informed consent form before they join the study and they were free to decide whether or not to attend or withdraw at any time and for any reason without changing the medical care.

3 | RESULTS

The median for maternal weight for subjects over 35 years old was higher than the other group (but not significant: $p = 0.437$). The median BMI of the A group was significantly higher than the other group (31.64 vs. 30.47, respectively; $p = 0.011$; Table 1)

Median and interquartile ranges of GA were not significantly different, comparing the two groups ($p = 0.415$), although these variables were significantly different regarding maternal height among the two groups ($p = 0.007$). 14.1% (29 patients) in the B group had a history of at least one abortion or miscarriage, compared to a significantly higher rate of 23% (43 patients) in the A groups ($p = 0.026$; Table 1).

There were no significant differences regarding pregnancy-associated hypertensive disorders or gestational diabetes incidence among the two groups ($p = 0.474$, $p = 0.494$, respectively), using χ^2 data analysis. The frequency of the indications of labor induction is listed in Table 1, revealing, for instance, 8% and 9.7% ranges attributed to gestational diabetes as an indicator, in the B and A groups. Further analysis with the χ^2 test, showed that there were no significant differences between the indications of labor induction based on the age of participants ($p = 0.135$).

There was a significant relationship between the type of labor induction among the two groups ($p = 0.005$), revealed by Fisher's exact test application and (in 33% and 30.1% of subjects the labor was augmented by Cytotec [misoprostol] in the A, B groups, respectively; Table 2).

Duration of labor was also evaluated which revealed no significant relationship between outcomes among the two groups ($p = 0.309$, with Mann–Whitney test analysis). There was a statistical prominent relationship between (a) C/S deliveries and also (b) indications of C/S among the two groups ($p = 0.004$ and $p = 0.033$, respectively: with χ^2 test analysis).

There were no significant relationships among the two groups, regarding: (a) maternal and neonatal complications (Table 3).

Univariate regression logistic test was measured for OR of C/S among the two age groups and each variable was separately evaluated. This, revealed maternal age groups, neonatal weight, and history of underlying diseases had significant results ($p < 0.05$). Multivariate logistic regression was also applied to define the OR of C/S in the two age groups, with adjustments of confounders of neonatal weight and maternal factors (i.e., BMI, GA, number of abortions past medical history of underlying diseases, and type of labor induction). This analysis was significant for age groups, neonatal weight, types of labor induction, and positive past medical history. Also, the following results were achieved with otherwise equal variables. (A) C/S's OR was 1.998 times in the B group versus A group ($p = 0.002$) (b) OR of Cytotec administered group versus oxytocin group was 1.894 times ($p = 0.017$) (c) OR of subjects with positive past medical history was 1.652 times ($p = 0.025$) and (d) each

TABLE 1 Definition and comparison of demographic features of subjects in the two study groups.

Variables	Age group < 35 years old (n = 206)	Age group ≥ 35 years old (n = 187)	Statistic	p-Value
Age (years)				
Median interquartile range (1st–3rd)	24 (21–28)	37 (36–38)	-17.165	0.000
BMI (kg/cm ²)				
Median interquartile range (1st–3rd)	30.47 (28.65–32.87)	31.64 (30.84–31.64)	-2.559	0.011
History of abortion ≥ 1	29 (14.1%)	43 (23%)	5.208	0.026
Gestational diabetes	28 (13.6%)	30 (16.0%)	0.468	0.494
Pre-eclampsia	35 (17.0%)	37 (19.8%)	0.512	0.474
Comorbidity	101 (49.0%)	82 (44.1%)	0.96	0.327

Abbreviation: BMI, body mass index.

TABLE 2 Relationship between admission criteria, frequency of C/S, and indication of C/S in the two study groups.

Variables	Age group < 35 years old (n = 206)	Age group ≥ 35 years old (n = 187)	Statistic	p-Value
Gestational age (weeks)				
Median interquartile range (1st–3rd)	39 (38–40)	39 (38–40)	-0.815	0.415
Indication of labor induction				
Postterm	5 (2.4%)	13 (7.0%)	5.569	0.135
Diabetes	20 (9.7%)	15 (8%)		
Hypertension and pre-eclampsia	35 (17%)	37 (19.8%)		
Fetal growth restriction	26 (12.6)	20 (10.6)		
Abnormal biophysical profile	82 (39.8)	73 (39)		
Elective induction	38 (18.4)	29 (15.5)		
C/S	93 (45.1%)	111 (59.7%)		
Indications of C/S				
Abnormal fetal heart rate	33 (35.5%)	56 (50.9%)	8.716	0.033
Failure to progress	21 (22.6)	21 (19%)		
Meconium passage	39 (41.9%)	33 (30.0%)		
Duration of admission (day)				
Median interquartile range (1st–3rd)	3 (2–3.25)	3 (2–3)	-1.398	0.162

TABLE 3 Relationship between postpartum complication, neonate variables between two study groups (based on the maternal age).

Variables	Age group < 35 years old (n = 206)	Age group ≥ 35 years old (n = 187)	Statistic	p-Value
Gender (male)	86 (41.7%)	93 (50.3%)	2.852	0.091
1-min APGAR score	3 (1.5%)	7 (3.7%)	-	0.203
5-min APGAR score	0	1 (0.5%)	-	0.476
NICU admission	8 (3.9%)	8 (4.3%)	0.048	0.826
Neonatal weight	3220 (3100–3392.5)	3480 (3030–3480)	-1.318	0.188
Median interquartile range (1st–3rd)				

Abbreviation: NICU, neonatal intensive care unit.

kilogram increase in neonatal weight, raised the chances of C/S for 1.002 times more ($p = 0.001$; Table 4).

4 | DISCUSSION

Our study aims to evaluate the effects of maternal age on the mode of delivery among nulliparous women with term pregnancies who underwent labor induction shows the rates of OR attributed to cesarean deliveries increased. Many recent studies suggest that advanced maternal age is a potential risk factor for higher rates of

cesarean deliveries and elevated rates of obstetric adverse complications.^{5,6,10,11} Although, in the former studies, elective labor induction was not definitely recommended, probably due to possible disadvantages and its role in raising the rates of cesarean section, new approaches support this method of induction for labor among not only the pregnant women with underlying diseases (e.g., maternal hypertension, premature rupture of membranes: gestational diabetes and macrosomia) but also in the ones with older age at the time of delivery.^{20–24} In favor of such approach, many recent studies, question the former thoughts of the inefficiency of labor induction among older mothers at term pregnancies before the spontaneous

TABLE 4 Regression logistic to define the underlying factors, affecting C/S rates.

Variable	OR (95% CI) ^a	p-Value	Adjusted OR (95%CI) ^b	p-Value
Age range (reference: <35 years old)	1.798 (1.204–2.686)	0.004	1.998 (1.282–3.114)	0.002
Body mass index (BMI)	1/033 (0.994–1.073)	0.100	1.013 (0.973–1.055)	0.518
Neonatal weight	1.002 (1.001–1.003)	0.000	1.002 (1.001–1.003)	0.0001
No. of abortions	1.037 (0.621–1.730)	0.890	0.945 (0.533–1.673)	0.845
Gestational age	1.504 (0.892–1.245)	0.537	0.963 (0.798–1.163)	0.696
Past medical history	1.695 (1.135–2.531)	0.010	1.652 (1.066–2.558)	0.025
Type of labor induction: (reference: oxytocin)	1.455 (0.911–2.324)	0.116	1.894 (1.122–3.197)	0.017
Constant			0.002	0.112

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

^aUnivariate regression logistic.

^bMultivariate logistic regression adjusting for age, BMI, neonatal weight, no. of abortions, gestational age, past medical history, type of labor induction.

start of labor.^{9,25,26} The importance of such interventions lies in the fact that with age, the risk of stillbirth increases among pregnant women, therefore, inducing labor in such timelines, could decrease this devastating complication.

As Walker et al.^{17–19} reported, inducing labor in women at GA of 39 weeks or more was not related to higher rates of cesarean deliveries or other obstetric complications. Considering the fact that the least collective rate of risk of prenatal deaths is in this GA of around 39 weeks, labor induction could be beneficial for women aged 35 years old or more. It seems that, to better understand the differences between Walker et al.'s study and ours, factors like demographic features (incl. maternal BMI, height, and weight) or even race and maternal morbidities of the assigned subjects should come into account.

Kwayke-Ackah et al.¹² found no significant differences among women over 35 years old versus younger ages in terms of age-related factors on the rates of cesarean sections and type of labor after labor induction. However, unlike our study, they used various means of labor induction. Longer duration of the study course and different labor induction methods and the fact that they conducted the research only among women over 35 years old could be the underlying etiologies responsible for different outcomes.

We found that, with age, the risk of cesarean deliveries rises (1.9-fold in women less than 35 vs. 35 years old or more, ($p = 0.002$). In a recent retrospective registry-based national study in Nordic countries, Bergholt et al.'s¹¹ study, it is reported that the risk of C/S increases with age, regardless of labor mode (induced or spontaneous), among nulliparous and multiparous women. These findings could arise from the fact that, younger women are probably healthier and do not suffer from potential pregnancy-threatening diseases. It is also stated that institutional cultures and the expertise level of the obstetrician or the midwives could potentially affect the decision-making process of women, when the labor is being induced.¹²

We reported higher rates of cesarean deliveries in patients with misoprostol induction versus oxytocin (1.89-fold), indicating that

labor induction could be related to higher rates of cesarean section in women over 35 years old. To understand this, we think that other variables like initial Bishop scores and cervical ripening have significant effects on the final rates of cesarean section. This is also supported by Kwayke-Ackah et al.'s¹² study, mentioning that Bishop scores less than five are significantly related to higher rates of cesarean deliveries among women (either 35 years old, older or younger). However, we only used misoprostol and oxytocin to induce labor in women with Bishop scores less than five, unlike various methods of labor induction in Kwayke-Ackah et al.'s study.¹² Higher risks of cesarean sections with heavier fetuses in our study seem reasonable as increased fetal weights are definite risk factors of cesarean sections.

5 | CONCLUSION

In the present study, it is revealed that, women 35 years old or older, the ones with lower heights (shorter mothers), higher BMIs and the ones with prior history of abortions/miscarriages had higher risks of cesarean deliveries among the two age groups. The most common reasons to perform cesarean section were abnormal FHRs and arrest of labor, which are consistent with the findings of former studies and could suggest biological effects of aging on the final outcome of maternal health and course of labor.

We think that conducting such study in a tertiary university hospital along with applying similar treatment standards for all patients is the strength of our study.

Due to the increased chance of cesarean section in women over 35 years of age and having a history of underlying maternal disease, women over 35 years of age should be adequately educated and informed before pregnancy. Also, clarify the importance of perinatal care to reduce pregnancy complications for them. Second, obstetricians should pay special attention to prenatal and postnatal care to reduce complications and potential risks in the age group over 35 years.

5.1 | Limitations

We consider the small sample size of the study, as our major limitation factor, as we initially intended to perform such study in larger sample sizes and for older mothers. However, as some women met the exclusion criteria, the sample size of the study in our medical center was finally restricted to the aforementioned amount.

5.2 | Recommendations

Future multicentric national and worldwide studies with larger sample sizes are highly recommended. Adjustment of demographic or cultural features of the individuals participating in the studies could lead to a precise conclusion.

AUTHOR CONTRIBUTIONS

Conceptualization: Seyedeh Hajar Sharami, Roya Kabodmehri, Fatemeh Hosseinzadeh. **Formal analysis:** Maryam Ghalandari. **Writing – review and editing:** Seyedeh Hajar Sharami, Roya Kabodmehri, Fatemeh Hosseinzadeh, Sina Montazeri, Maryam Ghalandari, Seyedeh Fatemeh Dalil Heirati, Sarvenaz Ershadi. **Writing – original draft:** Sina Montazeri.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data that support the findings of this study are available from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

Seyedeh Hajar Sharami (lead author) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, and no important aspects of the study have been omitted.

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