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Original Research Article

Exploring the impact of early-term labor induction on cesarean section risk in gestational diabetes mellitus: insights from a tertiary care hospital study in Pakistan

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is the most common endocrine disorder in pregnancy. It is associated with significant perinatal morbidity and mortality, therefore, an early-term delivery by routine induction of labor is proposed by some societies, to prevent/reduce these complications.
Methods: This cross-sectional study was conducted between 1st January 2019 and 30th June 2020 at Aga Khan University Hospital, Pakistan to compare the pregnancy outcomes of patients with GDM when induced at 37, 38, and 39 weeks in comparison to women with GDM managed expectantly. The study included all women with singleton pregnancy and vertex presentation. Women induced after 41 weeks, previous cesarean delivery, placenta previa, major fetal anomalies, chronic maternal medical conditions that necessitate delivery, and those women presenting with spontaneous onset of labor were excluded. Data was analyzed in SPSS v.19.
Results: A total of 293 women were included. The mean age of women was 27 years, and the mean BMI was 27.8 kg/m^2. We found that women who were induced at earlier gestational weeks were managed with a combination of diet and pharmacological therapy in comparison to those induced at later gestational weeks and achieved glycemic control with diet and lifestyle modifications only. Around 77% of women required pharmacological therapy. The mode of delivery was not significantly different for women induced at different gestational weeks after 37 completed weeks. For neonatal outcomes, the birth weight was significantly greater for women induced at later gestational weeks.
Conclusions: In women with gestational diabetes induced after 37 weeks at various gestational weeks, the mode of delivery is not significantly different.

Keywords: Cesarean section, Gestational diabetes mellitus, Induction of labor, Labour, Outcome of pregnancy

INTRODUCTION

Gestational diabetes mellitus (GDM) is the most common endocrine disorder affecting pregnancy.[1] It has a profound impact on maternal, fetal, and neonatal outcomes, including macrosomia, shoulder dystocia, and cesarean section. The prevalence of this disease has drastically increased over the years, with global findings indicating that 16% of pregnancies are complicated by gestational diabetes.[2] At our institution, the audit has revealed a steady rise in GDM prevalence from 6.3% in 2005 to 19.3% in 2018.[3]

Data has shown that southeast Asians are at a particularly high risk of developing diabetes mellitus due to genetic predisposition and rapidly changing lifestyles consistent with industrialized dietary patterns.[4] These rising trends in GDM prevalence is also confirmed by a similarly high prevalence of type II diabetes mellitus among young populations.[1,4]

The management of GDM requires a comprehensive approach including lifestyle modification, nutritional intervention, and medical therapy.[5] The aim is to achieve optimal maternal and perinatal outcomes.[6-8] The ideal timing for delivery in women with GDM is intricate and influenced by a combination of maternal and fetal factors including maternal blood sugar control, comorbidities, and fetal growth parameters.[9-11] For women that do not go into spontaneous labor, the recommendations regarding the exact time of delivery are confusing.[6-12] Some recommend an early-term delivery by routine induction of labor to prevent/reduce the risk of the above-mentioned complications, especially in women on pharmacological treatment for blood sugar control or where strict euglycemia cannot be achieved.[12] On the flip side, induction of labor would increase the risk of cesarean delivery and neonatal morbidity due to respiratory distress.[13,14]

Despite a high prevalence of GDM, no local data exists till now to guide on the ideal time of delivery in our pregnant population. Although the Society of Obstetrics and Gynecology (SOGP) has recently released national guidelines for managing GDM, including recommendations for timing of delivery, there is a lack of comprehensive information regarding outcomes when comparing labor induction to expectant management after 37 completed weeks of gestation.[15] Therefore, our study aimed to assess the timing of delivery and compare perinatal outcomes in women with gestational diabetes mellitus. We examined those women with GDM, who underwent induction at 37, 38, or 39 weeks in comparison to those who received expectant management until 40 weeks and 6 days.

METHODS

This cross-sectional study was conducted between 1st January 2019 till 30th June 2020 at Aga Khan University Hospital, Pakistan. The study included all women with GDM, in whom labor was induced after 37 completed weeks, with singleton pregnancy and vertex presentation. GDM was diagnosed as per the institutional screening guidelines, i.e. early pregnancy booking 75-gram oral glucose tolerance test (OGTT) or fasting blood glucose when OGTT could not be tolerated due to nausea and vomiting of early pregnancy. If the early screening showed normal results, a repeat OGTT is performed at 28 weeks of pregnancy. We also included women when their ultrasound revealed polyhydramnios or fetal macrosomia (fetal abdominal circumference or expected fetal weight >95th centile) combined with deranged blood sugar levels. Prior approval was obtained from the hospital's ethical review committee (REF: 2021-6019-17971). The outcomes were compared between women delivered at different gestational weeks after 37 completed weeks. Exclusion criteria included women induced after 41 weeks, previous cesarean delivery, placenta previa, major fetal anomalies, chronic maternal medical conditions that necessitate delivery, and those women presenting with spontaneous onset of labor (as it naturally increases chances of normal delivery).

We compared women who underwent induction of labor (IOL) from 37+0 to 37+6 weeks (group 1A) with women who were expectantly managed from 38-40+6 weeks (group 1B). Women induced at 38-38+6 weeks (group 2A) were compared with those managed expectantly from 39-40+6 weeks (group 2B). Women induced at 39-39+6 weeks (group 3A) were compared to women who were expectantly managed between 40+0 to 40+6 (group 3B). Institutional guidelines were followed to decide on the timing of induction, with women who had their GDM well controlled with either metformin or insulin or combination to be induced after 38 completed weeks taking into account the bishop score, while women on diet control were allowed to be induced at or after 40 weeks but not later than 41 weeks. However, in cases where euglycemia was not achieved, or where other complications were developed e.g., fetal growth restriction (FGR) or late-onset preeclampsia (complications that have an association with GDM) were the indications for early-term induction at 37 weeks onwards whenever diagnosed.

Demographic details of the mother were collected from the hospital medical records and labor room management system database. Details of the newborn were obtained from the hospital medical records of the neonates. The following outcomes were examined and considered: mean gestational week at diagnosis of GDM, mean gestational week at delivery, blood sugar control during the weeks preceding delivery, development of other GDM-associated complications e.g., FGR and preeclampsia, mode of delivery, newborn birth weight, Apgar score, neonatal intensive care unit (NICU) admission, neonatal hypoglycemia, and neonatal death (NND).

All statistical analyses were performed using SPSS 19.0 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA). Frequency and percentages were computed for categorical variables and analyzed by chi-square test or fisher exact test. Histograms, Q-Q plots, and Kolmogorov-Smirnov test used to observe normality of continuous data. Mean and standard deviation were estimated for normally distributed observation and analysis by independent sample t test and median and IQR were reported for non-normal distributed observation and analyzed by Mann Whitney U test. Multivariable logistic regression analysis was performed at different gestational week at term to compute adjusted odds ratio for mode of delivery and composite neonatal morbidity after controlling the effect of potential confounders such as maternal age, therapy, and BMI. A p value less than and equal to 0.05 was significant.

RESULTS

During the study period from January 2019 to June 2020, 8924 women gave birth in Aga Khan University Hospital,

Karachi. There were 324 patients who underwent labor induction due to gestational diabetes between 37+0 to 40+6 weeks. Out of those, 293 were found to be eligible for the study. There were 78 women who underwent induction of labor at 37+0 to 37+6 weeks of gestation for GDM-related reasons (group 1A) were compared with 215 women who remained undelivered until at least 40+6 weeks (group 1B). Similarly, 151 women who underwent IOL at 38+0 to 38+6 weeks of gestation for GDM-related reasons (group 2A) were compared with 64 women who remained undelivered until 40+6 weeks of gestation (group 2B). The third group represented 43 women who were induced at 39+0-39+6 weeks (group 3A) and were compared to 21 undelivered women till 40+6 (group 3B).

Table 1: Demographic characteristics of the patients (n=293).

Variables	Statistics
Age (years)	29.49±4.77
BMI (kg/m^2)	27.97±5.11
Gestational age at diagnosis of GDM	27.42±5.71
Gestational age at induction	38.02±0.84
Parity	
Nulliparous	167 (57%)
Multiparous	126 (43%)

The baseline demographics of the study population and parameters related to GDM are shown in Tables 1 and 2 respectively. The mean age among all women was 29 years (SD ±4.7 years), almost the same across all groups as seen in Table 2. The mean gestational age for induction of labor due to gestational diabetes was recorded as 38 weeks (±0.84) and the body mass index (BMI) was found to be higher with a mean of 27.9 (±5.1).

Table 2: GDM relevant parameters (n=293).

Variables	Count (%)
GDM diagnosed	
Fasting sugar	10 (3.4)
OGTT	209 (71)
Sugar series	74 (25)
Treatment	
Diet	72 (24.6)
Oral hypoglycemic drug	179 (61.1)
Insulin	29 (9.9)
Oral hypoglycemic drug + insulin	13 (4.4)
Blood sugar of last 1 week	
Uncontrolled	43 (14.7)
Well controlled	250 (85.3)
EFW (>4 kg or fetal AC above 95th centile or presence of poly hydramnios)	27 (9.2)
Evidence of intrauterine growth restriction or abnormal doppler	
SGA	7 (2.4)
IUGR	6 (2)

Table 3: Characteristics of women in the induction and expectant management groups.

Variables	Weeks of gestation								
	37 weeks			38 weeks			39 weeks		
	Induction group 1A n=78 (%)	Expectant group 1B n=215 (%)	P value	Induction group 2A n=151 (%)	Expectant group 2B n=64 (%)	P value	Induction group 3A n=43 (%)	Expectant group 3B n=21 (%)	P value
Age (years)	30.12±5.31	29.26±4.54	0.176	29.22±4.62	29.36±4.38	0.377	29.49±4.44	29.10±4.36	0.739
BMI (kg/m^2)	28.74±5.44	27.68±4.96	0.195	28.11±5.23	26.69±4.19	0.520	27.38±4.43	25.22±3.30	0.113
Parity	-	-		-	-		-	-	
Nulliparous	40 (51.3)	127 (59.1)	0.234	91 (60.3)	36 (56.3)	0.584	23 (53.5)	13 (61.9)	0.524
Multiparous	38 (48.7)	88 (40.9)		60 (39.7)	28 (43.8)		20 (46.5)	8 (38.1)	
Treatment	-	-		-	-		-	-	
Insulin	12 (15.4)	17 (7.9)		12 (7.9)	5 (7.8)		4 (9.3)	1 (4.8)	
Metformin	44 (56.4)	135 (62.8)	0.076	99 (65.6)	36 (56.3)	0.072	29 (67.4)*	7 (33.3)	0.010*
Insulin + metformin	6 (7.7)	7 (3.3)		7 (4.6)	0		0	0	
Diet	16 (20.5)	56 (26)		33 (21.9)	23 (35.9)		10 (23.3)	13 (61.9)	
Mode of delivery	-	-		-	-		-	-	
SVD	53 (67.9)	147 (68.4)	0.945	103 (68.2)	44 (68.8)	0.938	29 (67.4)	15 (71.4)	0.747
C/S	25 (32.1)	68 (31.6)		48 (31.8)	20 (31.3)		14 (32.6)	6 (28.6)	
Evidence of IUGR or abnormal Doppler						-	-		
SGA	0.1411 (1.3)	6 (2.8)	0.67	6 (4)	0	0.182	0	0	NA
IUGR	1 (1.3)	5 (2.3)	0.99	5 (3.3)	0	0.141	0	0	
Bishop score at time of induction	4.09±1.83	4.19±1.74	0.67	4.31±1.69	3.91±1.81	0.123	4.02±1.84	3.67±1.77	0.465

Table 4: Neonatal outcome in the induction and expectant management groups.

Variables	Weeks of gestation								
	37 weeks			38 weeks			39 weeks		
	Induction group 1A n=78	Expectant group 1B n=215	P value	Induction group 2A n=151	Expectant group 2B n=64	P value	Induction group 3A n=43	Expectant group 3B n=21	P value
Birth weight (kg)	2.88±0.33	3.05±0.36	0.001	3.00±0.36	3.15±0.36	0.008	3.08±0.36	3.28±0.32	0.031
Apgar score at 5 minutes	8.91±0.29	8.94±0.24	0.381	8.93±0.26	8.97±0.17	0.24	8.98±0.15	8.95±0.22	0.606
NICU admission	1 (1.3%)	0	0.266	0	0	NA	0	0	NA
Cord PH	1 (1.3%)	6 (2.8%)	0.45	5 (3.3%)	1 (1.6%)	0.672	1 (2.3%)	0	0.999
Blood sugar level (mg/dl)	63 (55.75-78)	64 (55-81)	0.718*	64 (55-84)	64 (56-80)	0.871*	63 (58-80)	65 (55-77)	0.830*

Data are presented as mean±SD, n (%) and median (25-75th percentile)

Table 5: Multivariable analysis showing the association of IOL with adverse maternal and neonatal outcome.

Outcome Induction versus expectant management	Nulliparous		Multiparous	
	AOR (95%CI)	P value	AOR (95%CI)	P value
At 37-week gestation				
Cesarean delivery	1.05 (0.50-2.19)	0.89	1.00 (0.25-3.92)	-
Vaginal delivery	Ref		Ref	
Composite neonatal morbidity*	1.70 (0.57-5.06)	0.34	1.53 (0.49-4.73)	0.45
At 38 weeks gestation				
Cesarean delivery	0.62 (0.28-1.37)	0.24	3.68(0.38-34.90)	0.25
Vaginal delivery	Ref		Ref	
Composite neonatal morbidity	5.07(0.62-41.38)	0.13	2.18 (0.38-12.55)	0.38
At 39 weeks gestation				
Cesarean delivery	1.74 (0.42-7.26)	0.45	NA	NA
Vaginal delivery	Ref			
Composite neonatal morbidity	NA	NA	NA	NA

Ref: Values reflect the results of multivariable logistic regression analysis, with adjustment for the following potential confounders: maternal age, insulin and metformin therapy, BMI. *Composite neonatal morbidity: NICU Admission, birth weight <2.5kg, cord PH. AOR= Adjusted odds ratio; NA= Not applicable.

In our study, 57% of women included were nulliparous. Table 3 shows the comparison of different outcomes in women induced at 37, 38, and 39 weeks with their respective expectant groups (groups 1B, 2B, 3B). It was observed that the group 1A had a higher rate of patients who required insulin therapy when compared with the expectant group (1B) and successive induction groups i.e., groups 2A and 3A (15.4% versus 9.3%). In contrast, most of the patients were managed with dietary modification in the group 3B (62%). For the mode of delivery, there was no significant difference observed in the induction at gestational weeks of 37, 38, and 39 weeks (group 1A, group 2A and group 3A) when compared to their expectant groups (group 1B, group 2B and group 3B respectively). The cesarean section rate was 32.1% for group 1A in comparison to 31.6% for group 1B. (p value =0.945) for group 2A the rate was 31.8% in comparison to 31.3 % for group 2B (p value =0.938). Similarly, the cesarean delivery rate for group 3A was 32.6%, in comparison to 28.6% for group 3B. (p value =0.747).

A small number of women in the 37- and 38-weeks groups 1(A+B) and 2(A+B) also had evidence of fetal growth restriction which was the concomitant indication for induction of labor along with GDM. The bishop score was low across all groups regardless of gestational weeks.

Table 4 shows neonatal outcomes. The birth weight was significantly low for newborns delivered at earlier gestational weeks. There was only one infant in group 1A who was shifted to NICU post-delivery due to neonatal hypoglycemia.

Table 5 shows the results of multivariable logistic regression analysis to adjust for potential confounders such as maternal age, insulin and metformin therapy, and BMI while studying the different characteristics of the induction and expectant groups (group A and B respectively). This confirmed that induction of labor at any given gestational age after term did not result in any difference in the mode of delivery and remained the same in 37, 38, and 39 weeks of gestation in comparison to expectant groups.

DISCUSSION

The main outcome of our study was the mode of delivery. Our results showed no statistically significant difference in the rate of cesarean delivery across all the groups of women with gestational diabetes induced at different weeks when compared with their respective expectant groups (p value 0.945, 0.938 and 0.747 for group 1, 2 and 3 respectively). A similar conclusion was made by S Alberico, in a randomized controlled trial showing no difference in the mode of delivery in women with GDM induced versus those in the expectant group.[16] In the landmark HAPO study 16% of participants underwent emergency cesarean section.[17,18] Similarly high rate of emergency cesarean section has been reported by different investigators in other studies in women with GDM.[19,20] Even when GDM was controlled with pharmacotherapy, the rate of cesarean section remained as high as 33% in a study conducted in three different hospitals in Canada.[21] Our results are in agreement with the findings of a high cesarean delivery rate as reported by other researchers.

Apart from gestational diabetes, obesity was common in our study participants regardless of being in the induction group or expectant group with a mean BMI of 27.9 kg/m^2. This reflects high prevalence of obesity in Pakistan.[22] Even lower cutoffs of the BMI have been suggested for the Asian population due to the ethnic differences and their relationship with health outcomes. Strong epidemiological association has been established between obesity and gestational diabetes mellitus especially pre-pregnancy obesity increases the risk of GDM significantly which is in conformity with our study findings.[23]

In our data set it was observed that most women (75.4%) were managed with pharmacotherapy combined with medical nutritional therapy to control blood sugars. Excellent control was achieved in 85.3% of women as evident by the documentation in the medical record files. We observed that women who were induced at early term were more likely to receive insulin in comparison to those who were induced at late term. Most of the international and national guidelines have allowed women on diet control to continue pregnancy till 40-40+6 weeks.[6,7] According to literature, the rate of cesarean section is not higher when use of metformin is compared with that of insulin.[24] However, in a study by Incencio it was concluded that initiation of insulin therapy early in pregnancy was associated with an increased risk of cesarean section.[25,26] In another study, it was demonstrated that starting therapy can prevent macrosomia.[27] However, even though it offers protection against macrosomia, it does not reduce the risk of cesarean delivery.[28] Probably good glycemic control played a role in the prevention of macrosomia as no case was found. Similarly, no significant perinatal morbidity and mortality was observed, except for only one newborn shifted to the neonatal intensive care unit for the management of hypoglycemia which was statistically insignificant (p value =0.266).

Nulliparity is a significant risk factor for cesarean section and 57% of our women were nulliparous. In a recent study, a risk scoring system was developed, which confirmed a direct relationship between nulliparity, use of insulin therapy and gestational weight gain with cesarean section.[29] In addition to nulliparity, an unfavorable bishop score is also a major determinant of the mode of delivery. A higher bishop score indicates a more favorable cervix, which is more likely to dilate and efface during labor. In our study, all of the women who were induced had an unfavorable bishop score. A meta-analysis of studies has shown that bishop score is a significant determinant of successful vaginal delivery. Nulliparity combined with unfavorable cervical findings, is a further contributing factor for abdominal delivery.[30] This shows that unfavorable bishop score and parity are the primary determinant of the mode

Our study possessed several notable strengths that contributed to its robustness. One of the most prominent strengths was meticulous data maintenance. We ensured comprehensive and precise record-keeping of all relevant information pertaining to pregnancy and its outcomes in the patients who were induced for gestational diabetes mellitus. This rigorous approach to data collection allowed us to maintain a high level of accuracy and reliability throughout the study, providing a strong foundation for our findings.

Nevertheless, it's essential to acknowledge the limitations that were present in our study. Perhaps the most significant limitation was the relatively small sample size. While comprehensive data collection was ensured, the size of our patient cohort was small. This limitation could potentially affect the generalizability of our results to a broader population. Additionally, our study primarily focused on an urban population, which might not fully represent the diversity of experiences and outcomes that could be observed in more rural or diverse settings. Therefore, the results of our study should be interpreted with caution when considering their applicability to different populations.

CONCLUSION

Our study shows that induction of labor in women with gestational diabetes after 37 completed weeks till 40+6 weeks does not increase the risk of cesarean delivery. Parity and Bishop score prior to induction are major contributing factors to influence the mode of delivery. Based on our study, it can be deduced that in the presence of other concomitant indications like fetal growth restriction or preeclampsia-induction at early term after 37 completed weeks can be offered without having any effect on mode of delivery.

Recommendations

Similar large scale multicenter study should be conducted in both rural and urban populations of low middle income countries to understand the differences in the prevalence of GDM, and its effect on maternal and perinatal outcomes and impact on mode of delivery.

It is imperative to extend our focus on this matter by planning and executing extensive multi-center studies on a larger scale, encompassing both rural and urban regions in low and middle-income countries. Such research endeavors are essential for comprehending the variations in the prevalence of gestational diabetes mellitus (GDM) and its implications on maternal and perinatal outcomes, in addition to the influence it exerts on the mode of delivery. These comprehensive studies will contribute significantly to the development of more effective antenatal care strategies, ultimately improving the overall well-being of expectant mothers and their newborns in these diverse settings.

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