Obstetric and neonatal complications in large for gestational age pregnancy with late gestational diabetes

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Abstract

Objective: Gestational diabetes (GDM) is increasing in prevalence with effects starting in-utero, leading to excessive fetal growth. It is the leading cause of many perinatal complications. The aim was to determine the rate of obstetric and neonatal complications in pregnant women with high fetal weight and a recent diagnosis of GDM during the third trimester, despite normal earlier glycemic control.

Material and Methods: Prospective cohort study over four years involving pregnant women regularly visiting a single center who had normal glycemic index at 24-28 gestational weeks and ultrasonography (US) suggested high fetal weight during the third trimester. Oral glucose tolerance test was given, dividing the sample into the late GDM (LGDM) and the non-LGDM group.

Results: Of 176 women, 24 (13.64%) had LGDM, and 152 (86.36%) had non-LGDM. After exclusions these groups' sizes were (n=21) in LGDM and (n=132) in non-LGDM. Hemoglobin A1c level was significantly higher in LGDM than non-LGDM (5.9% versus 5.1%). However, obstetric and neonatal complications were largely comparable ($p \geq 0.05$) but higher in LGDM than non-LGDM women. Exceptions to this were birth weight (3219 g versus 3326 g), large for gestational age at delivery (85.72% versus 88.64%), and gestational age at delivery (37.9 versus 38.2 weeks) in the LGDM vs. non-LGDM groups, respectively. There was a significantly higher cesarean section (CS) rate (76.19% versus 51.52%; $p<0.05$) in the LGDM group.

Conclusion: The rate of newly diagnosed LGDM in pregnant women with high fetal weight during the third trimester by US was 13.64%. They had comparable obstetric and neonatal complications with non-GDM women, except for the rate of CS that was significantly higher in LGDM women. (J Turk Ger Gynecol Assoc 2023; 24: 12-7)

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Introduction

Gestational diabetes mellitus (GDM) is a state of glucose intolerance during pregnancy and affects 3.2% of pregnancies in Iraq and 3-10% globally, varying by sample populations and diagnostic criteria (1,2). GDM exaggerates fetal growth and directly influences adverse obstetric and neonatal events (1,3). The diagnosis of GDM is usually confirmed by an oral glucose tolerance test (OGTT), which is undertaken between 24-28 gestational weeks, while fetal growth has the fastest increase between 20-28 gestational weeks, that is prior to or concurrent with the OGTT. Correct diagnosis and effective management of GDM as early as possible may improve fetal weight, obstetric complications, which include, high cesarean section (CS) rate,

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postpartum hemorrhage, preterm delivery (PD), pregnancy-induced hypertension, and polyhydramnios, and neonatal adverse events, such as shoulder dystocia, hypoglycemia, and high admission rate to neonatal intensive care (4,5).

A high glycemic index in pregnant women is a major cause of excessive fetal growth, constituting up to 45% of elevated fetal weight cases. However, many pregnancies are complicated with high fetal weight after 28 weeks' gestation with normal earlier glucose measurements. There is limited published evidence concerning diagnosis and management in this situation (2,6,7).

The aim of this study was to investigate obstetric and neonatal complications in pregnant women during the third trimester, who had high fetal weight suggested by ultrasonography (US) after 28 weeks of gestation and were recently diagnosed with GDM, despite an earlier normal glycemic index.

Material and Methods

The study was carried out over a four-year period, from May 4, 2017 until May 3, 2021. The study design was a prospective cohort study and involved pregnant women visiting the Obstetrics and Gynecology Department of Medical City Hospital in Baghdad, Iraq. This is the main tertiary referral hospital in the country. This work was approved by the ethical and scientific committees of the College of Medicine and Al-Kindy College of Medicine/University of Baghdad (approval number: 547, date: 29.03.2017). Informed consent was taken from all involved women.

Inclusion criteria

Singleton pregnant women who had regular antenatal care (ANC) visits starting from the first trimester until delivery, with no diagnosis of GDM during the second trimester, either by screening OGTT or blood sugar measurements (fasting and postprandial) at 24-28 weeks' gestational age and who had the suspicion of large for gestational age (LGA) fetus by US examination at 32 weeks' gestational age during the third trimester.

Exclusion criteria

Multiple pregnancy, congenital anomalies diagnosed by US, irregular ANC, pre-pregnancy diabetes mellitus, diagnosis of GDM during the second trimester, and women who missed glucose measurements during the period 24-28 gestational weeks. Women who lost contact with the researchers during the study period or delivered outside the hospital were also excluded.

Carpenter-Coustan criteria were applied to diagnose GDM using OGTT (100 gram) with the following blood sugar reference readings: 95, 180, 155, and 140 mg/dL of fasting, one hour, two hours, and three hours postprandial, respectively. If the pregnant women had (or exceeded) at least two of these thresholds, the diagnosis of GDM was confirmed (8). In addition, hemoglobin A1c (HbA1c) was also measured in the involved women at this stage.

The weight of the fetus was estimated by US using the Hadlock formula, and LGA pregnancy was assumed when the estimated weight of the fetus exceeded 90th percentile of weight for gestational age (9).

When the included pregnant women had the suspicion of LGA during the third trimester, OGTT was done within 2-3 days. Subsequently, two study groups were created; the late GDM (LGDM) group, and non-LGDM group. In LGDM women, lifestyle management was advised with frequent blood glucose monitoring and management was undertaken by an expert obstetrician.

The following obstetric complications were investigated: PD, polyhydramnios, pregnancy induced hypertension, shoulder dystocia, and operative delivery by CS, while the observed neonatal complications were hypoglycemia and admission to the neonatal intensive care unit (NICU). These complications were documented for all included women and compared between the GDM and non-GDM groups. Labor was managed for all involved women by the attending obstetrician and neonatologist, and all perinatal events and delivery details were documented.

Statistical analysis

Mann-Whitney U test was used for continuous parameters, while Pearson's χ^2 test or Fisher's exact test was performed for proportions. Statistical Package for the Social Sciences statistics software, version 23.0 (IBM Corp., Armonk, NY, USA) was used to complete the calculations. A p-value <0.05 was considered significant.

Results

The total number of involved pregnant women was 176 were tested using OGTT after an excessive fetal weight had been suggested on US during the third trimester. Of them, 24 women (13.64%) had abnormal OGTT, indicating a diagnosis of LGDM (LGDM group), while the remainder, 152 women (86.36%), had normal OGTT (non-LGDM group). For LGDM and non-LGDM groups, 3 and 20 women, respectively, were excluded from the study because of missed data or delivery outside the research center. Thus, final total in the LGDM group was 21, while it was 132 for the non-LGDM group. In the LGDM group, three women were managed by diet while the remaining 18 were on medical treatment.

General characteristics of both groups were comparable without statistical significance ($p \geq 0.05$), with the exception of

HbA1c, which was significantly higher in the LGDM than in non-LGDM women (5.9% versus 5.1%) (Table 1).

Table 2 shows all neonatal and obstetric complications, compared between the two groups. Most variables were statistically comparable, although there was a tendency for babies in the LGDM group to be lighter weight at birth, to have an earlier gestational age at birth and to be less likely to be LGA.

Table 3 compares the characteristics of the women in the two groups at the time of OGTT. Gestational age (34.7 versus 35.2) and estimated fetal weight (2674 versus 2719) were comparable ($p \geq 0.05$) between both groups, while OGTT, as expected, was significantly different ($p < 0.05$).

Details of delivery mode are shown in Table 4. LGDM women had significantly ($p < 0.05$) higher rates of CS and lower rates of normal delivery than non-LGDM women (76.19% versus 51.52%, and 23.8% versus 48.48%, respectively). The rates of induction of labor and premature rupture of membranes did not differ between the groups. Frequencies of different indications of CS, including

Table 1. General features of involved women

Variable	LGDM (n=21)	Non-LGDM (n=132)	p
Age (years), median (range)	23.4 (18-43)	22.7 (19-46)	0.62
Nulliparous, n (%)	13 (61.90%)	79 (59.85%)	0.81
Family history of diabetes mellitus, n (%)	4 (19.05%)	22 (16.67%)	0.53
Pre-pregnancy body mass index (kg/m^2), median (range)	26.1 (17.4-38.3)	25.8 (17.2-39.8)	0.14
Hemoglobin A1c, median (range)	5.9 (4.8-7.3)	5.1 (4.4-6.2)	<0.05
LGDM: Late gestational diabetes mellitus			

Table 2. Obstetric and neonatal outcomes of involved groups

Variable	LGDM (n=21)	Non-LGDM (n=132)	p
Birth weight (g), median (range)	3219 (2472-4596)	3326 (2411-4480)	0.38
Polyhydramnios, n (%)*	1 (4.76%)	5 (3.79%)	0.79
Pregnancy induced hypertension, n (%)*	1 (4.76%)	3 (2.27%)	0.09
Large for gestational age at delivery, n (%)**	18 (85.72%)	117 (88.64%)	0.46
Gestational age at delivery (weeks), median (range)	37.9 (34.3-41.1)	38.2 (34.5-40.8)	0.18
Shoulder dystocia, n (%)*	1 (4.76%)	5 (3.79%)	0.42
Preterm delivery, n (%)*	2 (9.52%)	9 (6.82%)	0.39
Fetal sex (male), n (%)*	12 (57.14%)	65 (49.24%)	0.61
Neonatal hypoglycemia, n (%)*	1 (4.76%)	4 (3.03%)	0.34
Neonatal intensive care unit admission, n (%)*	2 (9.52%)	10 (7.58%)	0.22
*Data are presented as n (%) and were compared with Fisher's exact test, **Data were compared with Pearson's χ^2 test, LGDM: Late gestational diabetes mellitus			

Table 3. Data of involved women at time of oral glucose tolerance test during the third trimester

Variable	LGDM (n=21)	Non-LGDM (n=132)	p
Gestational age at presentation (weeks), median (range)	34.7 (29.5-39.2)	35.2 (30.3-40.6)	0.28
Estimated fetal weight at presentation (g), median (range)	2674 (1253-3587)	2719 (1304-3926)	0.31
Oral glucose tolerance test measurements (mg/dL), median (range)			
- Fasting	88 (64-128)	80 (61-105)	<0.05
- After 1-hour	191 (156-280)	149 (73-212)	<0.05
- After 2-hours	169 (101-274)	124 (82-165)	<0.05
- After 3-hours	136 (58-221)	104 (53-158)	<0.05
High oral glucose tolerance test, n (%)*			
- Fasting	4 (19.05%)	4 (3.03%)	<0.05
- After 1-hour	15 (71.43%)	6 (4.55%)	<0.05
- After 2-hours	17 (80.95%)	7 (5.30%)	<0.05
- After 3-hours	13 (61.90%)	8 (6.06%)	<0.05
*Data are presented as n (%) and compared with Fisher's exact test, LGDM: Late gestational diabetes mellitus			

Table 4. Details of delivery characteristics

Variable	LGDM (n=21)	Non-LGDM (n=132)	p
Delivery type, n (%)*			
- Normal vaginal delivery	5 (23.8%)	64 (48.48%)	<0.05
- Cesarean section	16 (76.19%)	68 (51.52%)	-
Labor induction, n (%)*	13 (61.90%)	69 (52.27%)	0.69
Premature rupture of membranes, n (%)*	3 (14.29%)	22 (16.67%)	0.75
Cesarean section indication, n (%)*			
- Previous cesarean section	10 (47.62%)	58 (43.94%)	0.56
- Placental abnormalities	1 (4.76%)	6 (4.55%)	0.91
- Fetal deceleration	2 (9.52%)	11 (8.33%)	0.64
- Failure to progress	4 (19.05%)	23 (17.42%)	0.72
- Malpresentation	1 (4.76%)	3 (2.27%)	0.09
*Data were compared with Fisher's exact test, LGDM: Late gestational diabetes mellitus			

previous CS, placental abnormalities, fetal deceleration, failure to progress, and malpresentation, were higher in the LGDM than non-LGDM group but failed to reach significance.

Discussion

Many previous studies have discussed obstetric and neonatal complications in GDM pregnancy, but few have addressed the issue of LGDM in the third trimester (1,6,10). In this study, we tried to select pregnant women with suggested high fetal weight during the third trimester who surprisingly appeared to have GDM despite their prior normal glucose readings during the second trimester.

The prevalence rate of LGDM women during the third trimester in our sample was 13.64%, which was comparable with one previous study (13.5%) (11) but twice that of another earlier study (6.7%) (12). The reason behind that might be due to the feature of excessive fetal weight in our sample of pregnant women who are likely to have high blood sugar as insulin resistance is a progressive phenomenon during pregnancy, and GDM is the primary etiology of increased fetal growth (13).

HbA1c was significantly elevated in LGDM women, indicating higher glucose readings for the previous 2-3 months. However, this interpretation may be unreliable during pregnancy due to physiological changes, including rapid erythrocyte turnover (14).

In our study, although LGDM women had higher suggested fetal weight during the third trimester, neonatal birth weight and LGA at delivery were lower than non-LGDM women. This may be explained by effective GDM management, which influenced perinatal outcomes (15). Other reported perinatal outcomes including polyhydramnios, pregnancy-induced hypertension, shoulder dystocia, PD, neonatal hypoglycemia, and admission to NICU, were slightly higher in the LGDM group, in agreement with local and international figures (13,16,17).

The LGDM women in this cohort had significantly higher OGTT measurements, including fasting and 1-, 2-, and 3-hour postprandial readings, confirming the diagnosis of GDM in these women (18).

Rates of CS were significantly higher in LGDM women, which might be due to increased but not significantly increased rates of CS indications, including previous CS, placental abnormalities, fetal deceleration, failure to progress, and malpresentation.

Higher chances of operative delivery in GDM patients were reported in several previous studies, while our non-GDM women had a rate of CS delivery similar to the local rate (17,19-21).

The significantly high rate of CS in LGDM women in our sample was higher than the local rates of CS in adult and adolescent pregnant women (22,23).

This study has the advantage of a prospective assessment of newly diagnosed GDM women during late pregnancy in the third trimester, with suspected excessive fetal growth and normal earlier glucose measurements. LGDM could be missed because of comparable obstetric and neonatal complication rates (11), unless identified using the approach described herein. Although obstetric and neonatal complications were slightly but insignificantly increased in LGDM compared to non-LGDM women, the benefit of identifying women with GDM may extend beyond the current pregnancy. This is because GDM in a previous pregnancy is considered a risk factor for early GDM in subsequent pregnancies with more severe perinatal complications that may be similar to pre-pregnancy diabetes. Moreover, GDM diagnosis may suggest increased monitoring for diabetes and it may predict overt diabetes within some subsequent timeframe (24).

Study Limitations

This study has some limitations. OGTT was not routinely applied to all pregnant women during mid-pregnancy because

of limited resources in our setting, and was replaced by blood glucose profile (fasting and postprandial) in some pregnant women, which is less sensitive for diagnosing GDM (25). In addition, the small sample size could be considered a limitation and may make the findings less reliable despite the long study period. In addition, the single-center design of the study may affect the generalizability of the results. However, this rare presentation of pregnant women with LGDM needs to be given more consideration, to prevent possible complications in the existing pregnancy and possible complications in future pregnancies.

Conclusion

The rate of newly diagnosed GDM during the third trimester in pregnant women high fetal weight suggested by US was 13.64%. LGDM and non-LGDM pregnant women had comparable non-significant obstetric and neonatal complication rates. Operative delivery by CS was significantly more likely in LGDM women, possibly due to increased concerns about CS indications, despite the rates of these being similar between the two groups.

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