

Vicissitudes in the Placental Cotyledon Number in a Singleton Pregnancy with Gestational Diabetes

Abstract

Background: Placenta is a transient organ during pregnancy, connects the fetus to the uterine wall. Pregnancy is frequently complicated by gestational diabetes, which might cause morphological changes in the placenta (weight, diameter, and cotyledons number); consequently, it may affect both fetus and mother. **Aim:** The aim of this study was to determine the difference in placental cotyledons number between pregnant with gestational diabetes versus without gestational diabetes, then correlate it with the weight and diameter between groups. **Materials and Methods:** A comparative study (gestational diabetes Group A and nongestational diabetes Group B) included mothers with a singleton baby delivered at term (37–40 weeks) after acceptance of the informed consent. Women with pregestational diabetes and other chronic diseases and those with intrauterine fetal death were excluded. Postdelivery placentae were accurately prepared and examined in detail. The placental weight, diameter, and cotyledons number were recorded and analyzed by SPSS version 21. The correlation was measured between the two groups in terms of cotyledons count, placental diameter, and weight. **Results:** The study included 385 participants (128 Group A and 257 Group B). Placental number of cotyledons, weight, and diameter in Group A were higher than in Group B, and the difference was significant ($P = 0.000$, $P = 0.021$, and $P = 0.000$, respectively). In Group A, there was a significant correlation between the placental weight, diameter, and number of its cotyledons ($r = 0.23$, $P = 0.011$). Cotyledon count was significantly affected by diabetic control ($P = 0.021$). **Conclusions:** Gestational diabetes increases placental cotyledons number, weight, and diameter.

Keywords: Cotyledons, diameter, gestational diabetes, placenta, weight

Introduction

Gestational diabetes mellitus (GDM) is a common glucose metabolic disorder, resulting from alterations in glucose homeostasis that occurs during the second and third trimesters of pregnancy, and is clearly not preexisting or overt diabetes.^[1-5] It is one of the common complications encountered during pregnancy.^[3,6] The precise prevalence of GDM remains vague;^[2] on the other hand, the prevalence of GDM showed a dramatic annual increase that is affected by the diagnostic tests applied and the population included in the research.^[2,4,6,7]

The exact causative mechanism of gestational diabetes is still unclear,^[6] observed extra demand on the pancreas in pregnancy causes some of pregnant ladies to develop gestational diabetes.^[8] The manner of development of a disease is an intricate matter that is triggered

by many factors such as insulin intolerance, impairment of islet β -cells function, and inflammatory factors.^[1] It had maternal and neonatal adverse consequences. In maternal site, it increases the mode of delivery by cesarean section.^[4]

The placenta is a newly formed complex, and transient organ between mother and fetus. It possesses various vital functions such as elimination of wastes, nutritional transportation, gas exchange, and hormones production that sustain fetal growth and development during intrauterine life.^[8-11]

It is an oval organ possessing three surfaces – a rough maternal surface containing 15–30 cotyledons, a fetal surface, and a peripheral margin which is the outer limit of the vascular plate.^[9] These cotyledons are the functional unit of the placenta.^[12] Their number is extremely variable. The factors that determine its number are unknown, though they may depend on events in early

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gestation. Each cotyledon is lined by trophoblast cells and partially or entirely separated from adjacent cotyledon by connective tissue partition. Each cotyledon receives blood from one or more maternal spiral arteries.^[13]

Placenta is subjected to changes throughout the pregnancy in the circulation of both mother and fetus.^[10] It is considered as a window by which one can acknowledge any maternal functional impairment and their adverse effects on the fetus.^[9] As fetus grows, many structural changes will happen in placenta.^[14] In GDM, the cotyledon experiences a diversity of changes that subsequently affect placental morphology and function.^[8] This study was aimed to discover the change in the placental cotyledon number in pregnant women with GDM in comparison with non-GDM, as well as placental weight and diameter.

Materials and Methods

A comparative study was conducted in Omdurman Maternity Hospital (OMH) after approval from the research committee, Faculty of Medicine, Alzaiem Alazhari University, Sudan, from January 2018 to September 2020. OMH is a tertiary hospital located in Khartoum, the capital of Sudan, and receives patients from different regions in the country. The studied groups were divided into Group A and Group B. The Group A (GDM group) comprised women with GDM admitted in labor and fulfilling the criteria of the research, whereas Group B (non-GDM group) comprised women whose pregnancy was not complicated by GDM admitted in labor at OMH during the study period, after acceptance of a pre-given informed consent.

The selection criteria were singleton delivery at term (37–40 weeks) in both groups, as well as mothers' willingness to participate in the study, and acceptance of the informed consent. The gestational age was determined by the last menstrual period. Women with a history of pregestational diabetes, hypertension, other chronic diseases, with more than singleton pregnancy, preterm pregnancy, and postterm pregnancy and those with intrauterine fetal death were excluded from this study.

The diagnosis of GDM was made if any of these criteria were met: fasting plasma glucose of 7.0 mmol/L (126 mg/dL); 2-h plasma glucose of 11.1 mmol/L (200 mg/dL) following a 75 g oral glucose load; or random plasma glucose 11.1 mmol/L (200 mg/dL) in the presence of diabetic symptoms.

Postdelivery placentae from both groups were collected in a clean tray. An accurate preparation of the placentas was performed by trimming off all membranes, superficial fetal vessels were drained of all blood, adherent blood clots were removed from the maternal surface, and the umbilical cord was severed at the insertion site on the placenta surface.

Then, the placentae were put in a hard surface for detailed examination and measurements. The placenta

was gently pressed on its fetal surface to facilitate bulging of cotyledons, and then, the maternal surface was well inspected, and cotyledons were counted systematically, from the right side of one terminal and working through leftward in a curved fashion, as well as their number was recorded [Figure 1].

The minimum sample size was determined statistically and found to be 384 using the formula.^[15] The collected data were managed statistically using Chi-square test and Student's *t*-test where appropriate. $P < 0.05$ was considered to be statistically significant (confidence interval: 95%). The correlation (*r*) was measured between the number of cotyledons, placental diameter, and weight.

Results

A total of 385 participants were included in the study – 128 participants in Group A, and 257 in Group B. Mean age for GDM group (Group A) was 31 ± 5.8 years (range, 15–45), whereas it was 38 ± 7.3 years (range, 15–45) in non-GDM group (Group B). The difference was statistically significant ($P < 0.03$). The mean gestational age at delivery was 37.3 ± 1.011 (range, 37–39 weeks) in Group A versus 37.7 ± 1.5 (range, 37–40 weeks) in Group B. The difference was significant ($P < 0.002$). In Group A, 80.5% were adequately adherent to regular antenatal care visits, whereas it was lower in Group B as only 66.5% were found adequately adherent to regular antenatal care visits [Table 1].

Table 1: Antenatal care attendance among the study groups

ANC	Frequency (%)	
	Group A	Group B
Regular	103 (80.5)	171 (66.5)
Absent	25 (19.5)	86 (33.5)
Total	128 (100)	257 (100)

$P=0.004$. ANC: Antenatal care



Figure 1: Cotyledons in maternal surface

Para 5–7 were seen in 15.6% in Group A, whereas it was seen in 10.5% in Group B. Para >7 cases were seen in 8.6% in GDM group and in 8.9% in Group B. More than Para 2 in GDM group was 68% whereas in Group B was 54.1%. In the both groups, all participants were having normal spontaneous pregnancy. The incidence of cesarean delivery was more in Group A (83.6%) than Group B (9.7%). The difference was statistically significant ($P < 0.000$).

The mean body mass index (BMI) of Group A was 27.6 ± 3.45 kg/m² (range, 22–29) and 22.4 ± 2.22 kg/m² (range, 18.5–28) in Group B. The difference was statistically significant ($P < 0.0001$). The studied placental morphological variables were weight, diameter, and number of cotyledons [Table 2].

The mean placental weight in Group A was 660 ± 116 g (range, 470–900 gm), whereas it was less in Group B as 545 ± 206 g (range 300–900 gm), and the difference was significant ($P < 0.021$). The various placental weights are shown in Table 3.

The mean placental diameter was 17.9 ± 1.9 cm (range 15–25) in Group B, whereas it was 21.7 ± 2.3 cm (range 14–26) in Group A, and the difference between both groups was highly significant ($P < 0.000$) [Table 2]. In Group A, the diameter of 58% of placentae was 19–23 cm, whereas 68% in Group B has 14–18 cm diameter [Table 4].

The mean number of cotyledons in maternal surface in Group A was 19.8 ± 1.44 (range, 16–23), whereas it was lower in Group B as 17.7 ± 1.95 (range, 15–22). The difference was highly significant ($P < 0.000$) [Table 2]. Placentae in Group A tended to have more cotyledons than Group B. The majority of placentae (31.2%) in Group A had 20 cotyledons, whereas in the Group (B), the majority (28.9%) had 18 cotyledons. Collectively, in Group (A), 64% of the placentae contained 20–23 cotyledons, in contrary to that in Group (B) where 74.4% of placentae contained 15–18 cotyledons ($P < 0.001$) [Table 5].

In Group A, the placenta of pregnant who are adequately adherent to regular antenatal care visits and having good diabetic control had significantly less number of cotyledons when compared to those with less diabetes control or who were not having regular antenatal care ($P = 0.021$). In Group A, a significant correlation was found between the placental weight, diameter, and number of its cotyledons ($r = 0.23$, $P = 0.011$), as placental weight and diameter increased, the cotyledons number increased. A significant correlation was found between the GDM and non-GDM groups, in terms of cotyledons number ($r = 0.32$, $P = 0.007$).

Discussion

It was found that the optimal age of women for childbirth is between 20 and 29 years, conception in women

Table 2: Placental morphology in the study groups

Placental morphology	Group A		Group B		P
	Mean±SD	Range	Mean±SD	Range	
Weight (g)	660±116	470-900	545±206	300-900	0.021
Diameter (cm)	21.7±2.3	14-26	17.9±1.9	15-25	0.000
Cotyledons	19.8±1.44	16-23	17.7±1.95	15-22	0.000

SD: Standard deviation

Table 3: The weight of placenta in study groups

Placental weight (g)	Frequency (%)	
	Group A	Group B
<500	3 (2.3)	74 (28.8)
500-599	54 (42.2)	154 (60)
600-699	36 (28.2)	15 (5.8)
700-799	20 (15.6)	6 (2.3)
800-900	15 (11.7)	8 (3.1)
Total	128 (100)	257 (100)

Table 4: The diameter of placenta among study groups

Placental diameter (cm)	Frequency (%)	
	Group A	Group B
14-18	14 (11)	175 (68)
19-23	74 (58)	82 (32)
24-28	40 (31)	0
Total	128 (100)	257 (100)

Table 5: The cotyledons number among study groups

Cotyledon	Frequency (%)	
	Group A	Group B
15	0	45 (17.5)
16	3 (2.3)	33 (12.8)
17	5 (3.9)	39 (15.2)
18	20 (15.6)	74 (28.9)
19	18 (14.1)	19 (7.4)
20	40 (31.2)	30 (11.7)
21	32 (25)	5 (1.9)
22	8 (6.2)	12 (4.7)
23	2 (1.6)	0
Total	128 (100)	257 (100)

$P < 0.001$

over 35 years is disadvantageous and carrying maternal and fetal risks. Nowadays, improved economic resources have made it possible to improve lifestyles worldwide; as a result, the average childbearing age of women has increased globally.^[16]

The mean maternal age among participants was 34.5 ± 6.55 years. This was in concordance with the study in Norway by Roum *et al.*^[17] whereas it was higher than that reported in Turkey by Erbil *et al.*^[18] In this study, the mean age for Group A was lower than Group B. On the contrary, this was reversed in Egyptian study by Abdelghany *et al.* when they reported a higher mean maternal age in GDM

group than that of control,^[19] whereas in the study by Saini *et al.* in India, the mean maternal age for GDM and control groups was almost similar.^[20]

Obesity is a known risk factor for GDM. In general, the recent increasing rate of obesity simultaneously led to a significant increase in the prevalence of GDM.^[21] The current study had a similar result as the mean BMI in the GDM Group A ($27.6 \pm 3.45 \text{ kg/m}^2$) was higher than in non-GDM Group B ($22.4 \pm 2.22 \text{ kg/m}^2$).

It is proven that women who have fewer hospital visits have more probability to be diagnosed with GDM than women who are on regular antenatal care visits.^[22] On the contrary, the findings in the current study showed that 80.5% of participants in GDM group were adequately adherent to regular antenatal care visits, whereas in non-GDM group, only 66.5% were found adequately adherent to regular antenatal care visits.

In diabetes, the magnitude of the placenta structural changes depends on the precision of glycemic control accomplished during placental development.^[23] Currently, in GDM group, the cotyledons number is significantly less in the placenta from mothers having good diabetic control when compared to those with less diabetes control or whom not on regular antenatal care.

Some studies have found that higher parity is concomitant with a greater prevalence of gestational diabetes. In the current study, 68% of women in GDM group were multiparous with parity more than two. Similarly, Agarwal (2020) stated that multiparity has a greater incidence of GDM.^[24]

Managing GDM is one of the most worthwhile clinical experiences. An efficient treatment regimen comprises dietary control, monitoring of blood glucose, and management with insulin if blood glucose targets are not achieved by diet alone. About 40% of patients with gestational diabetes require insulin.^[25] The higher incidence (50%) of insulin usage for glycemic control was due to illiteracy and low knowledge in the principles of good diabetes control.

With the rise of complications related to GDM in fetal and maternal, it is clear that nonnormal vaginal delivery is preferred by numerous obstetricians. As observed in this study, 83.6% of patients with GDM had undergone cesarean section (CS), whereas in the nonGDM group, only 9.7% of their mode of delivery was CS. However, GDM *per se* is not an indication for CS or termination of pregnancy before 38 weeks. In Brazilian study by Zanrosso *et al.* (2015), CS was the delivery route adopted in 60.5% of the women with GDM.^[26]

Placenta is a transient organ between fetus and mother, preserves pregnancy, and promotes fetal growth.^[27] Its weight is an imperative and functionally noteworthy factor.

It is one of the most important factors responsible for fetal growth. Placenta from women with GDM is heavier than those without diabetes at the equal gestational age.^[28] This was in concordance with the findings in this study that the placenta from women with GDM tends to be heavier than normal healthy mothers. The increased placental weight and volume in diabetic mothers were also stated by various authors.^[19,20,28-32] The mean placental diameter of study populations was 19.8 cm. This was in agreement with that reported from different nations and countries in literature.^[28,29,31]

The documented maternal cotyledon number was variable in the literature. It was reported in many studies to be ranging from 10 to 38. The number of cotyledons in the current study was less than that reported by Sharmila *et al.* in India;^[29] whereas it was in consistent with the reports by others.^[29,33]

Various pathological and physiological factors can considerably influence morphological changes in placenta.^[9] The number of cotyledons of placentae from diabetic mothers was significantly more than those from uncomplicated pregnancies. This was well supported by published literature.^[20,28-30] On the contrary, Elshennawy in Egypt, in his study of 60 placentae, reported that the mean cotyledons number was 19.8 and it was remarkably equal in both groups (GDM vs. non-GDM).^[32] Conversely, Hussain and Islam in Pakistan studied 50 placentae (Group A 25-GDM and Group B 25-normal control). The mean number of cotyledons in the control group (22.56 ± 1.98) was significantly higher than that of the GDM group (17.88 ± 1.66)^[31] [Table 6].

In GDM, as the weight of the placenta is increased, concomitantly, other morphological parameters such as volume, diameter, and cotyledons numbers increase.^[29] Similar results were found in this study, as there was a significant correlation between the placental weight, diameter, and the number of its cotyledons, and when the

Table 6: Comparative studies of placental cotyledons number in gestational diabetes mellitus versus nongestational diabetes mellitus

Author name	Year	Country	Mean cotyledons number		P
			GDM	Control	
Akhter <i>et al.</i> ^[28]	2010	Bangladesh	18.555	17.953	>0.05
Hussain <i>et al.</i> ^[31]	2013	Pakistan	17.88	22.56**	0.001
Khaskhelli <i>et al.</i> ^[30]	2013	Pakistan	24.46	16.13	0.0001
Saini <i>et al.</i> ^[20]	2015	India	18.38	16.93	0.05
Elshennawy ^[32]	2016	Egypt	19.86	19.8*	-
Sharmila <i>et al.</i> ^[29]	2017	India	19.38	15.38	0.0001
The current study	2021	Sudan	19.8	17.7	0.000

*Cotyledons number was equal in both groups, **Cotyledons number was greater in control than GDM group. GDM: Gestational diabetes mellitus

placental weight and diameter increased, the cotyledons number also increased. The strength of the present study is that it was done prospectively, using the standard technique for placental preparation.

Limitation of the study

The sample size in GDM group was small. Before pregnancy, BMI was unknown, so the BMI was calculated at the time of presentation to the labor room. The study did not rely on maternal prepregnancy weight which was self-reported and this may be subject to error. As a consequence, this might lead to inaccurate categorizations of obesity.

Conclusions

The study participants are of descent from different country regions, they constitute homogeneous inhabitants in terms of ethnic background. It is more likely to have an impact on generalizability than inner validity. The number of cotyledons is considerably higher in the placentae of GDM mothers compared with placentae from non-GDM mothers. The concomitant increase in the diameter and weight of the placenta of GDM mothers as compared to the non-GDM group could be an adaptive reaction. Further validation of the finding of the current study in a larger sample including histobiochemical changes should be considered in the future.

Ethical clearance

The study was conducted after approval from the Institutional Ethics Committee.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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