

GROSS MORPHOLOGICAL STUDY OF GESTATIONAL DIABETES MELLITUS PLACENTA FROM SOUTH INDIAN MOTHERS COMPARED WITH CONTROL PLACENTA

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ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) is an ever increasing threat in Indian women, is found up to 10% of the total pregnancies and is mainly due to diet, obesity and sedentary life style. Placenta, considered being the vital organ of intrauterine life, form the representation of whole pregnancy. The present study has undertaken to observe the morphological changes of the GDM and control placenta.

Material and Methods: Total number of 96 placentas, out of which 48 are GDM and 48 from control were procured for the present study along with mother's age, gestational age and baby's weight. All samples were studied morphologically.

Result: The morphological aspects of GDM were found be more significant when compared to normal. In GDM placentas, mean placental weight was 537.27 ± 131.97 with a range of 330 to 890g, mean placental volume was $482.61 \pm 142.17 \text{ ml}^3$ in GDM with a range of 144.12-700 ml^3 , and mean placental diameter was $168.2 \pm 13.23\text{mm}$ with a range of 147-186 mm. Thickness in GDM was $23.69 \pm 5.08\text{mm}$. The average number of placental cotyledons was 19.38 ± 3.4 in GDM, which was significantly higher, revealed its excessiveness. In GDM feto-placental ratio calculated from dividing baby birth weight by placental weight was 5.96 ± 1.06 .

Conclusion: Significant placental morphological changes of GDM observed in the present study may be considered as a clinical importance. The impact of these changes may reflect on the perinatal outcome of the pregnancy, resulting in macrosomia, congenital malformations and intrauterine growth retardation.

KEY WORDS: Gestational diabetes, GDM, Placenta, Morphology, pregnancy, feto-placental ratio.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is described as glucose intolerance of varying severity with the onset of first recognition

during pregnancy and disappears with delivery [1,2]. GDM is a common metabolic problem complicates approximately 2-4% of pregnancies and it is the major cause of macrosomia and

perinatal mortality and usually associated by clinical hyperglycemia, hyperlipidemia, hyperinsulinemia and placental endothelial dysfunction [3]. In India the prevalence of GDM is 4-11.6% and varies according to geographical areas and diagnostic methods employed [4,5]. With a multifaceted trait, placenta is exposed to the regulatory influence of hormones present in both fetal and maternal circulations and affected by changes in any of these. As a fundamental organ with complexities of intrauterine life, placenta seizes an adaptive response and tries to compensate to prevent any foetal complications. It undergoes a change in weight, volume, structure, shape and functions continuously throughout gestation in order to support prenatal life [6].

Diabetes mellitus (DM) in pregnancy is associated with a variety of placental abnormalities. The extent of these changes depends on a number of factors, particularly the quality of glycemic control achieved during the critical periods in placental development [7,8]. Examination of placenta immediately after delivery provides much insight into the prenatal health of the baby and the mother [9]. The aim of the present study is to observe the morphological changes of the placenta from control and GDM mothers.

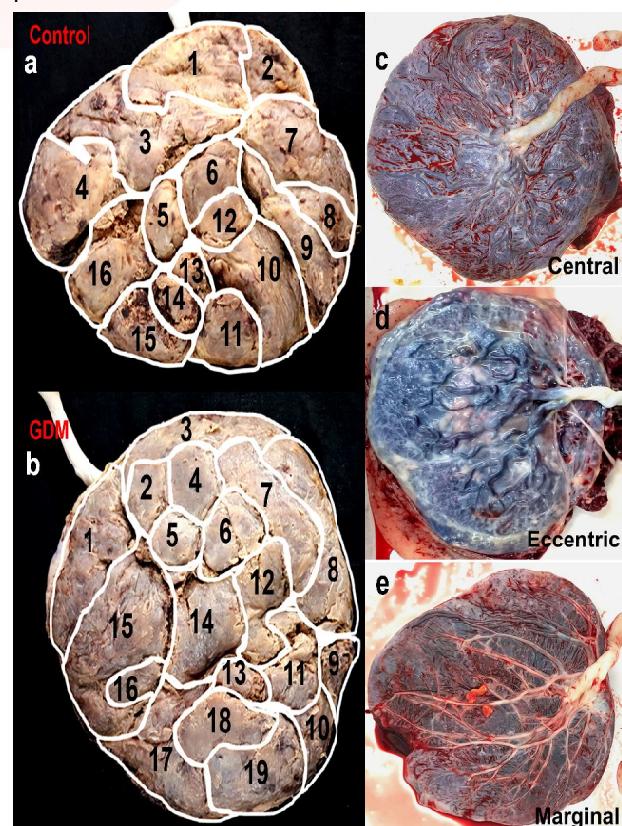
MATERIALS AND METHODS

For the present study, 96 placentas (48 from GDM and 48 from controls) were collected from Obstetrics and Gynaecology department and were sent to Anatomy department, Narayana medical college and general hospital, Nellore. The gestational age of the women was between 36-40 weeks. GDM cases were identified if they had two or more blood glucose values greater than or equal to the defined threshold levels (plasma glucose level of ≥140 mg/dL is taken as cut off for diagnosis of GDM) on a 100-g oral glucose tolerance test (OGTT). As a criterion, only those who delivered full term, singleton live births were selected for this study ($n=96$) and mothers in the age group of 21-39 years. The exclusion criteria from the study are Type-1DM, combined DM and hypertension and severe anaemia. All participants completed informed written consent to encompass this study, and

the study protocol was approved by the Institutional Ethical Committee. Immediately after the delivery, placenta with attached membranes and umbilical cord was collected; membranes were trimmed and blood coagulants were removed. The placental weight, volume, diameter, central thickness, cotyledon numbers and attachment of umbilical cord were recorded. For volume, the water displacement method of placenta was adopted [10] and for cotyledon number estimation, the placentas were fixed in formalin for 3-5 days, as a result the placental tissues were hardened and slight pressure applied on fetal surface, thus the cotyledons become prominent and separated from adjacent ones [11].

The data was fed in computer program SPSS ver.15 for Windows (SPSS Inc, Chicago, IL, USA). The statistical significance of difference between the two groups was evaluated by using Student unpaired t-test. Data were presented as mean \pm SD. P-value less than 0.05 were considered statistically significant.

Fig.1: Placentas from control (a) and GDM (b) showing the number of placental cotyledons. All the placentas were photographed on maternal surface containing the cotyledons, and then drawn lines on intercotyledonary areas with the help of Adobe Photoshop software for Windows. c-e: Showing the three different attachments (central, eccentric and marginal) of umbilical cord on placenta.



RESULTS

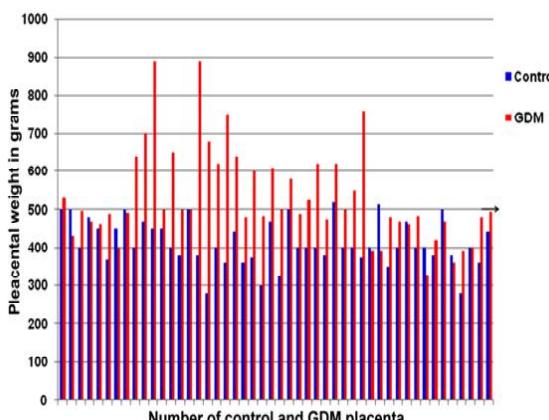
Mean birth weight of the new born babies was 2527 ± 516 gms in the control group and 3040 ± 464 gms in the GDM group which was highly significant ($p < 0.0001$) with a range of 1500-3800g in control and 2600-4000g in GDM. The range (minimum to maximum) of placental weight, volume, diameter, central thickness and number of cotyledons were significantly more in GDM compared to control group (Table-1). In GDM, 18 placentas showed >500 g (37.5%) whereas in control only 2 (4.2%) placentas showed >500 g (Graph 1). The placental weight, volume, diameter and central thickness showed significantly higher in GDM group ($p < 0.0001$) than the control (Table-2).

Table 1: Comparison of ranges of placental parameters and baby's birth weight between the control and GDM.

Parameter	Control (n=48) range (mini-maxi)	GDM (n=48) range (mini-maxi)
Placental weight (g)	280-520	330-890
Placental volume (ml ³)	125-520	144.12-700
Placental diameter (mm)	143-182	147-186
Placental central thickness (mm)	10-30	12-40
Number of placental cotyledons	10-22	11-25
Baby's birth weight (g)	1500-3800	2600-4000

g, gram; mm, millimetre; ml, millilitre; mini, minimum; maxi, maximum

Graph 1: Bar diagram showing the placental weight in grams in relation to Control and Gestational diabetes mellitus (GDM).



In control group, mean placental weight was 412.08 ± 54.03 g and in GDM it was 537.27 ± 131.97 with a range of 280 -520 and 330 to 890g in control and GDM respectively. Mean placental volume was 366.55 ± 123.13 ml³ in control with a range of 125 -520 ml³ and 482.61 ± 142.17 ml³ in GDM with a range of 144.12-700 ml³. Mean placental diameter was 156.4 ± 6.64 mm in a

range of 143-182 in normal and 168.2 ± 13.23 mm in GDM with a range of 147- 186mm. Thickness of normal placenta were 18.71 ± 5.37 mm in range of 10 -30mm and in GDM it was 23.69 ± 5.08 with a range of 12-40mm. The average number of placental cotyledons was 15.38 ± 3.3 and 19.38 ± 3.4 in controls and GDM respectively (Fig. 1a-b), which was significantly higher, revealed an overabundance of cotyledons in GDM (Table-2). The feto-placental ratio calculated from dividing baby birth weight by placental weight was 5.96 ± 1.06 in normal and 6.44 ± 1.41 in GDM.

Table 2: Comparison of placental weight, volume, diameter, central thickness, cotyledons and baby's birth weight between the control and GDM.

Parameter	Control (n=48)	GDM (n=48)	t-value	P-value
Placental weight (g)	412.08 ± 54.03	537.27 ± 131.97	5.71	0.0001**
Placental volume (ml ³)	366.55 ± 123.13	482.61 ± 142.17	4.27	0.0001**
Placental diameter (mm)	156.4 ± 6.64	168.2 ± 13.23	6.08	0.0001**
Placental central thickness (mm)	18.71 ± 5.37	23.69 ± 5.08	4.71	0.0001**
Placental cotyledons	15.38 ± 3.3	19.38 ± 3.4	5.81	0.0001**
Baby's birth weight (g)	2527.50 ± 516.05	3040.00 ± 464.09	5.27	0.0001**
Feto-Placental weight ratio	5.96 ± 1.06	6.44 ± 1.41	2.03	0.04*

Values are presented as mean \pm SD. g, gram; mm, millimetre; ml, millilitre; ** extremely significant; * significant

In the present study, the umbilical cord attachment in GDM and control were observed under three types centric, eccentric and marginal (Fig. 1c-e). Most of GDM placenta had eccentric type found to be 43.75%. The next observed type was marginal with 33.33% and centric positions were 22.92%. However the normal placentas also had a higher percentage, 39.59% of eccentric types than the other two types (Table-3).

Table 3: Attachment of umbilical cord to the placentas of control and GDM.

Parameter	Centric (n=48)	Eccentric (n=48)	Marginal (n=48)
Control	16 (33.33%)	19 (39.59%)	13 (27.08%)
GDM	11 (22.92%)	21 (43.75%)	16 (33.33%)

DISCUSSION

Maternal hyperglycemia is believed to be the cause of impaired placental function in conditions of gestational diabetes mellitus (GDM) and is been reflected in both microscopical [12] and

morphological aspects of the developing placenta. In turn GDM is also characterized by number of abnormalities in developing fetus such as macrosomia, congenital mal formations and intrauterine growth retardation [13].

In the present morphological study of placenta, there were significantly larger placental diameter, weight, volume and thickness in GDM group than control group. The increased placental weight and volume in diabetic mothers were also stated by various authors [14-19]. Mayhew et al [20] demonstrated that the placental weight was due to hyperplasia throughout the gestation that was reflected by higher DNA contents and may be endocrine effect of hyperinsulinaemia. Magee et al [21] studied that the increased mass in placentas was associated with significantly reduced apoptosis in the trophoblast in GDM patients. According to Boyd et al [22] the volume of the placenta in diabetic mothers on average was 12% more than that of the non-diabetic controls. In the present study it was found to be more significant than Boyd et al [22] findings of which was 23% more in GDM than the normal. Also the numbers of cotyledons were increased in GDM [23] in the present study.

Once the placental weight is increased, subsequently all the other morphological parameters such as volume, diameter, thickness and cotyledons are also increased in the GDM as observed in the present study. These changes collectively can be correlated and supported with the previous findings which state that insulin regulates the fetal and placental development and in any instance if this is altered can reflect on placental morphology [24]. However, both in diet controlled and drug controlled cases of GDM were also found to deliver with large placentas and macrosomic babies [25,26]. The increased baby weight as found in the present study may be one of the consequence of the placental weight and also intrinsic placental dysregulation factors such as glucose transport during pregnancy [27] which is statistically related by strong association with one another and is concordant with other authors [28,29].

According to Pathak et al [30] the cord insertion did not show any marked importance between normal and pregnancies complicated by GDM,

preeclampsia, and pregnancy induced hypertension. In the present study cord attachment does not show any significance between normal and GDM which convincing with the other findings. An increased placental ratio represents an adaptive process by feto placental unit in unfavourable maternal environment. When there is a limitation imposed on fetal growth velocity due to nutritional deficiencies, the placenta may undergo hypertrophy in an attempt to compensate. An increase in placental ratio would be a sign of fetal growth disturbance [31] and can lead to intrauterine fetal death [32].

Infants born to GDM mothers with glucose intolerance were at an increased risk of morbidity and mortality associated with respiratory distress, intrauterine growth retardation (IUGR), large for gestational age, congenital malformations, hypoglycemia, etc [33]. Impaired placental function, in terms of abnormal placental morphology and histology may state for the unexplained intrauterine fetal death and other complications met with the perinatal outcome in GDM [34].

CONCLUSION

Adverse morphological and histological changes in the GDM placenta resulting in the altered feto placental unit are predictable to have long-term impact on adult health and morbidity. Further exploration in aspects of histological and inflammatory processes can necessitate the role of pathophysiology in GDM placentas. From the present study altered placental morphology may account for the fetal growth and weight as a compensatory factor or vice-versa and could be a thrive for the placenta to maintain the good intrauterine environment for the developing fetus.

Conflicts of Interests: None

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