Original Article

COMPARING GROSS MORPHOLOGICAL AND HISTOPATHOLOGICAL CHANGES IN PLACENTA OF MOTHERS WITH GESTATIONAL DIABETES MELLITUS WITH NORMAL PREGNANCY

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Abstract

Background: Placentas in GDM pregnancy are large, heavier and shows microscopic alterations in form of villous edema, immaturity and fibrinoid degeneration. Such abnormal modifications in placentas are accountable for fetal hypoxia and raised perinatal morbidity and mortality. Studying of placental structure and its effect on fetus development is essential for developing effective screening, prevention, and management methods.

Objectives: Studying gross morphological and histopathological changes in placenta of mothers with Gestational Diabetes Mellitus (GDM) and comparing them with normal pregnancy.

Methodology: Present cross-sectional comparative study of placenta was conducted in 50 GDM and 50 normal pregnancies at tertiary care center of Pune, Maharashtra during September 2020 to August 2022.

Results: Among GDM pregnancy, mean gestational age was significantly lower, mean fasting blood sugar was significantly higher compared to normal pregnancy ($p<0.05$). There was significantly higher placental weight, fasting sugar among GDM pregnancy, relationship of increased syncytial knots, villous stromal fibrosis, fibrinoid necrosis and chorangiosis between both groups was statistically significant ($p<0.05$).

Conclusion: Placenta among GDM pregnancy were heavier with raised syncytial knots, presence of villous stromal fibrosis, fibrinoid necrosis and chorangiosis compared to normal pregnancy. Hence, we conclude that studying the histomorphology of the placentas in GDM can help with screening and management of both mother and fetus.

Key words: GDM, Placenta, Chorangiosis, Fibrinoid necrosis

Introduction

Human placenta is important organ for survival of fetus in mother's womb being the only medium by which nutrition provision, removal of waste from fetus, and gas exchange is possible. It has nutritional, endocrine and immunologic functions for supporting fetal growth and development. Placenta is important for synthesis of hormones like progesterone and HCG (human chorionic gonadotropin) which preserves pregnancy [1]. Therefore, dysfunction of placenta can lead to various adverse fetal consequences. In diabetes mellitus, various alterations arise in placental morphology like placental size, hyper-vascularization, higher branching capillaries of villi and higher glycogen deposits [2].

Diabetes Mellitus (DM) is a disorder which complicates pregnancy. It affects 0.5% to 2% of pregnancies. This leads to substantial effects, since pre-existing diabetes (both type 1 and type 2) is related with various pregnancy complications like macrosomia, congenital anomaly, caesarean section deliveries, still births [3,4]. Among developed nations, gestational diabetes complicates around 5% to 7% of pregnancies. Gestational diabetes is worldwide health problem, and in India, it affects more than 5 million pregnant females yearly. Prevalence of gestational diabetes in India, varies from 4% to 18% [5].

Gestational diabetes mellitus (GDM) during pregnancy is responsible for gross and microscopic alteration in placenta which is responsible for fetal hypoxia and raised perinatal morbidity and mortality. It is metabolic disorder, defined as glucose intolerance with onset or first detection during pregnancy [2]. GDM during pregnancy leads to gross and microscopic alteration in placental area and volume resulting in functional alteration thus restricting well-being of growing fetus [2]. Past studies had found that maternal postprandial glucose concentration was vital determining factor for overgrowth of fetus. Such findings reveal constant risk for fetal morbidity related with raising maternal glucose intolerance during pregnancy [7].

Placenta from GDM pregnancies vary from nondiabetic pregnancies by raised placental to fetal ratio and by histological changes such as villous immaturity, villous fibrinoid necrosis, chorangiosis, and ischemia. Early onset diabetes is commonly related with noticeable structural alteration of placenta, while GDM at late gestation is related with placental functional alteration. This placental alteration, causing raised intervillous diffusion space of immature villi and placental size to perfusion discrepancy, might affect fetus to chronic and acute variations in gas and nutrient exchange thus converting placenta from being "fetus protector" to possible source of adverse outcome. Studying of placental alteration and how they affect fetus development is essential in order to develop effective screening, prevention, and management methods [6].

Materials and methods

Current non-randomized hospital based cross sectional study was conducted in 100 placentas of mothers, 50 placentas of GDM and 50 placentas of normal uncomplicated pregnancy during September 2020 to August 2022 at Department of Pathology Dr. D. Y. Patil Medical College, Hospital & Research Center, Pimpri, Pune.

Placentas of women who were diagnosed as diabetic during period of gestation (gestational diabetes mellitus) considered as cases, while placentas of women with normal pregnancy and with no associated diabetes were considered as control. Patients suffering from pregnancy induced hypertension or preeclampsia, hypothyroidism, Type 1 or Type 2 Diabetes (Overt Diabetes) before pregnancy, chronic illness and toxaemia during pregnancy were excluded from study.

After approval from ethics committee, 50 placentas from GDM pregnancy and 50 placentas from normal pregnancy were selected who had given informed and written consent. After delivery, weight of newborn was noted and all placentas were collected in fresh state. Afterwards, placentas were washed, blood and blood clots were removed and then weighed. All placentas were evaluated for clinical examination, necessary macroscopic and microscopic investigations. Volume of fresh placenta was determined by water displacement technique. Any abnormal finding on gross examination such as cord pathology, or any calcifications or infarctions were recorded.

Following this, placentas were fixed in 10% formal saline, after adequate fixation, sections for microscopic examination were taken and processed. Tissues were taken from following placental sites for histopathological studies such as centre of placenta, umbilical cord, membrane and any other area showing significant abnormality.

After the completion of data collection, data entry was done into MS Excel spreadsheets and data was analyzed by using IBM SPSS (Statistical Package for Social Science) version 20.

Results

In present hospital-based study, mean age and parity had non-significant relation between both GDM and normal pregnancy ($p>0.05$). Though, mean gestational age was significantly lower and mean values of fasting blood sugar (FBS) was significantly higher among GDM pregnancy patients compared to normal pregnancy ($p<0.05$). Oval shaped placenta (54%) and centrally located cord (98%) were commonest among GDM pregnancy, while round shaped placenta (52%) and centrally located cord (80%) were common among normal pregnancy. However, relationship of placental shape and cord location between both groups was statistically non-significant ($p>0.05$) (Table 1).

Table 1: Comparison of various parameters between GDM and Normal pregnancy

Parameters		**GDM Pregnancy n=50**	**Normal Pregnancy n=50**	P value
Age (Years)	*Mean ± SD*	25.6 ± 5.6	24.9 ± 6.8	0.178
Gestational age (weeks)	*Mean ± SD*	37.6 ± 3.1	39.5 ± 1.8	<0.001*
FBS (mg/dl)	*Mean ± SD*	162.8 ± 24.8	78.4 ± 6.7	<0.001*
Placental weight (gm)	*Mean ± SD*	611.2 ± 52.3	460.7 ± 34.3	<0.001*
Parity	Primi	31 (62%)	29 (58%)	0.683
	Multipara	19 (38%)	21 (42%)	
Placental Shape	Oval	27 (54.0)	24 (48.0)	0.548
	Round	23 (46.0)	26 (52.0)	
Cord location	Central	49 (98.0)	44 (88.0)	0.050
	Marginal	1 (2.0)	6 (12.0)	
Syncytial knots	Increased	41 (82.0)	1 (2.0)	<0.001*
	Not increased	9 (18.0)	49 (98.0)	
Villous stromal fibrosis	Present	26 (52.0)	2 (4.0)	<0.001*
	Absent	24 (48.0)	48 (96.0)	
Fibrinoid necrosis	Present	31 (62.0)	2 (4.0)	<0.001*
	Absent	19 (38.0)	48 (96.0)	
Chorangiosis	Present	29 (58.0)	0	<0.001*

	Absent	21 (42.0)	50 (100.0)	
* p values <0.05 was considered as statistically significant. GDM- Gestational Diabetes Mellitus, FBS- Fasting Blood Sugar				

Mean placental weight was significantly higher among GDM pregnancy compared to normal pregnancy (611.2 ± 52.3 vs 460.7 ± 34.3 gm); p<0.05). Additionally, among GDM pregnancy higher percent of patients were found with increased syncytial knots (82% vs 2%), villous stromal fibrosis (52% vs 4%), fibrinoid necrosis (62% vs 4%) and chorangiosis (58% vs none) compared to normal pregnancy. These relationships of increased syncytial knots (Figure 1), presence of villous stromal fibrosis, fibrinoid necrosis (Figure 2) and chorangiosis(Figure 3) were statistically significant (p<0.05) (Table 1).

Figure 1: Hematoxylin & Eosin-stained microphotograph (200X) showing syncytial knots (black arrow), which is aggregation of syncitio-trophoblastic cells nuclei in surface of terminal villi.

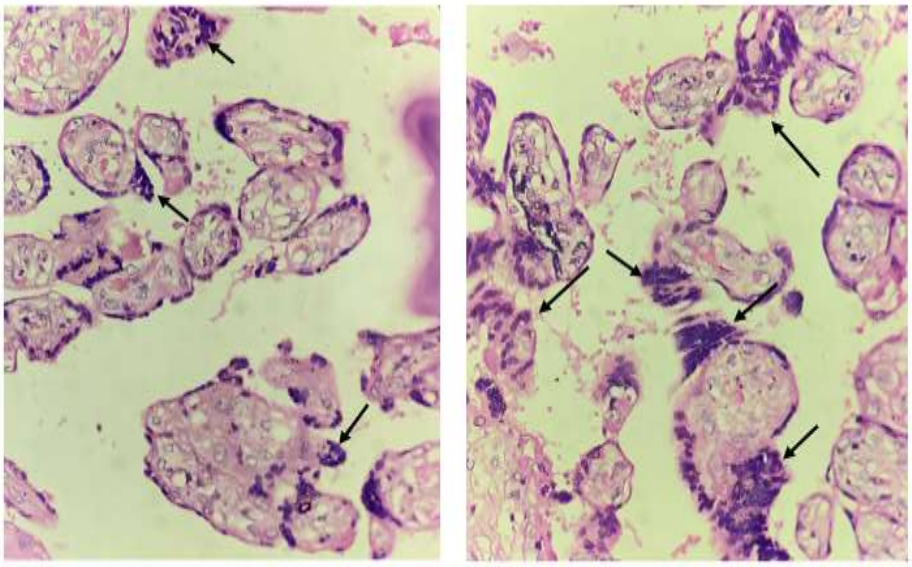


Figure 2: Hematoxylin & Eosin-stained microphotograph (400X) showing fibrinoid necrosis.

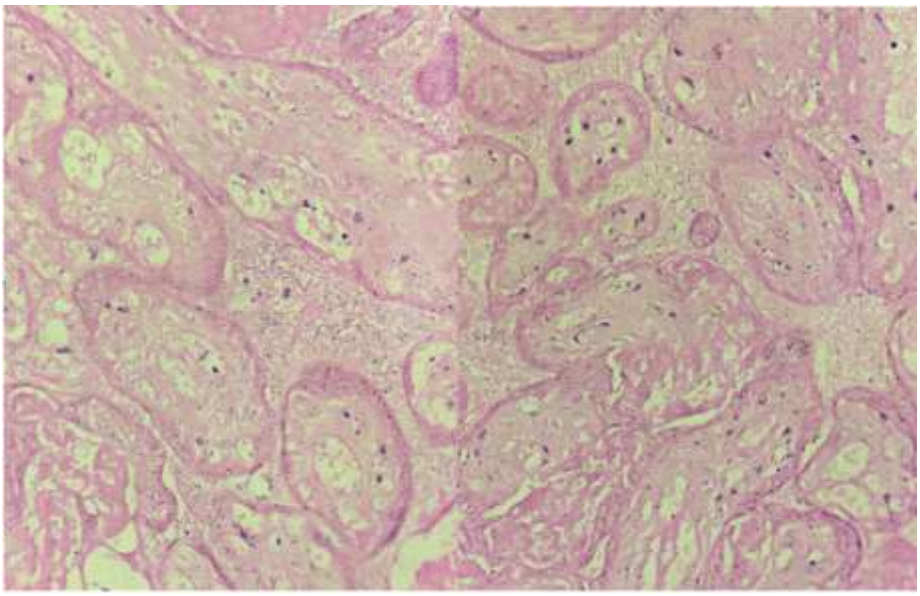
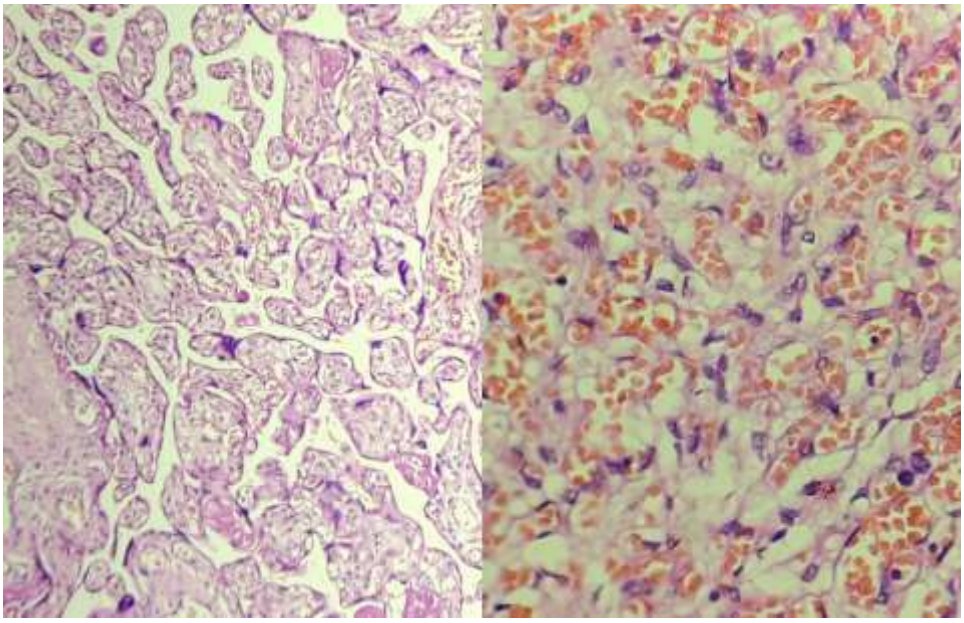


Figure 3: Hematoxylin & Eosin-stained microphotograph showing chorangiosis, 100X(A) and 400X(B), which is proliferation of capillaries in chorionic villi.



Discussion

Placenta is morpho-functional organ and major metabolic part during pregnancy, as it is vital organ accountable for nutritional uptake, waste removal and gas exchanges between mother and fetus, hence understanding morphology of placental is essential [2]. Growth of placenta in diabetic patients has structural and functional transformations, which depends on glucose control during placental growth, types of management and duration of time when diabetes was uncontrolled [8]. Current prospective cross-sectional study was conducted in 50 GBM patients for analyzing gross morphological and histopathological changes in placenta and to compare them with 50 normal pregnancies. Comparison of current study with other studies is stated in table (Table 2).

Table 2: Comparison of current study GDM Placental findings with various other studies

Study	Placenta weight (grams)	Syncytial knots	Villous stromal fibrosis	Fibrinoid necrosis	Chorangiosis
Current study	611.2 ± 52.3	82%	52%	62%	58%
Anjum et al [12]	586 ± 53.6	85%	75%	90%	65%
Daskalakis et al [13]	734 ± 105	-	80%	82.5%	40%
Augustine et al [16]	560.1 ± 155.9	56.7%	-	46.7%	46.7%

In this study, mean age of patients was non-significantly higher in GDM patients in contrast to normal pregnancy and similar findings were found in study conducted by Tandon et al [9] and Pooransari et al [10] studies. In this study, majority of GDM patients and normal pregnancy patients were primipara, which was comparable to study done by Saini et al [11] and Pooransari et al [10]. Mean gestational age was significantly lower in GDM patients in

contrast to normal pregnancy patients in current study and similarly in studies done by Anjum et al [12] and Daskalakis et al [13].

Shapes of placenta had non-significant relationship with gestational diabetes and this finding of current study was supported by various others studies done by Tandon et al [9], Saini et al [11] and Pooransari et al [10] ($p>0.05$). Moreover, location of umbilical cord on placenta had non-significant relationship between gestational pregnancy and normal pregnancy. Similarly cord insertion in Pooransari et al [10] study was more common at paracentral in GDM (60%) and in control (68.3%) and this was statistically non-significantly related ($p>0.05$).

Weight of newborn and placenta at birth were commonly used for determining health of intrauterine milieu and morphological features of placenta acting as an indicator of in-utero fetal development. In this study, mean placental weight was significantly higher among GDM pregnancy patients (611.2 ± 52.3 gm) compared to normal pregnancy (460.7 ± 34.29 gm, $p<0.05$). Similarly, significantly higher mean placental weight among GDM pregnancy compared to control groups was found by study conducted by Anjum et al [12], Asha et al [14], Bhanu et al [15] and Augustine et al[16]. Though study by Daskalakis et al [13] had found significantly lower fetal/placental weight ratio among diabetic patients. Moreover, study done by Anjum et al [12] had found increase in placental weight among GDM patients which might be related to upsurge in both parenchymatous (syncytio-vascular) and non-parenchymatous tissues (stroma, lipids, glycogen, tissue fluid edema) in responses to gestational diabetes. Study done by Bhanu et al [15] also noted that placental volume, diameter, central thickness and number of cotyledons were significantly more in GDM in contrast to control group ($p<0.05$).

Current study had found presence of villous stromal fibrosis, fibrinoid necrosis, chorangiosis and increased syncytial knots in GDM patients compared to normal pregnancy with statistically significant relationship between them ($p<0.05$). Commonest histological features of GDM pregnancy in Tandon et al [9] study was syncytial knots cytotrophoblastic cell proliferation, fibrosis of villous stroma, fibrinoid necrosis, calcified and hyalinised spots within villi. In addition, endothelial proliferation and fibromuscular sclerosis of stem arteries and presence of Hofbauer cells were detected. Study by Daskalakis et al [13] found presence of apparent degenerative lesions like fibrinoid necrosis and vascular lesions such as chorangiosis among diabetes pregnancy and they also found villous immaturity and presence of NFRBC as signs of chronic fetal hypoxia which were significantly raised in gestational diabetes placentas compared to normal pregnancy placentas. Though Anjum et al [12] had found significant relationship of Chorangisis between GDM patients and normal pregnancy ($p<0.05$). In Augustine et al [16] study, excessive syncytiotrophoblastic knot was histopathologic marker of excessive chorionic villous capillary proliferation and exaggerated senescence prompted by fetal hypoxia. They also found that chorangiosis was numerically raised in capillaries inside peripheral, placental villi and might be indicator of chronic prenatal hypoxia.

Conclusion

Current cross-sectional study was performed to compare placenta of normal term delivery and term placenta of gestational diabetes mellitus mothers. The study found significantly higher Placental weight. Relationship of increased syncytial knots, presence of villous stromal fibrosis, fibrinoid necrosis and chorangiosis between both groups was significant statistically. Hence studying these features can help the treating obstetrician in the further management of the mothers and can reduce fetal hypoxia, perinatal morbidity and mortality.

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