Original Article

Gestational Diabetes

Consequences of Gestational Diabetes Mellitus on Plancentae in Rural Area of Sindh

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ABSTRACT

Objective-To determine the changes in placentae in pregnant ladies suffering from pregnancy induced gestational diabetic mellitus.

Study Design: A cross sectional study

Place and Duration of Study: Sampling was done of the patients from the OPD's of Taluka hospital Hala and basic health unit Hala old, with collaboration of department of Anatomy, Baqai Medical University, Karachi from Jan-2011 to June 2011.

Materials and Methods: Placentae were preserved in 10% formalin of Merck Company and studied macroscopically as well as microscopically. These features include shape, size, and site of attachment of umbilical cord, central thickness and diameter (in centimeter, diameters) and weights (in grams) of fully developed placentae. Microscopic feature will include infarction, placental haemorrhage, villous edema, hyper vascularity and increase production of syncytial epithelial knots.

Results: Central thickness (Mean ± S.D ± SEM) diabetic placenta 3.8 ± 1.15 ± 0.21 were significantly high ($p<0.01$) as compared normal placenta. In diabetic placenta (Mean ± S.D ± SEM) of diameter 34.5 ± 7.93 ± 1.45 and weight 1478.8 ± 699.6 ± 127.7 were significantly ($p<0.01$) high as compared to normal placenta diameter 21.1 ± 3.37 ± 0.62, weight 557.8 ± 33.85 ± 6.18.

Conclusion: Gestational diabetes causes significant morphological changes in placenta that affects fetal and maternal wellbeing. This study is helpful for those who are concerned for mother and child health.

Key Words: Placentae, diabetes, macroscopy, microscopically,

INTRODUCTION

The placental foetal vessels are contained in chorionic villi composed of an outer trophoblast layer and a mesenchymal core[1]. The umbilical system is lost at birth, the vitelline contributes to the portal system and the systemic (embryonic) is extensively remodeled to form the cardiovascular system[2]. The villi lie bathed in maternal blood. The trophoblast and endothelium together regulate the transfer of nutrients and oxygen between maternal and foetal blood. Therefore, the successful development, growth and maturity of the foeto-placental vessels are vital to foetal growth and survival. Moreover, the foeto-placental vasculature is continuous with the foetal circulation and any changes here may reflect and affect the vascular functioning of the foetus[3]. The placenta brings the maternal and foetal circulation in close contact over a large surface area involved in the transfer of maternal nutrients, oxygen and heat to the foetus and transfer of metabolic waste products to the maternal circulation. In normal placenta protein synthesis and degradation rates progressively declines over the last weeks of gestation[4]. Classically, previous histological studies of type 1 diabetic placentae have described grossly abnormal placentae that are enlarged, thick, and plethoric, with abnormalities of villous maturation. These changes support the increased incidence of placental-related complications observed in diabetic pregnancy. However, other historical series have not detected significant differences, and more recent stereological studies continue to differ with either no disparity in placental composition or isolated changes including increases in capillary volume and surface area, increased villous surface area, increased total diffusive conductance, and increased intervillous and trophoblast volume. This lack of consistency reflects a combination of small series, grouping of different classes of maternal diabetes, differences in glycemic control between individual patients, recent improvements in antenatal care, and differing methodology[5].

In diabetes, the placenta undergoes a variety of structural and functional change. The nature and extent depend on a range of variables including the quality of glycemic control achieved during the critical periods in placental development, the modality of treatment, and the time period of severe departures from metabolic control of a non diabetic environment[6].

This review highlights the possible cellular/molecular mechanisms by which hyperglycemia and hyper-insulinaemia may alter vascular permeability and angiogenesis in the diabetic placenta. It also reveals the mechanistic information regarding the effects of diabetes on the growth, development and functioning of

the human placenta. Given the acceptance of the consequences of maternal diabetes on the growing foetus and also on later vascular diseases in adulthood, this area of placental research needs to be of more importance[7].

The trophoblast of human placenta is directly exposed to the maternal circulation. It forms the main barrier to maternal–foetal glucose transport. Prolonged hyperglycemia in vitro reduces trophoblast glucose uptake at substrate concentrations corresponding to blood levels of poorly controlled diabetic gravidas[8].

Aims and Objective: Present study aims to determine the changes in placentae in pregnant ladies suffering from pregnancy induced gestational diabetic mellitus so as to help the obstetrician for management of these problems during gestational period.

MATERIALS AND METHODS

Research Design:-A cross sectional study

Data Collection Procedures: This study was carried at the department of gynae and obs Taluka hospital Hala, and Basic health unit Hala old cases were examined and identified for diabetes and during pregnancy for the parameters mentioned successively. All the samples from these hospitals were collected personally as the patient came to the OPD'S and some of them were selected from the patients already admitted to the hospital for prenatal care. With the help of the hospital staff the placentae were collected in formalin containing plastic jars from labor room and operation theaters and weighed and labeled.

The samples divided into three groups: Group A: This group comprised of 30 placentas from pregnancies, which were not suffering from any disease, and served as control.

Group B: This group comprised of 30 full term placentae from mothers suffering from diabetes.

In this study 60 full term placenta were taken and divided into three groups of equal in number. The duration of this study was one year. All subjects in this study were mothers of any age. There were no racial, cultural or environmental differences among the subjects.

Parameters: The data was recorded for this study by following variables classified as

- Independent variables
- Dependent variables

Independent Variables: These included all the maternal variables;

- Patient's clinical history
- Clinical examination
- Lab investigation

All recorded on patient's record Proforma, designed specifically for this study, these variables included:

- Age
- Blood group
- Gravidity
- Parity
- No of abortions / still birth
- Blood pressure systolic
- Blood pressure diastolic
- Mode of delivery
- HbA1c
- RBS

Dependent variables: These included the following

- Variables related to placenta

Gross Examination: Weight, diameter, size, completeness, color, consistency, site of insertion of cord, site of insertion of membranes, length of cord, diameter of cord, true knots, no. of vessels in cord, hemorrhage, infarction, calcification and necrosis.

Microscopic Examination: These included following variables that were recorded on the Proforma.

- Syncytial knots
- Hemorrhage
- Villous congestion
- Endothelial proliferation
- Inflammation of membrane
- Thrombosis of cord vessels

Ethical Consideration: The written informed consent was taken from the patients, consultant and hospital administration of Taluka Hospital Hala and Basic Health Unit Hala old.

Inclusion and Exclusion Criteria:

- For this study only mature placenta were taken, Premature and Post mature placenta were not considered in this study.
- Only diabetic placentae were closely monitored.
- Also hypertensive placentae were taken without any other complications.
- These placentae were preserved in 10% formalin after half hour after the delivery.

Statistical Data: The data feeding and analysis was on computer package SPSS (Statistical Packages of Social Sciences) version 11.0. Clinical characteristics were be summarized in terms of frequencies and percentages for qualitative variables (shape, size of attachment of umbilical cord, hemorrhage, infarction, villous edema, hypervascularity and syncytial epithelial knots of placenta) mean S.D. for quantitative variables (central thickness, diameter and weight) of placenta. Statistical comparison was performed by analysis of variance (ANOVA) with tukey test with multiple comparisons for quantitative and chi-square test/fisher exact test for

qualitative variables. In all statistical analysis only p-value <0.05 was be considered significant.

RESULTS

Table No.1 showed that total 60 placentae, 30 from normal, 30 from diabetic. The study shows that shape discoid were significantly less compared to 16 (53.3%) diabetic placenta and normal placenta ($p<0.01$), bilobed in 6 (20.0%) diabetic placenta. In central attachment of umbilical cord, diabetic 22 (73.3%) and normal 30(100%) results showed non-significance in this comparison.

Table No.2 showed that central thickness (Mean ± S.D ± SEM) diabetic placenta 3.8 ± 1.15 ± 0.21 were significantly high ($p<0.01$) as compared normal placenta 3.0 ± 0.03 ± 0.01. In diabetic placenta (Mean ± S.D ± SEM) of diameter 34.5 ± 7.93 ± 1.45 and weight 1478.8 ± 699.6 ± 127.7 were significantly ($p<0.01$) high as compared to normal placenta diameter 21.1 ± 3.37 ± 0.62, weight 557.8 ± 33.85 ± 6.18.

Table No.1: Morphological changes between Normal (Group A) and Diabetic (Group C) placenta

	Group A Normal placenta (n=30)		Group B Diabetic placenta (n=30)	
	No.	%	No.	%
Discoid	30	100.0	16	53.3
Small discoid	-		-	
Star discoid	-		8	26.7
Bilobed discoid	-		6	20.0
Acentric	30	100.0	22	73.3
Marginal	-		8	26.7
Hemorrhage	-		17	56.7
Infarction	-		18	60.0
Villous edema	-		22	73.3
Decreased	-		6	20.0
Increased	-		15	50.0
No	30	100.0	9	30.0
Syncytial Epithelial knots	-		9	30.0

Table No.2: Comparison of Central thickness (cm), Diameter (cm) and Weight (gm) between Normal (Group A) and Diabetic (Group B) placenta Statistically

	Group A Normal placenta (n=30)	Group C Diabetic placenta (n=30)	P-value
	Mean ± S.D ± SEM	Mean ± S.D ± SEM	
Central thickness (cm)	3.0 ± 0.03 ± 0.01	3.8 ± 1.15 ± 0.21**	0.001
Diameter (cm)	21.1 ± 3.37 ± 0.62	34.5 ± 7.93 ± 1.45 **	0.001
Weight (gm)	557.8 ± 33.85 ± 6.18	1478.8 ± 699.6 ± 127.7 **	0.001

significant ** $p<0.01$

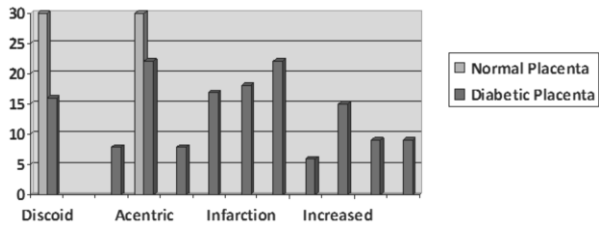
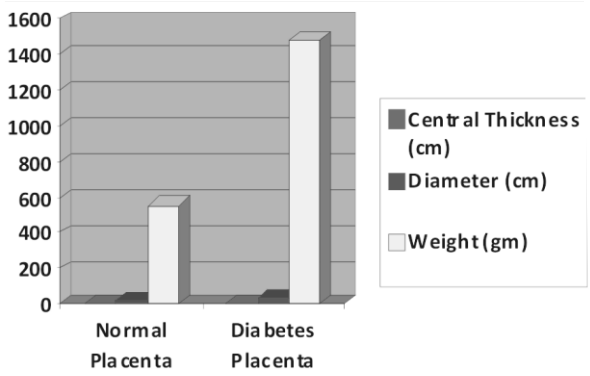


Figure No.1:



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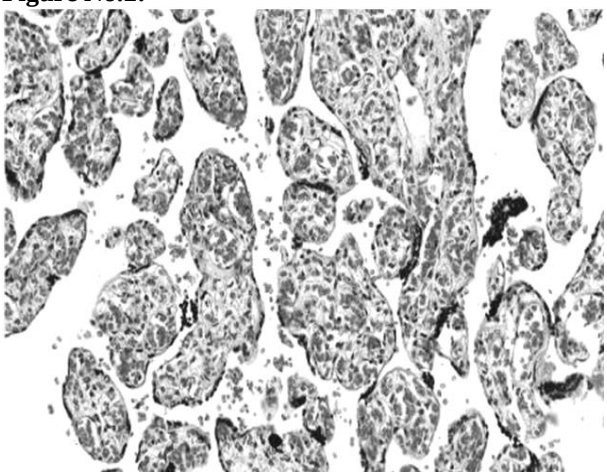
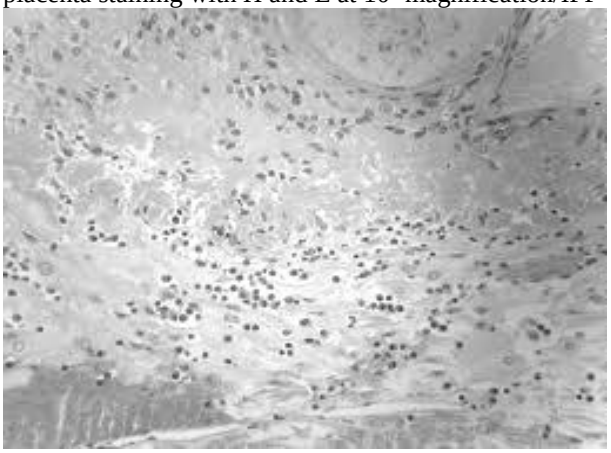
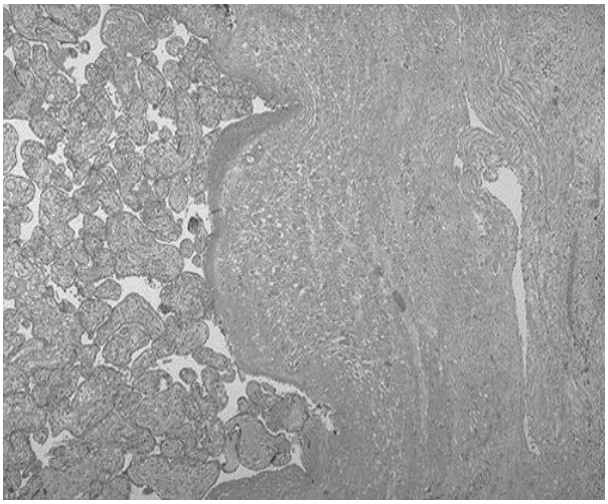


Photomicrographs 3: Showing villous edema in diabetic placenta staining with H and E at 10×magnification/IPF



Photomicrographs 4: Showing hypervascularity in diabetic placental tissue with masons trichome staining at 10× magnification/IPF



Photomicrographs 5: Showing villous adema in diabetic placenta staining withg H and E at 10x magnifaication / IPF

DISCUSSION

In present study showed in 60 placentae, 30 from normal, 30 from diabetis shape discoid were significantly less compared to 16 (53.3%) diabetic placenta and normal placenta ($p<0.01$), bilobed in 6 (20.0%) diabetic placenta. In central attachment of umbilical cord, diabetic 22 (73.3%) and normal 30(100%) results showed non significace in this comparison.Central thickness (Mean ± S.D ± SEM) diabetic placenta 3.8 ± 1.15 ± 0.21 were significantly high ($p<0.01$) as compared normal placenta 3.0 ± 0.03 ± 0.01. In diabetic placenta (Mean ± S.D ± SEM) of diameter 34.5 ± 7.93 ± 1.45 and weight 1478.8 ± 699.6 ± 127.7 were significantly ($p<0.01$) high as compared to normal placenta diameter 21.1 ± 3.37 ± 0.62, weight 557.8 ± 33.85 ± 6.18.Maternal diabetes is associated with changes of the placental structure. This is true as we noted similar changes in our study. These changes include great variability of vascularity manifested by strikingly hypovascular as well as hypervascular terminal villi. In our study, hypervascularity of villi noted in 15 out of 30 diabetic patient placentae.[9]

Present study correlates with the study of Guaster M et al., 2012 by its location between maternal and foetal blood streams the human placenta not only handles the materno-foetal transport of nutrients and gases, but may also be exposed to intrauterine conditions adversely affecting placental and foetal development. Such adverse conditions exist in pregnancies complicated by gestational diabetes mellitus (GDM), and have been associated with alterations in placental anatomy and physiology. These alterations are mainly based on changes on the micro-anatomical or even molecular level including aberrant villous vascularization, a misbalance of vaso active molecules, and enhanced oxidative stress. The consequence thereof may be impaired foetal oxygenation and changes in transplacental nutrient supply. Although transplacental glucose flux is flow limited and independent of glucose transporter availability, transport of essential and nonessential amino acids and expression of genes involved in lipid transport and metabolism are significantly affected by GDM[10].

This study showed similarity with the Guzmán-Gutiérrez E et al., 2011 Gestational diabetes mellitus (GDM) is a syndrome compromising the health of the mother and the foetus. Endothelial damage and reduced metabolism of the vasodilator adenosine occur and foetal hyper insulinemia associated with deficient insulin response and a metabolic rather than mitogenic phenotype is characteristic of this pathology. These phenomena lead to endothelial dysfunction of the foeto placental unit. Major databases were searched for the relevant literature in the field. Special attention was placed on publications related with diabetes and hormonal metabolic disorders. We aimed to summarize the information regarding insulin sensitivity changes in GDM and the role of adenosine in this phenomenon. Evidence supporting the possibility that foetal endothelial dysfunction involves a functional link between adenosine and insulin signaling in the foetal endothelium from GDM pregnancies is summarized. Since insulin acts via membrane receptors type A (preferentially associated with mitogenic responses) or type B (preferentially associated with metabolic responses), a differential activation of these receptors in this syndrome is proposed[11].

This study is correlated with the Rudge MV , Placentas from MGH group presented 17 types of histopathological change and higher rates of syncytial nodes and endarteritis. GDM placentas presented only nine types of histopathological change, high rates of dysmaturity, low rates of calcification and no syncytial nodes. Overt DM placentas showed 22 types of histopathological change, 21 of which were present in the preterm period. There were histopathological similarities between MGH and DM placentas, but the former exhibited a higher incidence of endarteritis, which has been described as a "post-mortem" phenomenon. Our results confirmed that the distinct placental changes associated with DM and MGH depend on gestational period during which the diabetic insult occurs. It may reasonably be inferred that subclinical maternal hyperglycemia during pregnancy, as showed in MGH group, is responsible for increased placental endarteritis, a postmortem lesion in the live foetus[12]

CONCLUSION

Gestational diabetes causes significant morphological changes in placenta that affects fetal and maternal wellbeing. This study is helpful for those who are concerned for mother and child health.

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