Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Histo pathological changes in the placenta of women with gestational diabetes mellitus

Dr. Rakesh Kumar Shukla[1], Dr. Suniti Pandey[2], Dr. Mirza R. U. Beg[3], Dr. Archana Mishra[4*]

[1]Assistant Professor of Anatomy, Autonomous State Medical College, Mirzapur, UP, India

[2]Professor & Head, Dept. of Anatomy, GSVM Medical College, Kanpur, UP, India

[3]Professor & Head, Dept. of Anatomy, Autonomous State Medical College, Mirzapur, UP, India

[4]Assistant Prof. of Biochemistry, MLN Medical College, Prayagraj, UP, India

***Corresponding Author-** Dr. Archana Mishra, Assistant Prof. of Biochemistry, MLN Medical College Prayagraj, UP, India

E-mail ID: - 0522archana@gmail.com

ABSTRACT

Background: - Gestational diabetes mellitus (GDM) is a common metabolic complication in pregnancy affecting the maternal and foetal wellbeing.

Aim: - The aim of this original research article is to investigate the histological changes in placenta of GDM and control women.

Method: - This study was done in Rama Medical College & Hospital Kanpur. Placenta sample from 100 cases of GDM and 150 of control women collected and histological changes studied.

Result: - In this study, the histological changes revealed that Fibrin was in 78% of GDM. Calcification was seen in 42% of GDM. Infarction was found in 4% of GDM, but in control the histological changes revealed Fibrin in 40%, Calcification was 25.3% and Infarction was 4%.

Conclusion: - Gestational diabetes mellitus causes significant histological changes.

Key Words: - GDM, Gestational diabetes mellitus, Placenta, Fibrin, Calcification, and Infarction

---

INTRODUCTION

Placenta is circular, discoid organ. The development of this is directly affected by the maternal health conditions. It also affects the intra-uterine status of the foetus. It is a structure where maternal and foetal tissues come in direct contact. It also suggests the immunological acceptance of foetal graft by the mother. Placenta is a potent endocrine, immunologic and metabolic organ. It is also responsible for nutrition, respiration and excretion for the foetus [1].

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Diabetes mellitus (DM) is one of the major actual public health issues consisting of chronic hyperglycaemia which can damage body organs and systems [2]. Gestational diabetes mellitus (GDM) is the most common metabolic disorder of pregnant women with an estimated prevalence ranging from <1% to 28%. However, in the countries where universal screening is recommended, the percentage of pregnant women screened ranges from 10% to >90% [3].

The prevalence of GDM in women in Asian countries is between 3.0-21.2%. The risk of developing GDM for South-Asian women is higher than the South East Asian and the East-Asian women [4, 5]. Among different ethnicities, also mother and child outcomes have important variations. Newborns from Pacific Island countries have higher rates of macrosomia. However, children with Chinese backgrounds have lower adverse outcomes [5].

Glucose is the main nutrient that passes to the fetus by facilitated diffusion. Thus, increased amounts of glucose may reach the fetus by facilitated transport through the placenta [6]. Therefore, adaptations in cells that are in contact with maternal and fetal circulation may occur in response to this abundant glucose supply [7]. GDM during pregnancy produces varieties of placental abnormalities such as distension of basal membrane of trophoblast proliferation of cells of the endothelium and decreased vascular surfaces of terminal villi. These changes depend upon the quality of glycemic control achieved during the critical period of the placental development [8].

MATERIAL AND METHODS

Study site

The study was conducted in the Department of Anatomy and Gynecology, Rama Medical College & Hospital Kanpur.

Study population

Placentas of full-term and preterm pregnancy were collected from labor room of Rama Hospital, Rama Medical College Kanpur of all reproductive age after obtaining the ethical clearance from ethical committee and consent from each individual of case and control. Placentas of Gestational diabetes mellitus (GDM) and control women were studied for histological changes.

Study design

Case-control

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Sample size:

Sample size was calculated using the Epitools software, keeping expected proportion in controls 0.05, and assumed odds ratio 4, confidence level 0.95 and power 0.8. Minimum sample size per group was calculated 98. Considering these minimum value 100 cases and 150 controls as sample size were kept for the study.

Study duration

Four years (2014-2018)

Inclusion criteria

- Gestational Diabetes mellitus

Exclusion criteria

- Pre-existing Diabetes mellitus (IDDM-Type 1)
- Pre-existing Diabetes mellitus (NIDDM-Type 2)
- Chronic hypertension
- Essential hypertension
- Chronic renal disease (renovascular)
- Coarctation of aorta
- Pheochromocytoma
- Thyrotoxicosis
- Connective tissue disease-systemic lupus erythematosus
- Twins pregnancy

Methods

Pregnant women were diagnosed with GDM under the standard protocol of Diabetes in Pregnancy Study Group India (DIPSI) and WHO. In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination had given a 75 g oral glucose load, irrespective of whether she had fasting or nonfasting state and without regard to the time of the last meal. A venous blood sample was collected at 2 hours for estimating plasma glucose by the GOD-POD method. GDM was diagnosed if 2-hour PG is ≥ 140 mg/dL.

Gestational weeks for Screening Recommended

Following the usual recommendation for screening between 24 weeks and 28 weeks of gestation, the chance of detecting unrecognized type 2 diabetes before pregnancy (pre-GDM) is likely to be missed. If the 2-hour PG is > 200 mg/dL in the early weeks of pregnancy, she may be a pre-GDM and A1C of ≥ 6.5 is confirmatory. A pregnant woman found to have normal glucose tolerance (NGT), in the first

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

trimester, should be tested for GDM again around 24th–28th weeks and finally around 32nd–34th weeks.

Methodology followed for Histological Examination

- Two cm wedge of tissue required for histopathology from
    a. Maternal & fetal surface 2 cm from periphery
    b. Maternal & Fetal surface from centre
- Tissue packed in disposable cassettes with proper labeling.

Processing

- Tissue processing were done under automated tissue processing machine, the Thermo Scientific™, Excelsior AS™

Embedding

- Embedding done using automated Tissue-Tek TEC Machine.
- Placed the base mould over Tissue-Tek for 2 hrs.

Freezing

- Paraffin blocks were stored at 0^0C 2hrs for 30 minutes.

Trimming

- Trimming was usually done at thickness between 10 and 30 µm with the help of Leica RM 2125 RT microtome.

Section Cutting

- Used the adjusting knob on the right side of the Leica RM 2125 RT microtome front panel to select the 5-micron section thickness.

Hot Water Bath

- Picked the ribbon gently to the MAC tissue floater hot water bath and attached a single floating film of paraffin at the midway of the slide.

Deparaffinization

- This is done by placing the slide over Macro Scientific slide warming table at 60^0C for 20 min.

Staining

- This is done by automated tissue strainer Tissue-Tek DRS.

Cover Slip

- Slide covered by cover slip and prepared for microphotography.

Histological appearances of placentas assessed for:-

- Fibrin deposition, Calcification and Infarction.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Microphotography

- Microphotography done with Magnus theia – I trinocular digital microscope.
- Slide observed at 100X and 400X.

Microphotographs

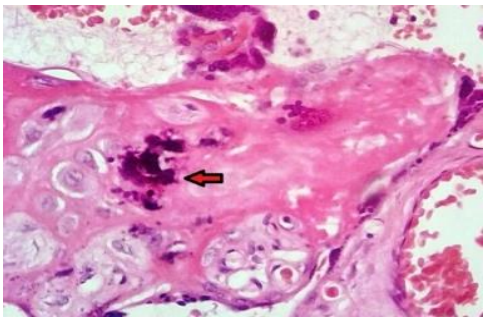

Fig. 1.Microphotograph of Peripheral Fetal Surface In GDM. Showing Areas of Calcification. H-E Stain at 400X.

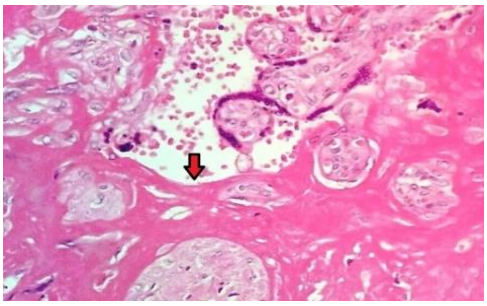

Fig. 2.Microphotograph of Peripheral Fetal Surface In GDM showing area of intervillous fibrin deposition. H-E Stain at 400X.

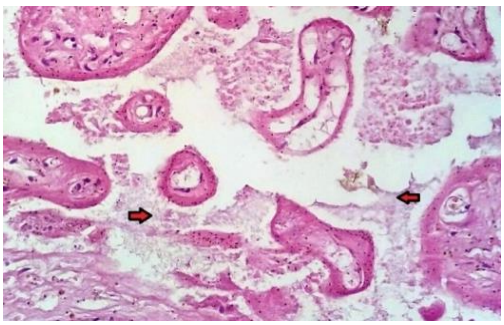

Fig. 3.Microphotograph of Central Fetal Surface In GDM Showing areas of inter villous necrosis. H-E Stain at 400X**.**

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

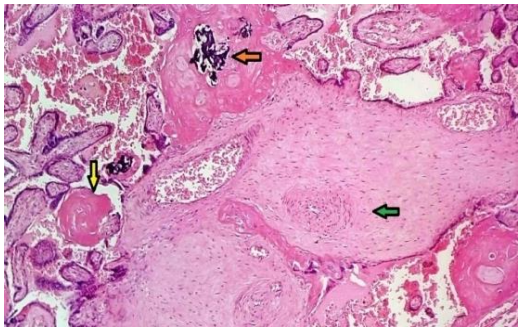

Fig. 4.Microphotograph of Peripheral Maternal Surface In GDM Showing areas of calcification (orange arrow), fibrin (yellow arrow) And fibrosis (green arrow). H-E Stain at 400X.

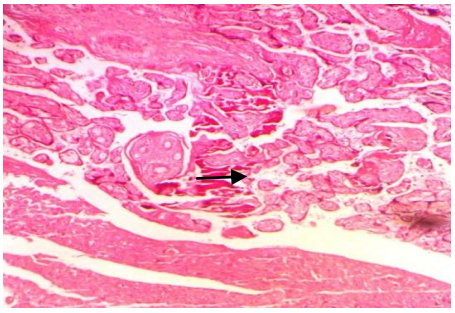

Fig.5.Microphotograph of Peripheral Maternal Surface Showing Calcification in Control. H & E Stain at 100X

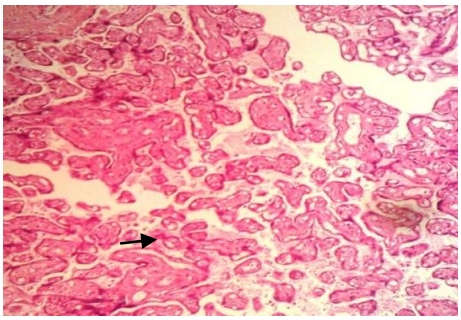

Fig.6. Microphotograph of Central Maternal Surface Showing Fibrin Deposition In Control. H & E Stain at 100X

OBSERVATIONS AND RESULTS

The present study was undertaken to find out the histological changes in the placenta of GDM and Controls women. A total of 100 cases of GDM and 150 controls were included in the study.

TABLE-I: Comparison of maternal age among the groups

Groups	**Age in years (Mean±SD)**
GDM	31.28±1.99

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Controls	28.44±3.03
p-value[1]	0.09

[1]ANOVA test

TABLE-II: Comparison of OGTT between the groups

Groups	OGTT (mg/dl) (Mean±SD)
GDM	186.50±15.02
Controls	97.15±10.05
p-value[1]	0.06

[1]ANOVA test

TABLE-III: Comparison of parity among the groups

Parity	GDM (n=100)		Controls (n=150)		p-value[1] GDMvs Controls
	No.	%	No.	%	
Nullipara	4	4.0	28	18.7	0.0001*
Primipara	18	18.0	34	22.7	
Multi para	78	78.0	88	58.7	

[1]Chi-square-test, *Significant

TABLE-IV: Comparison of histological changes among the groups

Deposition	GDM (n=100)		Controls (n=150)		p-value[1] GDMvs Controls
	No.	%	No.	%	
Fibrin					
Yes	78	78.0	60	40.0	0.0001*
No	22	22.0	90	60.0	
Calcification					
Yes	42	42.0	38	25.3	0.0001*
No	58	58.0	112	74.7	
Infarction					

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Yes	4	4.0	6	4.0	0.0001*
No	96	96.0	144	96.0	

[1]Chi-square-test,*Significant

DISCUSSION

In this study, the mean age of GDM cases was 31.28±1.99 years. In a study reported that the mean age of the GDM women being 28.5±5.71 years [9]. The mean age of controls in the present study was 28.44±3.03 years.

Maternal age is proven risk factor for GDM. But there is no consensus on the age after which there is significantly increased the risk of GDM. In the literature, the lowest cut off is ≥25 years as recommended by the American Diabetes Association.

In this study, 78.0 % multipara, 18.0 % primipara and 4.0% nullipara cases were found. It has been found that there was a higher proportion of multigravida than secundigravida and primigravida women (23 cases [37.1%], 11 cases [17.7%], and 9 cases [14.5%], respectively) among women with GDM [9].

In the present study, OGTT was significantly (p=0.0001) higher among GDM (186.50±15.02) patients compared to controls (97.15±10.05).In a study found that OGTT was significantly higher in GDM cases compared to control [10].

In GDM, many biologic and molecular mechanisms of regulating glucose levels are involved. It has been demonstrated that inadequate decrease of the renal threshold for glucose (RTG) that is determined by the nephron's reabsorption capacity, play a role in the development of GDM. In fact, glucose is reabsorbed through sodium glucose transporters in the proximal tubules. During pregnancy, the renal glucose reabsorption capacity reduces because of decreased glucose transporter expression leading to lower glucose elimination [11].

Histological studies have revealed apparent fibrinoid necrosis and vascular lesions such as chorangiosis, and thickening of the basement membrane more frequently in placentas from pregnancies complicated by GDM. When compared with normal placentas. In other studies, poorly controlled GDM placentas have shown villous edema, fibrin deposit in the syncytiotrophoblast, and hyperplasia of cytotrophoblast. These changes have been less distinct in placentas from well-monitored diabetic mothers and hardly observed in normal cases [12].

In present study, the histological changes revealed that Fibrin was in 78% of GDM. Calcification was seen in 42% of GDM. Infarction was found in 4% of GDM. Chorioamnionitis was in 18% of GDM. It

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

has been demonstrated in a study that the assessment of an association between GDM and placental changes showed that all 43 women with GDM (100%) demonstrated some sort of change in either the foetal or maternal placental surface [9]. The most common placental changes included in study are calcification (19; 44.1%), fibrin (11; 25.6%), and placental infarction (1; 2.3%) on the maternal surface; and fibrin (35; 81.4%), calcification (4; 9.3%), and hematoma (1; 2.3%) on the foetal surface. There were no placental changes in the maternal surface in 12 cases (28%) and on the foetal surface in three cases (7%). A study reveals 50 PIH cases and 50 control and found mean Infarcted area 16.5 ± 4.6, mean Calcification 33.3± 3.15 and mean Fibrinoid necrosis 11.3±2.3 in PIH and Mean Infarcted area 3.77 ± 1.87, mean Calcification 4.125± 1.15 and mean Fibrinoid necrosis 3.13±1.87 in control [13].

In present study, the histological changes revealed that Fibrin seen in 40% of controls. Calcifications were seen in 25.3% of controls and Infarctions were found in 4% of controls. In a study it was observed that infarction in 6.7% of controls; Calcification in 23.3% of controls [14].

CONCLUSIONS

- The mean age of GDM and controls was 31.28±1.99 and 28.44±3.03 years respectively.
- Primipara were in 18% of GDM and 22.7% of controls.
- OGTT was significantly (p=0.0001) higher among GDM (186.50±15.02) patients compared to controls (97.15±10.05).
- Fibrin was higher in GDM than controls.
- Calcification was higher in GDM than controls.
- Infarction was found in same percentage in GDM and controls but lowers than other histological changes.

Gestational diabetes mellitus cause significant histological changes in the placenta that affects foetal and maternal well-being. This study is helpful for those who are concerned for mother and child health.

DISCLOSURE: The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Concept and Design: Dr. Suniti Pandey

Collection and Assembly of data: Dr. Rakesh Kumar Shukla

Data Analysis and Interpretation: Dr. Mirza R. U. Beg

Manuscript Writing: Dr. Archana Mishra

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

Final approval of Manuscript: All authors

BIBLIOGRAPHY

1. Datta AK. Essentials of human embryology. 5th ed. Kolkata: Current Books International; 2007. p. 57-69.

2. Karamanou M, Protogerou A, Tsoucalas G, Androutsos G, Poulakou-Rebelakou E. Milestones in the history of diabetes mellitus: Th e main contributors. World J Diabetes. 2016;7(1):1-7. doi: 10.4239/wjd.v7.i1.1, PMID 26788261.

3. Jiwani A, Marseille E, Lohse N, Damm P, Hod M, Kahn JG. Gestational diabetes mellitus: results from a survey of country prevalence and practices. J Matern Fetal Neonatal Med. 2012;25(6):600-10. doi: 10.3109/14767058.2011.587921, PMID 21762003.

4. Chu SY, Abe K, Hall LR, Kim SY, Njoroge T, Qin C. Gestational diabetes mellitus: all Asians are not alike. Prev Med. 2009;49(2-3):265-8. doi: 10.1016/j.ypmed.2009.07.001, PMID 19596364.

5. Yuen L, Wong VW. Gestational diabetes mellitus: challenges for diff erent ethnic groups. World J Diabetes. 2015;6(8):1024-32. doi: 10.4239/wjd.v6.i8.1024, PMID 26240699.

6. Holemans K, Aerts l. Lessons from experimental research: lasting consequences of fetal development in an abnormal intra-uterine milieu. Eur Pract Gynecol Obstet Diabetes Pregnancy. 2004:124-39.

7. Desoye G, Myatt G. The placenta. Diabetes in women—adolescent, pregnancy, and menopause Reece EA, Coustan DR, Gabbe SG, editors. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 147-57. 3.

8. Desoye G, Shafrir E. The human placenta in diabetic pregnancy. Diabetes Rev. 1996;4:70-89.

9. Ana K M S, Karlla M N R, Raphaela M X,Wilzianne S R, Érika L R, Janaína VG, Rocha KM, Xavier RM, Ramalho WS, Rocha ÉL, Guimarães JV et alMacroscopic placental changes associated

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE02, 2023

with fetal and maternal events in diabetes mellitus. Clin (S Paulo). 2012;67(10):1203-8. doi: 10.6061/clinics/2012(10)13, PMID 23070348.

10. Chitme HR, Al Shibli SA, Al-Shamiry RM. Risk factors and plasma glucose profile of gestational diabetes in Omani women. Oman Med J. 2016;31(5):370-7. doi: 10.5001/omj.2016.73, PMID 27602192.

11. Klein P, Polidori D, Twito O, Jaffe A. Impaired decline in renal threshold for glucose during pregnancy – a possible novel mechanism for gestational diabetes mellitus. Diabetes Metab Res Rev. 2014;30(2):140-5. doi: 10.1002/dmrr.2474, PMID 24106177.

12. Gauster M. DG, Tötsch M, Hiden U the placenta and gestational diabetes mellitus. Current. 2011;12;614. Diabetes record:16-23.

13. Majumdar S, Dasgupta H, Bhattacharya K, Bhattacharya A. A study of placenta in normal and hypertensive pregnancies. J Anat Soc India. 2005;54(2):1-9.

14. Ranga MK, Sree S, Kumar KV, Adaline T, Vasantha MMC. Morphological variations of human placentae in preterm labor, pregnancy-induced hypertension, and gestational diabetes mellitus. Int J Sci Study. 2017;4(11).