

## Gestational Diabetes-Induced Alterations in Placental Morphology and Microarchitecture: A Quantitative Comparative Study

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### ABSTRACT

**Background:** Gestational Diabetes Mellitus (GDM) is a common pregnancy related disease. Diabetes mellitus affects 2.5% of pregnancies of which 65% are gestational diabetes mellitus and 35% are complicated by pre-existing diabetes mellitus. The placenta is an important organ serving as a connection between mother and growing fetus. This critical organ undergoes drastic modification in response to hyperglycemic condition. Previous studies have shown that GDM alters placental morphology, vascular patterns and histopathological features. However, a detailed comparative study of these parameters across different treatment modalities in GDM remain limited. This study aims to identify and analyze placenta changes associated with GDM across different treatment modalities.

**Objective:** To compare the changes in morphological, histopathological and vascular features between normal pregnancies and pregnancies complicated with GDM- classified by different treatment modalities as diet-controlled, tablet- treated or insulin- treated patients.

**Methods:** In our study we have analyzed 70 placentas 50 normal pregnancies and 20 GDM pregnancies across different modalities. Placental samples were collected from OBG department of Adichunchanagiri Institute of Medical Sciences, soon after the delivery, analyzed for morphometric (cotyledon number, weight, thickness), and vascular (umbilical vein/artery pattern), then tissue samples were taken for histopathological examination for different quantitative and qualitative parameters. Statistical analyses included independent t-tests, one-way ANOVA, and chi-square tests. Findings are presented in tables and graphs.

**Results:** Significant abnormalities were found in placental morphometry, architecture, and histopathology for GDM, most marked in insulin-treated cases. Magistral vascular patterns predominated in GDM groups. Syncytial knots, chorangiosis, and infarction emerged as qualitative discriminators.

**Conclusion:** Morphometric, vascular, and histopathological placental parameters are all significantly altered in GDM pregnancy. More severe changes were observed in the Insulin-treated patients. This suggest that the routine placental assessment can help us in stratifying the perinatal risk and modulate the treatment strategies in GDM patients

**KEY WORDS:** Gestational Diabetes Mellitus (GDM), Morphology, Magistral, Villi, Syncytial Knots, Chorangiosis.

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## INTRODUCTION

Gestational diabetes mellitus (GDM) is a very common disease during pregnancy which is globally affecting 2-10% of the pregnancies. GDM is characterized by intolerance to the Glucose which is first recognized during pregnancy [1]. In this condition the developing fetus is exposed to hypoxic stress which may lead to many adverse pregnancy outcomes such as premature delivery or pre-eclampsia. With the increased incidence of obesity there is an increased number of pregnancies diagnosed with GDM [2-4].

Placenta is a vital connection between mother and the fetus. The survival of the fetus completely depends on it [5]. Placenta word is derived from Latin word Plakos, which means cake [6]. The development of placenta occurs in three stages an early stage where there is continuous proliferation and differentiation of the trophoblast forming the primary villi. In the second stage villi undergoes branching and the villous core is filled with the mesoderm forming secondary villi, then the secondary villi are invaded by the embryonic blood vessels forming the tertiary villi. During the first half of pregnancy trophoblast undergoes drastic change while in the second half of pregnancy there will be an extensive angiogenesis and vascularization which leads to vascular remodeling and vascular stabilization [7,8].

GDM alters the intrauterine environment which affects the placental morphology, development and function leading to many fetomaternal complications [9]. It undergoes a significant adaptive changes in case of GDM. GDM management involves dietary modifications and drug therapy (tablets or insulin), when the Glycemic control cannot be achieved through dietary modifications alone. The effect of these treatment modalities on placenta morphology and histopathology is still poorly understood [10].

Understanding these relationship is important for preferring therapeutic approaches for improving pregnancy outcomes.

Previous research has reported many conflicting results about the placenta morphology in GDM patients like placenta weight and

number of cotyledons [11-13]. While in other studies they have given variable results depending on the treatment modalities and degree of glycemic control [14,15]. The systemic reviews have highlighted and suggested the need of more detailed comparative studies on morphological and histopathological parameters among the different treatment modalities in GDM patients [10,16].

In our study we are aiming to provide a comprehensive analysis on placental morphometry and histopathology between normal placenta and placenta of GDM patients managed with different treatment modalities.

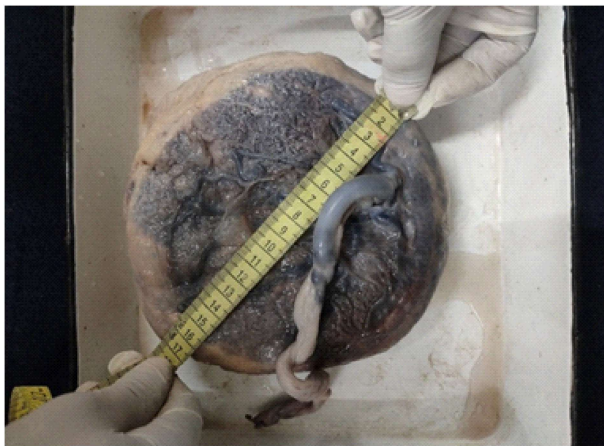
## MATERIALS AND METHODS

**Study Design and Participants:** This prospective observational study was conducted in the department of Anatomy Adichunchanagiri Institute of Medical Science, B G Nagara, Mandya, Karnataka from January 2023 to December 2024. The study included 70 placentae from singleton pregnancies: 50 Normal 20 GDM patients. The GDM placenta were further divided into 3 categories depending upon their treatment modalities: diet control (n=5), oral hypoglycemic tablets (n=8), and insulin therapy (n=7). The informed consent was taken from the study participants and Institutional Ethics committee approval was obtained (IEC letter number AIMS/IEC/030/2022 dated 12/04/2022).

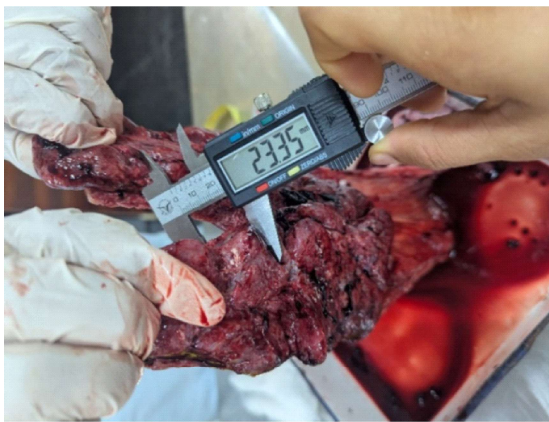
**Inclusion and Exclusion Criteria:** Inclusion criteria comprised singleton pregnancies delivered at term (37-42 weeks), confirmed GDM diagnosis according to International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for the study group, and normal glucose tolerance for controls. Exclusion criteria included multiple pregnancies, pregestational diabetes, pregnancies complicated with hypertension, congenital anomalies, and intrauterine growth restriction not related to GDM.

**Morphometric Analysis:** Placenta was collected from the OBG department immediately after delivery, placenta was stored in normal saline for half an hour, then taken for the gross examination. Placental weight was measured

using a calibrated digital scale. Placental diameter was measured in centimeter; two diameters were taken then the average of two measurements were taken for the study (**Figure 1**). Site of attachment of umbilical cord, pattern of distribution of umbilical vessels was observed. Cotyledon counting was performed systematically across the maternal surface. Central and peripheral thickness measurements were obtained using digital Vernier caliper at standardized locations [**17,18**]. (**Figure 2&3**).



**Fig. 1:**Measuring the diameter of the placenta.



**Fig, 2 & 3:** Measuring the central and peripheral thickness of the placenta using digital Vernier caliper

## Histopathological Examination

From each placenta three sections were taken i.e. central, paracentral and peripheral areas. Tissues were fixed in 10% formalin solution for 24 hours, and embedded in paraffin, blocks were made. 4-5  $\mu$ m thickness sections were taken from the blocks and stained with hematoxylin and eosin for routine histological examination [19,20].

Quantitative histomorphometric analysis was performed using light microscopy with digital image analysis. Parameters measured included villous count per high-power field, villous diameter and perimeter, trophoblast thickness, number of capillaries per villus, capillary diameter, and blood vessel wall thickness. At least 10 random fields were examined per case [21,22].

## Statistical Analysis

Data analysis was performed using SPSS version 26.0. Descriptive statistics were calculated for all variables. Independent samples t-tests were used to compare continuous variables between normal and GDM groups. Chi-square tests analyzed categorical variables including cord insertion site and vascular patterns. One-way ANOVA compared multiple groups (normal vs. different GDM treatment modalities) with post-hoc Tukey's test for pairwise comparisons. Statistical significance was set at  $p < 0.05$  [23,24].

## RESULTS

### Demographic and Treatment Modality Comparisons:

The study population comprised 70 participants with mean maternal age of  $28.4 \pm 4.2$  years in the normal group and  $29.8 \pm 3.9$  years in the GDM group ( $p=0.154$ ). Mean gestational age at delivery was significantly lower in GDM cases ( $37.8 \pm 1.4$  weeks) compared to normal pregnancies ( $39.2 \pm 1.1$  weeks) ( $p < 0.001$ ). ANOVA analysis across different treatment modalities within the GDM group revealed significant differences in gestational age at delivery ( $F=3.794$ ,  $p=0.031$ ). Diet-controlled GDM cases had the earliest delivery ( $36.4 \pm 1.5$  weeks), while tablet-treated cases delivered later ( $39.0 \pm 1.4$  weeks). This pattern

suggests that more intensive treatment may be associated with prolonged gestation, although the relationship requires further investigation.

Extended ANOVA comparing normal pregnancies with GDM treatment subgroups showed significant differences in placental weight (F=3.627, p=0.018), neonatal birth weight (F=8.104, p<0.001), and gestational age (F=11.890, p<0.001). These findings indicate that treatment modality influences pregnancy outcomes and placental characteristics.

Neonatal birth weight was significantly lower in the GDM group (2.6 ± 0.5 kg) compared to controls (2.9 ± 0.3 kg) (p=0.020).

**Morphometric Analysis Results:** Significant differences were observed in several key morphometric parameters between normal and GDM groups. The number of cotyledons was markedly elevated in GDM cases (21.3 ± 3.2) compared to normal pregnancies (14.6 ± 3.9) (p<0.001). Placental weight showed no significant difference between groups (694.39± 200.0 g in GDM vs. 682.6 ± 149.7 g in normal, p=0.81), but the placental weight across the GDM treatment groups and normal group shows a significant difference (p=0.012). **(Table 1)**

**Categorical Variable Analysis:** The categorical variable analysis (site of attachment of cord and vascular patterns of the umbilical vessels)

revealed a significant variation between GDM and Normal Pregnancies. Site of cord attachment showed significant differences ( $\chi^2=19.058$ , p=0.008), with GDM cases more commonly exhibiting eccentric cord insertion compared to the normal pregnancies where it showed predominantly central insertion of the cord.

Vascular pattern analysis demonstrated highly significant differences in both umbilical vein ( $\chi^2=52.519$ , p<0.001) and umbilical artery patterns ( $\chi^2=9.381$ , p=0.002). The GDM group exhibited magistral vascular patterns more predominantly than the dispersal pattern, while normal pregnancies exhibited dispersal patterns.

**Histopathological Findings:** Quantitative histopathological analysis revealed striking differences between GDM and normal placentas across all measured parameters. The number of villi per high-power field was significantly increased in GDM cases (152.2 ± 17.2) compared to normal pregnancies (118.5 ± 2.1) (p<0.001) **(Figure 4)**.

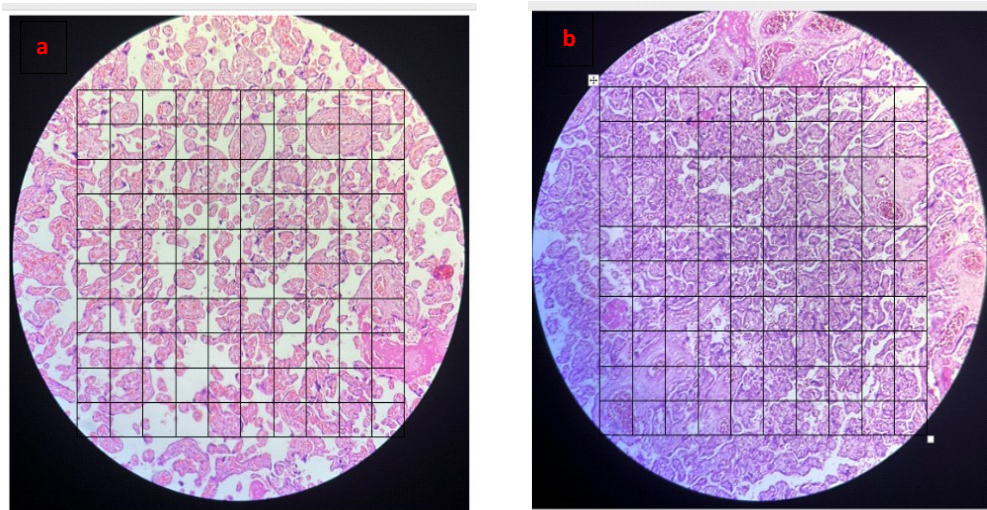
Villous diameter showed significant enlargement in GDM placentas (0.0785 ± 0.0114 mm vs. 0.0640 ± 0.0000 mm, p<0.001), Similarly, villous perimeter was significantly increased (0.331 ± 0.059 mm vs. 0.268 ± 0.018 mm, p<0.015), reflecting the overall enlargement of villous structures. **(Table 2, Graph 1&2)**

**Table 1:** Baseline and Morphometric Comparison between Normal and GDM Placentas, and GDM placenta with different treatment modalities.

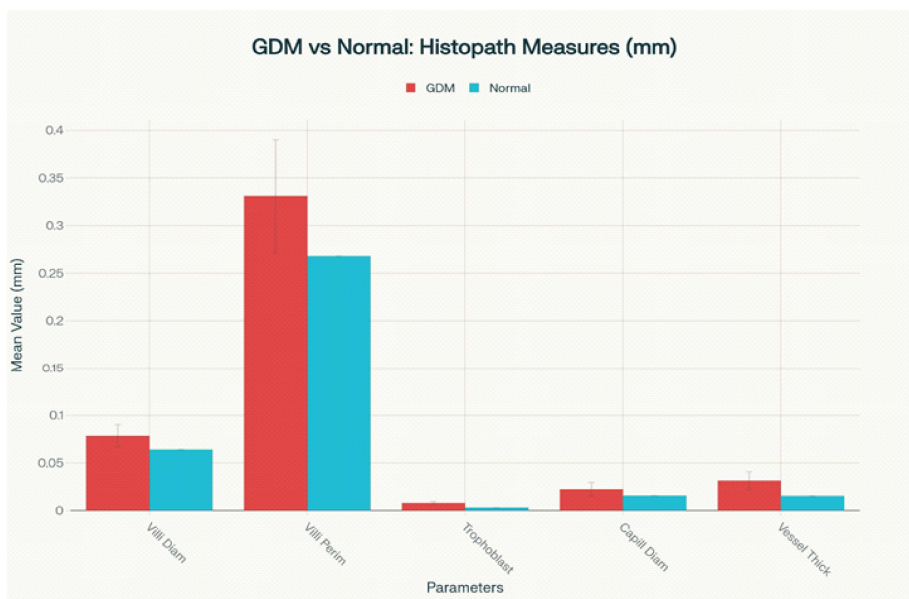
| Parameters               | Normal (n=50)   | GDM (overall) (n=20) | Diet controlled (n=5) | Oral-hypoglycemic (n=8) | Insulin treated (n=7) | ANOVA p-value |
|--------------------------|-----------------|----------------------|-----------------------|-------------------------|-----------------------|---------------|
| Cotyledon number         | 14.56 ± 3.89    | 21.3 ± 3.21          | 20.80 ± 3.49          | 20.62 ± 3.11            | 22.29 ± 3.35          | 0.001         |
| Placental weight (gms)   | 682.57 ± 149.66 | 684.27 ± 199.95      | 724.70 ± 138.85       | 563.69 ± 143.11         | 793.20 ± 235.08       | 0.049         |
| Placental thickness (cm) | 2.1 ± 0.46      | 2.66 ± 0.35          | 2.5 ± 0.46            | 2.6 ± 0.27              | 2.9 ± 0.38            | 0.007         |

**Table 2:** Showing the quantitative histopathological comparison between Normal and GDM with different treatment modalities.

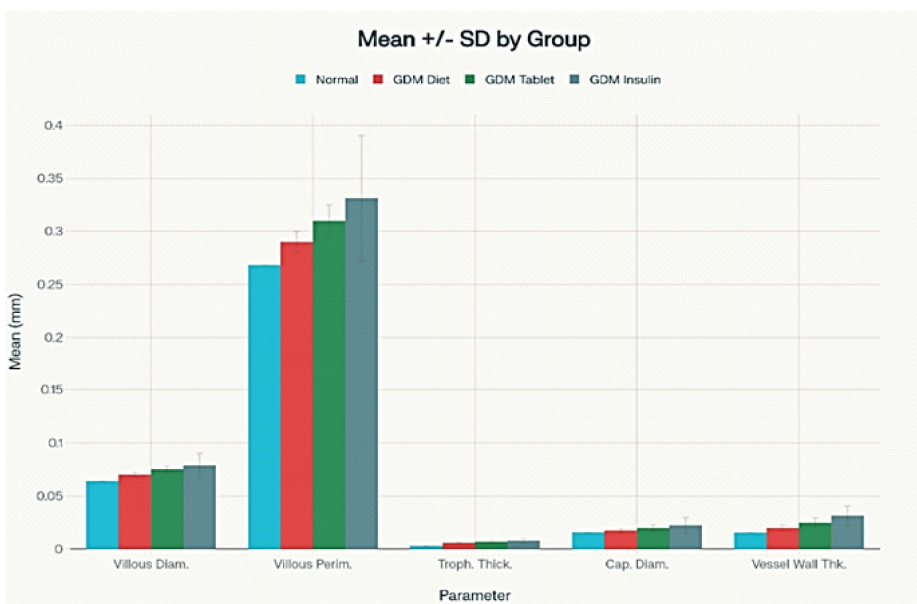
| Parameters                 | Normal           | Overall GDM    | GDM (Diet-controlled) | GDM (oral-hypoglycemic agent) | GDM (Insulin-treated) | ANOVA p-value |
|----------------------------|------------------|----------------|-----------------------|-------------------------------|-----------------------|---------------|
| Villi Count/HPF            | 125.7200 ± 8.273 | 152.2 ± 17.2   | 140 ± 10              | 145 ± 12                      | 152 ± 17.2            | 0.002         |
| Villous Diameter (mm)      | 0.0552 ± 0.007   | 0.079 ± 0.0114 | 0.070 ± 0.01          | 0.075 ± 0.003                 | 0.079 ± 0.0114        | 0.01          |
| Villous Perimeter (mm)     | 0.268 ± 0.018    | 0.33 ± 0.59    | 0.290 ± 0.29          | 0.310 ± 0.015                 | 0.331 ± 0.59          | 0.015         |
| Trophoblast Thickness (mm) | 0.0036 ± 0.0005  | 0.01 ± 0.002   | 0.006 ± 0.001         | 0.007 ± 0.0015                | 0.008 ± 0.002         | 0.005         |
| Capillary Count/Villus     | 10               | 22 ± 2.5       | 18 ± 1.8              | 20 ± 2                        | 22 ± 2.5              | 0.001         |
| Capillary Diameter (mm)    | 0.0164 ± 0.0007  | 0.022 ± 0.01   | 0.018 ± 0.002         | 0.020 ± 0.003                 | 0.022 ± 0.007         | 0.02          |
| Vessel Wall Thickness (mm) | 0.0153 ± 0.0004  | 0.031 ± 0.01   | 0.020 ± 0.003         | 0.025 ± 0.004                 | 0.031 ± 0.009         | 0.008         |



**Fig. 4:** a. H&E 10X stained slide of normal placenta with the grid for counting the number of villi  
b. H&E 10X stained slide of GDM placenta with the grid for counting the number of villi



**Graph 1:**Quantitative Histopathological parameter comparison between GDM and Normal groups showing significantly elevated values in GDM cases (all  $p < 0.01$ ).



**Graph 2:**Quantitative Histopathological parameter comparison between Normal and GDM with different treatment modalities showing significantly elevated values in GDM cases (all  $p < 0.01$ )

**Table 3:** Showing the qualitative histopathological comparison between Normal and GDM with different treatment modalities.

| Parameter                      | Normal (%) | GDM Diet (%) | GDM Tablet (%) | GDM Insulin (%) | Chi-square p-value |
|--------------------------------|------------|--------------|----------------|-----------------|--------------------|
| Syncytial Knots (More)         | 0          | 100          | 100            | 100             | 0.0001             |
| Chorangiosis (Present)         | 0          | 100          | 100            | 100             | 0.0001             |
| Villous Immaturity (Present)   | 0          | 100          | 67             | 33              | 0.002              |
| Villous Edema (Present)        | 0          | 50           | 33             | 33              | 0.01               |
| Fibrinoid Necrosis (Present)   | 0          | 0            | 63             | 86              | 0.005              |
| Nucleated Fetal RBCs (Present) | 0          | 40           | 75             | 57              | 0.001              |
| Infarction (Present)           | 0          | 100          | 100            | 100             | 0.0001             |
| Calcification (Present)        | 25         | 40           | 40             | 40              | 0.45               |

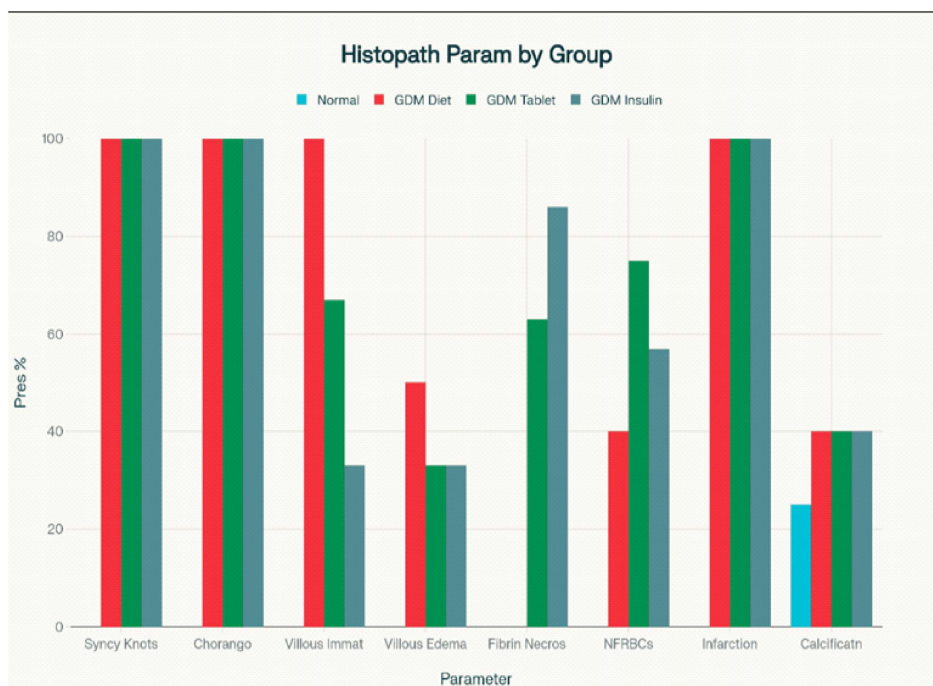
Trophoblast thickness demonstrated the most dramatic difference, with GDM cases showing values of  $0.008 \pm 0.002$  mm compared to  $0.003 \pm 0.000$  mm in normal pregnancies ( $p < 0.001$ ). Vascular parameters also showed significant alterations, with capillary diameter increased in GDM cases ( $0.0224 \pm 0.0072$  mm vs.  $0.0156 \pm 0.0000$  mm,  $p = 0.002$ ) and blood vessel wall thickness significantly elevated ( $0.0313 \pm 0.0094$  mm vs.  $0.0153 \pm 0.0000$  mm,  $p < 0.001$ ).

### Qualitative Histopathological Features

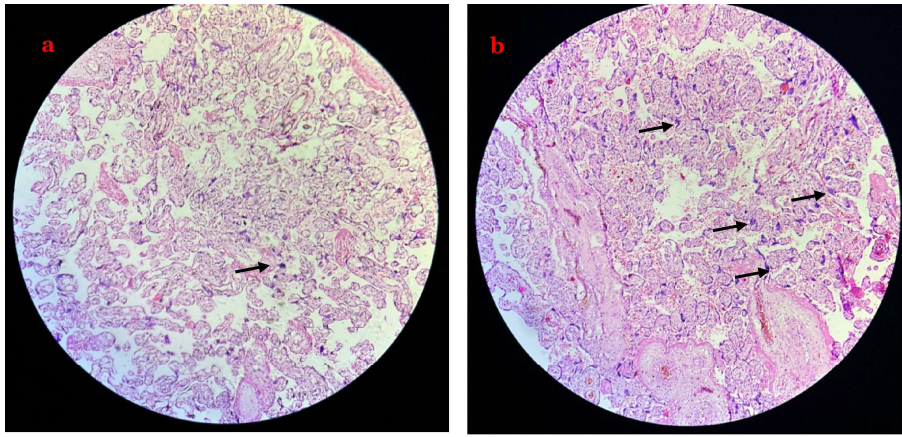
Categorical histopathological analysis revealed several important differences between GDM

and normal placentas. Syncytial knot formation was universally increased in GDM cases (“more” in 100% vs. “less” in 100% of normal cases), indicating accelerated placental maturation and potential hypoxic stress (Figure 5 a&b).

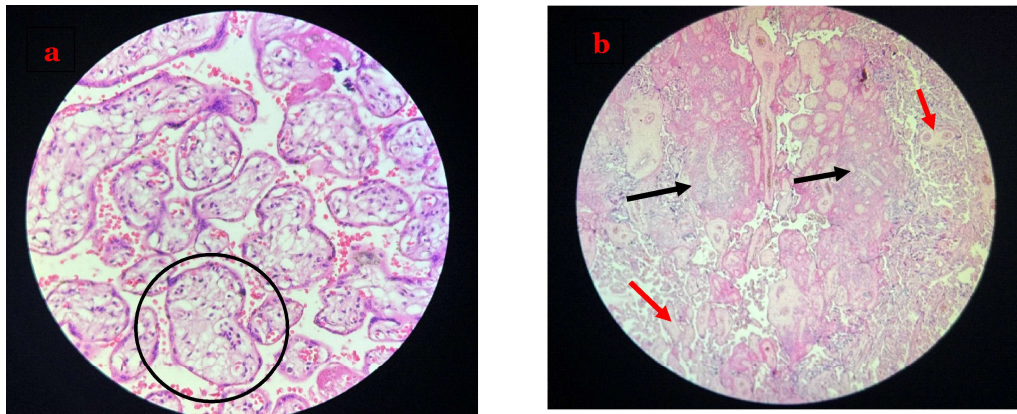
Chorangiosis, characterized by increased villous capillarization, was present in all GDM cases but absent in normal pregnancies, supporting the concept of adaptive angiogenesis in response to metabolic stress. (Figure 6 a & b, Table 3, Graph 3)



**Graph 3:** Qualitative Histopathological parameter comparison between Normal and GDM with different treatment modalities showing significantly elevated values in GDM cases (all  $p < 0.01$ )



**Fig. 5:** a. H&E stained slide of normal placenta with less syncytial knots and more intervillous space  
b. H&E stained slide of GDM placenta with increased syncytial knots and decreased intervillous space



**Fig. 6:** a. H&E 40X stained slide of GDM placenta showing Chorangiosis  
b. H&E 10X stained slide of GDM placenta showing extravillous fibrinoid (red arrow) and calcification (black arrow)

## DISCUSSION

The present study affirms that GDM induces consistent and measurable changes and abnormalities in placental morphometry (elevated cotyledon number, weight, thickness), vascular architecture (dominant magistral vein/artery patterns), and histopathological features. The Insulin-treated GDM cases exhibit the greatest deviations, suggesting a dose-response relationship between disease severity/intervention and placental remodeling [17,18].

Mean gestational age at delivery was significantly lower in GDM cases ( $37.8 \pm 1.4$  weeks) compared to normal pregnancies ( $39.2 \pm 1.1$  weeks) ( $p < 0.001$ ) this finding is in accordance with the studies done by George Daskalakis et.al [25]. This association may be due to chronic inflammation, oxidative stress, and altered prostaglandin metabolism in the diabetic environment.

Interestingly, our study found significantly lower neonatal birth weights in the GDM group ( $2.6 \pm 0.5$  kg) compared to controls ( $2.9 \pm 0.3$  kg) ( $p = 0.020$ ) this finding differs from the other studies. Although macrosomia is commonly associated with poorly controlled gestational diabetes mellitus (GDM), this outcome is not always observed [26,27].

This finding likely reflects the effectiveness of treatment interventions in preventing excessive fetal growth, and possibly indicates a degree of growth restriction in some cases due to placental vascular compromise. Recent studies have similarly reported that well-controlled GDM may be associated with appropriate-for-gestational-age or even small-for-gestational-age births [25].

Comparing normal pregnancies with GDM treatment subgroups showed significant differences in placental weight, neonatal birth weight, and gestational age. These findings indicate that treatment modality influences

pregnancy outcomes and placental characteristics. (Comparison)

Number of cotyledons and thickness of placenta was significantly increased with values approximately 46% higher than normal controls. This finding aligns with previous reports demonstrating increased cotyledon number as a consistent feature of diabetic placentas [12,13,15]. Previous studies have reported an increased placental weight in GDM patients but in our study the results are contradictory to others. This contrasting result may reflect the relatively good glycemic control achieved in our study population through appropriate treatment methods [28,29].

In the present study the site of attachment of umbilical cord and vascular pattern presented a significant variation between GDM and normal study population. In GDM patients the umbilical cord was eccentrically attached. The GDM patients exhibited predominantly magistral type of vascular distribution, these changes may reflect adaptive responses to the altered metabolic environment in GDM patients [30-33]. These pattern changes could have functional implications for placental blood flow and resistance [32].

Histopathological changes have provided a better understanding of the fundamental cellular mechanism and placental dysfunctions associated with GDM cases. In the present study the significant increase in villous number, diameter and thickness of trophoblast suggests compensatory hypertrophy and hyperplasia in response to hypoxic stress in GDM cases [34-36]. These changes depict the placental attempt to maintain the proper fetomaternal exchange.

Chorangiomas were uniformly observed in all GDM placentas which represent the adaptive response to metabolic stress and hypoxic condition. Previous studies have proved that chorangiomas are associated with maternal diabetes and it also acts as a compensatory mechanism to improve nutrient and oxygen delivery to the fetus [17,37].

The analysis on different treatment modalities revealed that diet-controlled cases had

earliest delivery and also had different placental characteristics compared to pharmacologically treated cases. This suggests that the type of treatment may also influence the placental modification and gestational age [37-38]. However, the studies with larger numbers would strongly confirm these relationships.

The clinical implications of these findings are significant for obstetric management and counseling. The consistent morphometric and histopathological changes observed in GDM placentas may serve as markers for placental dysfunction and guide monitoring strategies. Additionally, understanding these changes may help predict pregnancy outcomes and guide timing of delivery decisions.

The study was limited by a comparably less number of sample sizes for each subgroup. Additional study on molecular correlations like certain biomarkers, gene expression could have clarified the molecular reasons behind these placental changes.

## CONCLUSION

Our comprehensive study provides a significant insight on the morphometric and histopathological changes in placenta of GDM pregnancies in comparison with the normal pregnancies. The changes observed in the study persist in all GDM cases despite of different treatment modalities and it may represent the adaptive response to the diabetic intrauterine environment.

The parameters observed in our study may serve as biomarkers for assessing placental function in GDM patients. This can also be incorporated as a clinical assessment protocol. Continued research in this area will enhance our ability to predict and prevent adverse outcomes in pregnancies complicated by gestational diabetes mellitus.

We have also observed the difference in placental characteristics across the treatment modalities suggesting that better therapeutic approaches can influence the placenta and pregnancy outcomes, although further research is needed to establish definitive relationships.

This study has provided important implications for understanding GDM pathophysiology, guiding clinical management, and developing strategies to optimize maternal and fetal outcomes.

#### ABBREVIATIONS

**GDM** - Gestational Diabetes Mellitus

**OBG** – Obstetrics and Gynecology

**ANOVA** - Analysis of Variance

**IADPSG** - International Association of Diabetes and Pregnancy Study Groups

**SPSS** - Statistical Package for the Social Sciences

#### Author Contributions

**SKL:** Concept and design, acquisition, analysis, and interpretation of data, drafting of the manuscript, critical review of the manuscript for important intellectual content, accountable for all aspects of the work, review of the final version to be published and supervised the work

**YAB:** Drafting of the manuscript, critical review of the manuscript for important intellectual content, accountable for all aspects of the work and review of the final version to be published

**AN:** Drafting of the manuscript, critical review of the manuscript for important intellectual content, accountable for all aspects of the work and review of the final version to be published.

**THL:** Concept and design, critical review of the manuscript for important intellectual content, accountable for all aspects of the work, review of the final version to be published and supervised the work.

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**ETHICS APPROVAL:** This study was approved by the Institutional Ethical Committee of Adichunchanagiri Institute of Medical Sciences (IEC letter number AIMS/IEC/030/2022 dated 12/04/2022)

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**Conflicts of Interests: None**

#### REFERENCES

- [1]. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care*. 2010;33(3):676-82. <https://doi.org/10.2337/dc09-1848> PMID:20190296 PMCID:PMC2827530
- [2]. Sweeting A, Wong J, Murphy HR, et al. A clinical update on gestational diabetes mellitus. *Endocr Rev* 2022; 43: 763-793. <https://doi.org/10.1210/endrev/bnac003> PMID:35041752 PMCID:PMC9512153
- [3]. Casson IF, Clarke CA, Howard CV, McKendrick O, Pennycook S, Pharoah PO, et al. Outcomes of pregnancy in insulin dependent diabetic women: results of a five year population cohort study. *Br Med J*. 1997; 315: 275-8., <https://doi.org/10.1136/bmj.315.7103.275> PMID:9274545 PMCID:PMC2127202
- [4]. Mondestin MAJ, Ananth CV, Smulian JC, Vintzileos AM. Birth weight and fetal death in the United States: the effect of maternal diabetes during pregnancy. *Am J Obstet Gynecol*. 2002; 187: 922-6. <https://doi.org/10.1067/mob.2002.127458> PMID:12388978
- [5]. Udainia A, Jain ML. Morphological study of placenta in pregnancy induced hypertension with its clinical relevance. *J Anat Soc India*. 2001;50:24-7.
- [6]. Huppertz B, Kingdom J.C.P. The placenta and Foetal membranes In :Edmond DK editor. *Dew hurts Text book of Gynaecology and Obstetrics*. 7th ed. London: Blackwell the d publisher;2007.p.19-25.
- [7]. Kaufmann P, Mayhew TM, Charnock-Jones DS, Aspects of human fetoplacental vasculogenesis and angiogenesis. II. Changes during normal pregnancy, *Placenta*, 2004, 25(2-3):114-126. <https://doi.org/10.1016/j.placenta.2003.10.009> PMID:14972444
- [8]. Mayhew TM, Fetoplacental angiogenesis during gestation is biphasic, longitudinal and occurs by proliferation and remodeling of vascular endothelial cells, *Placenta*, 2002, 23(10):742-750.
- [9]. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008;358(19):1991-2002. <https://doi.org/10.1056/NEJMoa0707943> PMID:18463375
- [10]. Carrasco-Wong I, Moller A, Giachini FR, Lima VV, Toledo F, Stojanova J, et al. Placental structure in gestational diabetes mellitus. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(2):165535. <https://doi.org/10.1016/j.bbadis.2019.165535> PMID:31442531 PMCID:PMC9477341
- [11]. Desoye G, Hauguel-de Mouzon S. The human placenta in gestational diabetes mellitus. The insulin and cytokine network. *Diabetes Care*. 2007;30 Suppl 2:S120-6. <https://doi.org/10.2337/dc07-s203> PMID:17596459
- [12]. Hiden U, Glitzner E, Hartmann M, Desoye G. Insulin and the IGF system in the human placenta of normal and diabetic pregnancies. *J Anat*. 2009;215(1):60-8. <https://doi.org/10.1111/j.1469-7580.2008.01035.x> PMID:19467150 PMCID:PMC2714639
- [13]. Edu A, Teodorescu C, Dobjanschi CG, Socol ZZ, Teodorescu V, Matei A, et al. Placenta changes in pregnancy with gestational diabetes. *Rom J Morphol Embryol*. 2016;57(2):507-12.

- [14]. Huynh J, Xiong G, Bentley-Lewis R. A systematic review of metabolite profiling in gestational diabetes mellitus. *Diabetologia*. 2014;57(12):2453-64. <https://doi.org/10.1007/s00125-014-3371-0> PMID:25193282 PMCID:PMC4221524
- [15]. Mitanchez D, Yzydorczyk C, Siddeek B, Boubred F, Benahmed M, Simeoni U. The offspring of the diabetic mother—short- and long-term implications. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(2):256-69. <https://doi.org/10.1016/j.bpobgyn.2014.08.004> PMID:25267399
- [16]. Ornoy A, Reece EA, Pavlinkova G, Kappen C, Miller RK. Effect of maternal diabetes on the embryo, fetus, and children: congenital anomalies, genetic and epigenetic changes and developmental outcomes. *Birth Defects Res C Embryo Today*. 2015;105(1):53-72. <https://doi.org/10.1002/bdrc.21090> PMID:25783684
- [17]. American Diabetes Association. Management of diabetes in pregnancy: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):S200-S210. <https://doi.org/10.2337/dc21-S014> PMID:33298425
- [18]. Brown J, Alwan NA, West J, Brown S, McKinlay CJ, Farrar D, et al. Lifestyle interventions for the treatment of women with gestational diabetes. *Cochrane Database Syst Rev*. 2017;5(5):CD011970. <https://doi.org/10.1002/14651858.CD011970.pub2> PMID:28472859
- [19]. Lowe WL Jr, Scholtens DM, Lowe LP, Kuang A, Nodzenski M, Talbot O, et al. Association of Gestational Diabetes With Maternal Disorders of Glucose Metabolism and Childhood Adiposity. *JAMA*. 2018;320(10):1005-1016. <https://doi.org/10.1001/jama.2018.11628> PMID:30208453 PMCID:PMC6143108
- [20]. Rodrigues P, Furtado J, Sarmiento P, Santos AC, Almeida MC. Microscopic changes and gross morphology of placenta in women with gestational diabetes mellitus under dietary control: A systematic review. *Placenta*. 2025;156:1-9.
- [21]. Elamin A, Mohammed Ahmed M, El Elhaj A, Ahmed Hussien T, Abdelrahman Mohamed A, Mohamed H, et al. Vicissitudes in the placental cotyledon number in a singleton pregnancy with gestational diabetes. *Int J Appl Basic Med Res*. 2022;12(1):24-28. [https://doi.org/10.4103/ijabmr.ijabmr\\_230\\_21](https://doi.org/10.4103/ijabmr.ijabmr_230_21) PMID:35265477 PMCID:PMC8848564
- [22]. Khaskheli MN, Baloch S, Baloch A. Effect of gestational diabetes mellitus on placental morphology. *Pakistan J Med Health Sci*. 2013;7(3):632-636.
- [23]. Sharmila T, Gunapriya R, Jaya V. Morphometric study of placenta in gestational diabetes and its correlation with fetal outcome. *J Clin Diagn Res*. 2017;11(2):AC05-AC08.
- [24]. Daskalakis G, Marinopoulos S, Krielesi V, Papapanagiotou A, Papantoniou N, Mesogitis S, et al. Placental pathology in women with gestational diabetes. *Acta Obstet Gynecol Scand*. 2008;87(4):403-7. <https://doi.org/10.1080/00016340801908783> PMID:18382864
- [25]. Go M. Gestational Diabetes Mellitus and Associated Placental Histopathology: A Narrative Literature Review. *Brown Public Health J*. 2024;4(1):1-12.
- [26]. Mayhew TM, Sorensen FB, Klebe JG, Jackson MR. The effects of mode of delivery and sex of newborn on placental morphology in control and diabetic pregnancies. *J Anat*. 1993;183(Pt 3):545-52.
- [27]. Salafia CM, Zhang J, Charles AK, Bresnahan M, Shrout P, Sun W, et al. Placental characteristics and birthweight. *Paediatr Perinat Epidemiol*. 2008;22(3):229-39. <https://doi.org/10.1111/j.1365-3016.2008.00935.x> PMID:18426518
- [28]. Khong TY, Mooney EE, Ariel I, Balmus NC, Boyd TK, Brundler MA, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. *Arch Pathol Lab Med*. 2016;140(7):698-713. <https://doi.org/10.5858/arpa.2015-0225-CC> PMID:27223167
- [29]. Roberts DJ, Post MD. The placenta in pre-eclampsia and intrauterine growth restriction. *J Clin Pathol*. 2008;61(12):1254-60. <https://doi.org/10.1136/jcp.2008.055236> PMID:18641412
- [30]. Jarmuzek P, Wielgos M, Bomba-Opon D. Placental pathologic changes in gestational diabetes mellitus. *Neuro Endocrinol Lett*. 2015;36(2):101-5.
- [31]. Mayhew TM. A stereological perspective on placental morphology in normal and complicated pregnancies. *J Anat*. 2009;215(1):77-90. <https://doi.org/10.1111/j.1469-7580.2008.00994.x> PMID:19141109 PMCID:PMC2714641
- [32]. Altman DG, Bland JM. Statistics notes: the normal distribution. *BMJ*. 1995;310(6975):298. <https://doi.org/10.1136/bmj.310.6975.298> PMID:7866172 PMCID:PMC2548695
- [33]. Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE, et al. The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes. *Diabetes Care*. 2012;35(4):780-6. <https://doi.org/10.2337/dc11-1790> PMID:22357187 PMCID:PMC3308300
- [34]. Higgins L, Greenwood SL, Wareing M, Sibley CP, Mills TA. Obesity and the placenta: A consideration of nutrient exchange mechanisms in relation to aberrant fetal growth. *Placenta*. 2011;32(1):1-7. <https://doi.org/10.1016/j.placenta.2010.09.019> PMID:21030077

- [35]. Raio L, Ghezzi F, Di Naro E, Buttarelli M, Franchi M, Dürig P, et al. Umbilical cord insertion in gestational diabetes. *Arch Gynecol Obstet.* 2002;267(1):61-3.
- [36]. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med.* 2005;352(24):2477-86. <https://doi.org/10.1056/NEJMoa042973> PMID:15951574
- [37]. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;1(8476):307-10. [https://doi.org/10.1016/S0140-6736\(86\)90837-8](https://doi.org/10.1016/S0140-6736(86)90837-8)
- [38]. Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD. Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. *Diabetologia.* 2016;59(7):1396-9. <https://doi.org/10.1007/s00125-016-3985-5> PMID:27174368 PMID:PMc6364673

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