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Morphological Alterations Of The Placenta In Pregnant Women With Diabetes Mellitus: Pathophysiological Insights And Clinical Implications

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Abstract

Diabetes mellitus during pregnancy, including pregestational and gestational forms, is associated with significant structural and functional alterations in the placenta, which may adversely affect maternal and fetal outcomes. The placenta, as a critical interface between mother and fetus, undergoes adaptive as well as pathological changes in response to hyperglycemic intrauterine environments. This study aims to comprehensively analyze the morphological changes observed in placental tissues of diabetic pregnancies, with a focus on recent advances in histopathological and ultrastructural findings.

Chronic maternal hyperglycemia induces a cascade of metabolic and vascular disturbances, including oxidative stress, endothelial dysfunction, and inflammatory activation, which collectively contribute to placental remodeling. Common morphological features include villous immaturity, increased syncytial knots, thickening of the basement membrane, fibrinoid necrosis, chorangiosis, and enhanced angiogenesis. Additionally, alterations in trophoblastic proliferation and apoptosis have been reported, suggesting impaired placental development and function.

Recent studies utilizing advanced imaging and molecular techniques have revealed that diabetic placentas often exhibit dysregulated expression of growth factors, such as vascular endothelial growth factor (VEGF), and increased deposition of extracellular matrix components. These changes may lead to reduced placental efficiency, contributing to complications such as

fetal macrosomia, intrauterine growth restriction, and preeclampsia.
Furthermore, the severity of placental morphological changes appears to correlate with the degree of glycemic control, highlighting the importance of early diagnosis and effective management of diabetes during pregnancy. Understanding these structural alterations provides valuable insights into the pathophysiology of diabetic pregnancies and may guide the development of targeted therapeutic strategies.
In conclusion, placental morphology in diabetic pregnancies reflects a complex interplay between metabolic, vascular, and inflammatory factors. Detailed morphological assessment of the placenta can serve as an important tool for predicting adverse perinatal outcomes and improving clinical management.

Keywords: Diabetes mellitus, gestational diabetes, placenta, placental morphology, histopathology, trophoblast, villous structure, hyperglycemia, angiogenesis, chorangiosis, oxidative stress, fetal outcomes

Introduction

Diabetes mellitus represents one of the most common metabolic disorders complicating pregnancy worldwide, with an increasing prevalence driven by rising rates of obesity and sedentary lifestyles. It encompasses both pregestational diabetes mellitus (type 1 and type 2) and gestational diabetes mellitus (GDM), the latter being defined as glucose intolerance with onset or first recognition during pregnancy. Regardless of the type, maternal hyperglycemia has profound effects on placental development, structure, and function.

The placenta plays a central role in maintaining fetal homeostasis by regulating nutrient exchange, gas transfer, hormone production, and immunological protection. As a highly dynamic organ, it adapts continuously to changes in the maternal environment. However, in the presence of chronic hyperglycemia, these adaptive mechanisms may become dysregulated, leading to structural and functional abnormalities that compromise placental efficiency.

Hyperglycemia-induced metabolic disturbances contribute to oxidative stress, inflammation, and endothelial dysfunction, all of which are key drivers of placental pathology. These processes affect the villous architecture, vascular network, and trophoblastic integrity of the placenta. Previous studies have documented a wide range of morphological alterations in diabetic pregnancies, including villous

immaturity, thickened basement membranes, increased syncytial knot formation, fibrinoid deposition, and abnormal angiogenesis. Such changes may impair maternal-fetal exchange and are associated with adverse pregnancy outcomes, including fetal macrosomia, intrauterine growth restriction, preeclampsia, and stillbirth.

Recent advances in histopathology, immunohistochemistry, and molecular biology have enhanced our understanding of the mechanisms underlying placental changes in diabetes. In particular, the role of growth factors, cytokines, and signaling pathways involved in angiogenesis and cellular turnover has gained significant attention. Despite these developments, there remains a need for comprehensive and integrative studies that correlate morphological findings with clinical parameters and pregnancy outcomes.

Therefore, this study aims to investigate the morphological alterations of the placenta in pregnancies complicated by diabetes mellitus, with an emphasis on histopathological features and their clinical relevance. By providing a detailed analysis of placental changes, this research seeks to contribute to a better understanding of the pathophysiological mechanisms involved and to support improved diagnostic and therapeutic approaches in diabetic pregnancies.

Materials and Methods

This comparative observational study was conducted at the Departments of Obstetrics and Gynecology and Pathological Anatomy of a tertiary medical institution over a two-year period (2023–2025). The aim of the study was to evaluate morphological changes in placentas obtained from pregnancies complicated by diabetes mellitus and to compare them with those from normal pregnancies.

A total of 60 pregnant women were included in the study. The participants were divided into two groups: 30 women diagnosed with diabetes mellitus (including both gestational and pregestational diabetes) and 30 healthy pregnant women serving as the control group. Only singleton pregnancies with a gestational age of 37 weeks or more were included. Women with multiple pregnancies, hypertensive disorders such as preeclampsia, infectious diseases, congenital fetal anomalies, or other systemic conditions were excluded from the study. Informed consent was obtained from all participants prior to inclusion.

Placental samples were collected immediately after delivery and subjected to detailed macroscopic examination. Parameters such as placental weight, diameter, thickness, umbilical cord insertion, and the presence of infarctions or calcifications

were recorded. Representative tissue samples measuring approximately 1–2 cm were taken from both central and peripheral regions of each placenta.

The collected tissues were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Sections of 4–5 µm thickness were prepared and stained with hematoxylin and eosin for general histological evaluation, as well as Periodic acid–Schiff stain for assessment of basement membrane changes. Microscopic examination focused on identifying key morphological features, including villous maturity, syncytial knot formation, basement membrane thickening, fibrinoid necrosis, chorangiosis, and vascular alterations.

Morphometric analysis was performed using light microscopy combined with digital image analysis software. Quantitative parameters such as villous diameter, capillary density per villus, and thickness of the trophoblastic basement membrane were measured in multiple high-power fields, and mean values were calculated for each case.

Statistical analysis was conducted using SPSS software (version XX). Quantitative data were expressed as mean ± standard deviation, while categorical variables were presented as percentages. Comparisons between the diabetic and control groups were performed using the independent sample t-test, and a p-value of less than 0.05 was considered statistically significant.

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board, and all procedures were performed with respect for patient confidentiality and safety.

Results

A total of 60 placentas were examined, including 30 from pregnancies complicated by diabetes mellitus and 30 from normal pregnancies. Both macroscopic and microscopic differences were identified between the two groups.

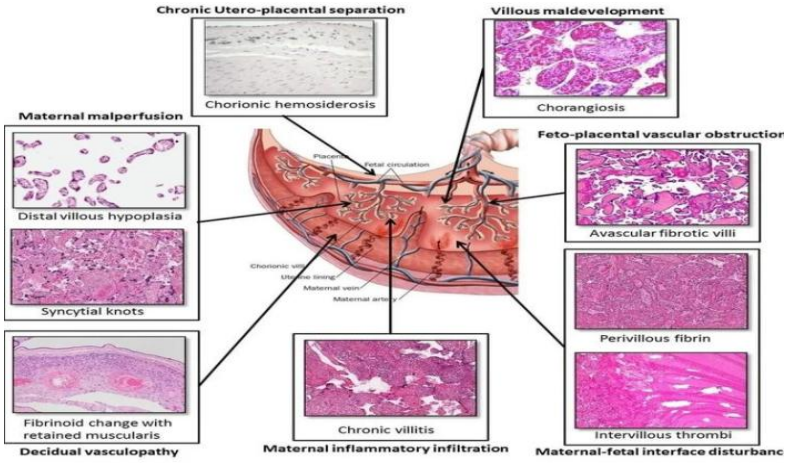
Macroscopically, placentas from the diabetic group demonstrated increased weight and thickness compared to the control group. Areas of calcification and infarction were more frequently observed in diabetic pregnancies.

Microscopic examination revealed significant structural alterations in placentas of diabetic mothers. These included villous immaturity, increased syncytial knot formation, thickening of the trophoblastic basement membrane, chorangiosis, and fibrinoid necrosis. Vascular changes such as capillary proliferation and congestion were also more prominent in the diabetic group.

Table 1. Morphological and Morphometric Parameters of the Placenta

Parameter	Diabetic Group (n=30)	Control Group (n=30)	p-value
Placental weight (g)	620 ± 85	480 ± 60	<0.01
Villous diameter (µm)	210 ± 25	180 ± 20	<0.05
Capillary density (/villus)	8.5 ± 1.2	6.2 ± 1.0	<0.01
Basement membrane thickness (µm)	6.8 ± 0.9	4.5 ± 0.7	<0.01
Syncytial knots (%)	35 ± 6	20 ± 5	<0.01
Chorangiosis (%)	40%	10%	<0.01

Quantitative analysis showed a statistically significant increase in placental weight, villous diameter, capillary density, and basement membrane thickness in the diabetic group compared to controls ($p < 0.05$). The frequency of syncytial knots and chorangiosis was also markedly higher in diabetic placentas.



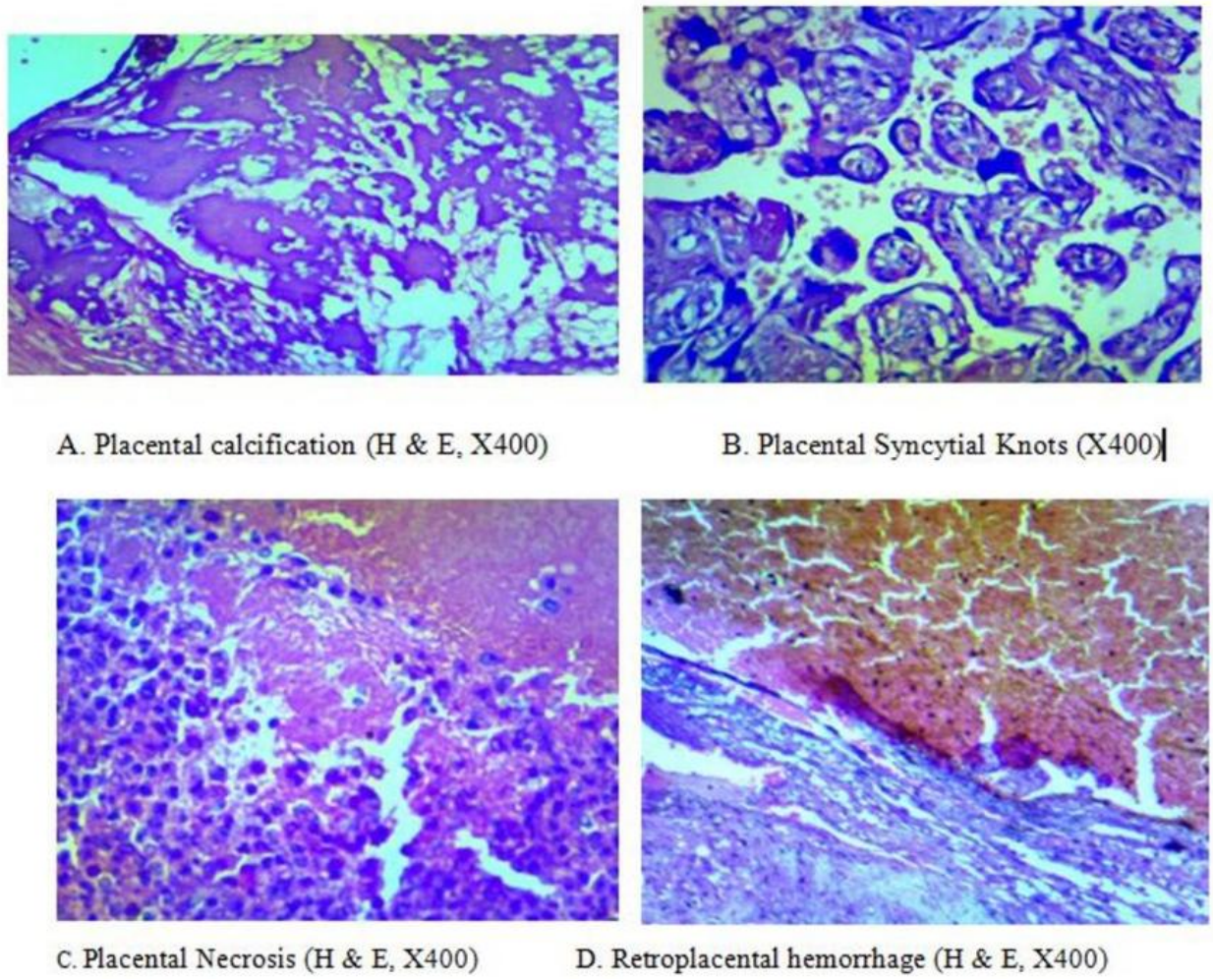


Figure 1. Histopathological Features of Diabetic Placenta

Figure description:

Histological sections of placental tissue from diabetic pregnancies show increased syncytial knot formation (A), thickened trophoblastic basement membrane (B), chorangiosis with increased capillary number (C), and immature villi (D) (H&E staining, high magnification).

Overall, the results indicate that diabetes mellitus during pregnancy is associated with significant morphological and morphometric alterations in placental structure. These changes may impair placental function and contribute to adverse fetal outcomes.

Discussion

The present study demonstrates that diabetes mellitus during pregnancy is associated with significant morphological and morphometric alterations in placental structure.

These findings support the concept that maternal hyperglycemia exerts profound effects on placental development and function, ultimately influencing fetal outcomes.

One of the key findings of this study was the increased placental weight observed in the diabetic group compared to controls. This is consistent with previous studies, which have reported placentomegaly as a compensatory response to chronic intrauterine hyperglycemia. The enlargement of the placenta may reflect an adaptive mechanism aimed at enhancing nutrient and oxygen transfer; however, such compensation is often insufficient and may be associated with functional impairment.

Histopathological examination revealed a higher prevalence of villous immaturity in diabetic placentas. This finding suggests delayed or abnormal maturation of placental villi, which can compromise the efficiency of maternal-fetal exchange. Similar observations have been reported in recent studies, where hyperglycemia disrupts normal trophoblastic differentiation and villous development.

Another significant observation in this study was the marked increase in syncytial knot formation in the diabetic group. Syncytial knots are considered indicators of placental stress and hypoxia. Their increased presence may reflect underlying oxidative stress and altered oxygen dynamics in diabetic pregnancies. This is in agreement with previous research indicating that oxidative stress plays a central role in the pathophysiology of diabetic placental changes.

The study also demonstrated significant thickening of the trophoblastic basement membrane in diabetic placentas. This structural alteration is likely a result of chronic hyperglycemia-induced accumulation of extracellular matrix components and glycoproteins. Basement membrane thickening may act as a barrier to efficient nutrient and gas exchange, thereby contributing to fetal complications.

Chorangiosis, characterized by an increased number of capillaries within the villi, was significantly more frequent in the diabetic group. This finding is indicative of chronic placental hypoxia and represents a compensatory angiogenic response. Increased capillary density, as observed in this study, further supports the presence of altered placental vascularization in diabetic pregnancies.

In addition, fibrinoid necrosis and vascular congestion were more commonly observed in the diabetic group, suggesting endothelial dysfunction and impaired placental circulation. These changes may further exacerbate placental insufficiency and are associated with adverse pregnancy outcomes such as fetal macrosomia, intrauterine growth restriction, and preeclampsia.

Importantly, the severity of morphological changes observed in this study appears to correlate with the degree of metabolic disturbance, highlighting the critical role of glycemic control during pregnancy. Early diagnosis and proper management of diabetes may reduce the extent of placental damage and improve both maternal and fetal outcomes.

Despite its strengths, this study has certain limitations. The relatively small sample size and the lack of molecular-level investigations may limit the generalizability of the findings. Future studies incorporating larger populations and advanced molecular techniques are recommended to further elucidate the mechanisms underlying placental alterations in diabetic pregnancies.

In conclusion, the findings of this study confirm that diabetes mellitus induces significant structural changes in the placenta, affecting both villous architecture and vascular components. These alterations reflect underlying pathophysiological processes and may serve as important indicators of placental dysfunction in diabetic pregnancies.

Conclusion

This study demonstrates that diabetes mellitus during pregnancy is associated with significant morphological and morphometric alterations in placental structure. Key findings include increased placental weight, villous immaturity, enhanced syncytial knot formation, thickening of the trophoblastic basement membrane, and a higher incidence of chorangiosis.

These structural changes reflect underlying metabolic, vascular, and hypoxic disturbances caused by maternal hyperglycemia and may compromise placental function. As a result, they contribute to an increased risk of adverse fetal outcomes, including macrosomia and intrauterine growth abnormalities.

The findings highlight the importance of strict glycemic control during pregnancy to minimize placental damage and improve perinatal outcomes. Furthermore, detailed histopathological examination of the placenta can serve as a valuable tool for understanding the severity of diabetic impact and guiding clinical management.

Future research incorporating larger sample sizes and molecular approaches is recommended to further elucidate the mechanisms of placental adaptation and injury in diabetic pregnancies.

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