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Placental Histomorphological and Radiological Changes and Their Association with Maternal Insulin Resistance in Gestational Diabetes Mellitus.

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ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) is associated with maternal metabolic disturbances, particularly insulin resistance, leading to structural and functional alterations in the placenta. These changes can be evaluated through histomorphological and radiological assessment.

Objective: To evaluate placental histomorphological and radiological changes in GDM and determine their association with maternal insulin resistance.

Methods: This comparative cross-sectional study included 80 pregnant women (40 diagnosed with GDM and 40 normoglycemic controls). Maternal insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Antenatal placental evaluation was performed using obstetric ultrasonography, assessing placental thickness, grading, and vascularity. Placental tissues were collected after delivery and examined histologically for villous immaturity, syncytial knots, fibrinoid necrosis, chorangiosis, and intervillous hemorrhage.

Results: Radiological assessment revealed significantly increased placental thickness in the GDM group (4.6 ± 0.7 cm) compared to controls (3.8 ± 0.5 cm, $p < 0.001$). Advanced placental grading (Grade III before 37 weeks) was observed in 42.5% of GDM cases versus 12.5% of controls ($p = 0.002$). Increased placental vascularity on Doppler was noted in 60% of GDM cases compared to 22.5% in controls ($p < 0.001$).

Histologically, syncytial knots were present in 72.5% of GDM placentae versus 32.5% of controls ($p < 0.001$), villous immaturity in 65% vs 27.5% ($p = 0.002$), chorangiosis in 55% vs 20% ($p = 0.001$), fibrinoid necrosis in 60% vs 25% ($p = 0.003$), and intervillous hemorrhage in 47.5% vs 17.5% ($p = 0.004$).

Mean HOMA-IR levels were significantly higher in the GDM group (4.8 ± 1.2) compared to controls (2.1 ± 0.9, $p < 0.001$). A strong positive correlation was observed between HOMA-IR and placental thickness ($r = 0.59$), vascularity ($r = 0.61$), syncytial knot density ($r = 0.62$), and villous immaturity ($r = 0.58$), all statistically significant ($p < 0.01$).

Conclusion: GDM is associated with significant radiological and histomorphological placental alterations, strongly correlated with maternal insulin resistance. Combined imaging and histological evaluation provides a comprehensive understanding of placental pathology in GDM and may aid in early identification of high-risk pregnancies and improved maternal-fetal outcomes.. .

Keywords: Gestational Diabetes Mellitus, Placenta, Histomorphology, Radiology, Insulin Resistance, HOMA-IR, Chorangiosis, Syncytial Knots

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a common metabolic disorder of pregnancy characterized by glucose intolerance and heightened maternal insulin resistance (1,2). The placenta, a transient yet vital organ, plays a central role in mediating nutrient exchange, hormonal signaling, and fetal growth (3). In GDM, chronic hyperglycemia and insulin resistance induce structural, vascular, and functional alterations in the placenta (2,4). These changes are largely driven by oxidative stress, inflammatory cytokine release, and endothelial dysfunction, which disrupt normal placental development and function (5,6). These alterations can be studied through histomorphological examination (microscopic tissue changes) and radiological imaging, particularly obstetric ultrasound and Doppler studies (7,8). Advances in imaging have enabled early detection of placental abnormalities, including altered thickness, premature maturation, and abnormal vascular patterns (8,9). Understanding these changes provides insight into fetal complications such as macrosomia, intrauterine hypoxia, preterm birth, and long-term metabolic risk, including childhood obesity and type 2 diabetes (10,11). Therefore, integrating structural, functional, and metabolic assessment of the placenta is essential for improving maternal and fetal outcomes (12).

Objectives

1. To evaluate placental histomorphological changes in GDM.
2. To assess radiological alterations in placental structure and vascularity.
3. To determine the association between these changes and maternal insulin resistance using Homeostatic Model Assessment of Insulin Resistance.

MATERIALS AND METHODS

This comparative cross-sectional study included a total of 80 pregnant women from a tertiary care hospital in Rawalpindi. Subjects were aged 20-40 years, delivered at 37+ weeks of gestation. They were divided into two groups: 40 women diagnosed with Gestational Diabetes Mellitus (GDM) and 40 normoglycemic pregnant women serving as controls. Mothers having comorbid conditions like hypertension, Hepatitis, HIV and pre diagnosed Diabetics (Type 1 & 2) were excluded from the study. Maternal insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index, calculated from fasting glucose and insulin levels. Antenatal placental evaluation was performed using obstetric ultrasonography, focusing on placental thickness, placental grading according to the Grannum classification, and Doppler-based assessment of placental vascularity. Following delivery, placental samples were collected, fixed in formalin, and processed for histopathological examination. Key histomorphological parameters evaluated included villous immaturity, syncytial knot formation, fibrinoid necrosis, chorangiosis, and intervillous hemorrhage. Statistical analysis was carried out using SPSS version 25, with continuous variables expressed as mean ± standard deviation and categorical variables presented as percentages. Pearson's correlation analysis was used to assess associations between HOMA-IR and placental parameters, and a p-value of less than 0.05 was considered statistically significant.

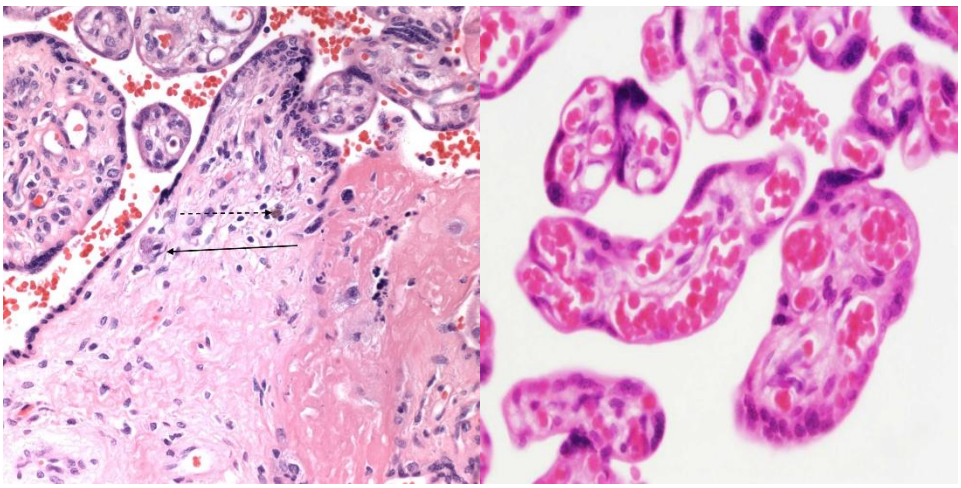
RESULTS

The figures demonstrate a progressive spectrum of placental changes from normal morphology to advanced pathological alterations in GDM. Figure 1 shows normal placental histology with well-formed chorionic villi, uniform capillary distribution, and minimal syncytial knot formation, indicating efficient placental function. Figure 2 illustrates early pathological changes in GDM, including increased syncytial knots and villous immaturity, reflecting hypoxic stress and delayed maturation. Figure 3 represents more advanced injury, demonstrating chorangiosis and fibrinoid necrosis, which indicate chronic hypoxia, excessive vascular proliferation, and placental damage. Moving to radiological findings, Figure 4 depicts a normal placenta on ultrasound with appropriate thickness and homogeneous echotexture. In contrast, Figure 5 shows increased placental thickness and premature Grade III maturation in GDM, suggesting accelerated placental aging. Figure 6 further demonstrates increased placental vascularity on Doppler imaging, reflecting compensatory hyperperfusion in response to metabolic stress. Together, Figures 1–6 provide a comprehensive visual correlation between structural, microscopic, and imaging changes in GDM.

The tabulated data further quantify and support these observations. Table 1 summarizes the radiological findings, showing

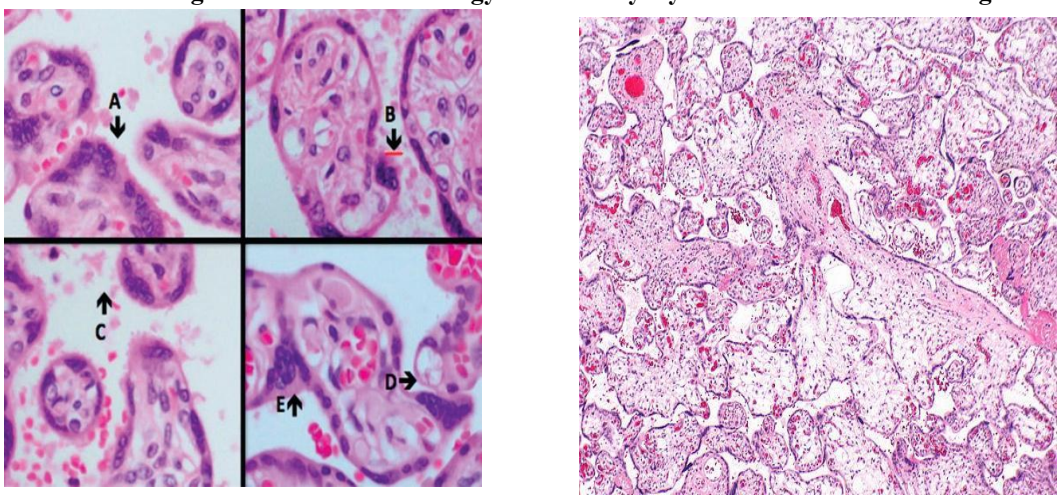
significantly increased placental thickness, a higher frequency of premature placental grading, and increased vascularity in GDM pregnancies, confirming early structural and hemodynamic alterations. Table 2 presents the histomorphological changes, demonstrating a significantly higher prevalence of syncytial knots, villous immaturity, chorangiosis, fibrinoid necrosis, and intervillous hemorrhage in GDM placentae, all of which reflect hypoxia, vascular compromise, and tissue injury. Table 3 highlights the significantly elevated HOMA-IR levels in the GDM group, confirming increased maternal insulin resistance. Finally, Table 4 shows a strong positive correlation between HOMA-IR and key placental parameters, including placental thickness, vascularity, syncytial knot density, and villous immaturity. Collectively, these results establish a clear association between maternal insulin resistance and both radiological and histological placental abnormalities, reinforcing its central role in the pathophysiology of placental dysfunction in GDM.

Figure 1: Normal Placental Histology (Control)



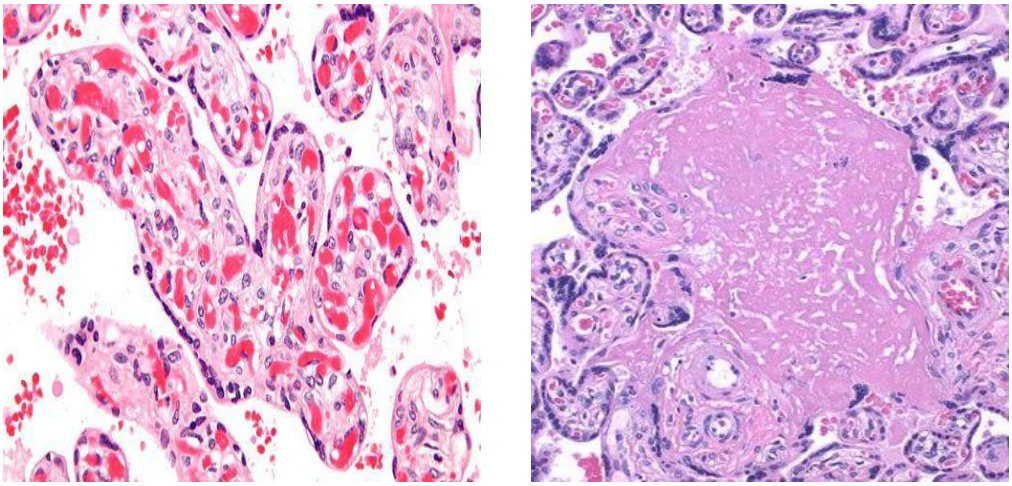
Photomicrograph of a normal placenta showing well-formed chorionic villi with uniform distribution of fetal capillaries, intact syncytiotrophoblast layer, and minimal syncytial knot formation (H&E stain, 40×).

Figure 2: Placental Histology in GDM: Syncytial Knots & Villous Changes



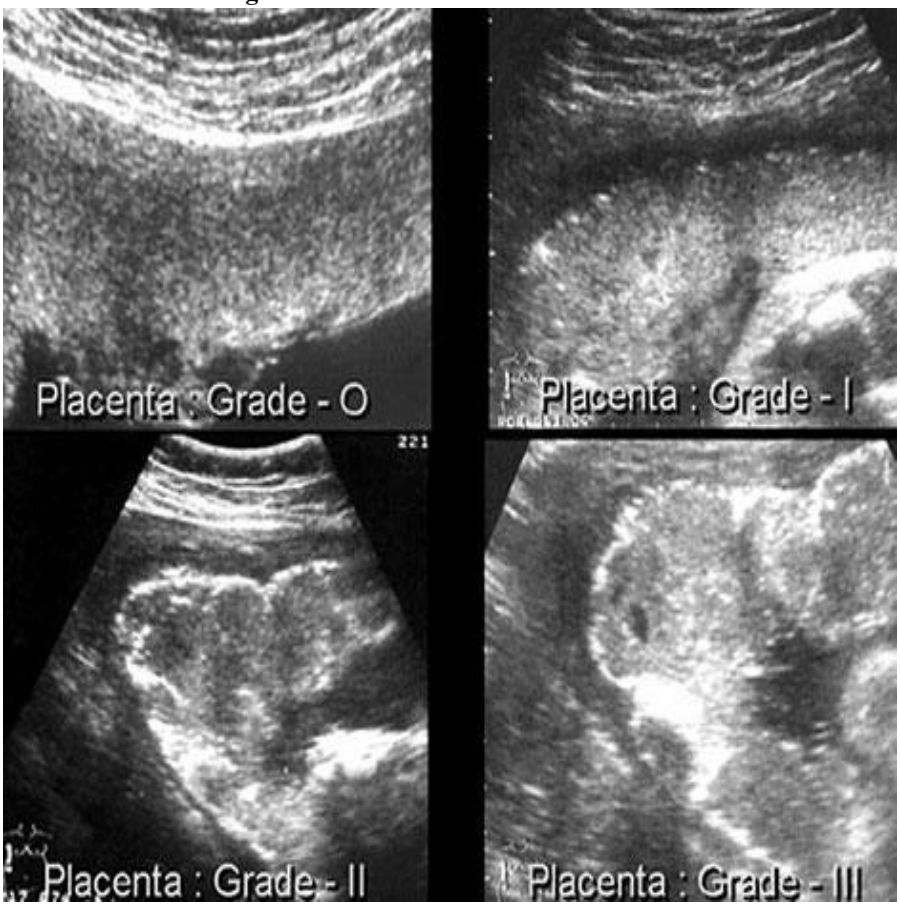
Placental section from GDM pregnancy showing increased syncytial knot formation, villous immaturity, and stromal edema. These features reflect hypoxic stress and altered placental maturation (H&E stain, 40×).

Figure 3: Chorangiosis and Fibrinoid Necrosis



Histological features of GDM placenta demonstrating chorangiosis (increased capillary proliferation within villi) and fibrinoid necrosis, indicating chronic hypoxia and vascular injury (H&E stain, 100×).

Figure 4: Ultrasound – Normal Placenta

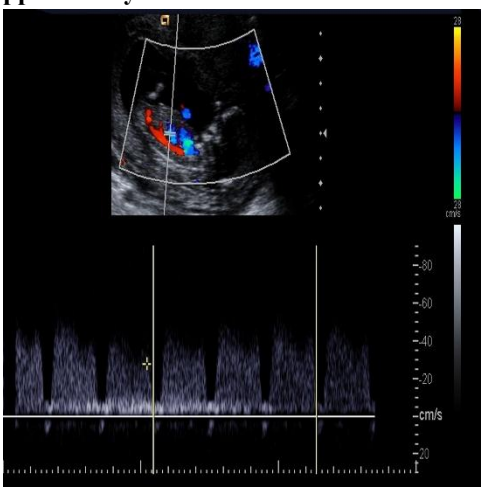


Obstetric ultrasound image of a normal placenta showing appropriate thickness, homogeneous echotexture, and normal grading corresponding to gestational age.

Figure 5: Ultrasound in GDM – Increased Thickness & Advanced Grading

Ultrasound image of placenta in GDM showing increased placental thickness and premature Grade III maturation with calcifications, indicating accelerated placental aging.

Figure 6: Doppler Study – Increased Placental Vascularity in GDM



Color Doppler ultrasound demonstrating increased placental vascularity in GDM pregnancy, reflecting compensatory hyperperfusion due to altered metabolic demands.

Table 1: Radiological Characteristics of Placenta in GDM and Control Groups

Parameter	GDM (n = 40)	Control (n = 40)	p-value
Placental Thickness (cm)	4.6 ± 0.7	3.8 ± 0.5	< 0.001
Advanced Placental Grading (Grade III <37 wks)	42.5%	12.5%	0.002
Increased Placental Vascularity (Doppler)	60%	22.5%	< 0.001

Table 2: Histomorphological Changes in Placenta

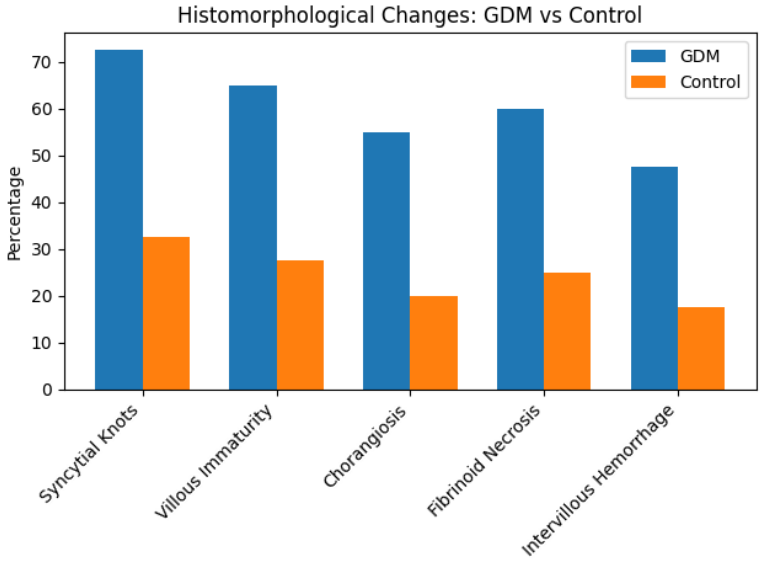
Parameter	GDM (n = 40)	Control (n = 40)	p-value
Syncytial Knots	72.5%	32.5%	< 0.001
Villous Immaturity	65%	27.5%	0.002
Chorangiosis	55%	20%	0.001
Fibrinoid Necrosis	60%	25%	0.003
Intervillous Hemorrhage	47.5%	17.5%	0.004

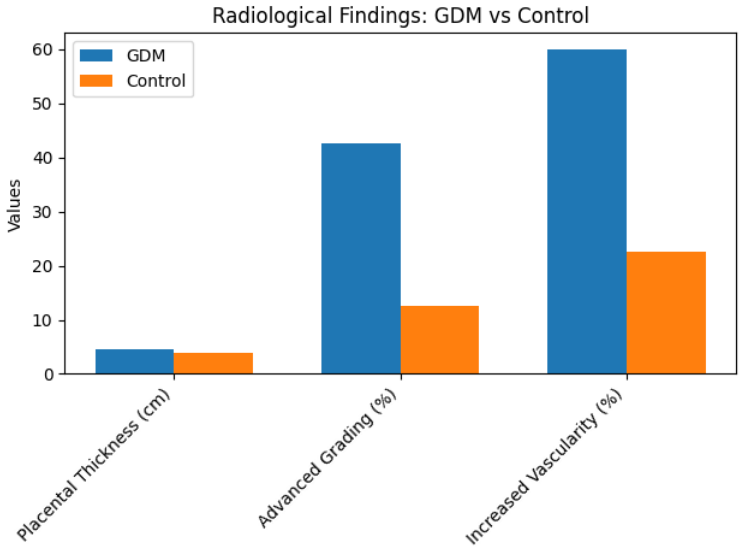
Table 3: Comparison of Insulin Resistance (HOMA-IR)

Parameter	GDM (n = 40)	Control (n = 40)	p-value
HOMA-IR	4.8 ± 1.2	2.1 ± 0.9	< 0.001

Table 4: Correlation of HOMA-IR with Placental Parameters

Variable	Correlation Coefficient (r)	p-value
Placental Thickness	0.59	< 0.01
Placental Vascularity	0.61	< 0.01
Syncytial Knot Density	0.62	< 0.01
Villous Immaturity	0.58	< 0.01





DISCUSSION

The present study demonstrates that GDM significantly affects placental morphology and function through mechanisms closely linked to insulin resistance. Hyperglycemia induces oxidative stress, mitochondrial dysfunction, and endothelial injury, leading to altered angiogenesis and impaired placental perfusion (5,6). These pathophysiological processes manifest

as both radiological and histological abnormalities (13).

Radiological findings such as increased placental thickness, premature maturation, and enhanced vascularity represent early, non-invasive indicators of placental dysfunction and may serve as useful screening tools in high-risk pregnancies (14). Histological features including chorangiosis, syncytial knots, villous immaturity, and fibrinoid necrosis reflect chronic hypoxia and compensatory adaptations to metabolic stress (13,14). The observed strong correlation between Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and placental changes highlights insulin resistance as a central pathogenic driver (2). These findings are consistent with recent literature demonstrating that maternal metabolic dysregulation adversely affects placental efficiency, fetal programming, and long-term offspring health outcomes (10,11,15). Early identification and management of insulin resistance may therefore play a critical role in reducing placental dysfunction and improving pregnancy outcomes (1,16).

Conclusion

Gestational Diabetes Mellitus (GDM) is associated with significant placental histomorphological and radiological changes linked to maternal insulin resistance. These alterations reflect metabolic and vascular disturbances that impair placental function. A combined approach using ultrasound and histopathology enables early detection, supports risk stratification, and allows timely intervention, ultimately helping to prevent adverse maternal and fetal outcomes and improve pregnancy prognosis.

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Authors' Contribution:

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Final Approval of Version: All authors approved the final version.

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