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Research Article

Placental Histomorphological Alterations Associated with Excessive Gestational Weight Gain

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Abstract

Background: Excessive gestational weight gain has been associated with adverse pregnancy outcomes and placental dysfunction. However, the histopathological alterations occurring in placental tissue under these conditions have not been fully elucidated. This study aimed to evaluate placental histomorphological changes in women with excessive gestational weight gain.

Methods: Placental tissues were obtained from healthy pregnant women and women with excessive gestational weight gain. Histopathological evaluation was performed using hematoxylin and eosin staining. Villous architecture, trophoblastic morphology, stromal organization, syncytial knot formation, and fibrinoid deposition were examined and compared between groups.

Results: Control placentas demonstrated preserved villous architecture, regular syncytiotrophoblast morphology, well-organized stromal structures, and minimal fibrinoid deposition and syncytial knot formation. In contrast, placentas from women with excessive gestational weight gain exhibited disrupted villous architecture, trophoblastic thickening, stromal edema and vacuolization, increased syncytial knot formation, fibrinoid deposition, and degenerative villous changes. These alterations were accompanied by impaired cellular organization and reduced structural integrity of the villi.

Conclusion: Excessive gestational weight gain is associated with significant placental histopathological alterations, including villous degeneration, stromal edema, trophoblastic thickening, increased syncytial knot formation, and fibrinoid deposition. These findings suggest that excessive maternal weight gain may adversely affect placental structure and potentially compromise placental function.

Keywords: Placenta; excessive gestational weight gain; histopathology; villous degeneration; pregnancy.

Introduction

Excessive gestational weight gain is an increasingly common condition that has been associated with adverse maternal and fetal outcomes[1]. Maternal overnutrition during pregnancy may lead to metabolic disturbances, oxidative stress, systemic inflammation, and vascular dysfunction, all of which can influence placental development and function [2]. Because the placenta serves as the primary interface between the mother and fetus, structural alterations within placental tissue may have important consequences for fetal growth and pregnancy outcome[3].

The placenta undergoes continuous morphological adaptation throughout pregnancy to maintain adequate oxygen and nutrient exchange. However, maternal metabolic disturbances may impair these adaptive mechanisms and lead to abnormal placental development [4]. Previous studies have reported that excessive maternal weight gain and obesity are associated with villous immaturity, trophoblastic abnormalities, stromal edema, increased fibrinoid deposition, and vascular alterations. Such changes may reduce placental efficiency and contribute to fetal complications[5,6].

Histopathological examination of placental tissue provides valuable information regarding the effects of maternal metabolic status on placental structure. In particular, alterations in villous architecture, syncytial knot formation, trophoblastic integrity, and stromal organization may reflect underlying disturbances in placental maturation and function[7,8].

Despite growing evidence linking excessive gestational weight gain to placental dysfunction, the histomorphological changes associated with this condition remain incompletely characterized. Therefore, the present study aimed to evaluate placental histopathological alterations in women with excessive gestational weight gain and compare these findings with those observed in healthy pregnancies.

MATERIALS AND METHODS

Ethical approval

This study was approved by the Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Approval date: 16 April 2025; Approval number: 2025/146). All procedures were conducted in accordance with the ethical standards of the institutional and national research committees and with the principles of the Declaration of Helsinki.

Patient Selection

This observational case–control study was conducted using placental tissues obtained from women who delivered at the Department of Obstetrics and Gynecology, Dicle University Faculty of Medicine, between June 2025 and December 2025. A total of 90 placentas were included in the study and allocated into two groups according to maternal body mass index (BMI). The control group consisted of 45 healthy pregnant women with a BMI <30 kg/m^2, whereas the excessive gestational weight gain/obese group comprised 45 pregnant women with a BMI ≥30 kg/m^2. All participants were between 18 and 40 years of age and had singleton pregnancies resulting in live births. Women with pregnancy-related complications, including preeclampsia, gestational diabetes mellitus, fetal growth restriction, preterm delivery, or any other obstetric complication, were excluded from the study. In addition, subjects with chronic systemic diseases, metabolic disorders, autoimmune diseases, infectious diseases, or other significant medical conditions were not eligible for inclusion. Following delivery, placentas that were not required for routine pathological examination were collected. Representative tissue samples were obtained from placental regions free of gross pathological lesions and processed for histopathological evaluation.

Tissue Processing and Histopathological Examination

Placental tissues were collected immediately after delivery and transported to the laboratory under appropriate conditions. Representative tissue samples were excised from the placentas and subjected to routine histological processing. The specimens were fixed in 10% neutral buffered formalin (catalog no: Z2902-3.75L, Sigma, Germany) for 24 h. Following fixation, the tissues were washed under running tap water overnight and dehydrated through ascending ethanol series (50%, 70%, 80%, 90%, 96%, and absolute ethanol). Subsequently, the samples were cleared in xylene (3 × 30 min) and infiltrated with paraffin at 58°C for 3 × 45 min before being embedded in paraffin blocks. Paraffin-embedded tissues were sectioned at a thickness of 4 µm using a rotary microtome (Leica RM2265, Wetzlar, Germany) and mounted on positively charged glass slides. Histopathological evaluation was performed using hematoxylin and eosin (H&E) staining[9, 10].

Hematoxylin and Eosin Staining

Paraffin sections were initially placed in a 37°C water bath and subsequently incubated at 58–62°C for 6 h to ensure adequate adhesion and removal of excess paraffin. The sections were deparaffinized in xylene (3 × 15 min) and rehydrated through descending ethanol concentrations (100%, 96%, 90%, 70%, and 50%) for 10 min each. Following rinsing in distilled water for 5 min, the sections were stained with hematoxylin and eosin according to standard histological procedures. After staining, the sections were dehydrated through ascending ethanol series (80%, 90%, and 96%), immersed in absolute ethanol for 2 min, and cleared in xylene (3 × 15 min). Finally, the slides were coverslipped using Entellan mounting medium and examined under a Zeiss Imager A2 photomicroscope (Carl Zeiss, Germany). Representative images were captured for histopathological assessment[11, 12].

Histopathological Scoring

Placental histopathological alterations were evaluated semi-quantitatively by two blinded observers using hematoxylin and eosin-stained sections. Six histopathological parameters, including villous architectural disruption, stromal edema/vacuolization, trophoblastic thickening, syncytial knot formation, fibrinoid deposition, and villous degeneration, were scored independently. Each parameter was graded on a four-point scale: 0 = absent, 1 = mild, 2 = moderate, and 3 = severe. Scores obtained for all parameters were summed to generate a total histopathological score ranging from 0 to 18 for each specimen. Five randomly selected non-overlapping microscopic fields per section were evaluated, and the mean score was used for statistical analysis.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software (version 25.0; IBM Corp., Armonk, NY, USA). Histopathological scores were evaluated for villous architectural disruption, stromal edema/vacuolization, trophoblastic thickening, syncytial knot formation, fibrinoid deposition, and villous degeneration. Each parameter was graded on a four-point scale ranging from 0 to 3, and the individual scores were summed to obtain a total histopathological score for each specimen.

The distribution of continuous variables was assessed using the Shapiro–Wilk test. As histopathological scores represented ordinal data and did not demonstrate a normal distribution, results were expressed as median (minimum–maximum). Comparisons between the control and excessive gestational weight gain groups were performed using the Mann–Whitney U test. A two-tailed p value < 0.05 was considered statistically significant.

RESULTS

Histopathological Findings of Control Group

Placental sections obtained from the control group demonstrated preserved villous architecture. Terminal villi exhibited regular morphology characterized by a thin syncytiotrophoblast layer and well-organized stromal structure. Fetal capillaries were evenly distributed within the villi, and no apparent stromal

edema or inflammatory cell infiltration was observed. Fibrinoid deposition and syncytial knot formation were minimal throughout the examined sections (Figures 1 and 2).

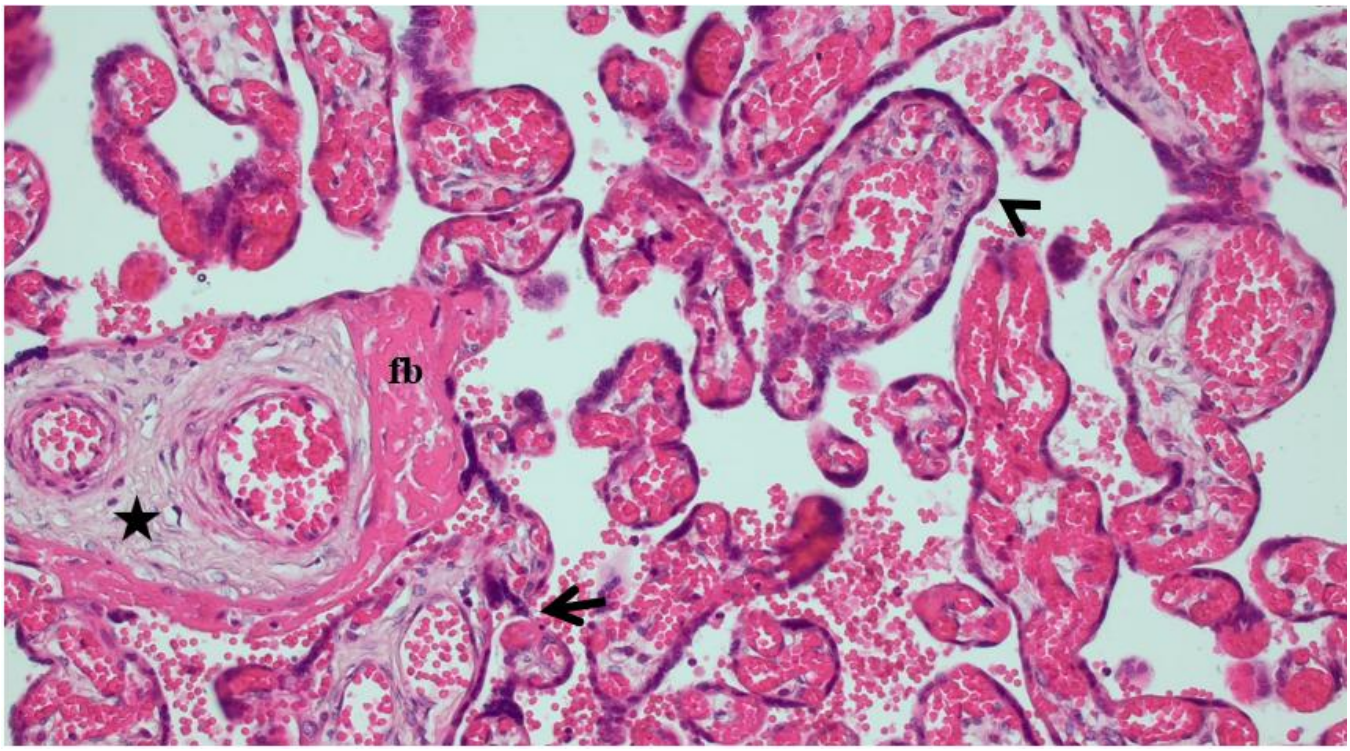

Figure 1: Representative hematoxylin and eosin (H&E)-stained placental section from the control group. Preserved villous architecture with normal stromal organization and an intact syncytiotrophoblast layer is observed. *: stromal area; arrow: syncytial knot; arrowhead: syncytiotrophoblast layer; fb: fibrinoid deposition. Scale bar = 50 µm. Magnification = ×20.

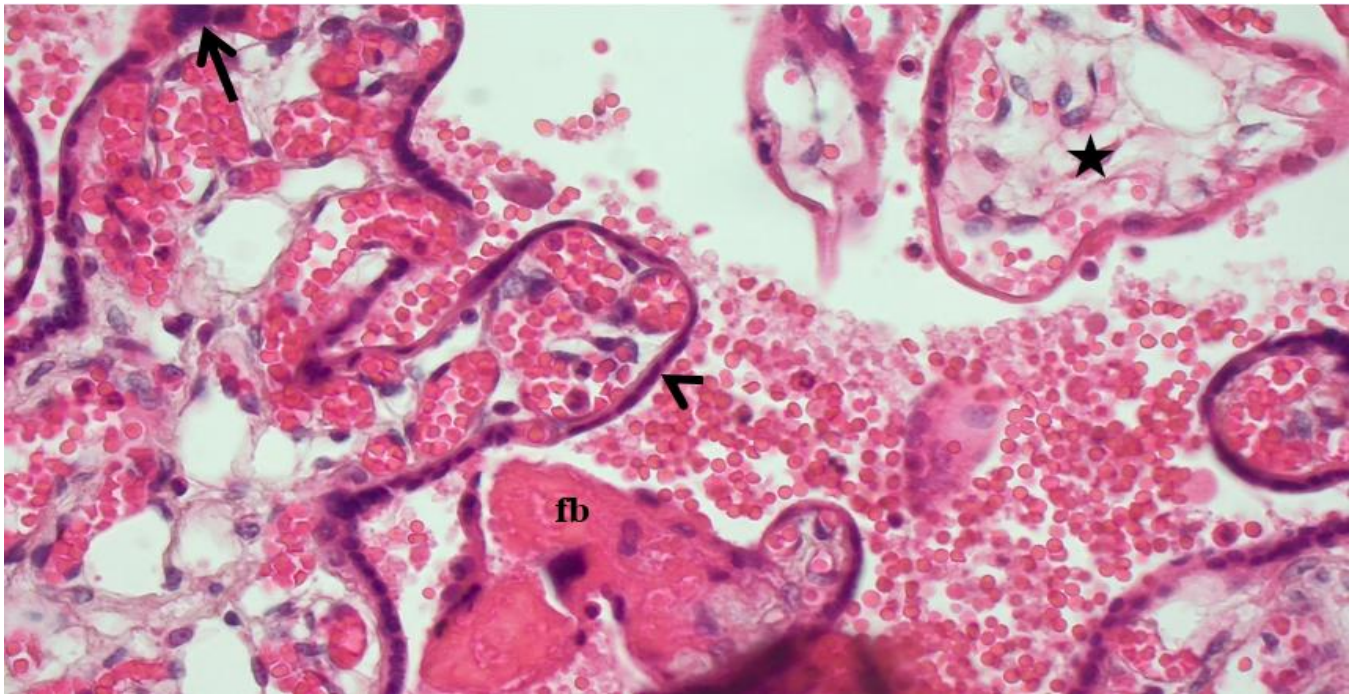

Figure 2: High-magnification image of an H&E-stained placental section from the control group. Terminal villi exhibit normal morphology with preserved syncytiotrophoblast integrity and minimal fibrinoid deposition. *: stromal area; arrow: syncytial knot; arrowhead: syncytiotrophoblast layer; fb: fibrinoid deposition. Scale bar = 20 µm. Magnification = ×40.

Histopathological Findings of Excessive GWG Group

In contrast, placental samples from women who experienced excessive gestational weight gain exhibited prominent histopathological alterations. Villous architecture was markedly disrupted, with irregularly shaped villi and focal fragmentation. Thickening of the trophoblastic layer was evident in several areas. The villous stroma displayed loosening and vacuolization consistent with stromal edema. An increased number of syncytial knots was observed compared with the control group. Furthermore, focal fibrinoid deposits and degenerative villous changes were identified. The affected villi exhibited disturbed cellular organization and reduced structural integrity, indicating impaired villous maturation and placental remodeling (Figures 3 and 4).

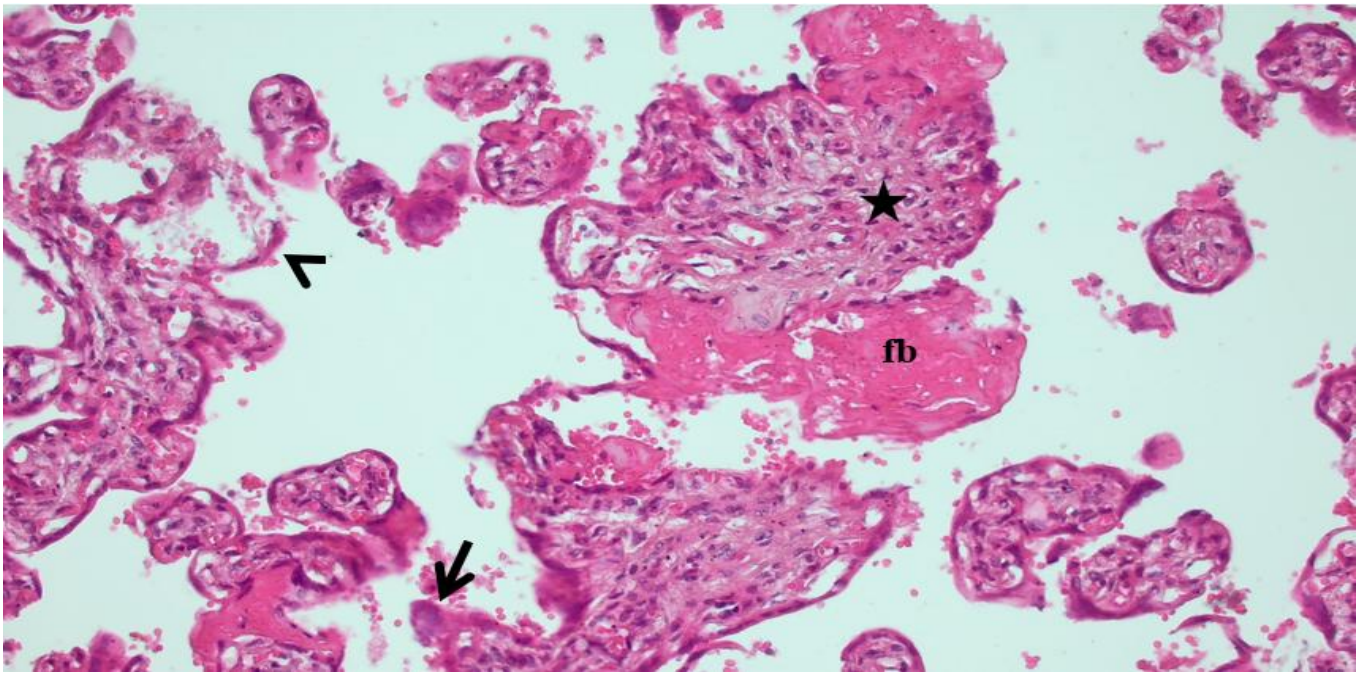

Figure 3: Representative hematoxylin and eosin (H&E)-stained placental section from women with excessive gestational weight gain. Villous architectural disruption, stromal loosening, increased syncytial knot formation, trophoblastic thickening, and focal fibrinoid deposition are evident. *: stromal area; arrow: syncytial knot; arrowhead: syncytiotrophoblast layer; fb: fibrinoid deposition. Scale bar = 50 µm. Magnification = ×20.

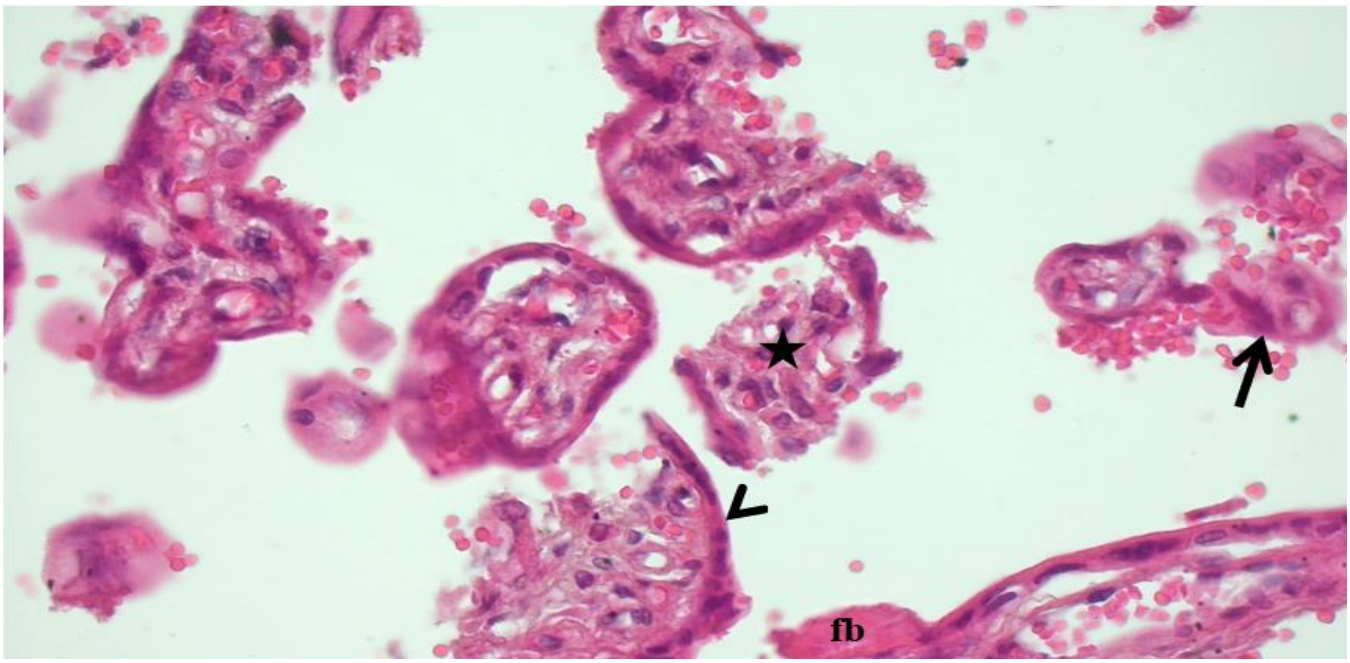

Figure 4: High-magnification image of an H&E-stained placental section from women with excessive gestational weight gain. Degenerative villous changes, stromal edema and vacuolization, increased syncytial knot formation, trophoblastic thickening, and focal fibrinoid accumulation are observed. *: stromal area; arrow: syncytial knot; arrowhead: syncytiotrophoblast layer; fb: fibrinoid deposition. Scale bar = 20 µm. Magnification = ×40.

Histopathological Scoring Results

Semi-quantitative histopathological evaluation revealed significantly higher placental injury scores in the excessive gestational weight gain group compared with the control group (Table 1). Villous architectural disruption, stromal edema/vacuolization, trophoblastic thickening, syncytial knot formation, fibrinoid deposition, and villous degeneration scores were all significantly increased in placentas obtained from women with excessive gestational weight gain (all $p < 0.05$). Among the evaluated parameters, syncytial knot formation and villous architectural disruption demonstrated the most pronounced differences between groups. Furthermore, the total histopathological score was significantly higher in the excessive gestational weight gain group, indicating more extensive placental structural damage and impaired villous organization. These findings quantitatively support the histological observations obtained from hematoxylin and eosin-stained sections and suggest that excessive maternal weight gain is associated with substantial alterations in placental morphology.

Table 1: Semi-quantitative histopathological scores of placental tissues in the control and excessive gestational weight gain groups.

Histopathological parameter	Control (n=45)	Excessive GWG (n=45)	p value
Villous architectural disruption	0 (0–1)	2 (1–3)	<0.001
Stromal edema/vacuolization	0 (0–1)	2 (1–3)	<0.001
Trophoblastic thickening	0 (0–1)	2 (1–3)	<0.001
Syncytial knot formation	1 (0–2)	3 (2–3)	<0.001
Fibrinoid deposition	0 (0–1)	2 (1–3)	<0.001
Villous degeneration	0 (0–1)	2 (1–3)	<0.001
Total histopathological score	2 (0–5)	12 (7–17)	<0.001

Values are presented as median (minimum–maximum). Comparisons between groups were performed using the Mann–Whitney U test.

DISCUSSION

The present study demonstrated that excessive gestational weight gain is associated with substantial alterations in placental histomorphology. Compared with the control group, placentas from women with excessive weight gain exhibited villous architectural disruption, trophoblastic thickening, stromal edema, increased syncytial knot formation, fibrinoid deposition, and degenerative villous changes. These findings suggest that excessive maternal weight gain may adversely affect placental structure and potentially compromise placental function.

The preservation of normal villous architecture in the control group reflects adequate placental maturation and efficient maternal–fetal exchange. In contrast, the morphological abnormalities observed in the excessive weight gain group are consistent with previous reports describing placental adaptations in obese pregnancies. Maternal obesity and excessive gestational weight gain have been associated with altered placental development, increased oxidative stress, chronic low-grade inflammation, and impaired vascular remodeling, all of which can influence villous morphology and placental efficiency.

One of the most notable findings in the present study was the increased number of syncytial knots in placentas from women with excessive weight gain. Syncytial knot formation is generally considered a marker of trophoblastic turnover and placental stress. Increased syncytial knot density has frequently been associated with hypoxic conditions and altered placental perfusion. Therefore, the elevated syncytial knot formation observed in the present study may indicate an adaptive response to localized placental hypoxia resulting from obesity-related vascular dysfunction.[13]

The presence of stromal edema and vacuolization further supports the existence of impaired placental microcirculation. Villous edema may increase the diffusion distance between maternal and fetal blood compartments, thereby reducing the efficiency of oxygen and nutrient transfer. Similar findings have been reported in placentas from obese pregnancies, where altered angiogenesis and endothelial dysfunction contribute to disturbances in villous stromal homeostasis.[14]

Another important observation was the increased fibrinoid deposition within the villous structures. Excessive fibrinoid accumulation is generally regarded as a manifestation of placental injury and abnormal maternal–fetal interface remodeling[15]. Increased fibrinoid deposition may reflect chronic placental stress and has been associated with reduced exchange surface area and impaired placental function. The coexistence of fibrinoid deposition and villous degeneration in the present study suggests that excessive gestational weight gain may promote progressive structural deterioration of placental tissue[16].

The trophoblastic thickening observed in the excessive weight gain group may also represent a compensatory response to increased metabolic demand and altered oxygen availability. However, excessive trophoblastic proliferation and thickening may paradoxically impair transplacental exchange by increasing the diffusion barrier. Collectively, these histopathological findings

indicate that excessive maternal weight gain may induce a placental microenvironment characterized by hypoxic stress, altered villous maturation, and impaired tissue remodeling.[17]

Considering that the primary aim of this study was to investigate HIF-1α and TNF-α expression in placental tissue, the observed histopathological alterations provide important morphological evidence supporting the potential involvement of hypoxia- and inflammation-related pathways[18]. Increased syncytial knot formation, stromal edema, trophoblastic thickening, and fibrinoid deposition are findings commonly associated with placental hypoxia and inflammatory activation. Therefore, the histological observations are consistent with the proposed biological roles of HIF-1α and TNF-α in obesity-associated placental dysfunction[19, 20].

CONCLUSION

In conclusion, placentas from women with excessive gestational weight gain exhibited significant histopathological alterations characterized by villous architectural disruption, trophoblastic thickening, stromal edema, increased syncytial knot formation, fibrinoid deposition, and degenerative villous changes. These findings suggest that excessive maternal weight gain adversely affects placental structure and may impair placental function. The observed morphological abnormalities support the concept that obesity-related placental dysfunction is associated with hypoxic and inflammatory processes, providing a structural basis for the evaluation of HIF-1α and TNF-α expression in placental tissue.

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Ethical Approval: This study was approved by the Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Approval date: 16 April 2025; Approval number: 2025/146). All procedures were conducted in accordance with the ethical standards of the institutional and national research committees and with the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants prior to inclusion in the study.

Conflict of Interest: The author declares that there is no conflict of interest regarding the publication of this thesis.

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