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Histological Study of the Human Placenta Across Trimesters: Correlating Structure and Function

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ABSTRACT:

Background: The placenta is a dynamic fetomaternal organ whose structure undergoes continuous remodeling throughout pregnancy to meet the increasing functional demands of the developing fetus.

Objective: To evaluate the histological changes in the human placenta across the first, second, and third trimesters and to correlate these structural changes with progressive placental maturation and function.

Methodology: This observational comparative histological study was conducted at Department of Anatomy Dow University of Health Sciences Karachi from June 2025 to June 2026. A total of 90 human placental specimens were included in the study, with 30 specimens representing each trimester of pregnancy. Placental specimens obtained after delivery were categorized according to gestational age into first-, second-, and third-trimester groups.

Results: Placental weight increased from 112.6 ± 24.8 g in the first trimester to 298.4 ± 51.7 g in the second and 489.7 ± 78.5 g in the third trimester ($p<0.001$). Placental thickness also increased from 1.7 ± 0.3 cm to 2.5 ± 0.4 cm and 3.2 ± 0.5 cm, respectively ($p<0.001$). Mean villous diameter decreased significantly from 182.4 ± 31.6 μm to 145.7 ± 26.4 μm

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and 108.3 ± 21.7 μm ($p<0.001$), while trophoblastic thickness decreased from 28.6 ± 5.4 μm to 20.8 ± 4.1 μm and 13.7 ± 3.2 μm ($p<0.001$). Terminal villi increased from 8.4 ± 2.1 to 16.7 ± 3.5 and 27.9 ± 5.2 per field, while fetal capillaries increased from 2.1 ± 0.7 to 3.8 ± 1.0 and 6.2 ± 1.4 per villus (both $p<0.001$).

Conclusion: The human placenta undergoes significant structural remodeling throughout gestation. Advancing pregnancy is characterized by progressive villous specialization, attenuation of the trophoblastic barrier, increased terminal villous formation, and enhanced fetal vascularization.

INTRODUCTION

Placenta is a special fetomaternal organ that grows during pregnancy and has vital functions essential for fetal growth and maintenance of maternal–fetal homeostasis. It is the site of exchange of oxygen, nutrients, elimination of metabolic waste, endocrine regulation and immunological interactions between the mother and fetus. It is therefore closely related to its functional capacity and progressive histological remodeling is required to keep pace with the growing needs of the developing fetus [1]. The development of placenta starts with the differentiation of trophoblast and its implantation in the uterine wall, then the chorionic villous tree is formed and branched. Throughout gestation, the trophoblastic layers, connective tissue stroma and fetal capillaries of the villi are continuously remodelled [2]. In the early stages of pregnancy, the villi are underdeveloped with comparatively thicker trophoblastic barrier and poorly developed vascular network. During the course of gestation there is a gradual increase in the specialization of villous architecture, characterised by a progressive decrease of trophoblastic and stromal elements and the progressive increase of the fetal capillary network [3]. Changes in the histology are more noticeable in the second and third trimesters. The progressive vascularization, the development of the terminal villi, the attenuation of the syncytiotrophoblast and the closer approximation of fetal capillaries to the intervillous space are important for the formation of the syncytiocapillary membrane, which decreases the distance between the mother and the fetus for gas and nutrient exchange [4]. Villous area, stromal area, epithelial components, and vascular structures have all been found to undergo progressive functional maturation of the placenta, as revealed by morphometric studies [5]. During pregnancy the vascular system of the placenta is also significantly remodeled. More branching and expansion of the fetal capillary network provides more surface area for exchange and ensures good fetal oxygenation and nutrient delivery. The changes in the structure are accompanied by changes in villous morphology, such as the increasing expression of terminal and intermediate villi during the later gestation [6]. These changes illustrate the changing structure of the placenta to meet the greater and greater metabolic needs of the fetus.

The association of placental structure and function is of clinical relevance because abnormalities of placental development have been linked to foetal growth restriction, pre-eclampsia, still birth and other adverse pregnancy outcomes [7]. Histopathological examination can yield important clues to abnormalities of villous maturation, trophoblastic development, vascularization and stromal organization. These morphologic changes can thus be used to indicate a change in placental function and fetal health [8]. New stereological and three-dimensional techniques have also contributed to the better understanding of the architecture of the placenta, enabling quantitative evaluation of villous branching, vascular density, distribution of trophoblast and exchange surfaces [9]. These strategies have shown that placental growth is more than just size – it requires a coordinated remodeling of several components in the placenta. The variations in the villous morphology and vascular organization throughout gestation therefore offer a significant clue as to the development of the function of the placenta [10]. Therefore, it is important to understand the normal histological changes throughout the trimesters in order to provide a structural basis for placental function. Villous architecture, trophoblastic properties, stromal elements and vascularity of the placenta can be compared among the different gestation periods to better understand the progressive adaptation of the placenta to the changing fetal needs [11]. The creation of these normal morphological patterns can also serve as a valuable reference to detect pathological changes of complicated pregnancies [12].

OBJECTIVE

To evaluate the histological changes in the human placenta across the first, second, and third trimesters and to correlate these structural changes with progressive placental maturation and function.

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METHODOLOGY

This observational comparative histological study was conducted at Department of Anatomy Dow University of Health Sciences Karachi from June 2025 to June 2026. A total of 90 human placental specimens were included in the study, with 30 specimens representing each trimester of pregnancy. Placental specimens obtained after delivery were categorized according to gestational age into first-, second-, and third-trimester groups. Placentae from pregnancies with adequate clinical and gestational information were included. Specimens with grossly damaged or incomplete placental tissue, inadequate tissue for histological processing, or specimens with significant pathological changes that could interfere with assessment of normal trimester-wise morphology were excluded.

Data Collection Procedure

After obtaining appropriate consent, relevant maternal and gestational information was recorded using a structured proforma. Placental specimens were collected following delivery and examined for relevant gross morphological features. Representative tissue samples were obtained from the placenta and fixed in an appropriate fixative before routine histopathological processing. The tissue was dehydrated, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Microscopic examination was performed to assess chorionic villous architecture, trophoblastic characteristics, villous stroma, fetal capillaries, terminal villi, and vascularity. The observed histological characteristics were documented and compared across the first, second, and third trimesters to evaluate progressive structural changes associated with placental maturation. The primary outcome was the comparison of histological characteristics of human placenta across the three trimesters of pregnancy. Secondary outcomes included trimester-wise differences in chorionic villous architecture, trophoblastic characteristics, stromal components, terminal villi, fetal capillary development, and vascularity. The findings were correlated with the progressive structural maturation of the placenta and its increasing functional requirements throughout gestation.

Data Analysis

The collected data were entered and analyzed using SPSS version 25. Quantitative variables were summarized as mean ± standard deviation, while categorical and graded histological findings were presented as frequencies and percentages. Differences in quantitative histological parameters among the three trimester groups were assessed using one-way ANOVA for normally distributed variables, while the Kruskal–Wallis test was applied for non-normally distributed variables. The chi-square test was used for comparison of categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included a total of 90 placental specimens, with an equal distribution across the three trimesters. Thirty specimens (33.3%) were obtained from each trimester, ensuring balanced representation of placental tissue across gestational stages. This equal allocation allowed a direct comparison of structural and histological changes from early to late pregnancy.

Table 1. Distribution of placental specimens according to trimester

Trimester	Number of specimens	Percentage
First trimester	30	33.3%
Second trimester	30	33.3%
Third trimester	30	33.3%
Total	**90**	**100%**

Maternal age was comparable across the three groups, with mean ages of 27.4 ± 4.1 years in the first trimester, 28.2 ± 4.3 years in the second trimester, and 28.8 ± 4.6 years in the third trimester ($p=0.481$). In contrast, gestational age, placental weight, and placental thickness increased significantly across the trimesters (all $p<0.001$). Mean gestational age was 9.8 ± 1.7, 21.4 ± 2.3, and 37.2 ± 1.6 weeks, while mean placental weight increased from 112.6 ± 24.8 g to 298.4 ± 51.7 g and 489.7 ± 78.5 g. Placental thickness similarly increased from 1.7 ± 0.3 cm to 2.5 ± 0.4 cm and 3.2 ± 0.5 cm.

Table 2. Comparison of maternal and gestational characteristics across trimesters

Characteristic	First trimester (n=30)	Second trimester (n=30)	Third trimester (n=30)	p-value
Maternal age, years	27.4 ± 4.1	28.2 ± 4.3	28.8 ± 4.6	0.481
Gestational age, weeks	9.8 ± 1.7	21.4 ± 2.3	37.2 ± 1.6	<0.001
Placental weight, g	112.6 ± 24.8	298.4 ± 51.7	489.7 ± 78.5	<0.001
Placental thickness, cm	1.7 ± 0.3	2.5 ± 0.4	3.2 ± 0.5	<0.001

Progressive histological maturation was evident across gestation. Mean villous diameter decreased from 182.4 ± 31.6 μm in the first trimester to 145.7 ± 26.4 μm in the second and 108.3 ± 21.7 μm in the third trimester ($p<0.001$). Trophoblastic thickness and stromal area also decreased significantly, from 28.6 ± 5.4 to 20.8 ± 4.1 and 13.7 ± 3.2 μm, and from 61.8 ± 7.2% to 51.4 ± 6.5% and 42.3 ± 5.8%, respectively (both $p<0.001$). Conversely, terminal villi increased from 8.4 ± 2.1 to 16.7 ± 3.5 and 27.9 ± 5.2 per field, while fetal capillaries increased from 2.1 ± 0.7 to 3.8 ± 1.0 and 6.2 ± 1.4 per villus (both $p<0.001$).

Table 3. Comparison of villous histological characteristics across trimesters

Histological parameter	First trimester (n=30)	Second trimester (n=30)	Third trimester (n=30)	p-value
Mean villous diameter, μm	182.4 ± 31.6	145.7 ± 26.4	108.3 ± 21.7	<0.001
Trophoblastic thickness, μm	28.6 ± 5.4	20.8 ± 4.1	13.7 ± 3.2	<0.001
Stromal area, %	61.8 ± 7.2	51.4 ± 6.5	42.3 ± 5.8	<0.001
Terminal villi, per field	8.4 ± 2.1	16.7 ± 3.5	27.9 ± 5.2	<0.001
Fetal capillaries, per villus	2.1 ± 0.7	3.8 ± 1.0	6.2 ± 1.4	<0.001

Vascular development increased significantly with advancing gestation. The mean villous vascularity score increased from 1.8 ± 0.6 in the first trimester to 3.1 ± 0.8 in the second and 4.4 ± 0.9 in the third trimester ($p<0.001$). Capillary density increased from 42.6 ± 9.8 to 68.4 ± 12.7 and 96.7 ± 16.3 vessels/mm², while the capillary-to-villous ratio increased from 0.24 ± 0.07 to 0.41 ± 0.09 and 0.63 ± 0.12 (both $p<0.001$). Syncytiocapillary membrane formation was observed in 16.7%, 56.7%, and 93.3% of specimens across the three trimesters, respectively ($p<0.001$).

Table 4. Comparison of vascular characteristics of placental villi across trimesters

Vascular parameter	First trimester (n=30)	Second trimester (n=30)	Third trimester (n=30)	p-value
Villous vascularity score	1.8 ± 0.6	3.1 ± 0.8	4.4 ± 0.9	<0.001
Capillary density, vessels/mm²	42.6 ± 9.8	68.4 ± 12.7	96.7 ± 16.3	<0.001
Capillary-to-villous ratio	0.24 ± 0.07	0.41 ± 0.09	0.63 ± 0.12	<0.001
Syncytiocapillary membrane formation	5 (16.7%)	17 (56.7%)	28 (93.3%)	<0.001

Trophoblastic and stromal maturation also showed significant trimester-wise changes. A continuous cytotrophoblast layer was present in 90.0% of first-trimester specimens, compared with 53.3% in the second and 16.7% in the third trimester ($p<0.001$). Conversely, attenuated trophoblast increased from 10.0% to 46.7% and 83.3%, while increased stromal vascularity rose from 26.7% to 63.3% and 90.0% across the three groups (both $p<0.001$). Prominent terminal villi similarly increased from 13.3% in the first trimester to 56.7% in the second and 93.3% in the third trimester ($p<0.001$).

Table 5. Comparison of trophoblastic and stromal features across trimesters

Histological feature	First trimester n (%)	Second trimester n (%)	Third trimester n (%)	p-value
Continuous cytotrophoblast layer	27 (90.0%)	16 (53.3%)	5 (16.7%)	<0.001
Attenuated trophoblast	3 (10.0%)	14 (46.7%)	25 (83.3%)	<0.001
Prominent stromal cellularity	26 (86.7%)	15 (50.0%)	7 (23.3%)	<0.001
Increased stromal vascularity	8 (26.7%)	19 (63.3%)	27 (90.0%)	<0.001
Prominent terminal villi	4 (13.3%)	17 (56.7%)	28 (93.3%)	<0.001

DISCUSSION

In the present study, it has been shown that the placental morphology undergoes definite changes in each trimester which supports the notion of continuous change in the placental structure during pregnancy. Placental weight increased from 112.6 ± 24.8 g in the first trimester to 298.4 ± 51.7 g in the second and 489.7 ± 78.5 g in the third trimester ($p<0.001$). Placental thickness also increased from 1.7 ± 0.3 cm to 2.5 ± 0.4 cm and 3.2 ± 0.5 cm, respectively ($p<0.001$). The results are similar to those in earlier studies which found progressive development of placental parenchymal elements during mid gestation and maturing structure towards term [13]. In the present study, progressive decrease in mean villous diameter from 182.4 ± 31.6 µm at 1st trimester to 145.7 ± 26.4 µm at 2nd trimester and 108.3 ± 21.7 µm at 3rd trimester ($p<0.001$) has suggested that the villous diameter becomes smaller and more branched with advancing gestation. Quantitative morphometry studies of the villous size also found a progressive decrease in villous size during gestation and a progressive increase in terminal villous development [14]. Also, there was a substantial decrease in trophoblastic thickness, from 28.6 ± 5.4 µm of the first trimester, to 20.8 ± 4.1 µm for the second trimester and 13.7 ± 3.2 µm for the third trimester ($p<0.001$). This gradual decrease is similar to earlier histomorphometric data indicating there is an inverse relationship between the thickness of the trophoblastic and villous barrier and gestational age. Thinning allows for greater exchange of maternal blood and fetal capillaries and thus facilitates more efficient exchange during later pregnancy [15]. The stromal area decreased significantly from 61.8 ± 7.2% in the first trimester to 51.4 ± 6.5% in the second and 42.3 ± 5.8% in the third trimester ($p<0.001$). The decrease was accompanied by increasing vascularity and formation of terminal villi - indicating progressive replacement and/or attenuation of relatively large immature villous elements by a more specialized exchange architecture. Consistent with previous morphologic studies, early villi have also been found to be larger, and more stromal with decreasing stromal cell numbers and villous size with gestation [16]. Compared to decrease in the size of the villi and decrease in the stromal components, there was a progressive increase in the number of terminal villous from 8.4 ± 2.1 per field in the first trimester to 16.7 ± 3.5 in the second trimester and 27.9 ± 5.2 in the third trimester ($p<0.001$). This discovery is significant because the villi at the end of the villous are very specialized locations for maternal–fetal exchange. The data reported previously showed that the greatest increase in the number of terminal villi does not occur until about the mid-second trimester and that this increase plays a significant role in the increase in villous surface area needed for exchange [17].

The mean villous vascularity score increased from 1.8 ± 0.6 in the first trimester to 3.1 ± 0.8 in the second and 4.4 ± 0.9 in the third trimester ($p<0.001$), while the capillary-to-villous ratio increased from 0.24 ± 0.07 to 0.41 ± 0.09 and 0.63 ± 0.12, respectively ($p<0.001$). This pattern suggests that vascular development is not just related to the growth of the whole placenta, but it is also an important aspect of maturation of function. The relative degree of villous vascularisation has been shown to rise during gestation as do villous size, hence efficiency of exchange surface [18]. The formation of syncytiocapillary membrane was significantly higher in the second trimester (56.7% specimens) and third trimester (93.3% specimens) as compared with the first trimester (16.7% specimens) ($p<0.001$). This finding is the progressive approach of the fetal capillaries to the syncytiotrophoblast and the development of specialized exchange barrier. Histological description of the mature term placentae has described a significant proliferation of the terminal villi along with conspicuous capillaries and well-developed vasculosyncytial membranes as characteristics features of normal placental maturation [19]. There is also progressive villous specialization as the prominent terminal villi increase from 13.3% in the 1st trimester to 56.7% in the 2nd trimester and 93.3% in the 3rd trimester ($p<0.001$). This is consistent with previous studies that have reported that the intermediate villi mature to become mature intermediate villi in later pregnancy and that the terminal villi proliferate to a large extent in the third trimester

[20]. There are a number of limitations with this study. A small number of placental samples (n = 90) could reduce the ability to generalize the results. The study also has an observational nature and hence the causal relationship of gestaltional age with the observed histological changes cannot be established. Inter-observer variation may occur, especially for semi-quantitative features, in the histological assessment. Furthermore, factors that could affect the morphology of the placenta may not be fully controlled such as potential maternal, fetal, and pregnancy-related risks.

CONCLUSION

The study demonstrated significant trimester-wise changes in placental structure, with advancing gestation characterized by reduced villous diameter, trophoblastic thickness, and stromal proportion, alongside increased terminal villous formation, fetal capillary density, vascularity, and syncytiocapillary membrane development. These coordinated histological changes indicate progressive placental maturation and specialization of the maternal–fetal exchange surface. The findings support a close relationship between placental structure and its increasing functional requirements throughout pregnancy.

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