

Gurbanova S.G., Isayev O.R., Akhundova N.E., Aliyarbayova A.A., Aliyeva G.N.,
Aliyeva Sh.E., Hagverdiyeva R.R.
Azerbaijan Medical University, Baku, Azerbaijan

MORPHOMETRIC AND HISTOLOGICAL DIFFERENCES OF FULL-TERM HUMAN PLACENTAS DEPENDING ON THE SEX OF THE CHILD

e-mail: med_avtor@mail.ru

A prospective microscopic and statistical analysis of full-term placental tissue samples and macroscopic parameters obtained from 20 healthy women with uncomplicated singleton pregnancies (10 male placentas and 10 female placentas) was performed. Conventional tissue treatment, hematoxylin and eosin staining, and standard descriptive statistical estimates were used to assess placental size, thickness, weight, overall villous architecture, microvessel structure, and stromal cell distribution. Descriptive statistics demonstrated baseline physical variations: mean placental dimensions were 21.2 ± 1.3 cm for male placentas and 20.0 ± 1.5 cm for female placentas; thickness averaged 2.50 ± 0.47 cm in males versus 2.52 ± 0.27 cm in females; and mean weight was 499.9 ± 45.0 g for male cohorts compared to 474.6 ± 31.0 g for female cohorts. Histological evaluations showed mature villous architecture in both groups. Normal term placentas from this cohort display subtle morphometric and microvascular variations associated with fetal sex, specifically regarding weight tendencies and capillary caliber.

Key words: placenta, histology, mesenchymal stromal cells, microvasculature, fetal sex.

Гурбанова С.Г., Ісаяєв О.Р., Ахундова Н.Є., Аліярбекова А.А., Алієва Г.Н.,
Алієва Ш.Е., Хагвердієва Р.Р.

МОРФОМЕТРИЧНІ ТА ГІСТОЛОГІЧНІ ВІДМІННОСТІ ДОНОШЕНИХ ПЛАЦЕНТ ЛЮДИНИ ЗАЛЕЖНО ВІД СТАТІ ДИТИНИ

Було проведено проспективний мікроскопічний та статистичний аналіз доношених зразків плацентарної тканини та макроскопічних параметрів, отриманих від 20 здорових жінок з неускладненою одноплідною вагітністю (10 чоловічих і 10 жіночих плацент). Для оцінки розмірів плаценти, товщини, ваги, загальної архітектури ворсинок, структури мікросудин та розподілу стромальних клітин було використано звичайну обробку тканин, фарбування гематоксиліном та еозином, а також стандартні описові статистичні оцінки. Описова статистика виявила вихідні фізичні відмінності: середні розміри плаценти становили $21,2 \pm 1,3$ см для чоловічих плацент і $20,0 \pm 1,5$ см для жіночих; товщина плаценти становила в середньому $2,50 \pm 0,47$ см у чоловіків проти $2,52 \pm 0,27$ см у жінок; а середня вага становила $499,9 \pm 45,0$ г у групі чоловіків порівняно з $474,6 \pm 31,0$ г у групі жінок. Гістологічні дослідження виявили зрілу структуру ворсинок в обох групах. Доношені плаценти з цієї групи демонструють незначні морфометричні та мікросудинні відмінності, пов'язані зі статтю плода, зокрема щодо ваги та калібру капілярів.

Ключові слова: плацента, гістологія, мезенхімальні стромальні клітини, мікросудинна мережа, стать плода.

The human placenta is a specialized transient organ responsible for maternal-fetal metabolic exchange, gas transport, immune modulation, and hormone production [1, 14]. Throughout normal gestation, macroscopic physical parameters and microstructural angioarchitecture are influenced by multiple intrinsic and extrinsic variables [9]. Recent investigations indicate that fetal sex can shape placental development, morphometry, and adaptive mechanisms [2]. Consequently, comparative evaluations of male and female placental tissues contribute to our understanding of sex-dependent physiological variations during gestation [4].

Nevertheless, detailed structural and quantitative comparisons of normal term placentas derived strictly from uncomplicated pregnancies remain essential for establishing baseline morphological parameters [6]. The primary objective of this descriptive study is to compare macroscopic metrics—including dimensions, thickness, and weight—along with general histological features of villous, stromal, and vascular components between male and female placental cohorts [5]. In this study, all fundamental concepts and terms, including syncytiotrophoblast, cytotrophoblast, chorionic villi, and stromal elements, are standardized in accordance with modern morphological nomenclature. The issues of sex-related differences in placental morphogenesis are attracting increasing attention from researchers in

the field of perinatal pathology [13]. Analysis of literature sources indicates the necessity of detailed passportization of macro- and micrometric parameters of placentas during physiological gestation [8]. Understanding these baseline processes allows for the subsequent differentiation of pathological changes in obstetric complications [10, 7].

The purpose of the study was a comparative evaluation of macroscopic metric parameters and microscopic features of the stromal-vascular apparatus of normal term placentas from uncomplicated pregnancies according to fetal sex.

Materials and methods. In a prospective study, term placental specimens and physical measurements obtained from 20 healthy women with uncomplicated singleton pregnancies (10 male and 10 female neonates), delivered in the Department of Obstetrics and Gynecology at the Educational Surgical Clinic of Azerbaijan Medical University between 2025 and 2026, were examined. The study was conducted in compliance with the ethical principles of the World Medical Association Declaration of Helsinki, and all patients signed informed consent for the use of biological material for research purposes. Patient selection was carried out according to strict inclusion criteria: maternal age from 20 to 35 years, physiological course of pregnancy, absence of severe somatic pathology, gestational diabetes mellitus, preeclampsia, and intrauterine infection.

Placental tissue samples were fixed in 10% neutral buffered formalin (Sigma-Aldrich, USA), processed routinely in a closed-system tissue processor, and embedded in paraffin. Sections of 4–5 μ m thickness were stained with hematoxylin and eosin (H&E) according to standard procedures. Microscopic analysis was performed using an Olympus CX43 light microscope (Japan) equipped with a digital camera to evaluate overall tissue architecture and vascular patterns, as documented across the histological preparations.

Statistical processing of the results was carried out using the SPSS software package (version 26.0, IBM, USA). Quantitative parameters were tested for normal distribution. Mean values are presented as $M \pm m$, where M is the arithmetic mean and m is the standard error of the mean. Parametric criteria were used to assess differences, and confidence intervals (95% CI) were calculated at a significance level of $p > 0.05$.

Results of the study. Quantitative analysis revealed specific metric variations between the male and female groups within this cohort of 20 placentas.

Placental Dimensions. The male cohort ($n = 10$) exhibited a mean dimension of 21.2 ± 1.3 cm (range: 19–23 cm; 95% CI: 20.3–22.1), whereas the female cohort ($n = 10$) showed a mean dimension of 20.0 ± 1.5 cm (range: 18–22 cm; 95% CI: 18.9–21.1). The total cohort average for placental dimensions was 20.6 ± 1.5 cm (95% CI: 19.9–21.3) (Table 1).

Placental Thickness. Thickness measurements remained consistent across both groups. Male placentas averaged 2.50 ± 0.47 cm in thickness (range: 2.1–3.2 cm; 95% CI: 2.17–2.83), while female placentas averaged 2.52 ± 0.27 cm (range: 2.1–2.9 cm; 95% CI: 2.33–2.71). The overall mean thickness for the entire group was 2.51 ± 0.37 cm (95% CI: 2.34–2.68) (Table 1).

Table 1

Normal placental dimensions and thickness

Parameter	Group	N	Mean	SE	CI (Lower)	CI (Upper)	Min	Max
Dimensions (cm)	Male	10	21.2	0.4	20.3	22.1	19	23
	Female	10	20.0	0.5	18.9	21.1	18	22
	Total	20	20.6	0.3	19.9	21.3	18	23
Thickness (cm)	Male	10	2.50	0.15	2.17	2.83	2.1	3.2
	Female	10	2.52	0.08	2.33	2.71	2.1	2.9
	Total	20	2.51	0.08	2.34	2.68	2.1	3.2

Note: N – sample size; SE – standard error; CI – confidence interval for the mean.

Placental Weight. Observations indicated a slightly higher mean weight in male placentas compared to female cohorts. The mean weight for the male group was 499.9 ± 45.0 g (range: 450–578 g;

95% CI: 467.7–532.1), compared to 474.6 ± 31.0 g for the female group (range: 430–505 g; 95% CI: 452.4–496.8). The mean weight across the total cohort was 487.3 ± 39.8 g (95% CI: 468.6–505.9) (Table 2).

Table 2

Normal placental weight

Parameter	Group	N	Mean	SE	CI (Lower)	CI (Upper)	Min	Max
Weight (g)	Male	10	499.9	14.2	467.7	532.1	450	578
	Female	10	474.6	9.8	452.4	496.8	430	505
	Total	20	487.3	8.9	468.6	505.9	430	578

Note: N – sample size; SE – standard error; CI – confidence interval for the mean.

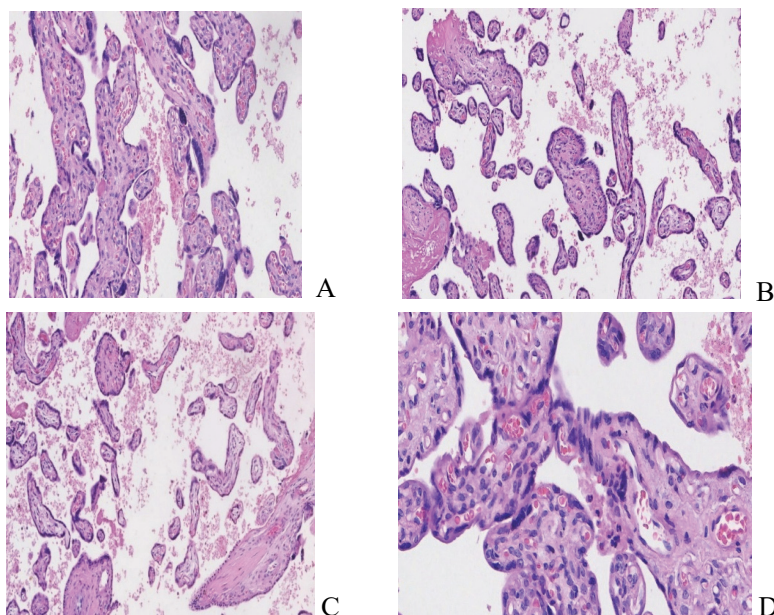


Fig. 1. (Male, H&E, 100x & 400x): Broad, rounded terminal villi with sinusoids (A); continuous syncytiotrophoblast layer (B, C, 100x); discrete cytotrophoblast cells (C, 100x); non-edematous myxoid stroma (A, D, 400x).

Histological examinations of male placental specimens ($n = 10$) demonstrated a mature villous branching architecture. As illustrated in Fig. 1A, terminal villi presented as broad, rounded profiles containing capillary sinusoids. The outer surface was lined by a continuous syncytiotrophoblast layer with basal nuclear clustering (Fig. 1B), while underlying cytotrophoblast cells appeared as discrete monolayered elements (Fig. 1C). The villous stroma consisted of a myxoid extracellular matrix without notable edema (Fig. 1D).

Fetal capillaries featured open lumina positioned in close apposition to the syncytial membranes. Furthermore, perivascular and stromal zones

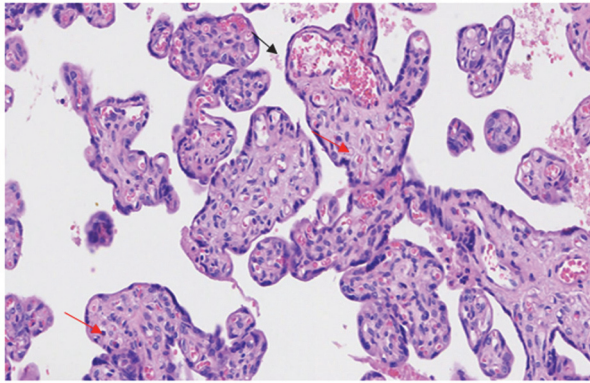
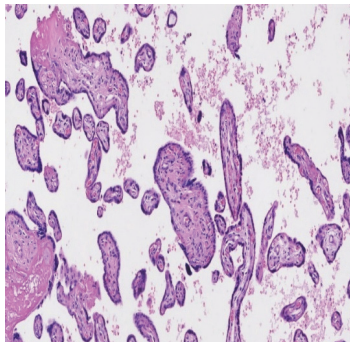
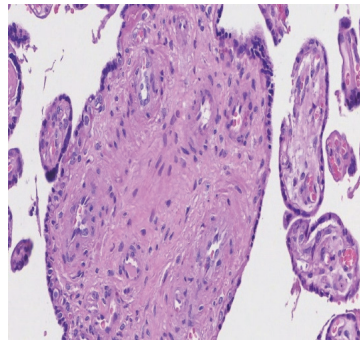


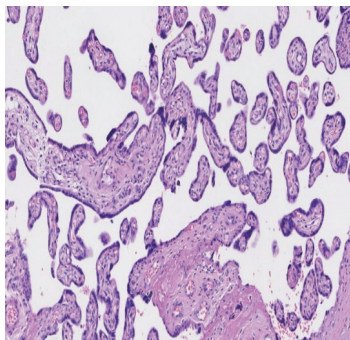
Fig. 2. (Male, H&E, 400x): Syncytial nuclear clustering, cytotrophoblast cells, and open capillaries. Perivascular stromal progenitor cells are marked by red arrows, and microvascular structures by black arrows.



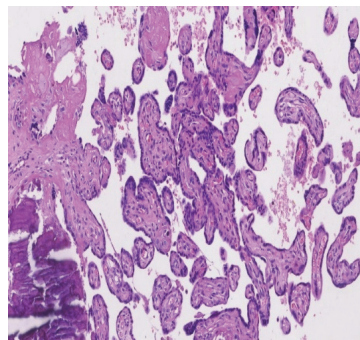
A



B



C



D

Fig. 3. (Female, H&E, 100x): Macroscopic villous architecture matching male controls (A); normal decidual cells and vasculature (B); fine-caliber terminal capillary networks (C & D).

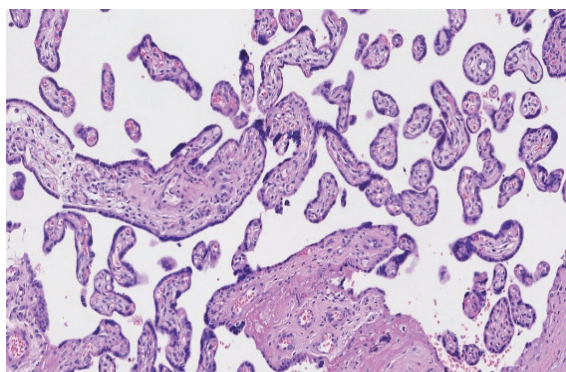


Fig. 4. (Female, H&E, 400x): High-power view of terminal villi showing intact syncytiotrophoblast layers, optimal stromal cellularity, and uncommitted stromal cells.

frequently contained cells exhibiting an immature morphology, high nuclear-to-cytoplasmic ratios, and euchromatic nuclei (marked by red arrows in Fig. 2), alongside vascular profiles indicative of active microvascular organization (marked by black arrows in Fig. 2).

Female placentas exhibited an overall macro- and microarchitecture comparable to male specimens, displaying normal macroscopic villous morphology (Fig. 3A), trophoblast layer continuity, and optimal stromal cellularity. Decidual components and vascular beds displayed typical histological traits (Fig. 3B). Morphological observation indicated that terminal villi in female specimens contained fine-caliber capillary loops that appeared narrower yet evenly distributed across the villous tissue (Fig. 3C and 3D).

High-power examination of terminal villi confirmed intact syncytiotrophoblast layers, optimal stromal cellularity, and uncommitted stromal cells with prominent euchromatin and high nuclear-to-cytoplasmic ratios (Fig. 4). Stromal collagen distribution, fibroblast density, and Hofbauer cell presence remained consistent with male specimens.

Discussion. The obtained data confirm the presence of certain sex-dependent features of placental morphometry and microstructure during physiological pregnancy. In particular, the registered tendency towards an increase in mass and linear dimensions of male placentas is consistent with the results of previously conducted studies [3, 12]. As clearly demonstrated by our microphotographic evaluations

(Figures 1–4), despite the overall conservation of histological architecture, subtle structural adaptations exist between sexes—specifically, the prevalence of broader capillary sinusoids in male terminal villi versus narrower, finely calibrated capillary networks in female specimens. This structural divergence points toward distinct sex-specific microcirculatory adaptations and hemodynamic adjustments during gestation, laying a solid morphological baseline for future targeted molecular and immunohistochemical investigations [11, 15].

Conclusion

Term placentas from uncomplicated pregnancies are characterized by a conservative baseline macro- and microstructural organization regardless of fetal sex, which is confirmed by standardized histological parameters.

Quantitative macroscopic analysis revealed a moderate trend towards an increase in the mean values of mass (499.9 ± 45.0 g versus 474.6 ± 31.0 g) and dimensions in male placentas compared to female ones.

Microscopic observations, as visualized through our histological preparations (Figures 1–4), demonstrate specific structural features of the terminal vascular bed: the predominance of wide sinusoids in the male cohort and narrower, evenly distributed capillary loops in the female cohort.

Prospects for further research. Prospects for further research include an in-depth study of the expression of angiogenic growth factors and immunohistochemical mapping of placental stromal elements taking into account the factor of fetal sex.

References

1. Al-Qraghouli M, Al-Attar N. Morphometric and Histological Study of Human Term Placenta in Normal Pregnancies. Iraqi Journal of Medical Sciences. 2019; 17(2): 140-148. doi: 10.22578/IJMS.17.2.6.
2. Barwari SS. Histological Evaluation of Placentas in Idiopathic Intrauterine Growth Restriction. Cureus. 2024 Oct 31;16(10):e72789. doi: 10.7759/cureus.72789.
3. Burton GJ, Fowden AL. The placenta: a memory for life? Journal of Physiology. 2015; 593(24): 5221-5233. doi: 10.1113/JP270385.
4. Dahlstrom JE, Subramaniam A, Faye-Petersen OM. Maternal Vascular Malperfusion and Associated Maternal Diseases. In: Baergen, R.N., Burton, G.J., Kaplan, C.G. (eds) Benirschke's Pathology of the Human Placenta. Springer, Cham. 2021; 507-554. doi: 10.1007/978-3-030-99166-1_15.
5. Ghani N, Yadav K. Comparative Study on Macroscopic Morphology of Human Placenta in Preterm, Term & Post Term Pregnancy. International Multispecialty Journal of Health. 2018; 4(4): 109-114. doi: 10.31143/imjh.2018.v4.i4.109.
6. Ileki JV, Tsilou E, Fisher S, Abrahams VM, Soares MJ, Cross JC, et al. Placental origins of adverse pregnancy outcomes: potential molecular targets: an Executive Workshop Summary of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. American Journal of Obstetrics and Gynecology. 2016; 215(1): S1-S46. doi: 10.1016/j.ajog.2016.03.001.
7. John MK, Sampson U, Sreedharan R. Placental Morphometry in Preterm and Term Neonates and its Association with their Birth Weights. Int J Anat Appl Physiol. 2020; 6(4): 152-155. doi: 10.19070/2572-7451-2000028.
8. Karmakar M, Kumar S, Chattopadhyay S, Kar S, Vaid L, Sen S. A study on the morphology and the morphometry of the human placenta and its clinical significance in rural population in Eastern India. Asian Pacific Journal of Health Science. 2018; 5(3): 202-209. doi: 10.21276/apjhs.2018.5.3.31.
9. Melbourne A, Aghwane R, Sokolska M, Owen D, Kendall G, Flouri D, et al. Separating fetal and maternal placenta circulations using multiparametric MRI. Magn Reson Med. 2019 Jan;81(1):350-361. doi: 10.1002/mrm.27406.
10. O'Connor BB, Pope BD, Peters MM, Ris-Stalpers C, Parker KK. The role of extracellular matrix in normal and pathological pregnancy: Future applications of microphysiological systems in reproductive medicine. Exp Biol Med (Maywood). 2020 Jul;245(13):1163-1174. doi: 10.1177/1535370220938741.
11. Salafia CM, Yampolsky M, Misra DP, Shlakhter O, Haas D, Eucker B, et al. Placental surface shape, function, and effects on fetal growth. Placenta. 2018; 68: 23-29. doi: 10.1016/j.placenta.2018.06.305.
12. Sgarbosa F, Silveira C, Silva MG, Ribeiro-Silva A. Quantitative Histological Evaluation of Term Placenta and Microvascular Architecture. Pathology - Research and Practice. 2021; 223: 153472. doi: 10.1016/j.prp.2021.153472.
13. Staud F, Karahoda R. Trophoblast: The central unit of fetal growth, protection and programming. The International Journal of Biochemistry & Cell Biology. 2018; 105: 35-40. doi: 10.1016/j.biocel.2018.09.014.
14. Sun C, Groom KM, Oyston C, Chamley LW, Clark AR, James JL. The placenta in fetal growth restriction: what is going wrong? Placenta. 2020; 96: 10-18. doi: 10.1016/j.placenta.2020.05.003.
15. Vambergue A, Fajardy I. Consequences of gestational diabetes mellitus on placenta: the impact of sexual dimorphism. Frontiers in Endocrinology. 2022; 13: 869226. doi: 10.3389/fendo.2022.869226.

Conflict of interest. The authors have no conflicts of interest to declare.

ORCID: Gurbanova Sh.G. <https://orcid.org/0009-0000-2307-5820>, Isayev O.R. <https://orcid.org/0000-0002-9673-7458>, Akhundova N.E. <https://orcid.org/0009-0002-1346-2389>, Aliyarbayova A.A. <https://orcid.org/0000-0003-0887-3132>, Aliyeva G.N. <https://orcid.org/0009-0001-8614-3015>, Aliyeva Sh.E. <https://orcid.org/0009-0006-3833-5668>, Hagverdiyeva R.R. <https://orcid.org/0000-0002-5394-8749>.

Article received: 18.09.2025