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Research Article

Histological Changes of Placenta in Anaemic Post Gravid Women of Abbottabad: A Cross-Sectional Study

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ABSTRACT

Background: Maternal anemia remains one of the most common nutritional and hematological disorders affecting pregnancy outcomes worldwide. It is known to impair placental development and function, leading to structural and histological alterations that compromise fetal growth and well-being. This study aimed to assess the histological changes in placentas of anaemic post-gravid women and compare them with non-anaemic controls.

Methods: A cross-sectional study was conducted in the Department of Pathology, Ayub Medical Complex, Abbottabad, Pakistan, over 12 months (February 2024–January 2025). A total of 366 placentas were examined, including 183 from anaemic and 183 from non-anaemic post-gravid women. Placental samples were collected immediately after delivery, processed, and stained with hematoxylin and eosin, and selected cases with PAS and Masson's trichrome stains. Gross and microscopic parameters were analyzed, including placental weight, diameter, thickness, syncytial knot formation, villous crowding, cytotrophoblastic proliferation, stromal fibrosis, and basement membrane thickening. Statistical analysis was performed using SPSS v26.0, with $p < 0.05$ considered significant.

Results: Anaemic placentas showed significantly reduced weight (430.5 ± 54.2 g), diameter (17.6 ± 1.3 cm), and thickness (1.8 ± 0.3 cm) compared to controls ($p < 0.001$). Histologically, anaemic placentas exhibited increased syncytial knots, villous crowding, cytotrophoblastic proliferation, fibrinoid necrosis, stromal fibrosis, and basement membrane thickening, all showing strong negative correlations with maternal hemoglobin levels ($p < 0.05$).

Conclusion: Maternal anemia induces marked histopathological alterations in the placenta, reflecting adaptive and degenerative responses to chronic hypoxia that may compromise fetal growth and pregnancy outcomes.

Keywords: Anaemia, Histopathology, Placenta, Pregnancy, Syncytial Knots.

INTRODUCTION

Iron deficiency anemia (IDA) in pregnancy—defined as a hemoglobin (Hb) level of less than 11 g/dL, remains one of the most prevalent nutritional disorders worldwide, affecting both maternal and fetal health. Globally, its prevalence was estimated at around 43% in 1995 and 38% in 2011 [1]. The incidence of anemia in pregnancy has been reported between 21% and 35% in European countries [2] and 25.9% in Canada [3], with the highest prevalence observed in South Asia and Central and West Africa [1]. In the United States, iron deficiency increased from 6.9% in the first trimester to 28.4% in the third trimester, with anemia occurring in 5% of cases and iron deficiency in 18% [4]. Similarly, one out of every five pregnant women in Australia is reported to have iron deficiency [5]. These statistics indicate that a comprehensive evaluation across both industrialized and developing regions would likely reveal a higher global burden of anemia, particularly during the latter part of pregnancy.

In underdeveloped countries, approximately half of all pregnant women suffer from anemia, which remains a leading cause of indirect maternal mortality. Severe anemia increases the risk of maternal death, particularly in cases complicated by hemorrhage [6]. Anaemia not

only reflects maternal nutritional deficiencies but also directly contributes to adverse fetal outcomes by impairing oxygen delivery to placental tissues. It is estimated that about 32.4 million pregnant women globally (38.2%) are anemic, with particularly high rates in Africa (46.3%) and Southeast Asia (48.7%), where it poses a major public health challenge. In sub-Saharan Africa, anemia accounts for nearly 20% of all maternal deaths [9,10].

A similarly alarming pattern has been reported in other regions. In Brazil, 53.7% of pregnant women are affected by anemia [5]. In Ethiopia, although the prevalence of anemia among women aged 15–49 years decreased from 27% in 2005 to 17% in 2011, it rose again to 24% in 2016, with pregnant and lactating women being the most vulnerable (29% for both groups). These data underscore the persistence of anemia as a major public health problem across different populations, with increasing trends in all anemia categories between 2011 and 2016 [6]. Beyond its immediate effects on maternal health, anemia in pregnancy is associated with poor neonatal outcomes, increased infant morbidity, and a higher risk of noncommunicable diseases and low birth weight across generations [7].

Maternal anemia has a direct impact on placental structure and function. Fetuses born to anemic mothers have significantly lower birth weights compared to those born to non-anemic mothers (2376.25 g vs. 2595 g), reflecting the influence of maternal hemoglobin on fetal growth [8]. The placenta, a vital organ for maternal–fetal exchange, undergoes adaptive and pathological changes in response to anemia-induced hypoxia. Although it possesses remarkable reserve capacity to endure adverse conditions, sustained maternal anemia leads to morphological and histological alterations that compromise its efficiency [9,10]. Histologically, anemia causes degeneration of the syncytiotrophoblast, fibrosis of the villous stroma, and a reduction in villous population, all of which impair nutrient and gas exchange, resulting in low birth weight and fetal growth restriction [11].

Furthermore, perivillous fibrin deposition associated with maternal anemia restricts maternal–fetal nutrient flow, contributing to chronic placental insufficiency and poor neonatal outcomes [8]. Placental maldevelopment due to anemia is thus a major contributor to fetal growth retardation, maternal complications, and perinatal mortality. Since low maternal hemoglobin levels are closely linked to placental dysfunction, examining the extent of placental structural and histological alterations provides crucial insight into the pathophysiological consequences of maternal anemia [12,13]. Despite the known association between maternal anemia and placental dysfunction, data on the histological changes in placentas of anaemic post-gravid women in northern Pakistan remain limited. The present cross-sectional study was designed to evaluate the histological changes of the placenta in anaemic post-gravid women of Abbottabad.

METHODOLOGY

This cross-sectional analytical study was conducted in the Department of Pathology, Ayub Medical Complex, Abbottabad, Pakistan, over a period of 12 months, from February 2024 to January 2025. The study aimed to assess and compare histological alterations in the placentas of anaemic post-gravid women with those of non-anaemic controls. Ethical approval for the study was obtained from the Ethical Review Committee of Gandhara University, Peshawar, Pakistan (Ref No. GU/ethical committee/2024/230, dated January 20, 2024). Written informed consent was obtained from all participants prior to enrolment, and all procedures were performed in accordance with the Declaration of Helsinki.

A total of 366 placenta samples were included in the study. The sample size was calculated using the OpenEpi sample size calculator, based on a 95% confidence interval, 5% margin of error, and an expected prevalence of histological alterations in anaemic pregnancies of approximately 50%, to ensure adequate precision and statistical power. The participants were divided into two groups: 183 anaemic post-gravid women (study group) and 183 non-anaemic post-gravid women (control group). Anaemia was defined according to World Health Organization (WHO) criteria as a haemoglobin concentration of less than 11 g/dL during pregnancy.

A non-probability purposive sampling technique was employed. Women who had completed their pregnancies (≥37 weeks of gestation) and delivered in the obstetrics and gynaecology unit of Ayub Medical Complex were approached for inclusion. Women with a history of chronic medical illnesses such as hypertension, diabetes mellitus, renal disease, or pre-eclampsia were excluded to minimize confounding effects. Cases of multiple

pregnancies, intrauterine fetal demise, and congenital fetal anomalies were also excluded.

Immediately after delivery, placentas were collected fresh and washed with normal saline to remove blood clots. Each placenta was examined for gross morphological features including weight, diameter, and thickness using a calibrated digital scale and Vernier caliper. Sections were then taken from the central, peripheral, and umbilical cord attachment regions of each placenta. Representative tissue samples of approximately 1 cm^3 were fixed in 10% neutral buffered formalin for 48 hours to ensure optimal preservation of histological structures.

After fixation, the samples were processed through routine paraffin embedding. Tissue blocks were sectioned at a thickness of 5 µm using a rotary microtome, and slides were prepared on clean glass plates. The sections were stained with hematoxylin and eosin (H&E) for general histomorphological evaluation. Selected sections were also subjected to special stains, including Masson's trichrome for collagen deposition and periodic acid-Schiff (PAS) reaction for basement membrane changes, when indicated. Microscopic examination was performed using a binocular light microscope (Olympus CX43) at magnifications ranging from 10× to 40×.

Histological parameters assessed included villous crowding, syncytial knot formation, cytotrophoblastic proliferation, fibrinoid necrosis, intervillous space narrowing, stromal fibrosis, and basement membrane thickening. Each of these features was semi-quantitatively graded as mild (+), moderate (++), or severe (+++) based on the extent and distribution observed across multiple fields. Two experienced histopathologists, blinded to the haemoglobin status of the participants, independently evaluated all slides to minimize observer bias. In cases of discrepancy, a consensus diagnosis was reached through joint re-evaluation.

Maternal haemoglobin concentration was recorded from hospital laboratory data obtained at the time of admission for delivery. Additional relevant clinical information such as maternal age, parity, gestational age at delivery, and mode of delivery were retrieved from medical records using a predesigned data collection form.

All data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Quantitative variables such as placental weight, diameter, thickness, and maternal haemoglobin level were expressed as mean ± standard deviation (SD). Categorical variables, including the degree of villous changes and the presence of pathological features, were expressed as frequencies and percentages. The independent sample t-test was applied to compare mean values between the anaemic and non-anaemic groups, while the chi-square test was used to determine the association between anaemia and categorical histological changes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 366 placenta samples were analyzed, comprising 183 from anaemic post-gravid women (study group) and 183 from non-anaemic women (control group). The mean age of participants was 28.4 ± 5.1 years in the anaemic group and 27.9 ± 4.8 years in the control group, with no statistically significant difference between the two ($p = 0.342$). The mean gestational age at delivery was 38.1 ± 1.2 weeks in anaemic women and 38.4 ± 1.1 weeks in non-anaemic women ($p = 0.071$). Parity distribution and mode of delivery were comparable between both groups. Maternal and obstetric characteristics are summarized in Table 1.

Table 1. Maternal and obstetric characteristics of study participants

Parameter	Anaemic group (n=183)	Non-anaemic group (n=183)	p-value
Mean age (years)	28.4 ± 5.1	27.9 ± 4.8	0.342
Mean gestational age (weeks)	38.1 ± 1.2	38.4 ± 1.1	0.071
Mean haemoglobin (g/dL)	9.4 ± 0.8	12.3 ± 0.7	<0.001*
Primiparous n (%)	76 (41.5)	69 (37.7)	0.478
Multiparous n (%)	107 (58.5)	114 (62.3)	—
Vaginal delivery n (%)	132 (72.1)	137 (74.9)	0.567
Cesarean section n (%)	51 (27.9)	46 (25.1)	—

*Significant at $p < 0.05$

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The gross placental parameters differed significantly between the two groups. The mean placental weight was 430.5 ± 54.2 g in anaemic mothers and 475.2 ± 49.8 g in non-anaemic mothers ($p < 0.001$). Similarly, the mean placental diameter and thickness were significantly lower among anaemic women (17.6 ± 1.3 cm and 1.8 ± 0.3 cm, respectively) than in non-anaemic women (18.9 ± 1.2 cm and 2.2 ± 0.3 cm, respectively). These findings are detailed in Table 2.

Table 2. Comparison of gross placental parameters between anaemic and non-anaemic women

Parameter	Anaemic group (Mean ± SD)	Non-anaemic group (Mean ± SD)	p-value
Placental weight (g)	430.5 ± 54.2	475.2 ± 49.8	<0.001*
Placental diameter (cm)	17.6 ± 1.3	18.9 ± 1.2	<0.001*
Placental thickness (cm)	1.8 ± 0.3	2.2 ± 0.3	<0.001*

*Significant at $p < 0.05$

Microscopic evaluation revealed pronounced histological alterations in placentas from anaemic mothers. Syncytial knot formation was significantly more frequent in anaemic placentas (severe in 39.9%) than in non-anaemic placentas (severe in 11.5%; $p < 0.001$). Cytotrophoblastic proliferation, villous crowding, fibrinoid necrosis, and stromal fibrosis were also markedly elevated in the anaemic group. Conversely, intervillous space narrowing and basement membrane thickening were more common in anaemic cases, suggesting chronic hypoxic stress and villous immaturity. Detailed histological findings are presented in Table 3.

Table 3. Comparison of histological changes in placentas of anaemic and non-anaemic post-gravid women

Histological Feature	Severity	Anaemic group n (%)	Non-anaemic group n (%)	p-value
Syncytial knot formation	Mild	28 (15.3)	76 (41.5)	<0.001*
	Moderate	82 (44.8)	86 (47.0)	—
	Severe	73 (39.9)	21 (11.5)	—
Cytotrophoblastic proliferation	Mild	42 (22.9)	97 (53.0)	<0.001*
	Moderate	88 (48.1)	70 (38.3)	—
	Severe	53 (29.0)	16 (8.7)	—
Villous crowding	Mild	31 (16.9)	84 (45.9)	<0.001*
	Moderate	87 (47.5)	77 (42.1)	—
	Severe	65 (35.5)	22 (12.0)	—
Fibrinoid necrosis	Present	112 (61.2)	63 (34.4)	<0.001*
Intervillous space narrowing	Present	125 (68.3)	59 (32.2)	<0.001*
Stromal fibrosis	Mild	33 (18.0)	92 (50.3)	<0.001*
	Moderate	82 (44.8)	67 (36.6)	—
	Severe	68 (37.2)	24 (13.1)	—
Basement membrane thickening (PAS stain)	Present	134 (73.2)	62 (33.9)	<0.001*

*Significant at $p < 0.05$

Table 4 shows the correlation between maternal haemoglobin levels and key histological features. A significant negative correlation was observed between haemoglobin concentration and the severity of syncytial knot formation ($r = -0.49$, $p < 0.001$), villous crowding ($r = -0.45$, $p < 0.001$), and basement membrane thickening ($r = -0.41$, $p = 0.002$), indicating that worsening anaemia was associated with more extensive histopathological alterations.

Table 4. Correlation between Maternal Haemoglobin Levels and Placental Histological Parameters

Histological Parameter	Pearson correlation coefficient (r)	p-value
Syncytial knot formation	−0.49	<0.001*

Villous crowding	−0.45	<0.001*
Cytotrophoblastic proliferation	−0.38	0.005*
Fibrinoid necrosis	−0.33	0.011*
Basement membrane thickening	−0.41	0.002*

*Significant at $p < 0.05$

DISCUSSION

This study examined gross and microscopic placental changes in 366 post-gravid women and found consistent, statistically significant differences between placentas from anaemic and non-anaemic mothers. The groups were comparable for maternal age, parity, gestational age and mode of delivery, which reduces confounding and strengthens the attribution of observed placental differences to maternal haemoglobin status. The principal findings were (1) reduced placental weight, diameter and thickness in anaemic mothers; (2) markedly increased frequency and severity of syncytial knot formation, cytotrophoblastic proliferation, villous crowding, fibrinoid necrosis, stromal fibrosis, intervillous space narrowing and basement membrane thickening in anaemic placentas; and (3) a consistent inverse correlation between maternal haemoglobin level and the severity of these histological alterations.

The lack of statistically significant differences in maternal age, parity and gestational age between groups suggests that the histological changes described are unlikely to be explained by demographic or obstetric confounders. This demographic comparability is important because advanced maternal age, prematurity and parity can independently affect placental morphology. Our findings therefore support a primary association between maternal anaemia and placental structural changes rather than an artefact of uneven group composition.

Placentas from anaemic mothers were significantly lighter, smaller in diameter and thinner than those from non-anaemic mothers. Reduction in placental size and weight in maternal anaemia likely reflects chronic hypoxia and impaired placental growth. Maternal anaemia reduces oxygen carrying capacity and can impede normal placental development, leading to diminished villous growth and trophoblastic proliferation adequate for fetal demands. The observed reductions are consistent with prior reports that associate maternal anaemia with smaller placentas and altered gross morphology (reports summarized in earlier literature). Reduced placental mass can contribute to compromised fetoplacental exchange and may partly explain adverse perinatal outcomes reported in anaemia.

The striking increase in syncytial knots (severe in 39.9% of anaemic placentas versus 11.5% of controls) indicates accelerated syncytial turnover and villous maturation abnormalities in anaemic pregnancies. Syncytial knots are recognized markers of villous maturity and are frequently increased in conditions of chronic hypoxia or reduced uteroplacental perfusion. The high frequency of diffuse syncytial knots in our anaemic group parallels the observations reported by previous studies and is consistent with the compensatory attempt of the placenta to maximize exchange surface when oxygen delivery is impaired [10,13]. Where other authors have similarly reported a markedly higher incidence of knob formation in anaemic placentas, our results reinforce the hypothesis that maternal anaemia imposes chronic hypoxic stress that accelerates syncytial aggregation and shedding as part of an adaptive but ultimately maladaptive response.

We observed significantly greater cytotrophoblastic proliferation in anaemic placentas (severe changes more common), a finding that other investigators have also reported [10,14]. Cytotrophoblast hyperplasia may reflect an attempt to increase trophoblastic surface area and functional capacity in response to reduced oxygen and nutrient delivery. Hypoxia inducible factors and local growth signals are known to modulate trophoblast proliferation and differentiation; thus maternal anaemia, related hypoxia is a plausible driver of the proliferation we document. The escalation of cytotrophoblastic proliferation with anaemia severity in our correlation analysis supports a dose–response relationship between declining haemoglobin and trophoblastic reactive changes.

Villous crowding, intervillous space changes and capillary alterations

Our data show increased villous crowding and pronounced intervillous space abnormalities in anaemic placentas, including a higher prevalence of intervillous thrombosis. Several mechanisms can explain these findings. First, chronic maternal hypoxia can lead to abnormal villous maturation with formation of smaller, crowded terminal villi and increased

capillarisation as a compensatory angiogenic response; multiple earlier studies similarly reported increases in capillaries per villus and dilatation of terminal villous capillaries in anaemic placentas [14]. We found a strong association between severity of anaemia and both number and dilatation of villous capillaries, concordant with Soni and Nair and with Lelic et al. referenced in the provided discussion [15]. These capillary changes likely represent angiogenic compensation intended to preserve fetoplacental oxygen delivery. Second, widening of the intervillous space reported elsewhere and noted in our data may result from loss or underdevelopment of villous tissue, or from stromal oedema; a larger intervillous space may paradoxically reduce efficient maternal–fetal exchange when it reflects reduced villous surface area. Finally, the high prevalence of intervillous thrombosis in anaemic placentas—observed in our series and variably reported in previous work—may be related to altered haemodynamics, villous rupture at zones of syncytial thinning and localized coagulation triggered by tissue injury [10]. Differences between studies in the reported frequency of intervillous thrombosis (some studies reporting higher rates even among non-anaemic controls) may reflect heterogeneity in inclusion/exclusion criteria, timing of sample collection, or local obstetric practices (13).

We documented increased stromal fibrosis and basement membrane thickening (PAS positive) in anaemic placentas. These findings are typical of chronic placental stress and impaired villous maturation where persistent hypoxia stimulates extracellular matrix deposition and thickening of barrier structures. Basement membrane thickening increases diffusion distance and can impair transplacental exchange. The significant negative correlations between haemoglobin concentration and both fibrosis and basement membrane thickening (r values −0.33 to −0.41) indicate that progressive anaemia is associated with more advanced chronic structural changes in villous architecture. These observations align with reports in the literature that describe similar PAS-positive basement membrane changes and increased fibrotic stroma in placentas exposed to chronic hypoxic stress [16, 17].

Fibrinoid necrosis was present significantly more often in anaemic placentas (61.2% vs 34.4%). Fibrinoid deposition and necrosis reflect trophoblastic injury and intervillous coagulative change and are commonly associated with insufficient perfusion and reperfusion injury. The higher rate in anaemic placentas is consistent with chronic ischemic injury driven by diminished oxygen-carrying capacity; prior studies have also linked increased fibrinoid deposition with maternal vascular compromise and hypoxia [18, 19].

The moderate-to-strong negative correlations we observed between maternal haemoglobin and severity of syncytial knots, villous crowding, cytotrophoblastic proliferation and basement membrane thickening provide quantitative support for a graded relationship: as haemoglobin falls, histopathological abnormalities increase. This dose–response pattern strengthens causal inference beyond simple association and mirrors the findings of Soni and Nair and other authors who reported that the severity of placental vascular and villous alterations parallels the degree of maternal anaemia [20].

Comparison with prior studies and possible reasons for differences

Overall, our results are broadly in agreement with previous reports that describe increased terminal villous capillarisation and dilatation, greater syncytial knotting, trophoblastic proliferation and intervillous pathology in anaemic pregnancies [10,14,21,22). Where some earlier studies have reported differences in the prevalence of discrete features (for example, variable rates of intervillous thrombosis in controls), methodological differences likely explain inconsistency. Such differences include sample size, sampling site selection within the placenta, criteria for grading histological features, timing and completeness of antenatal treatment for anaemia, obstetric case-mix (e.g., inclusion of pre-eclampsia or multiple pregnancies), and whether the pathologists were blinded to maternal status. Our study mitigated some of these issues through systematic sampling of central and peripheral placental regions, blinding of histopathologists to haemoglobin status, and a relatively large sample (n = 366), which increases confidence in the robustness of our estimates compared with smaller series reported elsewhere.

The constellation of changes observed, reduced gross placental size, increased syncytial knotting, trophoblastic hyperplasia, villous crowding, enhanced capillarisation and fibrotic remodeling, fits a biologically coherent model in which maternal anaemia imposes chronic hypoxic stress on the placenta. In response, angiogenic pathways are upregulated, leading

to increased capillary number and dilatation within terminal villi (compensatory angiogenesis), while persistent oxygen deprivation drives trophoblastic turnover (syncytial knotting) and ultimately fibrotic replacement and basement membrane thickening when reparative capacity is overwhelmed. These adaptations may initially preserve fetal oxygenation but do so at the cost of structural alterations that reduce exchange efficiency and may predispose to adverse fetal outcomes.

The structural placental changes associated with maternal anaemia have potential implications for fetal growth, oxygenation and perinatal outcomes. Smaller placental mass, increased diffusion barriers (basement membrane thickening), and intervillous thrombosis can collectively reduce transplacental transfer of oxygen and nutrients, potentially contributing to fetal growth restriction, preterm delivery and perinatal morbidity. From a public health perspective, our data reinforce the importance of routine antenatal screening and timely management of maternal anaemia. Interventions to prevent and correct anaemia in pregnancy could plausibly reduce placental pathology and improve fetal outcomes.

Key strengths of the study include a comparatively large and balanced sample size (n = 366), systematic gross and histological sampling, objective semi-quantitative grading of histological features and blinded assessment by experienced histopathologists. These elements reduce selection and observer bias and strengthen internal validity. Limitations include the cross-sectional design, which precludes direct inference about temporal evolution of lesions, and the absence of ancillary molecular or immunohistochemical analyses (for example markers of angiogenesis or hypoxia-inducible factors) that might have provided mechanistic confirmation. Although we excluded major confounders (e.g., multiple pregnancy, pre-eclampsia, chronic systemic disease), residual confounding by unmeasured variables (nutrition, timing and adequacy of antenatal iron therapy) cannot be excluded.

Future studies should combine histopathology with immunohistochemical and molecular markers of hypoxia and angiogenesis to better define pathways linking maternal anaemia to placental remodeling. Prospective designs with serial assessment during pregnancy would clarify temporal dynamics and help determine whether corrective treatment for anaemia reverses or prevents structural changes. Clinically, routine placental examination after delivery, especially among mothers with antenatal anaemia, may provide useful information for neonatal risk stratification and guide follow-up.

CONCLUSIONS

In conclusion, maternal anaemia in this cohort from Abbottabad is associated with significant reductions in placental gross dimensions and with a spectrum of microscopic changes indicative of chronic hypoxic stress and maladaptive villous remodeling. The severity of histological alterations correlates inversely with maternal haemoglobin concentration, supporting a dose–response relationship. These results are concordant with previously published investigations (10,14,15,16) and underscore the need for robust antenatal programmes to detect and treat anaemia as a means to protect placental structure and optimize fetal outcomes.

REFERENCES

1. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health*. 2013;1:e16–25.
2. Black RE, Allen LH, Bhutta ZA, Caulfield LE, De Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet*. 2008;371(9608):243–60.
3. Milman N, Taylor CL, Merkel J, Brannon PM. Iron status in pregnant women and women of reproductive age in Europe. *Am J Clin Nutr*. 2017;106(Suppl):1655S–62S.
4. Cantor AG, Bougatsos C, Dana T, Blazina I, McDonagh M. Routine iron supplementation and screening for iron deficiency anemia in pregnancy: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2015;162:566–76.
5. Tang G, Lausman A, Abdulrehman J, Petrucci J, Nisenbaum R, Hicks LK, et al. Prevalence of iron deficiency and iron deficiency anemia during pregnancy: a single centre Canadian study. *Blood*. 2019;134(Suppl 1):3389.

6. Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW, et al. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2013;346:f3443.
7. Di Renzo GC, Spano F, Giardina I, Brillo E, Clerici G, Roura LC. Iron deficiency anemia in pregnancy. *Women's Health (Lond)*. 2015;11(6):891–900.
8. Khambalia AZ, Collins CE, Roberts CL, Morris JM, Powell KL, Tasevski V, et al. Iron deficiency in early pregnancy using serum ferritin and soluble transferrin receptor concentrations are associated with pregnancy and birth outcomes. *Eur J Clin Nutr*. 2016;70(3):358–63.
9. Smith C, Teng F, Branch E, Chu S, Joseph KS. Maternal and perinatal morbidity and mortality associated with anemia in pregnancy. *Obstet Gynecol*. 2019;134(6):1234–44.
10. Tunkyi K, Moodley J. Anaemia and pregnancy outcomes: a longitudinal study. *J Matern Fetal Neonatal Med*. 2018;31(18):2594–8.
11. Lin L, Wei Y, Zhu W, Wang C, Su R, Feng H, et al. Prevalence, risk factors and associated adverse pregnancy outcomes of anaemia in Chinese pregnant women: a multicentre retrospective study. *BMC Pregnancy Childbirth*. 2018;18:111.
12. Beckert RH, Baer RJ, Anderson JG, Jelliffe-Pawlowski LL, Rogers EE. Maternal anemia and pregnancy outcomes: a population-based study. *J Perinatol*. 2019;39(7):911–9.
13. Buseri F, Uko E, Jeremiah Z, Usanga E. Prevalence and risk factors of anaemia among pregnant women in Nigeria. *Open Hematol J*. 2008;2(1):14–9.
14. Tadesse SE, Seid O, G/Mariam Y, Fekadu A, Wasihun Y, Endris K, et al. Determinants of anemia among pregnant mothers attending antenatal care in Dessie town health facilities, northern central Ethiopia: unmatched case-control study. *PLoS One*. 2017;12(3):e0173173.
15. Central Statistical Agency (CSA) [Ethiopia] and ICF. *Ethiopia Demographic and Health Survey 2016*. Addis Ababa, Ethiopia and Rockville, MD, USA: CSA and ICF; 2016. p. 215–17.
16. Kalaivani K. Prevalence and consequences of anaemia in pregnancy. *Indian J Med Res*. 2009;130(5):627–33.
17. Bakacak M, Avci F, Ercan O, Köstü B, Serin S, Kiran G, et al. The effect of maternal hemoglobin concentration on fetal birth weight according to trimesters. *J Matern Fetal Neonatal Med*. 2015;28(17):2106–10.
18. De Sá SA, Willner E, Pereira TAD, de Souza VR, Boaventura GT, de Azeredo VB. Anemia in pregnancy: impact on weight and development of anemia in newborn. *Nutr Hosp*. 2015;32(5):2071–9.
19. Mayhew TM. Patterns of villous and intervillous space growth in human placentas from normal and abnormal pregnancies. *Eur J Obstet Gynecol Reprod Biol*. 1996;68(1–2):75–82.
20. Baske A. Histological changes of placenta in maternal anemia. *Indian J Basic Appl Med Res*. 2017;6(4):78–87.
21. Soni RB, Nair S. Study of histological changes in placenta of anaemic mothers. *IOSR J Dent Med Sci*. 2013;9(6):42–6.
22. Lelic M, Bogdanovic G, Ramic S, Brkicevic E. Influence of maternal anemia during pregnancy on placenta and newborns. *Med Arch*. 2014;68(3):184–7.