GROSS MORPHOLOGICAL CHANGES OF PLACENTA ASSOCIATED WITH MATERNAL ANEMIA

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ABSTRACT

INTRODUCTION: Placenta is a feto-maternal organ composed of maternal part, decidua basalis, and a fetal part, chorion frondosum. The intra-uterine survival of the fetus is dependent on this vital organ.

AIM: The main aim of this study was to compare the macro architectural changes of placenta associated with maternal anemia in Dessie Referral Hospital, Northeast Ethiopia.

METHODS: A comparative cross-sectional study design was conducted from May 1-June 16, 2018 at Dessie Referral Hospital. A total of 96 placentas (48 anemic and 48 non-anemic) was collected after delivery at the labor room. EPI data version 4.2.0 was used to enter the data and analyzed by SPSS version 24. One way ANOVA and independent sample t- test was used to compare the mean differences of the groups.

RESULTS: In pregnancies with maternal anemia, the mean placental weight was 544±98 g and in non- anemic mother's it was 502±93 g ($p=0.03$). The mean birth weight in anemic group was 2502±360 g and in non-anemic group 3035±305 g ($p<0.001$). The mean number of cotyledons, was 13.5±1.8 and 17.6±1.1, ($p<0.001$) in anemic and non-anemic groups, respectively. There was a significant difference in the mean placental diameter of anemic 18±1.5 cm and in non-anemic 17±1.5 cm mothers ($p<0.001$).

CONCLUSIONS: The placenta was larger in anemic mothers than non-anemic mothers with amplifying in mean placental weight, thickness and diameter. It was bigger in weight, diameter and thickness in mild and moderate anemic but smaller in severe anemic mothers than non-anemic mothers.

KEYWORDS: Anemia, Placenta, Morphology, Dessie Referral Hospital

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INTRODUCTION

Placenta is a fetomaternal organ composed of maternal part, decidua basalis, and a fetal part, chorion frondosum[1]. During the period of pregnancy, it acts as the lungs, gut, kidneys, and liver of the fetus[2]. It plays a crucial role in fetal development and health by tightly regulating the exchange of endogenous and exogenous materials between the mother and the fetus. Placenta gives the picture of the most accurate record of the prenatal experience of an infant[3, 4]. Even though fetal growth and well-being depends on the functional and structural component of the placenta[5], this organ is affected by various defects and diseases just like the other vital organs of the body[6].

Various clinical conditions such as anemia, diabetes, hypertension and others have an injurious effect on the placenta occasionally resulting in morphological change. It undergoes different changes in weight, volume, structure, shape and function continuously throughout the gestation to support the prenatal life. This may seriously affect the health and even life of the fetus. Some researchers observed that the placenta has considerable functional reserve capacity; it can fix any damage it suffers from considerable damage. It has also its own compensatory mechanisms which tend to limit the ill-effects of both tissue injury and an unfavorable maternal situation like anemia[6]. Even though placenta has a remarkable reserve capacity to withstand noxious environment, it is equally true that some unfavorable changes due to maternal anemia causes adverse effect on placenta which ultimately might compromise the well-being of the fetus[7]. Severe abnormalities of the placenta lead to the adverse fetal outcome and some structural changes could be the consequences of poor fetal condition[8].

Anemia is a medical condition which defined as low hemoglobin level in the blood. It is a condition in which the hemoglobin content of the blood is lower than normal for a person's age, gender and environment resulting in oxygen carrying capacity of the blood is being reduced. World Health Organization classify anemia in pregnancy based on hemoglobin level as 10.0-10.9g/dl(mild anemia),7-9.9g/dl(moderate anemia) and <7g/dl (severe anemia) [9].

IIn fact, pregnancy is a state of increased iron demand which rises from 2.5mg/day in earlier weeks to 6.6mg/day in the third trimester. If demand and supply balance is not met, the women will develop anemia (10). Anemia during pregnancy affects about half of all pregnant mothers in developing countries and it is the major cause of indirect maternal mortality. For instance, severe anemia contributes to the risk of maternal death in cases of hemorrhage[11].

In Ethiopia, anemia prevalence among women aged 15-49 years declined from 27% in 2005 to 17% in 2011. But currently it has increased to 24% in 2016 and women who are pregnant or breastfeeding are more likely to be anemic (29% for both groups) as well; these data suggest that anemia is a public health problem in our country[12]. Anemia can directly cause poor growth of the fetus in utero due to inadequate oxygen flow to the placental tissue or it is an indirect indicator of maternal nutritional deficiency[13]. Mal-development of the placenta is the leading cause of maternal and perinatal mortality and an important factor of fetal growth retardation[14]. Therefore, there is a need to explore the extent of structural changes of placenta, because the severity of these morphological parameters change i.e. placental weight, shape, thickness and diameter is correlated with the efficiency of placenta to support the growth of the fetus, and low hemoglobin level is likely to be related to insufficient functioning of the placenta[7,15].

Morphological changes of the placenta due to anemia condition influences the placenta's exchange and hemodynamic processes[16]. Notably early examination of placental morphology in the postpartum period can improve the skill of clinicians to predict birth outcomes and will give a clue for earlier identification of the fetus at risk. After delivery, if the placenta is inspected meticulously, it can provide much insight into the prenatal health of the baby and the mother. Thus, it facilitates preparation for management at least in neonatal and childhood periods.

METHODS:

A comparative cross-sectional study design was conducted in Dessie referral hospital from May-June, 2018. Dessie town is Northeast of 401 Km from Addis Ababa the

capital of Ethiopia and 478 km far from Bahirdar which is the capital city of Amhara regional state. The Hospital is found in Dessie town serving 2.4 million peoples including neighboring zones. It has more than six wards including the obstetrics and gynecology ward and the hospitals monthly delivery report is above 500 mothers.

Source Population

All full term pregnant mothers who attend their delivery at Dessie referral hospital.

Study Population

Full term anemic and non-anemic mothers attend their delivery at Dessie referral hospital during data collection period.

Eligibility Criteria

Inclusion criteria

Group I; Anemic (mild, moderate and severe) pregnant mothers during our data collection period aged 20-35 years, diagnosed clinically and hematologically.

Group II; Non-anemic pregnant mothers aged 20-35 years having no signs and symptoms of anemia with their hemoglobin level recorded to be more than or equal to 11g/dl at any time during pregnancy.

Exclusion criteria

Any pathological condition which affect the placenta as well as fetus, such as; Pregnant mothers who experience any complication during pregnancy like gestational hypertension, chronic hypertension, Malaria, pre-existing diabetes mellitus, multiple pregnancy, fetal congenital anomaly, diagnosed single umbilical artery, IUFD, pre and post term pregnancies were excluded from this study.

Sample Size and Sampling procedure

The desired sample size was calculated by using Open Epi, version 3.0, using the difference of means formula, by considering two sided 95% confidence level and 80% power; comparison with equal number of cases and controls (n1= n2) was considered. Then, the final calculated sample size was 96 placentas (48 anemic, and 48 non-anemic).

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2)(Z_{\alpha/2} + Z_\beta)^2}{(\mu_1 - \mu_2)^2}$$

Sampling Technique and Procedure

Purposive sampling technique was employed to conduct this research; during the data collection period the number of mothers delivered in Dessie Referral Hospital were 550. From those 550 mothers delivered in the hospital, the sample was taken purposively till the total sample size was achieved.

For each case, a preliminary history was elicited from the mother and her clinical sheets regarding her current and past Medical, Surgical, Obstetrics and Gynecologic histories which affect the morphology of placenta. Then, the fresh placenta was collected as soon as delivery and checked for its completeness; secondly umbilical cord was cut 5cm away from its site of insertion and the membrane trimmed. Then it was washed by running water, cleaned up by towel and labeled with code numbers. After doing this the following placental parameters was observed and measured.

A. Shape:- Shape of the placenta was noted after proper inspection. Each placenta was categorized as circular, oval, and irregular in shape.

B. Diameter:-After putting the placenta on a flat tray, the maximum diameter was measured with a non-stretched wooden scale graduated in centimeters. Then the second maximum diameter was taken at right angles to the first one. The mean of the two measurements was considered as the diameter of the placenta expressed in centimeter (Figure 1).

Figure 1: Maximum diameter measured on the maternal surface in two axes at right angle to each other at Dessie Referral Hospital, Northeast Ethiopia.

C. Thickness:- With a long needle, placental thickness was measured at five points of each placenta. Each placenta was placed on fetal surface and divided

arbitrarily into three equal zones by drawing two circles on the maternal surface. One thickness was measured from the center of the central zone, two from middle and two from peripheral zones. Finally, the mean of all five measurements was calculated and considered as thickness of the placenta (Figure 2).

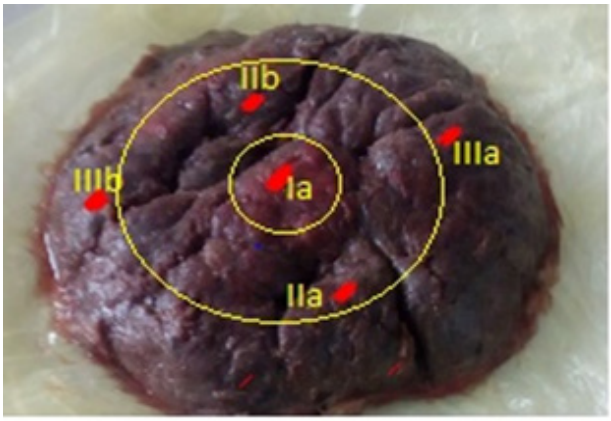

Figure 2: Method of selecting sites from different zones of placenta for measurement of placental thickness. Ia represents the site in the arbitrary central zone; IIa and IIb the sites in the middle zone; IIIa and IIIb represent the peripheral zones at Dessie Referral Hospital, North East Ethiopia.

D. Weight:- Weight of each placenta was recorded in grams by using a weighting machine scale after removal of membranes, umbilical cord and blood clots inside it (Figure 3).

Figure 3: Method of weighting placenta by standardized weighting machine at Dessie Referral Hospital, Northeast Ethiopia, May-June, 2018.

E. Number of Cotyledons:- After measuring and inspecting the above parameters placenta was fixed by 10% formalin for 24 hours to make the placental septum separation visible to count the cotyledon. Each formalin-fix placenta was taken on both hands; then gentle pressure was applied on the central part of the fetal surface with thumbs of both hands while holding the periphery of the placenta with the other fingers. As a result, the cotyledons on the maternal aspect become prominent. Then the placenta was put on a flat tray with maternal side facing upward by placing a wood block on the fetal side. Then counting was started from the left side of one end of the placenta going rightward and again turning back to the left in a manner of loop. This counting procedure was repeated until the other end of the placenta is reached. Then, the total number of cotyledons was recorded.

Data Quality Assurance

For insuring data quality training was given for data collectors and supervisors for 2 days concerning on the placental gross morphology, measurements, and appropriate disposal of the placenta. Data was collected and recorded on the checklist by 2 BSc midwifery staff members working in delivery room. Finally, the collected data was checked for completeness by the principal investigators.

Data Processing and Analysis

Data was entered using EPI-data Version 4.2.0 and exported to SPSS Version 22 for analysis. Descriptive statistics like frequency, ratio, mean and standard deviation was computed to describe the study variable and was presented by tables and graphs. Comparison of gross morphology of placenta in anemic and non-anemic mothers was analyzed by independent t-test and one way ANOVA. Differences $p<0.05$ was considered statistically significant.

4.13 Ethical Considerations

Ethical clearance for the beginning of the study was obtained from Research and Ethics committee of Department of Anatomy School of Medicine, College of Health Sciences, Addis Ababa University. Following

approval by the committee it was submitted to Institutional Review Board (IRB). After which, letter of cooperation was written by Department of Anatomy to Dessie Referral Hospital. Each study participant was adequately informed about the objective, benefit and risk of the study. Finally, individual verbal informed consent was obtained from every study participant and those who agree were included in the study. Then, giving due respect, confidentiality, and appropriate disposal of placenta was observed/done by the data collectors and the supervisors.

RESULTS

The mean maternal age in the study was 27±4 years and 67(69.7%) of the mothers age was within 25-29 years. The mean (±SD) gestational ages of mothers were 38±0.9 weeks. Regarding their mode of delivery 73(76%) of mothers delivered spontaneous by vaginal delivery, and 23(24%) of mothers delivered by cesarean section. Out of 96 deliveries 52(54.5%) of babies were males and (45.5%) of them were females. The majority (43.5%) of the mothers were multipara. In this study, the mean placental weight of anemic mothers was 544±98 g, and, in non- anemic mothers it was 502±93 g with (t =2.162, p = 0.03). The mean placental thickness of anemic mothers was 22.7 ±2.4mm, and in non-anemic mothers it was 20±0.6 mm with (t=5.742, p=0.001). In case of mean number of cotyledons, in anemic mothers it was 13.5±1.8 as compared to non- anemic mothers 17.6±1.1 (Table 1).

Table 1: Independent sample t- test of placental morphology and birth weight of fetus both in anemic and non-anemic mothers, at Dessie Referral Hospital, Northeast Ethiopia, May- June, 2018.

Variables	Anemic (case)	Non-anemic (control)	t- statistic	P- value
Placental weight	544 ±98 g	502±93 g	2.162	0.03
Placental diameter	18±1.5 cm	17±1.5 cm	3.14	0.002
Placental thickness	22.7±2.4 mm	20±0.6 mm	5.742	0.001
Placental thickness	22.7±2.4 mm	20±0.6 mm	5.742	0.001
Number of cotyledons	13.5±1.8	17.6±1.1	- 13.153	< 0.001
Birth weight of fetus	2562±360 g	3035±305 g	- 6.938	< 0.001

In the current study, the mean placental weight increases as the level of hemoglobin decreases from normal to moderate anemic mothers, then it decreases when the level of hemoglobin reaches at severe anemia level with significant difference in the mean placental weight between groups (ANOVA, F=8.974, P< 0.001) . In the case of mean number of cotyledons, as the level of hemoglobin decreases the number of cotyledons also decreases with significant difference between groups (ANOVA, F= 86.8, p<0.001) (Table 2).

Table 2: One way ANOVA result on morphologic characterstics of placenta and birth weight of fetus at different maternal hemoglobin levels in Dessie Referral Hospital, Northeast Ethiopia, May- June, 2018.

Variables	Group I (Non-anemic)	Group II (Anemic) Mild anemic n=23)	Moderate anemic (n=19)	Severe anemic (n=6)	ANOVA
Placental weight	502±93 g	510±41 g	612±116 g	455±39 g	8.974*
Placental diameter	17±1.3 cm	17.5±1.1 cm	19±1.2 cm	16±1. cm	0 13.89*
Placental thickness	20.0±0.6 mm	22±1.5 mm	23.8±2.4 mm	18±1.2 mm	38.4*
No. of cotyledons	17.5±1.1	14.3±1.9	13±0.9	11±1.1	86.8*
Birth weight of fetus	3035±305g	2721±261g	2536±318g	2033±314g	28.5*

(* significant)

DISCUSSION

Placenta is a functional component between mother and fetus. Any unpleasant incident related to mother or fetus may seriously distress the structure and function of placenta and even life of the fetus. The weight of the placenta has a significant importance and much information can be gathered by proper weight recording. In the current study the mean placental weight of anemic mothers was (544±98 g), which is significantly larger than that of non-anemic mothers (502±93 g) (t = 2.162, p= 0.03). This is in line with other studies conducted in India (502±50.7 vs. 466±20.7 g, p<0.025), and (512.8±89.8 g vs. 459.4±74.8 g, p=0.001) [6,17]. The mean placental enlargement in anemic mothers may be due to adequate compensatory capacity of anemic placentas to satisfy the intrauterine environment. An increase in placental weight in anemic mothers also confirmed by Biswas et al., even though there was no statistical significance difference between the two group (382g vs. 370.3g, p= 0.4)[18].

In this study, there was an increase in placental weight as the hemoglobin level decreases from non-anemic to moderate anemia. But when the hemoglobin levels of the mother reaches at severe anemia, the placental weight was decreased. This result is in contrary to other studies conducted in Norway; In pregnancies with hemoglobin concentrations <9 g/dl, mean placental weight was 701.2±160.6 g, followed by 678.1±150.2g for hemoglobin concentrations 9–13.5 g/dl, and 655.5±147.7 g for hemoglobin concentrations >13.5 g/dl[19]. This discrepancy may be due to the use of different cut off point for anemia severity, and 'it may be suggested that higher placental weight in pregnancies with low hemoglobin concentrations is only pregnancies with optimal potential for placental growth are successful. Hence, it is possible that women with low hemoglobin concentrations have higher risk of placental atrophy and miscarriage''. Decrease in weight of placenta when the level of hemoglobin decreases was also revealed (480g (non-anemic) vs. 350g(mild), 300g(moderate) and 250g(severe) mothers respectively, and(581.67 ± 83.97 g(non-anemic) vs. 545.95 ± 73.24 g (mild), 499.15 ± 87.52 g (moderate) and 373.60 ± 83.48 g (severe) mothers respectively [8,20]. This inconsistency may be due to the difference in mode of delivery, discrepancy in collection and processing techniques and difference in inclusion and exclusion criteria of study participants.

It is also evident that placental weight maintains more or less a constant relation with the fetal weight. In this study the placental-fetal weight ratio (P/F ratio) was varied among anemic and non-anemic mothers. The mean placental fetal ratio in this study was (0.212 vs. 0.166) in anemic and non-anemic mothers respectively. This result is in line with other studies conducted in Norway (0.203 vs. 0.193) and India (0.160 vs. 0.142) in anemic and non-anemic mothers respectively[6,19]. The high placental to birth weight ratio with low maternal hemoglobin concentrations may be due to the differences in placental growth relative to fetal growth across different maternal hemoglobin concentrations.

Placental shape is usually described as flattened discoid with an approximate circular margin. Even though it was statistically insignificant in the current study, placentas of anemic mothers were 4(8.3%) irregular in shape and 2 (2.1%) succenturiate lobes; which were somewhat deviates from its typical shape. This finding is parallel with other findings conducted by AL-Hakeem, in which 10 out of 50 placentas were irregular in shape [21]. On the other hand, another researcher reported on 60 mothers (30 anemic and 30 non-anemic) there was no difference in the shape of placenta in which 67% and 33% of both anemic and non-anemic placenta was circular and oval in shape respectively. This inconsistency may be due to the fact that the difference in the number of study participants and discrepancy in severity of anemia cases under the study [6].

The number of cotyledons shows discrepancy in anemic and non-anemic mother's placenta. Mongia et al, stated that, average number of cotyledons in non-anemic and anemic was 18 and12 respectively [20]. Similarly, another researcher revealed that maternal anemia showed reduced number of cotyledons and increase in incidence

of ill-defined cotyledons than non-anemic mothers[22]. Our study finding is in concurrence with the above results in which the average number of cotyledons was 13.5±1.8 in anemic and 17.6±1.1 in non-anemic mothers respectively. The reduction in number of cotyledons in anemic mothers may be due to the fact that the increase in number of ill-defined cotyledons.

The linear relationship between maternal hemoglobin and different components of fetal anthropometry indicates that fetal growth is compromised in maternal anemia, particularly when it is moderate and severe anemia. In the current study birth weight of fetus in non-anemic group was significantly larger (3035±305 g) than anemic mothers (2562±360 g) with (p<0.001). This result is comparable with others (2589 g vs. 2182g, p<0.001) and (2595 g vs. 2376 g p< 0.001) in non-anemic and anemic mothers respectively[6,18,23]. This reduction in birth weight of fetus in anemic mothers may be due to the fact that, a reduction in the exchange surface of the placenta which may be due to ongoing hypoxia of placenta causes direct deterioration of fetal growth.

The diameter and thickness of placenta gives an idea to the size of placenta. In the current study the mean diameter of placenta in non-anemic and anemic mothers was (16.4 ± 1.0 cm vs. 17.6±1.1cm, p< 0.001) respectively. This result is comparable with another studies conducted in India in which the mean placental diameter of anemic mothers was wider than non-anemic mothers (19.38±1.1 cm vs. 18.56±1.7cm) [6]. This may be due to the fact that the compensatory increment in the size of anemic placenta increases its diameter. Decrease in placental diameter in anemic mothers also reported by AL-Hakeem, the mean diameter of placenta in anemic mothers was 16.26 cm in comparison with non-anemic group which was 16.79 cm[21]. This discrepancy may be due to the difference in inclusion of study participants and difference in genetic and environmental factor.

In our study, as the level of hemoglobin decreases the diameter of placenta increases till it reaches at the level of severe anemia such; in non-anemic (17±1.3 cm), mild(17.5±1.1 cm), moderate (19±1.2 cm) and severe (16 ±1.0 cm) respectively with (t=13.9, p<0.001). This result was in line with other studies conducted in Bangladeshi with the diameter of non-anemic (15.60±0.74 cm); mild (18.041±1.32 cm) and moderate (18.80±1.96 cm), p<0.001) even though they couldn't incorporate severe anemia cases [24]. The decrease in diameter of placenta in severe anemic cases in the current study may be due to placental insufficiency as a result of irresistibility of the disease process.

The thickness of placenta gives an idea about the size of placenta which may intend to give indirect information about the fetal-placental ratio. In the current study the mean placental thickness of non-anemic mothers was significantly thinner than anemic mothers (p<0.001). This result is in line with other studies conducted in India, in which the mean placental thickness of anemic mothers was thicker (1.9 ±0.2 cm) than non-anemic mothers (1.79±0.1 cm)[6]. This may be due to the fact that the adequate compensatory hypertrophy due to anemia tends to increase its thickness as well.

In this study, as the level of hemoglobin decreases the mean placental thickness was 20.6±0.6mm, 22±1.5mm, 23.8±2.4mm and 18±1.2mm in non-anemic, mild, moderate and severe mothers respectively (p<0.001). This result is not comparable with other studies conducted in Bangladesh in which 2.14±0.26 cm, 2.10±0.16 cm and 2.19±0.13 cm in non-anemic, mild anemic and moderate anemic mothers with (p=0.1)[24]. This controversy may be due to the fact that discrepancy in method of data collection and processing techniques and difference in the inclusion and exclusion criteria of study participants.

CONCLUSIONS

Based on this study, the mean placental weight, thickness, and diameter were greater in anemic mothers than non-anemic mothers. Placenta was bigger in mild and moderate anemic mothers with increased weight, thickness and diameter, and it was small in weight, thickness and diameter in severely anemic mothers compared to non-anemic mothers. It was also observed

that maternal anemia resulted in decrease birth weight of fetus and number of cotyledons and it further decreased according to its severity.

LIMITATIONS

Due to budget constraint the study was conducted on small number of participants, hence difficult for generalization.

RECOMMENDATIONS

Clinicians should carry out routine placental examination and measurement during post-partum period; hence, this will provide better evidence for clinical decisions.

Prompt anatomic placental interpretation should be conducted on sick mothers and babies before referral to pathologists.

Large scale study should be conducted on the effects of anemia on placental morphological changes using this study as a baseline data.

DECLARATIONS

Ethical Approval and Consent to participate

Ethical clearance for the beginning of the study was obtained from Research and Ethics committee of Department of Anatomy School of Medicine, College of Health Sciences, Addis Ababa University. Following approval by the committee it was submitted to Institutional Review Board (IRB). After which, letter of cooperation was written by Department of Anatomy to Dessie Referral Hospital. Each study participant was adequately informed about the objective, benefit and risk of the study. Finally, individual verbal informed consent was obtained from every study participant and those who agree were included in the study.

CONSENT FOR PUBLICATION

"Not applicable"

AVAILABILITY OF SUPPORTING DATA

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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AUTHOR'S CONTRIBUTIONS

Teshome Gebremeskel, and Abay Mulu participated in designing the study, involved in the write up of methodology of the proposal, research work, and statistical analysis. Dr. Solomon Kumbi and Dr. Wondwossen Ergete participated in helped in drafting the paper, contributed to the designing of methodology and write up of the proposal and wrote up of the manuscript. All authors read and approved the final paper.

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