Relationship between Maternal Anemia during third trimester of pregnancy and Infant Low Birth Weight

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November 6, 2021

Conflict of interest: The authors report no conflict of interest.

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Abstract

Background: Anemia is a serious health problem associated with several types of maternal morbidity, and may negatively affect the pregnancy outcomes. There are multiple studies showing that maternal iron deficiency anemia during pregnancy can cause low birth weight, but there were conflicting results about the effect of anemia during the third trimester of pregnancy on the fetal weights.

Objective: The aim of this study is to determine the relationship between maternal anemia during the third trimester of pregnancy and infants' low birth weight.

Study Design: This is a cross-sectional case-control study recruiting all pregnant women who attended the Obstetrics Department at Tishreen University Hospital between July 2020 and July 2021. The sample included 280 patients who met the inclusion criteria. They were divided into two groups according to their hemoglobin concentration (threshold 10.5 g/dL). After delivery, the neonates were weighed within the first hour of birth. Maternal hemoglobin and birth weights were compared, also the relationship between anemia and maternal age, anemia and gestational age, and the relationship between neonates weights and genders were compared. Then the results were summarized in tables.

Results: The anemia prevalence was 38.9% (Hemoglobin < 10.5 g/dL). The number of neonates with low birth weight was 11 (3.9%); 8 of which were of anemic pregnant women. We found that there was a significant relationship between maternal anemia and low birth weight (p-value = 0.01, Odd Ratio = 4.4). The mean of Group 1 (anemic

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pregnant women) newborns weights was 2961 ± 371.3 gram, which was less than the mean of Group 2 (non-anemic pregnant women) newborns weights (3100.6 ± 391.3 gram). There was a significant inverse relationship between hemoglobin concentration and parity (p-value = 0.007). We also found that there was no relationship between anemia and maternal age or gestational age in third trimester of pregnancy. Also there was no relationship between infants birth weight and their gender.

Conclusion: Maternal anemia can be considered as a risk factor for low birth weight, and the average weight of neonates of anemic mothers is lower than the average weight of neonates of non-anemic mothers.

Keywords— Maternal anemia, Low Birth Weight, Pregnancy, Hemoglobin

1 Introduction

Anemia is a serious health problem during pregnancy and its incidence is still high. It is estimated that one-third of all women around the world, and 32.8% of women in Syria, of reproductive age (15-49 years) are anemic.[1] The prevalence of anemia among the pregnant women is 40%.[2]

Iron deficiency anemia is the most prevalent and also the most neglected nutrient deficiency in the world, particularly among children and pregnant women category and especially in developing countries.[3] During pregnancy, increased maternal iron is needed as a result of the demands of the growing fetus and placenta, increased erythrocyte mass and expanded maternal blood volume.[3] However, during pregnancy there are many risk factors for iron deficiency or iron deficiency

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anemia, including an iron-deficient diet, gastrointestinal issues affecting absorption, or a short interpregnancy interval.

Other causes of anemia include parasitic diseases, micronutrient deficiencies, and genetically inherited hemoglobinopathies.[3,4] Estimates vary, but each pregnancy requires at least 300 mg of iron taken from the mother's liver stores, and others have proposed that the value is even higher up to 500 mg. Late in pregnancy, an average of 5.6 mg of iron per day from dietary or endogenous maternal sources is transported across the placenta to cover fetal demands. The quantity of iron absorption during the second half of gestation, and principally in the third trimester, is around six times higher than the quantity of iron typically absorbed from dietary sources in non-pregnant women.

UK antenatal guidance[5] and Centers for Disease Control and Prevention guidance define anemia as Hemoglobin (Hb) concentration less than 11 g/dL in the first trimester and less than 10.5 g/dL in the second or third trimester (hematocrit (HCT) less than 33%).[3,6] It is important to know that anemia is not a diagnosis; it is a manifestation of an underlying disorder. Thus, even mild, asymptomatic anemia should be investigated so that the primary problem can be diagnosed and treated.[7] A strong association has been found between moderate to severe anemia at 28 weeks of gestation and the severity of intra and postpartum hemorrhage, which cause 23% of maternal deaths.[3] Also maternal anemia was frequently thought to be associated with a suboptimal fetal outcome, preterm delivery, and Low Birth Weight (LBW) infants.[4,8] However, data supporting this are not clear.

LBW is defined by the World Health Organization (WHO) as weight at birth less than 2500 g (5.5 lb).[9] Birthweight is the first weight of the fetus or newborn obtained after birth. For live births, birthweight should preferably be measured

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within the first hour of life, before significant postnatal weight loss occurs.[9] LBW occurs when a baby is born too early (before 37 weeks of pregnancy) or when a baby does not grow well during pregnancy (Intrauterine growth restriction).[9,10] LBW is a significant public health problem in many countries, especially in developing countries.[9,11] LBW is not only a major predictor of prenatal mortality and morbidity,[4,8,12] but recent studies have found that LBW also increases the risk of noncommunicable diseases such as diabetes and cardiovascular disease later in life.[13,14]

Since iron deficiency in pregnancy is identifiable, treatable and possibly preventable, early investigation and treatment of anemia can improve maternal and infant outcomes, and reduce the incidence of low birth weight. This is considered a global goal. WHO aims to achieve a 30% reduction of the number of infants born with a weight lower than 2500 g by the year 2025.[13,15]

1.1 The Objectives

The main aim of this study is to determine the relationship between maternal anemia during third trimester of pregnancy and fetal low birth weight. The minor aims are to determine the prevalence of maternal anemia among pregnant women and the prevalence of low birth weight among neonates.

2 Patients and Methods

This is a cross–sectional case–control study recruiting all pregnant women who attended the Obstetrics Department at Tishreen University Hospital in Latakia, Syria between July 2020 and July 2021. The number of studied patients is 280 out of 528 after applying the inclusion and exclusion criteria. Patients were divided

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into two groups according to hemoglobin concentration with a threshold of 10.5 g/dL.

- Group 1 (case): 109 patients whose hemoglobin concentration $< 10.5g/dL$
- Group 2 (control): 171 patients whose hemoglobin concentration $\geq 10.5g/dL$

The relationship between maternal anemia and each of birth weight, maternal age and gestational age were studied. Also the relationship between neonates birth weights and their gender was studied. The following baseline parameters were recorded: Maternal age, parity, Last Menstrual Period (LMP), gestational age, hemoglobin concentration, fetal gender, birth weight, mode of delivery, medical history, smoking or alcohol drinking, Body Mass Index (BMI), vital signs. After delivery, the weights of neonates were registered within the first hour.

2.1 Inclusion Criteria

Every singleton pregnant woman at third trimester of pregnancy whose age is between 17 and 35 years and BMI between 18 and 29.9

2.2 Exclusion Criteria

1. Who smoke or drink alcohol.
2. Existence of Placenta previa or any important bleeding during pregnancy.
3. Existence of Preeclampsia and gestational hypertension.
4. Gestational diabetes.
5. Preterm Premature Rupture of the Membranes (PPROM).
6. Anti-phospholipid syndrome.

7. Major fetal abnormalities.
8. Inherited hemoglobinopathies (sickle cell anemia, thalassemia).
9. Malabsorption disease.
10. Hemorrhagic disease, kidney or liver failure, thyroid disease.
11. SARS-CoV-2 infection during pregnancy.

2.3 Statistical Analysis

2.3.1 Descriptive Statistics

- Quantitative variables: By central tendency measure and dispersion.
- Qualitative variables: By frequencies and percentages.

2.3.2 Inferential Statistics

Chi-Square test was used to find the relationship between the qualitative variables (anemia of pregnant women and gestational age groups, maternal age groups, fetal gender). Pearson correlation coefficient was used to determine the relationship between two quantitative variables (interval/ratio) and the degree to which the two variables coincide with one another.

Independent T Student test was used to determine any statistically significant difference between the means in two unrelated groups (the mean of maternal anemia and the mean of neonates birth weights). Odd Ratio (OR) was used to compare the relative odds of the occurrence of the outcome of interest. A value of 2 is used for the OR. For all the tests conducted in the study, p-value < 0.05 was considered to indicate statistical significance. The data was analyzed using IBM® SPSS® (version 20)

3 Results

A total of 280 cases were studied. The mean of maternal age was 26.4 $\pm$ 4.8 years. In Table 1 we present the distribution of sample's maternal age across three groups. The highest percentage (122 patients, 43.6%) was for women between 24-30 years, 86 (30.7%) were between 17-24 years and 72 (25.7%) were between 30-35 years. Table 2 shows that out of the 280 patients, 109 (38.9%) were anemic (Hb$<$10.5g/dL) with a minimum Hb recorded of 7.1 g/dL and 171 (61.1%) were non-anemic (Hb$\geq$10.5 g/dL) with a maximum Hb recorded of 14.3 g/dL. 49 of the anemic women (45%) were in the age range (24-30 years), 31 (28.4%) were in the range (17-24 years), and the rest (29 patients, 26.6%) were in the range (30-35 years). Chi-square test shows no relationship between anemia and maternal age (p-value = 0.8). The mean age was 26.4$\pm$4.7 years for anemic women and 26.3$\pm$1.2 years for non-anemic women. This was studied by T Student test and we found that there is no relationship between the two groups according to age (p-value = 0.5). We presented these results in Table 3.

We also studied the sample according to parity. We divided the sample into 3 groups (Nulliparous, 1-2 births and 3 or more births). Table 4 shows that the highest percentage (49.3%) of the studied sample was for women with one to two previous births. 90 patients (32.1%) were Nulliparous and 52 (18.6%) had three or more previous births. In Table 5 we studied the relationship between maternal hemoglobin concentration and parity using Chi-square and we found a statistically significant differences with p-value=0.007 between maternal anemia and parity. This means that the probability of having anemia is higher in women with previous births. Using Pearson correlation, there was an inverse correlation as hemoglobin values decreased with the increase in the number of births (p-value=0.01 , r= -0.2). Figures 1 and 2 illustrate this clearly.

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In addition, we studied the sample according to gestational age. We divided the sample into three groups ([36-37], [38-39] and ≥40 weeks) and presented the data in Table 6. More than half (52.9%) the studied sample gave birth at 38-39 weeks. 94 women (33.6%) gave birth at 36-37 weeks and the rest (38 patients, 13.6 %) gave birth at 40 weeks or more.

By studying this data according to Hb concentration (Table 7), we found that 39 anemic women (35.8%) gave birth at 36-37 gestational weeks compared to 55 (32.2%) in the non-anemic group, 58 (53.2%) gave birth at 38-39 weeks compared to 90 (52.6%), and the rest of anemic women (12, 11%) gave birth at 40 weeks or above compared to 26 (15.2%) of non-anemic group. There was no relationship between maternal hemoglobin concentration and gestational age (p-value= 0.5). The mean age of gestation in anemic group was 38.1±1.1 weeks, and the mean age of gestation in non-anemic group was 38.2±1.2 with no statistically significant difference (p-value= 0.6).

We also studied the sample according to neonates' genders. We found that the proportions are similar for males and females (144 male neonates 51.4% and 136 female ones 48.6%) (Table 8). By studying the relationship between neonates weights and their genders, we found that 6 males (54.5%) and 5 females (45.5%) had low birth weight (<2500 grams). On the other hand, 138 males (51.3%) and 131 females (48.7%) weighed 2500 grams or more, with no statistically significant relationship (p-value = 0.8). The results were summarized in Table 10.

Moving to the main goal of the study, we found that 11 of the neonates (3.9%) had LBW, weighing less than 2500 grams, with a minimum recorded weight of 2000 grams, while the rest (269 neonates, 96.1%) weighed 2500 grams or more with a maximum recorded weight of 4600 grams (Table 9). Eight were to anemic women (7.3%). On the other hand, only three were to non-anemic women (1.8%).

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By applying Chi-square test we found statistically significant differences with p-value = 0.01 between maternal anemia and neonate weight in the studied sample. OR = 4.4 which means that women with anemia are *4.4 times more likely* to give birth to a child with LBW compared to the control group. Independent T Student test was used to study the differences in average weights of neonates between the two research groups. It was found that the average weight of neonates is lower among women with anemia (2961±371.3 grams) compared to (3100±391.3 grams) in non-anemic women, with statistically significant differences (p-value = 0.003). Table 11 presents the data and Figures 3 and 4 illustrate these findings clearly.

4 Discussion

4.1 Principal findings

This study demonstrated that maternal anemia in the third trimester increases the risk of infants' low birth weights. It also presented the inverse relationship between parity and hemoglobin concentration in pregnant women. In addition, it showed that neither maternal age nor gestational age affect maternal anemia. Finally, it proved that there is no relationship between neonates' genders and their weights.

4.2 Results

This study demonstrated that the prevalence of anemia is 38.9% (n=109) among pregnant women at Tishreen University Hospital in Latakia, Syria. Other studies have shown a higher prevalence of anemia in pregnancy such as 62.3% in India,[16] and 78% in Iraq.[17] The low prevalence of anemia in this study may be related to the different Hb threshold (11 g/dL in those studies while it is 10.5 g/dL in our

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study). Another factor may be a more frequent iron supplementation consumption, which was out side the scope of this research, and an increased awareness of the risks of anemia and malnutrition among patients.

Our study shows that anemia is more prevalent (45%) in pregnant women whose age between 24-30 years, this aligns with the results of Suryanarayana et al[16] (66.1% for 21-30 years) and Bedi et al[18] (83.62% for 20-29 years old). However, the relationship between maternal anemia and age groups was not significant in our study (p-value= 0.8) this again aligns with the results of Bedi et al[18] (p-value= 0.37) and Suryanarayana et al[16] (p-value = 0.766), but disagrees with Salman et al[17] and Bullens et al[19] where both show that there was a significant relationship between maternal anemia and age (p-value = 0.001 in both studies). The difference may be due to the difference in the age range of the accepted patients (15-52 years in Bullens et al[19] and 16-44 years in Salman et al[17]) and the age groups used in these studies.

There is an increased number of studies showing that maternal iron deficiency anemia during pregnancy can cause low birth weight, but there were conflicting results about the effect of anemia during the third trimester of pregnancy on the fetal weights. Our study indicates that there was a significant statistical relationship between maternal anemia and low birth weight (p-value = 0.01, OR = 4.4), this agrees with Saragih et al[20] (p-value = 0.047 , OR = 3.125), Sekhavat et al[21] (p-value = 0.001), Khan et al[22] (P-value = 0.001 , OR = 3.31), Bedi et al[18] (p-value<0.001, OR = 3.181, 95% CI: 1.778-5.693), and Salman et al[17] (p-value = 0.001).

We also found that the average weights of neonates is lower among women with anemia with statistically significant differences (p-value=0.003), which aligns with the results of Sekhavat et al[21] (p-value=0.01), Kumar et al[23] (p-value = 0.001) and

Tabrizi and Barjasteh.[24] Suryanarayana et al[16] (p-value = 0.406) and Rahmati et al systematic reviews in 2016[25] and 2017[26] show that there is no significant relationship between maternal anemia and birth weight (p-value>0.05, RR=1.23, 95%CI : 0.97-1055) (RR=1.21, 95%CI: 0.84-1.76) respectively. Our results prove the opposite. Hb concentration in the third trimester is an important factor in determining birth weight which could be explained by the rapid growth of fetus and the fact that Iron and other micronutrients accretion rates are the highest in this trimester.[23]

In addition, we found that Hb concentration decreases with the increase in the number of births, that agrees with Suryanarayana et al[16] (p-value = 0.001), Bullens et al[19] (p-value<0.001), Salman et al[17] (parity≥4 , p-value = 0.001) and Kavak and Kavak[27] results. This may be due to an increasing susceptibility to hemorrhage before, during and after delivery and to hormonal changes in plasma volume which causes reduction in hemoglobin levels.

This study found no relationship between fetal weight and gender. This disagrees with Kumar and Yadav[28] study in India and Taha et al[14] study in UAE which shows that Females were found to have double the risk of LBW (p-value<0.001, AOR 2.08, 95% CI 1.41- 3.08) than their male counterparts.

4.3 Clinical implications

The findings of this study will help achieve WHO goals in reducing infants low birth weight by increasing the early care of pregnant women. The results will prompt doctors to measure their patients' hemoglobin concentrations and to provide the required supplements to enhance their pregnancy outcome.

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4.4 Research implications

This study provides important data on maternal anemia in Latakia, which is located in the Mediterranean Basin, where there is a lack of information about this topic. However, it calls for a wider sample from multiple centers to better represent the society. It also recommends to take interpregnancy intervals and the consumption of iron supplements in consideration in future studies.

4.5 Strengths and limitations

The strengths of this study is that it is the first of its kind in Syria. It also adds reliable data to resolve the conflicting results on the effects of maternal anemia in the third trimester on infants' low birth weights in the region. This study comes with two limitations. The first one is the relatively small sample size which is caused by women in the sample stopping their followups at Tishreen Hospital where the study was conducted and a high percentage of smokers among the patients. The second limitation is not studying the effect of interpregnancy interval on maternal anemia and therefore on the pregnancy outcome.

4.6 Conclusion

Anemia should be detected and treated as early as possible to avoid the complications and health problems to the mothers and their pregnancy outcomes. This study demonstrated that anemia is a risk factor for fetal low birth weight, and the average weights of neonates of anemic mothers is lower than those of non-anemic mothers.

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Table 1: Distribution of the studied sample according to age groups

Age Group	**Number**	**Percentage**
[17-24[	86	30.7%
[24-30[	122	43.6%
[30-35]	72	25.7%
Total	**280**	**100%**

Table 2: Distribution of the studied sample according to Hb concentration

Hb Concentration	**Number**	**Percentage**
$< 10.5g/dL$	109	38.9%
$\geq 10.5g/dL$	171	61.1%
Total	**280**	**100%**

Table 3: The relationship between maternal anemia and age groups

Age Group	**Study Sample**		**P-Value**
	$< 10.5g/dL$	$\geq 10.5g/dL$	
[17-24[	31 (28.4%)	55 (32.2%)	0.8
[24-30[	49 (45%)	73 (42.7%)	
[30-35]	29 (26.6%)	43 (25.1%)	
Mean ± SD	**26.4±4.7**	**26.3±1.2**	**0.5**

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Table 4: Distribution of the studied sample according to parity

Parity	Number	Percentage
Nulliparous	90	32.1%
1-2	138	49.3%
≥3	52	18.6%
Total	**280**	**100%**

Table 5: The relationship between maternal anemia and parity

Parity	Study Sample		P-Value
	$< 10.5g/dL$	$\geq 10.5g/dL$	
Nulliparous	24 (22%)	66 (38.6%)	0.007
1-2	58 (53.2%)	80 (46.8%)	
≥3	27 (24.8%)	25 (14.6%)	

Table 6: Distribution of the studied sample according to gestational age

Gestational age (weeks)	Number	Percentage
36-37	94	33.6%
38-39	148	52.9%
≥40	38	13.6%
Total	**280**	**100%**

Table 7: The relationship between maternal anemia and gestational age

Gestational age (weeks)	Study Sample		P-Value
	$< 10.5g/dL$	$\geq 10.5g/dL$	
36-37	39 (35.8%)	55 (32.2%)	0.5
38-39	58 (53.2%)	90 (52.6%)	
≥40	12 (11%)	26 (15.2%)	
Mean ± SD	**38.1±1.1**	**38.2±1.2**	**0.6**

Table 8: Distribution of the studied sample according to neonate gender

Neonate Gender	Number	Percentage
Male	144	51.4%
Female	136	48.6%
Total	**280**	**100%**

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Table 9: Distribution of the studied sample according to neonate weight

Neonate Weight	Number	Percentage
<2500	11	3.9%
≥2500	269	96.1%
Total	**280**	**100%**

Table 10: The relationship between neonates weights and genders

Gender	Study Sample		P-Value
	$< 2500g$	$\geq 2500g$	
Male	6 (54.5%)	138 (51.3%)	0.8
Female	5 (45.5%)	131 (48.7%)	

Table 11: The relationship between maternal anemia and neonate weight

Neonate weight	Study Sample		P-Value
	$< 10.5g/dL$	$\geq 10.5g/dL$	
<2500g	8 (7.3%)	3 (1.8%)	0.01
≥2500g	101 (92.7%)	168 (98.2%)	
Mean ± SD	**2961.9±371.3**	**3100.6±391.3**	**0.003**

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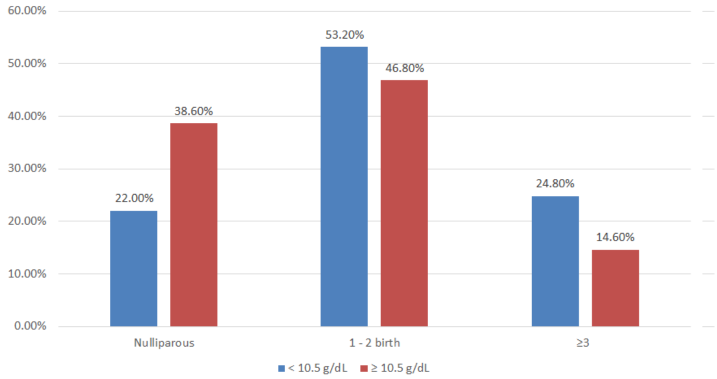

Figure 1: Distribution of the studied sample according to maternal anemia and parity

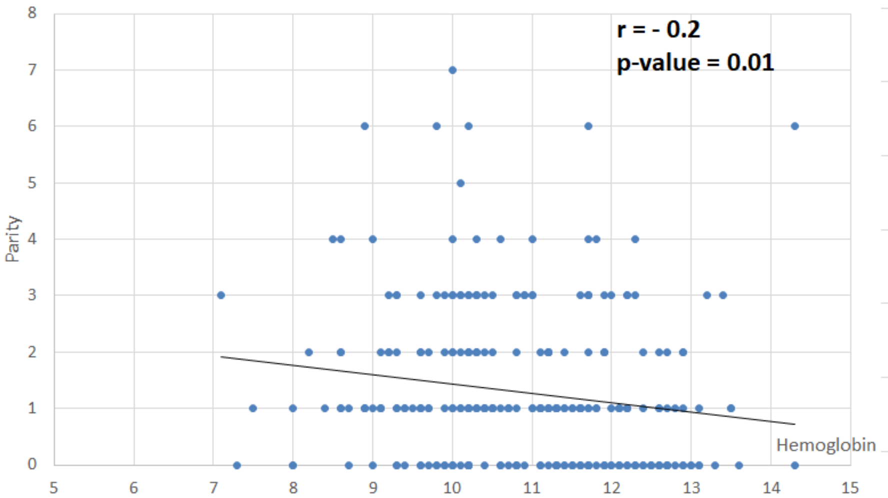

Figure 2: The relationship between maternal anemia and parity. There is an inverse correlation as hemoglobin values decrease with the increase in the number of births

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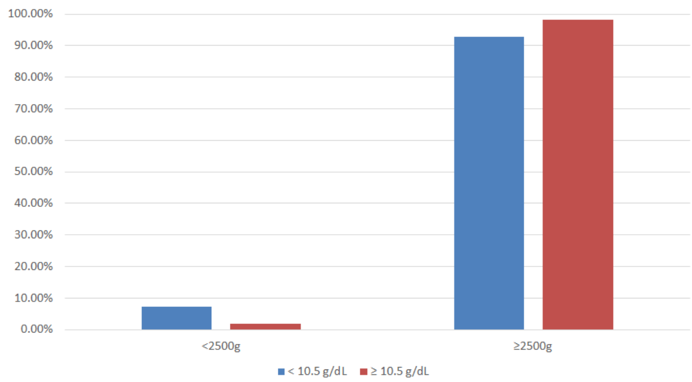

Figure 3: Distribution of the studied sample according to maternal anemia and the weights of the neonates

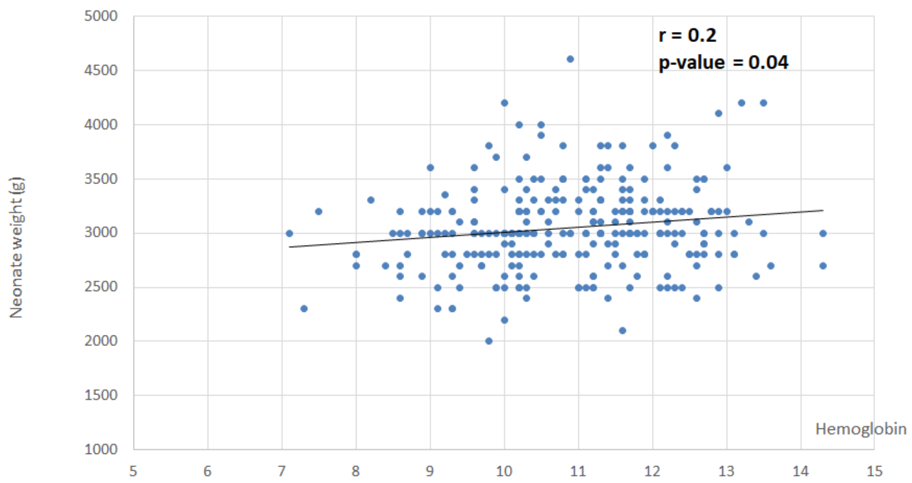

Figure 4: The relationship between maternal anemia and neonates weights. There is a positive correlation as the weights of the neonates decrease with the decrease of hemoglobin values.

http://dx.doi.org/10.29322/IJSRP.11.11.2021.p11960