WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 2, 1523-1536 Research Article ISSN 2278 – 4357

EFECT OF MATERNAL HEMOGLOBIN ON ANTHROPOMETRIC MEASUREMENTS OF PRE- TERM NEWLY BORN BABIES

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Article Received on
18 Dec. 2018,

Revised on 09 Jan. 2019,
Accepted on 31 Jan. 2019

DOI: 10.20959/wjpps20192-13235

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INTRODUCTION

Maternal Anemia: Anemia is defined as a condition in which there is a reduction in the number of circulating red blood cells or hemoglobin per unit of blood.[1] During pregnancy, anemia may occur most commonly due to iron deficiency or acute blood loss.[2] In a typical gestation with a single fetus, a need for an additional 1000 mg of iron is induced by the pregnancy, an amount that often exceeds the iron stores of most women.[2] In addition to this additional draw on iron stores, a reduction in the amount of hemoglobin available per g/L of blood results from natural processes that occur during pregnancy. During pregnancy, blood volume increases above non-pregnant levels, causing a modest fall in hemoglobin levels in healthy women who are not deficient in iron or folate.[2] This occurs because "a relatively greater expansion of plasma volume compared with the increase in hemoglobin mass and red blood cell volume results in plasma- dilution, an effect that accompanies all normal pregnancies" ..These changes in blood volume occur for three reasons; first, to meet the demands of the enlarged uterus, second, to protect the mother, and in turn the fetus, against the damaging effects of impaired venous return in the supine and erect positions, and third, to safeguard the mother against adverse effects of blood loss associated with delivery.[2]

What is anaemia?

Anaemia is the result of either not having enough red cells to take oxygen around the body, or having faulty red cells that are unable to carry enough oxygen. It is measured in the blood by the level of haemoglobin, sometimes called 'Hb'.

Blood is a complex fluid containing lots of proteins and a number of different types of cell to help our body to function correctly. These cells include white cells to help fight infection, platelets to help form clots when we bleed and red cells to carry oxygen. Oxygen is carried by

the red cells to all our organs, such as the brain, heart, kidneys, liver and tissues such as muscle, to convert food into energy for the body to work. Red blood cells last about 120 days so the body has to constantly make new ones in the bone marrow to replace them.

What are the signs and symptoms of anaemia?

The following can be features of anaemia

- Fatigue/tiredness
- Shortness of breath
- Dizziness
- Fast or irregular heartbeat
- Pounding or "whooshing" in your ears
- Headache
- Cold hands or feet
- Pale or yellow skin
- Chest pain
- Lack of concentration.

Are there different types of anaemia?

Yes, there are many different types of anaemia and they require different treatments. Some of the commonest types are listed below.

Anaemia due to an under-production of red cells can have different causes including

1. A shortage of iron or vitamins: Iron deficiency anaemia is common. It is caused by a lack of iron in the body. There might be a problem with not having enough iron in your diet or in absorbing it from your diet or you might have used it all up during pregnancy, surgery or because of bleeding.

2. Vitamin B12 or Folate deficiency: this is usually as a result of inadequate intake in food or more commonly the inability of the body to absorb it. Examples of the latter include pernicious anaemia and coeliac disease.

3. Anaemia of chronic illness: this is also sometimes called 'functional iron deficiency'. In this case the body has plenty of iron in stores but inflammation caused by chronic illnesses or infections can block access to the iron, so that the bone marrow does not have enough iron available to produce good quality red blood cells. This is more common as we get older.

Anaemia due to a problem in the bone marrow, where red cells are made: this can be caused by many different diseases, for example

- Patients with kidney failure may be unable to produce the hormone erythropoietin which is the messenger telling the bone marrow to produce more red cells.

- Cancer may invade the bone marrow or some drugs such as chemotherapy may also slow down the rate at which red cells are made.

- There are other types of bone marrow disease that can cause anaemia such as myelodysplastic syndrome or aplastic anaemia.

- Infections can also reduce red cell production.

Anaemia due to inherited disorders: these can affect haemoglobin production, for example thalassaemia.

Anaemia due to excessive destruction of red cells which occurs in immune haemolytic anaemia and inherited disorders such as sickle cell anaemia and sometimes an adverse reaction to certain medications.

Anaemia due to bleeding: this can be severe and sudden such as bleeding from a gastric ulcer or blood loss may be at a slower rate such as due to heavy periods or hidden blood loss from the bowel. When blood loss is slow, the anaemia develops gradually and is often associated with a shortage of iron as the iron is lost from the body.

Iron deficiency Mechanisms during Pregnancy

During pregnancy, the fetal demand for iron increases maternal daily iron requirements from <1 to 2.5 mg/d in early pregnancy and 6.5 mg/d in the third trimester. The average daily diet in the developed world contains <10–14 mg nonheme iron.but not all of this can be absorbed. Evidence from stable-isotope studies suggests that the percentage of nonheme iron absorbed from food during normal pregnancy increases from 7% at 12 wk of gestation to 36% at 24 wk and 66% at 36 wk. These dramatic changes enable the healthy pregnant woman to cope with the extra demands of pregnancy without becoming anemic. But only if there is adequate iron in her diet. If the woman's diet is deficient in iron, as is the case in many developing countries, fetal requirements can be met only by additional contributions of iron from maternal stores.

This demand by the developing fetus may cause the mother to develop iron deficiency anemia if she had inadequate iron stores at the beginning of pregnancy. Whether a pregnant woman is anemic cannot be assessed simply by measuring the blood hemoglobin concentration because a major factor influencing hemoglobin concentration in pregnancy is expansion of plasma volume. How this occurs is not fully established but part of the sequence might be as follows. Heat production by the fetoplacental unit causes a rise in body temperature. Heat loss is increased by peripheral vasodilatation, which causes a drop in blood pressure. This in turn stimulates the release of aldosterone from the adrenal gland, causing the retention of salts and water The drop in osmolality that occurs reduces blood viscosity and enhances blood flow in the low pressure system of the intervillous space. Enhanced blood flow improves fetal growth. In women who are not given supplemental iron, the hemoglobin concentration of the maternal blood falls from an average of <133 g/l in nonpregnant women to an average of <110 g/l at 36 wk of gestation.[4]

The fall is steepest up to 20 wk of gestation; the hemoglobin concentration remains fairly constant up to 30 wk and then rises slightly thereafter These changes in hemoglobin concentration are due mainly to changes in plasma volume; the red cell mass and total hemoglobin actually increase during pregnancy Failure of the plasma volume to expand adequately can lead to restricted fetal growth, resulting in the infant being small for gestation.

Regulation of iron transfer to the fetus: Transfer of iron from the mother to the fetus is supported by a substantial increase in maternal iron absorption during pregnancy and is regulated by the placenta. Serum ferritin usually falls markedly between 12 and 25wk of gestation, probably as a result of iron utilization for expansion of the maternal red blood cell mass. Most iron transfer to the fetus occurs after week 30 of gestation, which corresponds to the time of peak efficiency of maternal iron absorption.

Serum transferrin carries iron from the maternal circulation to transferrin receptors located on the apical surface of the placental syncytiotrophoblast, holotransferrin is endocytosed, iron is released, and apotrasferrin is returned to the maternal circulation. The free iron then bind to ferritin in placental cells where it is transferred to apotransferrin, which enters from the fetal side of the placenta and exist as holotransferrin into the fetal circulation. This placental iron transfer system regulates iron transport to the fetus.

When maternal iron status is poor, the number of placental transferrin receptors increases so that more iron is taken up by the placenta. Excessive iron transport to the fetus may be prevented by the placental synthesis of ferritin.

The capacity of this system may by inadequate to maintain iron transfer to the fetus when the mother is iron deficient.

Patients and Methods

This study is a cross- sectional study included 100 pregnant women who attended to the obstetrical ward in iraq in the period between the 20th of March to the 20th of May 2016, one hundred fifteen delivered by NVD, and Eighty five were delivered by C/S. All these 100 healthy pregnant women were studied have pre term babies all pregnant women with chronic diseases had been excluded from the study.

For each mother blood sample were aspirated, before delivery. Were sent for Hemoglobin analysis at the laboratory .Regarding the newborn of each mother only pre term were included in the study, all fullterm were excluded as well as, post date and any baby with obvious dimorphic feature.

Four measurements took for each baby (Weight, Length, Head Circumference and Chest Circumference). Immediately after birth the measurement done in neonatal intense care unit . The questionnaire It included information about age and parity of the mother, socioeconomic status, educational level, History of tonic during pregnancy (iron and folate) and attendance to the ANC.

Mothers according to their educational level were classified into illiterate, read and write only, primary school, intermediate school, secondary school and higher (Institute or collage). The questionnaire included another set of information belong to the newborns which were sex, gestational age, mode of delivery.

I. Weight measurement of baby used digital scale.

II. Lengths measurement of baby by Infantometer (studiometery) done by fix baby inside the box in supine position fix the head & lower limbs then attach the lower end of infantometer to sole of the feet.

III. Head Circumference measurements done according the following steps

1. Use non-stretch tape, such as flexible metal tape measure.
2. Warp the tap around the widest part of the child head.
3. Move the tape around a bit and record the largest possible measurement.

Measure the circumference of the head at the level of the plane passing above the glabella (the most anterior protrusion of the forehead) and over the opisthrocranion (the most posterior protrution from glabella on the back of the head), per-pendicular to the mid-sagittal plane. Three different measurements take for each baby & record the largest one.

IV. Chest Circumference measurement of baby, The infant lies on back. With an automated tape device, measure the circumference of the chest at the level of the nipples during normal breathing.

Normal values and measurements

According to the WHO definition of anemia in pregnancy, mothers with Hemoglobin <110 g/l considered as anemic mothers.[5]

pre term baby <37weeks.[11]

Low birth weight (LBW) <2500gram.

Very Low birth weight (VLBW) <1500gram.

Extremely low birth weight (ELBW) < 1000 gram.

Interpretation of growth parameters requires plotting the measurements on percentile charts constructed from a similar race and environmental population. If birth weight falls between the 10th and 90th percentiles for a given GA, the infant is appropriate for gestational age (AGA); if less than the 10th percentile, the infant is small for gestational age (SGA); and if above the 90th percentile, the infant is large for gestational age (LGA). Some literature cites the 3rd and 97th percentiles as outer limits. In term neonates, the chest circumference is 1 to 2 cm less than the head circumference.

Statistics: Data were analyzed and according to Chi- square test; p-value of less than 0.05 consider to be significant.

Note: A copy of the questionnaire sheet was placed at the end of this thesis.

RESULTS

The overall preterm birth (<37 weeks) rate of single-ton live-born infants in this cohort was 4.7%, with 4.1% for anaemic and 5% for non-anaemic pregnancy women (P < 0.05). The most prevalent preterm birth clinical subtype was spontaneous preterm labour (3.6%), accounting for 77% of all preterm births. Table 1 shows the rates of preterm birth by maternal characteristics and fetal gender. Nearly one-third of women (32.7%) had anaemia (haemoglobin <10 g/dl) sometime during their pregnancy, with the prevalence of anaemia being 11, 20 and 26% in the first, second and third trimesters, respectively. The distribution of gesta-tional age at delivery for women with and without anaemia was similar (data not shown). Distribution of preterm birth rates in relation to maternal anaemia status is shown in Tables 2–4. There were relatively more preterm PROM cases among moderate preterm births (32–33 weeks) of anaemic women (P < 0.05).

Associations between haemoglobin levelsin each tri-mester and risk of preterm birth, and preterm PROM and spontaneous preterm labour are, respectively. Haemoglobin values 9–10 g/dl in the first trimester was associated with slightly increased risk for all preterm births. Haemoglobin <11 g/dl in the first trimester was par-ticularly associated with increased risk for preterm PROM. Women with lowest haemoglobin levels were at highest risk for preterm PROM [adjusted hazards ratio (HR) 3.3, 95% CI 1.4–7.7 for haemoglo-bin 45 g/dl] with progressively declining risk with increasing haemoglobin levels up to 10 g/dl. In con-trast, haemoglobin 410 g/dl in the third trimester was associated with reduced risk for all preterm births and spontaneous preterm labour. Medically indicated preterm was not associated with maternal haemoglobin (data not shown). We also observed a stronger association between first trimester anaemia and very to moderate preterm birth (<34 weeks) (data not shown). In the subgroup analysis of women who were pregnant for the first time, the patterns of association were similar. Haemoglobin increases of 51 g/dl from previous trimester, as the proxy of haemo-dilution, were asso-ciated with reduced risks for all preterm birth.

Table. 3.1: The rate of Hemoglobin of Mother and Anthropometrics measurement of New Born were presented as Mean±SD (Range).

	Normal (Hb≥11.0)	Anemic (Hb<11.0)	P value
Hemoglobin (g/dl)	11.86±0.92 (11.00-15.80)	10.08±0.57 (8.20-10.80)	0.0001*
Weight (Kilograms)	3.47±0.48 (2.75-5.00)	3.29±0.63 (2.25-4.50)	0.031*
Length (cm)	49.52±1.81 (45.00-55.00)	48.72±2.31 (42.00-54.00)	0.009*
OFC (cm)	34.46±1.19 (31.00-38.00)	34.08±1.45 (30.00-37.50)	0.054
Chest circumference	33.13±1.50 (30.00-38.00)	32.43±1.63 (28.00-35.00)	0.004*

Table. 3.2: The rate of Gender of New Born with Hemoglobin of the Mother.

Gender	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
Male	33	47.9	15	51.7	0.621
Female	27	52.1	25	48.3	
Total	60	100%	40	100%	

Table. 3.3: The rate of Iron supplement of the Mother during Pregnancy with Hemoglobin of the Mother.

Iron supplement	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
Yes	42	60.7	17	56.7	0.593
No	18	39.3	23	43.3	
Total	60	100%	40	100%	

Table. 3.4: The rate of Mother age with Hemoglobin of the Mother.

Mother age (years)	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
<20	5	7.1	2	6.7	0.287
20-24	27	38.6	11	21.7	
25-29	20	28.6	10	33.3	
30-34	4	16.4	8	25.0	
35-39	3	7.1	7	10.0	
≥40	1	2.1	2	3.3	

Table. 3.5: The rate of Weight for age percentile of pre term New Born with Hemoglobin of the Mother.

Weight for age percentile	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
<3rd	1	0.7	4	6.7	0.001*
3rd-50th	35	52.9	24	66.7	
50th-97th	20	42.9	7	18.3	
>97th	4	3.6	5	8.3	

Table. 3.6: The rate of Length for age percentile of pre term New Born with Hemoglobin of the Mother.

Length for age percentile	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
<3rd	1	1.4	2	10.0	0.020*
3rd-50th	19	55.0	19	58.3	
50th-97th	17	42.1	8	31.7	
>97th	1	1.4	-	-	

Table. 3.7: The rate of Weight for Length percentile of pre term New Born with Hemoglobin of the Mother.

Weight for length percentile	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
<3rd	1	1.4	2	6.7	0.215
3rd-50th	21	37.9	9	31.7	
50th-97th	45	46.4	27	45.0	
>97th	15	14.3	13	16.7	

Table. 3.8: The rate of OFC for age percentile of pre term New Born with Hemoglobin of the Mother.

OFC for age percentile	Normal (Hb≥11.0)		Anemic (Hb<11.0)		P value
	No	%	No	%	
<3rd	1	0.7	1	5.0	0.063
3rd-50th	43	65.7	29	71.7	
50th-97th	16	33.6	10	23.3	
>97th	-	-	-	-	

*Significant difference using t-test for two independent means at 0.05 level of significance.

DISCUSSION

The various studies on maternal anaemia and adverse reproductive outcomes have produced inconsistent findings. This is largely mitigated by the fact that maternal anaemia has been analysed as an aggregated exposure such as 'any anaemia during pregnancy'. It is likely that anaemia diagnosed early in pregnancy may exert stronger associations on pregnancy out-comes than anaemia diagnosed later in gestation. Equally, studies on preterm birth have paid little attention to its heterogeneous underpinnings,[1] thereby combining aetiologically distinct endpoints as being homogeneous, and perhaps leading to atte-nuated association measures.[1,15,26] Finally, little attention has been devoted as to how anaemia affects the risk for preterm birth clinical subtypes, including previous Chinese studies.[4,8,9,13] Most studies have exclusively focused on spontaneous preterm births.[14,27] Our study was designed to overcome many of these limitations. In addition, we explored the potential effects of physiological haemo-dilution on preterm birth.

We found anaemia in the first trimester was asso-ciated with modestly increased risks for all preterm birth. These associations were considerably stronger for preterm PROM. However, third trimester anaemia was associated with reduced risk for all preterm birth, and this association was largely confined to sponta-neous preterm labour. Medically indicated preterm birth, on the other hand, was not associated with anaemia. These results underscore the strong

hetero-geneity in the risk profile for preterm birth based on underlying clinical subtypes, as well as by exposure window, i.e. trimester in pregnancy when anaemia was diagnosed.

Table. 2: Maternal anaemia and all preterm birth (<37 weeks) rates.

	Total live-born infants	With attribute (%) (95% CI)		Preterm birth rate (%) (95% CI)	
All women	100		–	4.7	(4.6–4.8)
Maternal anaemia status	95				
None	5	65.1	(64.8–65.4)	4.4	(4.2–4.6)
First trimester only	43	2.0	(1.9–2.1)	4.6	(3.7–5.5)
Second trimester only	27	5.3	(5.2–5.5)	3.5	(3.0–4.0)
Third trimester only	15	11.9	(11.7–12.1)	2.9	(2.6–3.3)
First and second trimesters	70	2.4	(2.3–2.5)	3.7	(2.9–4.5)
First and third trimesters	58	0.95 (0.89–1.01)		3.2	(2.1–4.4)
Second and third trimesters	42	6.7	(6.5–6.8)	3.5	(3.0–3.9)
All three trimesters	95	5.7	(5.5–5.7)	5.0	(4.5–5.6)

Our findings on all preterm birth were consistent with a meta-analysis[28] which concluded that early pregnancy anaemia was associated with slightly increased risk for preterm birth and late pregnancy anaemia was inversely associated with preterm birth. All four previous Chinese studies[4,8,9,13] con- ducted in the same or nearby regions as the present study, examined the association between anaemia and preterm birth without consideration of associa-tions by preterm birth clinical subtypes. Whereas some reported anaemia in the first trimester to be associated with increased risk of preterm birth,[4,8] others did not.[9] The last study reported that only the third trimester haemoglobin <7 g/dl (severe anae - mia) was associated with a marginally increased risk for preterm birth.[13] Previously, five studies[11,14,26,27,29] reported associations between maternal anaemia and preterm birth clinical subtypes. All these studies either dichotomized pregnant women as being anae-mic or non-anaemic using one cut-off point,[9,27,29] or have categorized them into multiple groups using several cut-off points.[4,8,13,14,26,29] Categorization of skewed exposures such as anaemia, assumes within-category homogeneity, degrades continuous exposure data and tends to be less accurate than spline analysis.[30] We analysed haemoglobin concen-trations as a continuous variable based on flexible spine transformation to account for non-linear effects.

Disaggregating preterm birth into more homoge-neous subtypes revealed considerable heterogeneity in their associations with anaemia. Anaemia present in all three trimesters was associated with increased risk for spontaneous preterm labour, whereas anae-mia in mid- and late pregnancy was associated with reduced risk. There were trends of increased risks for

preterm PROM in relation to anaemia exposure in early half or throughout pregnancy. Anaemia in early pregnancy or throughout pregnancy may repre-sent pre-existing, or early onset and persistent iron deficiency. Iron deficiency anaemia, in turn, could induce maternal infection, hypoxia and oxidative stress, and trigger the spontaneous onset of preterm labour.[16]

Previous studies mentioned the concern that normal physiological haemo-dilution during pregnancy, which usually reaches the nadir at the end of the second trimester and early the third trimester, might mask the true association between anaemia and pre-term birth.[9,12,31,32] However, the association between haemo-dilution in the second and third trimesters and preterm birth had not yet been assessed. In our study, we used the haemoglobin reduction across tri-mesters as the proxy of haemo-dilution, controlling for the first trimester haemoglobin level as the base-line. We found haemo-dilution was associated with reduced risk for preterm birth. This may partially explain the inverse association between the third tri-mester anaemia and preterm birth.

The overall preterm birth rate in this Chinese cohort was fairly low (4.7%) with spontaneous preterm labour (77%) being the most common clinical sub-type. This rate is consistent with earlier findings for other cohorts in this region;[4,9,13] Rates of obstetric interventions at preterm and term gestations were 11.6 and 16.7%, respectively, in our cohort. These rates are lower than reported in other populations and suggest that the threshold for intervention in the presence of impending in utero fetal compromise is far higher than in most industrialized societies.[1] It is therefore likely that differences in practice and threshold for intervention may have played an impor-tant, but yet uncharacterized, role in our findings. In addition, gestational age was estimated based on last menstrual period, and errors associated with men-strual dating may have affected our findings to some extent.

The observed association between preterm birth and anaemia in the first trimester possibly related to iron deficiency, which was less likely affected by iron sup-plementation as iron supplement was given after the diagnosis of anaemia. However, anaemic women in late pregnancy were more likely to take iron supple-ment as a treatment and receive more medical atten-tion. Besides the effects of the normal physiological haemo-dilution,[9] the observed inverse association between late pregnancy anaemia and spontaneous preterm labour might reflect an artefact partially due to the benefits of medical interventions. Whether early

prevention and prompt treatment of maternal anaemia can reduce the risks for spontane-ous preterm labour and preterm PROM warrants fur-ther investigation.

Biases, limitations and strengths of the data

Haemoglobin was assessed in local laboratories using the usual clinical methods without standardized pro-tocols. Haemoglobin values in the second and third trimesters pertained to the lowest of the assessments, which may blend real anaemia with the physiological haemo-dilution that reaches the nadir near the end of the second and early of the third trimesters in normal pregnancy.[33] Therefore, the observed association between anaemia and preterm birth may have been attenuated. Maternal socio-economic status, dietary factors, smoking and gestational age of each haemo-globin measurement could be related to anaemia and preterm birth. Unfortunately, these data were not col-lected. Data on individual iron supplementation was unavailable. However, it is likely that iron was pre-scribed to anaemic women as a treatment,[4,9] and this may have resulted in an attenuation of the associa-tions noted here. Finally, our estimation of gestational age was largely based on menstrual dates that are prone to some degree of inaccuracy.[34,35]

The abilities to separate preterm births by its clinical subtypes and to examine associations within more homogeneous groups in relation to maternal anaemia.

RECOMMENDATION

1. Further studies including longitudinal studies to follow mental and physical outcomes of babies whose mothers have Anemia are needed to provide more conclusive evidence of the long-term consequences.
2. Steps should be taken to ensure that maternal iron: folic acide. status is adequate early in pregnancy, throughout pregnancy and during the postpartum period.

CONCLUSIONS

Maternal anaemia in early pregnancy is associated with increased risk of preterm PROM and anaemia in late pregnancy is associated with reduced risk of spontaneous preterm labour. Adequate physiological haemo-dilution during mid- to late pregnancy may be associated with reduced risk for preterm birth. Early prevention and prompt treatment of maternal anaemia may be one avenue for intervention, and may be a topic worthy for further investigation. To unravel other possible explanations to our findings, and to further investigate the causal link

between anaemia and preterm birth, a randomized clinical trial could overcome some of the methodological lim-itations in the current studies.

Note: Whether maternal anaemia is associated with risk of preterm birth and their clinical subtypes remains unclear.

In this prospective cohort study from China preterm PROM, whereas anaemia in late pregnancy was associated with reduced risk for spontaneous preterm labour.

Adequate physiological haemo-dilution during mid- to late pregnancy may be associated with reduced risk for preterm birth.

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