MATERNAL ANEMIA AND ITS CONSEQUENCES ON CORD BLOOD HEMATOLOGIC PARAMETERS

By

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ABSTRACT:

Background: It is estimated that more than 50% of pregnant women in developing countries may be anemic. The most common cause of anemia in developing countries are: nutritional, hook worms infestation, repeated pregnancies and hemorrhages. Studies report that iron transfer to the fetus may depend on or be independent of maternal iron status.

Aim: To assess factors associated with maternal anemia and its implications on hemoglobin, iron and ferretin on cord blood.

Methodology: A cross-sectional study was conducted on 173 pregnant mothers. The study enclosed full term pregnant women attending the labour ward who will deliver single live birth at term gestation (37–41 weeks) at Woman's Health Center at Assiut University Hospital. A simple questionnaire was fulfilled by personal interview. Samples of maternal blood and cord blood were taken for hemoglobin, serum iron and serum ferritin measurement. Maternal blood samples were collected from the pregnant mothers during the first stage of labor. Cord blood was collected immediately after the placental delivery from the placental end of the umbilical cord without milking just after the second stage. The cutoff point to consider anemia when hemoglobin was <11 gm/dl while if hemoglobin was ≥11 gm/dl, the mother was considered to be non anemic.

Results: Anemic mothers were 89 (51.5%). There were no significant association as regards sociodemographic and reproductive history between both groups except the reproductive duration (p= 0.04). Drinking tea was higher among anemic group than the non anemic (75.5% and 24.5% respectively) with p= 0.021. There was a significant difference between both groups in mean hemoglobin, iron and ferretin levels. Cord blood hemoglobin, iron and ferretin levels were significantly lower in babies of anemic mothers (p= 0.023, 0.02 and < 0.0001 respectively). Significant negative correlation was found between mother iron level and number of pregnancies also between cord blood hemoglobin level and number of pregnancies. There was significant negative correlation between mother hemoglobin level and cord blood hemoglobin level. By using logestic regression analysis maternal age, number of pregnancies and drinking tea one hour before or after meals, were significantly associated factors with maternal anemia.

Conclusion: Maternal age, number of pregnancies and reproductive duration have a negative impact on maternal anemia in addition to drinking tea one hour before or after meals. Maternal anemia adversely affects cord blood iron status and haemoglobin level. Effective strategies are urgently needed to control maternal anemia in the developing world.

KEYWORDS:

Maternal anemia Cord blood Assiut University Hospital

INTRODUCTION:

According to the guidelines proposed by the expert group of the WHO, "maternal anemia should be considered when HB level is below 11 gm/dl". It is estimated that more than 50% of pregnant women in developing countries may be anemic. The prevalence of anemia in developed countries may not exceed 20% [1].

The most common causes of anemia in developing countries are: nutritional, hook worms infestation, repeated pregnancies and hemorrhages. Preterm labour, low birth weight infants and postpartum infection are associated with anemia during pregnancy. Maternal anemia associated with neonatal anemia and poor survival rate [2].

In societies where the status of women is low, women face overt discrimination in the distribution of food within the family. Although researches on infants and young children have shown cognitive, behavioral and anthropometric effects of iron deficiency [3].

An inverse type of relationship indirectly exists between maternal nutritional status and fertility levels. Virtually, in societies where women are well fed, the fertility levels are low, while societies where women are not well fed, the fertility levels are high [4].

Maternal anemia is widely prevalent and more severe in degree, frequently coexists with maternal malnutrition, and is of long duration, present since the beginning of pregnancy or antedating it in many mothers. Under these circumstances, the competing demands of mother and fetus may disturb the normal maternal-fetal iron homeostasis. Anemia or iron deficiency during pregnancy was reported to be a predictor of poor perinatal outcome including; intrauterine growth retardation, premature birth, low birth weight (LBW), increased labor time, higher risk of infection, elevated maternal and prenatal mortality, muscle dysfunction and low physical capacity [5].

Studies report that iron transfer to the fetus may depend on or be independent of maternal iron status. The relationship between maternal and fetal iron status is still disputed [6-8].

Aim:

To assess the factors associated with maternal anemia and its implications on hemoglobin, iron and ferretin on cord blood.

Methodology:

A cross-sectional study was carried out for target mothers during May 2011 at Woman's Health Center at Assiut University Hospital.

Participants:

The study was conducted on 173 full term pregnant women attending the labour ward who will deliver single live birth at term gestation (37–41 weeks) at Woman's Health Center at Assiut University Hospital. Those 173 mothers didn't fulfill the exclusion criteria and accepted to participate in the study out of all attendants during the study period. Exclusion criteria were preterm labour (before 37 weeks of gestation), mothers with chronic medical condition as diabetes mellitus, liver or kidney disorders and any other systemic illness. Mothers with bad obstetric conditions as bleeding during pregnancy, history of sever infections during pregnancy, history of sever hyperemesis, pre-eclampsia, eclampsia, previous history of hemoglobinopathy. Prolonged rupture

of membranes (>24 hours), fever, foul-smelling liquor or other medical complications during pregnancy. Gestational age was calculated from the first day of the last menstrual period.

A simple questionnaire was fulfilled by personal interview with the participants. The included questions were divided into first part: some sociodemographic questions as age, occupation (working or not), mother education, husband education. The second part included reproductive and obstetric history questions: Age at menarche, age at first pregnancy, reproductive duration (which is the duration between the first delivery and the last delivery), number of pregnancies, history of early delivery, history of still birth and history of low birth weight The third part was about nutritional history by using qualitative food frequency questionnaire, as: Eating meat, chicken, fish, fruits, vegetables, cereals and eggs. Answers were coded into daily, some days per week, rarely or never. A question about drinking tea within one hour before and after meals was included.

Weight measurement for the new baby was done. Samples of maternal blood and cord blood were taken for hemoglobin, serum iron and serum ferritin measurement.

Collection of samples and laboratory analysis:

Paired maternal and cord blood samples were collected and mother name was written on maternal sample tube and on the cord blood sample tube. Maternal blood samples were collected from the pregnant mothers during the first stage of labor. Cord blood was collected immediately after the placenta delivery from the placental end of the umbilical cord without milking just after the second stage. Analysis of maternal and cord blood for the estimation of hemoglobin level was performed on the same day of collection. Hemoglobin concentrations were measured by using (in an automated blood cell counter (Beckman Coulter). Maternal and cord blood serum samples were stored at −20°C until analyzed for serum iron and ferritin. Serum iron was measured by colorimetric assay (using Stanbio iron kits, Stanbio laboratories, Texas-USA), and serum ferritin by immunoenzymometric assay (using Accubind ELISA kit, Monobind Inc. - USA). The cutoff point for classification of anemic and non anemic mothers was (hemoglobin: <11 gm/dl) to be anemic mothers and (hemoglobin: ≥11 gm/dl) to be non anemic.

Statistical Analysis:

Statistical analysis was done with SPSS software (V.16 SPSS Inc., Chicago, Il, USA). The categorical variables were summarized as percentages and the continuous ones as means and standard deviations. Chi square test was used to compare the qualitative data. T test was used to compare two means. Spearman's rank correlation coefficient test (r) was used to assess the association between parameters. P value < 0.05 was considered statistically significant.

Ethical considerations:

Informed consent was taken from mothers, and the study protocol was approved by the ethical committee, Faculty of Medicine, Assiut University.

RESULTS:

Table (1): Anemic and non anemic mothers according to sociodemographic and reproductive characteristics

	Non anemic (n= 84)	**Anemic (n= 89)**	**P-value**
	mean ± SD	**mean ± SD**	
Age (yrs)	26.3 ± 5.4	27.8 ± 6.3	0.09
Age at menarche (yrs):	13.8 ± 1.2	13.8 ± 1.2	0.96
Age at first pregnancy:	21.7 ± 4.2	21.1 ± 2.3	0.12
No of pregnancies:	2.9 ± 1.7	3.2 ± 2.1	0.39
Reproductive duration:	4.5 ± 5.2	6.4 ± 6.8	0.04
Birth weight	3.3 ± 0.6	3.1 ± 0.6	0.12
Education: No (*%*)			
Illiterate	23 (*42.6*)	31 (*57.4*)	0.09
Read & write/ basic education	18 (*54.5*)	15 (*45.5*)	
Secondary	40 (*50.6*)	39 (*49.4*)	
High education	3 (*42.9*)	4 (*57.1*)	
Husband education: No (*%*)			
Illiterate	31(*43.7*)	40 (*56.3*)	0.20
Read & write/ basic education	18 (*56.2*)	14 (*43.8*)	
Secondary	35 (*52.2*)	32 (*47.8*)	
High education	0 (*0.0*)	3 (*100*)	
Mother's job: No (*%*)			
Working	81 (49.1)	84 (50.9)	0.72
Not working	3 (37.5)	5 (62.5)	
History of still birth: No (*%*)			
Yes	15 (48.4)	16 (51.6)	1.00
No	69 (48.6)	73 (51.4)	
History of intrauterine fetal death No (*%*)			
Yes	8 (42.1)	11 (57.9)	0.63
No	76 (49.4)	78 (50.6)	
History of low birth weight No (*%*)			
Yes	10 (40.0)	15 (60.0)	0.39
No	74 (50.0)	74 (50.0)	

Chi square test was done

Table (1) shows that out of 173 pregnant women, 89 (51.5%) were anemic and 84 (48.5%) were non anemic. The age ranged from 17 to 49 years old, age at menarche ranged from 11 to 16 years, the age at first pregnancy ranged from 14 to 35 years old and with range number of pregnancies from one to 11 pregnancies while the reproductive duration range was between zero and 32 years. Their newborn babies' range of weight was between 2.0 to 4.5 kgs. Mother hemoglobin ranged from 6.5 to 15.1 g/dl with mean ± SD of 10.7 ± 1.6. Between both groups there were no significant association as regards sociodemographic (age, educational level of the mother and the husband in addition to mother's job). The same

was found in reproductive history including age at menarche, age at first pregnancy and number of pregnancies while reproductive duration shows significance (p = 0.04). History of still birth, intrauterine fetal death and history of low birth weight showed no significant association with anemia in both groups.

Mean ± SD of maternal hemoglobin was 10.7±1.6 and ranged from 6.5 to 15.1 for all participants

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Table (2): Dietary habits of anemic and non anemic mothers

	Non anemic (n= 84)		Anemic (n= 89)		P-value
	No.	%	No.	%	
Frequency of eating meat:					
1-2 times weekly	74	46.8	84	53.2	0.32
>2 times weekly	3	75	1	25	
Rarely or no	7	63.6	4	36.4	
Frequency of eating chicken:					
Daily	2	50	2	50	
1-2 times weekly	62	48.4	66	51.6	0.98
>2 times weekly	2	40	3	60	
Rarely or never	18	50	18	50	
Frequency of eating fish:					
1-2 times weekly	50	55.6	40	44.4	0.04
Rarely or never	34	41	49	59	
Frequency of eating fruit:					
Daily	62	47.3	69	52.7	
1-2 times weekly	2	25	6	75	0.31
>2 times weekly	11	55	9	45	
Rarely or never	9	64.3	5	35.7	
Frequency of eating vegetables:					
Daily	28	49.1	29	50.9	0.57
1-2 times weekly	34	44.7	42	55.3	
>2 times weekly	22	55	18	45	
Frequency of eating cereals:					
Daily	41	56.9	31	43.1	
1-2 times weekly	15	45.5	18	54.5	0.30
>2 times weekly	25	41	36	59	
Rarely or never	3	42.9	4	57.1	
Frequency of eating eggs:					
Daily	52	46	61	54	
1-2 times weekly	7	36.8	12	63.2	0.20
>2 times weekly	4	80	1	20	
Rarely or never	21	58.3	15	41.7	
Drinking tea one hour before or after meals:					0.02
Yes	48	24.5	65	75.5	
No	36	60	24	40	

Chi square test was done

Table (2) shows that the dietary habits of the mothers, frequency of eating meat, chicken, fruits, vegetables, cereals, and eggs there is no significant association between anemic and normal mothers. On the other hand, eating fish was significantly higher among non anemic (55.6 % among those with 1-2 times weekly) with p= 0.04. Drinking tea was higher among anemic than in other group (75.5% and 24.5% respectively) with p = 0.021.

Table (3): Maternal and cord blood hemoglobin, iron and ferretin levels between normal and anemic mothers

	Non anemic (n= 84)	**Anemic (n= 89)**	**P-value**
	mean ± SD	**mean ± SD**	
Mother hemoglobin (g/dl)	12.1 ± 0.94	9.5 ±1.1	< 0.0001
Mother iron (µg/dl)	71.9 ± 29.4	49.8 ± 24.3	0.003
Mother ferretin (ng/ml)	36.7 ± 33.7	9.8 ± 11.8	< 0.0001
Cord blood hemoglobin (g/dl)	14.7 ± 1.4	14.1 ± 2.2	0.023
Cord blood iron (µg/dl)	84.2 ± 23.9	75.1 ± 27.4	0.02
Cord blood ferretin (ng/ml)	110.8 ± 58.6	69.6 ± 54.8	< 0.0001

t- Test was used

Table (3) found that there is a significant difference between mean mother hemoglobin, iron and ferretin levels between both groups. Cord blood hemoglobin, iron and ferretin levels were significantly lower in babies of anemic mothers (p= 0.023, 0.02 and < 0.0001 respectively).

Table (4): Pearson correlation among the studied mothers between the age, reproductive characteristics and maternal and fetal cord blood measurements

	Pearson correlation (r value)	**Significance**
Age and cord blood iron level	-0.058	0.013
Age and mother hemoglobin	-0.159	0.036
Cord blood hemoglobin level and number of pregnancies	-0.188	0.013
Mother iron level and number of pregnancies	-0.166	0.029
Mother iron level and cord blood iron level	0.272	< 0.0001
Mother iron level and cord blood ferretin level	0.178	0.019
Mother hemoglobin level and cord blood hemoglobin level	0.675	< 0.0001
Mother hemoglobin and cord blood iron level	0.541	< 0.0001
Mother hemoglobin and cord blood ferretin level	0.399	< 0.0001

Pearsons correlation coefficient test was done.

Table (4) shows significant negative correlation between number of pregnancies and mother iron level also between number of pregnancies and cord blood hemoglobin level. Positive significant correlation was found between mother iron level and cord blood iron level and cord blood hemoglobin level.

Table (5): Factors associated with maternal anemia assessed by logestic regression analysis

	B	Sig.	Exp(B)
Drinking tea1hour before or after meals	-.752	0.040	.472
Eating fish	.541	0.110	1.717
Mother education	-.069	0.709	.933
Maternal age	.883	0.006	2.418
Age at first pregnancy	-.351	0.225	0.704
No of pregnancies	-3.365	0.002	28.929
Reproductive duration	-.022	0.951	0.979
Constant	-4.672	0.013	0.009

Variable(s) entered on step 1: drinking tea one hour before or after meals, eating fish, mother education, maternal age, age at first pregnancy, no of pregnancies and reproductive duration.

Table (5) shows that by using logestic regression analysis drinking tea one hour before or after meals, maternal age and number of pregnancies were significantly associated factors with maternal anemia(0.040, 0.006 and 0.002).

DISCUSSION:

Maternal iron status has a crucial role in fetal development. Moreover, anaemia has been reported to be associated with fetal anaemia and still birth [9].

Maternal age, educational level, antenatal care and economic status play an important role in the incidence of LBW [10]. Out of 173 participants, 51.5% were anemic. The comparison of the prevalence is limited with that our study is a hospital based conducted in a limited population. But this percent is nearly in consistence with what was shown by the WHO that the prevalence in developing countries exceeds 50% [1] but it's lower than what was found in India (85%) [11].

In our study there was no great difference between anemic and non anemic mothers as regard maternal socio-demographic and reproductive studied characteristics with the exception of the reproductive duration which is significantly has higher mean years among anemic than that among non anemic. In addition, dietary habits on both groups have no statistical significant difference. Also socioeconomic conditions as education, husband education and job have no association with maternal anemia that nearly all mothers who are attending Assiut University Hospital to deliver in the popular sector are similar in socioeconomic status.

Gurav and Kartikeyan [12] found that multiparity is significantly associated with anemia which is in concordance with our study results that number of pregnancies is significantly differ between the anemic and non anemic mothers.

In the current study; newborn of anemic mothers had slightly LBW (3.12±0.56 vs 3.25±0.57) and the difference was not significant. This was not in accordance with Elhassan et al [13] that anemia was the main risk factor for LBW.

Our study found no great differences between anemic and non anemic mothers as regard the dietary habits except for eating fish it was significantly higher among normal (55.6 % and 44.4% respectively; p= 0.040). Drinking tea within one hour before or after meals was significantly associated with anemia among anemic than in non anemic (75.5% and 24.5% respectively; p= 0.02).

The possibility of neonatal iron deficiency (ID) when maternal iron stores (IS) are deficient has been previously suggested by Rao and Georgieff[14] as what found by our study.

Most iron transfer to the fetus occurs after week 30 of gestation, which corresponds to the time of peak efficiency of maternal iron absorption.

About 51 % of our study population was characterized by mild to moderate anemia; the serum ferritin levels were low in all of the anemic women in the study group, confirming the etiology of anemia as iron deficiency.

In accordance with other study [15] the present study, was documented that iron-deficiency anemia during pregnancy could compromise fetal iron status; significantly lower levels of hemoglobin, iron, and ferritin were found in the cord blood of infants born to anemic mothers.

Jaime-Perez et al [6] suggest that neonatal iron stores were influenced by maternal storage iron levels and there was a limit in the capacity of the fetus to accumulate iron at extremely low or absent maternal iron reserves as shown on our study results.

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. In the iron-deficiency state, there is up regulation of iron transport proteins in the placenta which ensures adequate iron supply to the growing fetus. This results in the majority of neonates being born with normal iron state (IS), whereas the majority of their mothers ended their pregnancy with deficient IS and/or iron deficiency anemia [16].

In accordance with other reports[17-19], our study showed that cord serum iron concentration was higher than those of maternal serum, suggesting an active transport system and implies the importance of iron for fetal growth. This finding is as what was found in our results that maternal iron level is positively highly significant correlated with cord blood iron level.

However, some investigators could not find any relationship between maternal and fetal iron status, thereby concluding that the fetus continues to extract iron efficiently from the mother regardless of her iron balance. They suggest that a protective mechanism might be present, aimed to secure the incorporation of whatever iron is available into fetal hemoglobin, to guarantee a sufficient level of oxygen delivery for the developing fetal tissues indicating that fetuses with reduced iron stores prioritized the available iron to sustain normal erythropoiesis[6]. This finding appears to be in consonance with the reported

increment on cord serum erythropoietin concentration in neonates born to anemic women, suggesting the existence of a mechanism for the induction of fetal erythropoiesis driven by maternal anemia. This efficient mechanism appears to have enabled most of the fetuses to obtain enough iron, even when maternal stores were already deficient[20]. This explains higher iron and ferritin levels in cord blood compared with the maternal blood,

Lack of an association between maternal and cord blood hemoglobin concentrations was reported in diverse countries [21- 23] in contrast our study reported a positive significant correlation between maternal hemoglobin concentrations and cord blood hemoglobin concentrations.

Cord blood ferritin was, however, related to maternal hemoglobin or maternal ferritin in most of studies[24,25] with few exceptions[26,27]. Here we found a positive significant correlation between mother iron level on one side and cord blood iron level and cord blood ferretin level on the other side.

The present study had the limitation of not assessing maternal iron and nutritional status from early gestation, which would have been more meaningful to see its effect on fetal iron nutrition. However, it was not possible to do so, because none of the study participants were registered in the first trimester and attended hospital for the first time only during delivery. Moreover, it would have been unethical to study the impact of maternal anemia from early pregnancy without supplementing them with iron.

In conclusion, the present study indicates that maternal age, numbers of pregnancies and reproductive duration have a negative impact on maternal anemia in addition to drinking tea one hour before or after meals. Maternal anemia adversely affects cord blood iron status and hemoglobin level. Nonetheless, the effect of the mother's iron status on her infant's iron stores postpartum needs to be clarified because of the known detrimental effects of iron deficiency anemia on the mental and motor development of infants.

Effective strategies are urgently needed to control maternal anemia in the developing world. Improving the nutritional status and iron status of pregnant and lactating women will have a favorable impact on maternal, fetal and infant iron status.

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أنيميا الأمهات و تأثيرها على قياسات الدم في الحبل السري

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مقدمة: تقدر الأنيميا بين الأمهات في الدول النامية بأكثر من 50%، ومن أكثر أسباب الأنيميا في الدول النامية التغذية والإصابة بالدودة الخطافية وتكرار الحمل والنزيف. وأسفرت الدراسات أن انتقال الحديد للجنين قد يعتمد أو لا يعتمد على نسبة الحديد في الأم.

الهدف من الدراسة: تحديد العوامل المصاحبة لأنيميا الأمهات وتأثيرها على الهيموجلوبين والحديد والفريتين في دم الحبل السري.

خطة البحث: تم اجراء دراسة مستعرضة على 173 سيدة حامل، وقد تضمنت الدراسة السيدات مكتملات فترة الحمل (من الأسبوع 37 الى الأسبوع 41) اللاتي أتين للولادة باستقبال مركز صحة المرأة بمستشفى أسيوط الجامعي ولم تنطبق عليهن معايير الإستبعاد من الدراسة.
استخدمت إستبانة تم استيفاؤها بالمقابلة الشخصية مع السيدة المستهدفة. وتم أخذ عينة من دم الأم في المرحلة الأولى من الولادة وعينة من دم الحبل السري بعد ولادة المشيمة من ناحية المشيمة بعد المرحلة الثانية مباشرة.
وقد تم اعتبار الأم مصابة بالأنيميا عند نسبة هيموجلبين ≤ 11 جم / دسل وغير مصابة عند نسبة > 11 جم / دسل.

النتائج: أوضحت الدراسة أن 89 سيدة (51.5%) مصابات بالأنيميا و 84 سيدة (48.5%) غير مصابات بالأنيميا. ولم يكن هناك اختلاف ذو دلالة احصائية بين المجموعتين في العوامل الإجتماعية والخصائص الديموغرافية والخواص الإنجابية، ما عدا فترة الإنجاب بدلالة احصائية (0.04). وكان شرب الشاي بعد أو قبل تناول الطعام بساعة أكثر في السيدات المصابات بالأنيميا بفارق ذى دلالة احصائية (0.02).

وأسفرت النتائج عن وجود فارق ذو دلالة احصائية بين المجموعتين في نسبة الحديد و الهيموجلوبين والفريتين وقد انخفضت القياسات في الحبل السري لأطفال الأمهات المصابات بالأنيميا.

وقد وجدت علاقة سلبية ذات دلالة احصائية بين نسب الحديد وعدد مرات الحمل، وبين الحديد في دم الحبل السري وعدد مرات الحمل أيضا. و أوضحت النتائج وجود علاقة ايجابية ذات دلالة احصائية بين نسبة هيموجلوبين الأم و نسبة هيموجلوبين الحبل السري. وباستخدام التحليل الإحصائي المتعدد وجد أن عمر الأم وعدد مرات الحمل وشرب الشاي بعد أو قبل تناول الطعام بساعة من العوامل المصاحبة لأنيميا الأمهات.

الخلاصة: عمر الأمهات وعدد مرات الحمل وفترة الإنجاب و شرب الشاي بعد أو قبل تناول الطعام بساعة من العوامل المصاحبة لحدوث أنيميا الأمهات. وقد أثرت أنيميا الأمهات على نسبة الهيموجلوبين والحديد و والفريتين في دم الحبل السري. ويوصى بحتمية وجود استراتيجية فعالة للتحكم في أنيميا الأمهات في الدول النامية. وإن تحسين الحالة الغذائية وتحسين نسبة الحديد للحوامل سيكون له مردود مطلوب على نسبة الحديد للجنين والطفل.