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Original Article

Iron Deficiency Anaemia is a Serious Maternal Health Issue During Pregnancy

Nadira jadoon[1], Muhammad Salman[2], Riffat Shaheen[3], Nadia Nisar[4], Uzma Bashir Amir[5]
Department of Hematology[1], Department of Microbiology[2], Public Health Laboratories Division[4,5], National Institute of Health, Federal Government Services Hospital[3], Islamabad.

Abstract

Background: Anaemia is commonly found in developing countries associated with nutritional deficiencies and multiple pregnancies. Iron Deficiency Anaemia in pregnancy is a risk for preterm delivery, low birth weight babies and adverse effects on infant development. The current study investigated frequency of iron deficiency anemia and beta thalassaemia trait during antenatal check up among pregnant women visiting a tertiary care hospital in Islamabad.
Objectives: To investigate iron deficiency anemia and beta thalassaemia trait among pregnant females visiting a tertiary care hospital in Islamabad.
Study design, settings and duration: The retrospective comparative study was done to investigate iron deficiency anemia among pregnant females visiting a tertiary care hospital in Islamabad from May 2006 to April 2009.
Subjects and Methods: The study was conducted at National Institute of Health (Department of Hematology) for Complete Blood Count and differential counts using Automated Hematology Analyzer (Sysmex KX-21). Serum Ferritin levels were measured by Electro-chemiluminescence technique using Elcys Ferritin Kit (Roche, Germany).
Results: Among 359 subjects, 237 (66%) had iron deficiency anemia. The mean age was 27.32 ± 4.9 years (range 18-50 years), 18 (5%) had beta thalassaemia trait and 104 (29%) had non-beta thalassaemia Trait. Forteen cases had concomitant iron deficiency anemia and beta thalassemia trait. The findings of this study indicate a relatively higher burden of iron deficiency anemia as compared to beta thalassemia trait.
Conclusion: Anemia is a neglected problem which needs priority. Routine iron supplementation should be given to women of child bearing age during pregnancy and post partum. Obstetricians have an important role to aware the women of reproductive age about the iron content in a balanced diet and motivation for iron supplements.
Key words: Iron deficiency anaemia, beta thalassaemia trait, complete blood count.

Introduction

Anemia during pregnancy is common problem among females of reproductive age group particularly in developing countries such as Pakistan, India and Bangladesh. The problem also poses a challenge for the antenatal physicians due to the associated mortality and morbidity for the mother and the child.[1,2] Iron deficiency in adults is caused by loss of blood while in childhood, faulty diet is to blame. The anemia result from quantitative defect of haemoglobin production.[3] Prevalence of maternal anemia varies considerably across Pakistan because of differences in socioeconomic conditions, life styles and health seeking behaviors.[1] Worldwide Iron Deficiency Anemia (IDA) is most common nutritional disorder effecting approximately 25% to 50% of population and burden is more in developing countries. In India, IDA is widely prevalent affecting 80% of pregnant mothers.[4] Iron Deficiency Anemia is the commonest nutritional deficiency among pregnant women worldwide. More than 56 million worldwide are estimated to have IDA with approximately 32 million of them been form Asia and it was estimated that 29% of IDA is in Sirilanka.[5,6]

Corresponding Author:
Nadira jadoon
Public Health Laboratories Division
National Institute of Health, Islamabad.
Email: drnadirajadoon@hotmail.com

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Authors Contribution

NJ, MS & RS conceptualized of project. MS did the data collection and literature search. Statistical analysis was done by NN. NJ, MS & UBA drafted the manuscript and did revision.

Women who start their pregnancy with low stored iron levels are at a greater risk to become anaemic during the course of pregnancy. Iron deficiency anaemia is more common in pregnancy on account of increased need of iron for the growing fetus, which is approximately twice times the demand in non- pregnant state. Once maternal stores are depleted, she becomes anaemic and transfer of iron to fetus is compromised. In pregnant women, iron and foliate deficiencies are common, these are related with nutritional factors, intestinal worm infestation etc. Low socioeconomic group in Pakistan is major cause of IDA. According to UNO, pregnant women of low income have 56% anaemia. Dietary habits of pregnant women affect the Haemoglobin level.[7] Anaemia in pregnancy is also directly associated with no previous antenatal checkups and low educational level. The WHO/World bank has ranked Iron Deficiency Anemia as the third leading cause of disability-adjusted life years lost for females 15-44 yrs of age.[8]

In Pakistan, the prevalence of anaemia is high and over 56% of the pregnant women are reportedly anemic.[9] Anemia is also associated with parity and gravity of human, No previous antenatal checkups, low educational level. Other causes include Vit B-12 and foliate deficiency, blood loss, intestinal worm infestations, malaria, inherited disorders and co morbid chronic diseases.[7] Prevalence of IDA among females of reproductive age exists up to 50%, therefore, maternal mortality rate is high and a growing concern has been raised by the local and international organizations to control IDA in Pakistan. According to Pakistan Demographic and Health Survey 2006-07, maternal mortality was shown to be high with 276 deaths per 100,000 live births as compared to 1 in 8,000 in the developed world.[2] Amongst 89 Pakistani women, one dies of child birth complications.[2] Anemia results from nutritional related caused inflammatory or infectious diseases, worm infestation and form blood loss.[10]

The pregnant women normally present with microcytic hypochromic anaemia and are put on iron therapy without ruling out the other causes specially those having same peripheral blood pictures like thalassaemia. Thalassaemia are heterogeneous group of genetic disorder of hemoglobin synthesis characterized by decrease globin chain production leading to microcytic anemia. Alpha and beta variants of Thalassaemia result from reduction of alpha and beta globulin chains respectively.[4]

Iron deficiency anemia in adults is caused by loss of blood and from quantitative defect of haemoglobin production. There is no haemolysis, erythrocytes survive normally and serum iron levels tends to be low.[11]

WHO/ World Bank has ranked iron deficiency anemia as third leading cause of disability-adjusted-life-years (DALYs).[8] WHO report on maternal health and safe motherhood program reveals an alarming rate of anemia among pregnant women in developing countries. A cycle of deteriorating health form pregnancy to pregnancy occur when these women are unable to replace blood loss during child birth.[12]

Microcytic hypochromic is very useful in picking up cases who have low MCV and MCH and require confirmatory tests like serum ferritin and HbA2 estimation. The presence of coexisting iron deficiency tends to increase the proportion of red cells with poor haemoglobinisation (Low MCH). The net result is lower M/H ratio.[13] MCV/RBC ratio was used to discriminate between iron deficiency and beta thelassamia trait and more than 14% was marked as iron deficiency.[14]

Subjects and Methods

The study was done to investigate Iron Deficiency Anemia among pregnant females visiting a tertiary care hospital in Islamabad from May 2006 to April 2009.

This study was conducted at the Department of Hematology, Public Health Laboratories Division (PHLD), National Institute of Health (NIH) in collaboration with Maternal and Child Health Centre (MCH), Federal Government Services Hospital (FGSH), Islamabad. All pregnant women were enrolled in the study from May 2006 to April 2009. The enrolled cases were referred to NIH for Complete blood count using hematology analyzer (Sysmex Kx-21), Serum ferritin levels measured by Electro-Chemiluminescence technique using Elcys Ferritin kit (*Roche, Germany). Comparison was done for beta thalassaemia trait by Haemoglobin Electrophoresis.

A total of 359 pregnant women were enrolled using non-probability convenient sampling technique. The cases were enrolled at the time of antenatal check up irrespective of the trimester with haemoglobin levels below or equal to 13gm/dl. Referred cases were interviewed using a pre-designed questionnaire which included information about the demographics, gestational age and other relevant clinical details.

Six milliliter venous blood was collected from each patient using aseptic technique with 3 ml into each of the 2 anti-coagulated venoject tubes. One sample was processed for CBC and differential counts using Haematology Analyzer (Sysmex KX-21, Japan), fully automated 5-part differential cell counter, working on the principle of light scattering.

The 2-level controls were run every day in the cell counter, and the counter was maintained according to the manufacturer's instructions. Preparation of slides for peripheral film examination was done by Leishman staining.[15]

From the second sample, haemolysate was prepared by standard method. The supernatant was applied on cellulose acetate strips (Bio system, France) and electrophoresis was carried out at a current of 5 mA in Tris EDTA buffer (pH:8.9) for 10-15 minutes . The separated HbA and HbA2 bands were cut and eluted in same buffer. Absorbance was read on a spectrophotometer (Sequa Turner-USA) at wavelength of 413nm and finally percentage of HbA2 was calculated by a standard formula. (A x 5 + A2 = (result)

A% = A2 / result x 100.[7]

Serum Ferritin levels were measured by Electro-chemiluminescence technique using Elcys Ferritin Kit (Roche, Germany) as per manufacturers' instruction. The diagnosis of beta thalassaemia trait was confirmed if serum ferritin level was increased (> than 13 µgm/l) or within normal range among cases having HbA2 levels more than 3.5%. Cases with normal HbA2 and serum ferritin levels were designated as the non-BTT group. The criteria to diagnose iron deficiency were transferrin saturation less than 16% and/or a serum ferritin level of less than 16 ng/mL. Serum iron level, total iron binding capacity, and serum ferritin level were done in each case. We applied the following five cell counter–based formulas: F1, Shine and Lal Index: MCV × MCV × MCH/100 (values¬_<-than 1530 in Thalassaemia trait, values >-than 1530 in IDA); F2, Mentzler Index: MCV/RBC count; F3, Srivastava Index: MCH/RBC count_ (values <13 then Thalassaemia trait, > than 13 Iron Deficiency anaemia; F4, England and Fraser Index: MCV– (5 × Hemoglobin) – RBC (Negative in thalassaemia trait and positive in IDA) ; F5, Ricerca Index: RDW/RBC count. The RBC count, MCH, RDW, and MCV were applied in each case.[14]

The study was approved by ethical committee of National Institute of Health, Islamabad.

Results

A total of 359 subjects were included in the study. The mean age was 27.32±4.9 (range 18-50 years). Iron Deficiency Anemia was present in 237 (66%), beta thalassemia trait (BTT) was confirmed in 18 (5%), and Non-BTT was present in 104 (29%) women. Out of these, there were 14 cases which have concomitant IDA and BTT. The mean age of BTT cases was 30±7.4 (25-30 yrs), 26.92±4.7 (range 18-48 yrs) for IDA and 28 ±4.7 (range 18-46 yrs) in non-BTT cases. There was statistically significant difference between the mean ages of IDA, BTT, and the non-BTT groups (p =0.012). Maximum number of cases was between age group 25-30 (in years) for both IDA and BTT (Table-1).

The mean and standard deviation were computed in all groups for hemoglobin, RBC, MCV, MCH, MCHC, Ferrtin and HbA2 levels (Table-1). The analysis of variance test showed significant difference in Hb, MCV, MCH, MCHC, Ferrtin and HbA2 levels (p =0.001).

The mean Hb level of the total subject was 9.37±1.52 (range 4-15 gm/dl). In IDA, the mean Hb level was 8.90±1.26 (range 4-11 gm/dl) and in BTT group was 9.8±1.59 (range 6 - 13 gm/dl) while there was a significant difference between Hb levels among BTT, IDA and non-BTT groups (p =0.001) Table-1. The mean RBC count of the all cases was 4.20±1.89 (range 2 - 38). Mean RBC count among BTT group was 4.71 ± .97 (range 3 - 7) while in IDA positive women, the mean RBC count was 4.20± 2.6 (range 3 - 43). There was a no significant difference between RBC count among BTT, IDA and non-BTT groups (p =0.587) Table-1.

The mean MCV of the all groups was 76.38±9.80 (range 30-111). In IDA the mean MCV level was 74±8.5 (range 30-97) while among the BTT group MCV was 70.46±10.47 (range 60 - 92). There was a significant difference between MCV among IDA, BTT and non-BTT groups (p = 0.001) Table-1.

Table 1: Comparison of age and hematological indices in IDA, BTT & normal cases.

Parameter	*BTT (n=18)*	*IDA (n=237)*	*Normal (n=104)*	*p-value*
Age	30±7.4 (23-50)	26.92±4.7 (18-48)	28±4.7 (18-46)	0.012
Hemoglobin (g/L)	9.8±1.59 (6-13)	8.90±1.26 (4-11)	10.37±1.55 (4-15)	0.001
RBC count	4.71±0.97 (3-7)	4.20±2.6 (3-43)	4.47±3.39 (2-38)	0.587
MCV	70.46±10.47 (60-92)	74±8.5 (30-97)	81.84±10.17 (34-111)	0.001
MCH	21.69±4.8 (17-31)	22.6±6 (13-92)	26.46±7.51 (15-92)	0.001
MCHC	29.51±3.05 (20-33)	29.74±2.1 (23-36)	31.23±1.69 (25-34)	0.001
Ferrtin	41.8±63.03 (4-218)	12.9±59 (1-908)	39.33±47.81 (6-371)	0.001
HbA2	4.81±1.295 (4-8)	2.37±0.618 (1-4)	2.44±0.7 (1-5)	0.001

In IDA, the mean MCH level was 22.6±6 (range 13-92). The mean MCH of the women's was 23.68±6.5 (range 13-92). Mean MCH among the BTT group was 21.69±4.8 (range 17-31) while there was a significant difference between MCH among IDA, BTT, and non-BTT groups (p =0.001) Table-1. The mean MCHC of the all cases was 30.16±2.17 (range 20-36). In IDA, the mean MCHC level was 29.74±2.1 (range 23 - 36), while the mean MCHC among the BTT group was 29.51±3.05 (range 20-33). There was a significant difference between MCHC level among BTT, IDA and non-BTT groups (p =0.001) Table-1.

The mean ferritin level for all subjects was 22.07±57 (range 1 - 908). In IDA, the mean ferritin level was 12.9±59 (range 1 - 908). Mean ferritin among the BTT group was 41.8±63.03 (range 4 - 218). There was a significant difference between ferritin level among IDA, BTT, and non-BTT groups (p =0.001) Table-1. Among all groups, the mean HbA2 level was 2.51±0.867 (range 1 - 18). In IDA, the mean HbA2 level was 2.37±0.618 (range 1-4) while among the BTT group mean HbA2 was 4.8±1.29 (range 4 - 8) while there was a significant difference between HbA2 levels among IDA, BTT, and non-BTT groups (p =0.001) (Table-1). As depicted in (Table-2), F1, F2, and F3 formulas, MCV, and MCH showed good specificity for MCH in IDA group.

Table 2: Distribution of true-positive among the BTT, IDA cases and false-negative cases in the normal groups.

Parameter & Formulas (Cutoffs)	*BTT (n=18)*	*IDA (n=237)*	*Normal (n=104)*
RBC count (>5×10$^{/L}$)	9 (50)	231(97.5)	95(91.3)
MCV (<76.5fL)	13(72.2)	141(59.5)	25(24)
MCH (27 pg)	14(77.8)	212(89.5)	56(53.8)
F1 (<1,530)	13(72.2)	164(69.2)	30(6.7)
F2 (<13.0)	9(50)	12(5.1)	7(6.7)
F3 (3.8)	18(100)	236(99.6)	102(98.1)
F4 (<0)	1(5.6)	41(17.3)	3(2.9)
F5 (<72)	18(100)	237(100)	103(99)

Discussion

Anaemia is major public health problem specially among poorer segment of population in developing countries like India, Pakistan and Bangladesh. The effects of anaemia on pregnancy outcome in Pakistan have not been evaluated systematically in randomized, prospective intervention trails that include a sufficient number of iron deficient women, while controlling for possible confounding factors.[1] Iron Deficiency Anemia in pregnancy is risk factor for preterm delivery and subsequent low birth weight and inferior neonatal health.[16] Maternal anemia measured as low haemoglobin in the blood during pregnancy remains a serious global health problem and WHO recommends the prevention efforts on treating iron deficiency with universal iron supplementation during pregnancy.[17]

Anaemia is one of the major nutritional deficiency health disorders particularly in developing countries.[2]

This study focused on 359 pregnant females visiting for antenatal checkup at MCH centre diagnosed with anemia. 63.5% of pregnant ladies were confirmed as Iron Deficiency Anaemia. The mean age was 27.29 years.

Mild or moderately sever hypochromic anemia may be more difficult to diagnose accurately. Both IDA and BTT have common causes and the hematological features. Previously it was recommended to do bone marrow staining for hemosiderin (stored iron) deposits to confirm or negate the presence of iron depletion as would be the case in IDA. However, today red cell indices (MCV, MCH) and red cell count are used for screening / differentiating IDA from BTT. Predictive values of discriminating factors are used to differentiate between IDA and BTT. MCV/RBCs count ratio was used to discriminate between IDA and beta thalassaemia trait.[13]

These discrimination factors are a mathematical manipulation of the red cell indices and generate a number which can be used to help differentiate between iron deficiency anemia and beta thalassaemia trait.[14]

Recently developed index, MCV-(10x RBC) for discrimination between beta thalassaemia trait and iron deficiency anemia. Sensitivity, specificity and Youden's index were compared between the proposed index and four other indices, namely England-Fraser, Mentzer, Srivastava and RBCs count.[18]

During pregnancy, approximately 75% of all anemia diagnosed are due to iron deficiency.[19]

In Pakistan, like other developing countries, we are facing major problems of high population growth. Resources are limited which badly effect socio economic development as a whole. Limited healthy care, poor hygiene, sanitation and low literacy rate are the main problems leading to various nutritional deficiencies including IDA, which is major health and serious hematological problems in pregnancy.[14] The prevalence of iron deficiency anemia to be estimated between 35% to 75 % (Average 56%) in developing countries.[20]

A study demonstrated 90% prevalence of anaemia in pregnancy in women attending antenatal clinics at a tertiary care hospitals of Pakistan ruling

out the efficient role of antenatal checkups and indicating week rule of Gynecologist to control anemia, however we believe that gynecologist can play very important role during antenatal period, when there is usually more opportunity to provide, encourage and monitor the use of supplement and proper food.[10] Iron deficiency anemia is common among pregnant women and its frequency varies in pregnant women of Karachi (64%), Lahore (73%) and Multan (76%).[21]

The ante-natal screening service may guide anaemic pregnant women regarding improvement of their nutritional status and propose supplements to improve their serum iron levels for a healthy pregnancy and also during the postpartum and nursing periods. Obstetricians have an important role to play by making women aware of the iron contepnt in a balanced diet and motivation for iron supplements especially during their reproductive age. Maternal mortality continues to be a major health problem in the developing world nearly 600,000 women die each year as a result of complications of pregnancy and child birth. A key component of safe motherhood is the eradication of anemia during pregnancy.[22]

Anemia is a neglected problem and needs to be dealt with on priority basis. Routine iron supplementation should be given to women of child bearing age, during pregnancy and post partum to cover the loss during delivery and lactation. Obstetricians have an important role to play by making women aware of the iron content in a balanced diet and motivation for iron supplements especially during their reproductive age.

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