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Red Blood Cell Indices Along With Hemoglobin and Serum Ferritin Estimation At Internal Correlation In Pregnant Females

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Abstract

Introduction: Anaemias occurring during pregnancy are known to increase maternal and perinatal morbidity and mortality, therefore it would be therapeutically important to be capable of selecting women who are in iron deficient prior to their developing a frank iron deficiency anemia. Red blood cell indices along with serum iron, serum ferritin, serum TIBC and serum transferrin parameters completely reflect the iron stores in pregnant females.

Aim and Objectives: To study red blood cell indices in context and correlation to serum ferritin levels. To measure the red blood cell indices in pregnant females expecting the women prior to expected date of delivery.

Materials and Method: The study was cross sectional type and carried out for two years in 100 consecutive pregnant women reporting to the antenatal OPD. Institutional ethical clearance was be obtained. The EDTA anticoagulated sample was used for estimation of Hb and the red cell indices on a Horiba Coulter Act 7part automated Haematology cell counter. The red cell indices were assayed.

Result: Analysis of the difference of means of various indices showed Hb, MCV, MCH, MCHC and total RBC to be significantly lower (p ¼ 0.000, 0.000, 0.000, 0.000 and 0.012, respectively) and RDW-CV% to be significantly higher (p ¼ 0.010) in the IDA cases. **Conclusion:** In view of this, 58% of non-anaemic pregnant women had iron deficiency, we recommend that all pregnant women in India should get iron supplements unlike what is recommended in the developed countries where iron supplementation is based on serum ferritin levels.

Keywords: Anaemia, iron deficiency, TIBC, transferrin, EDTA.

Introduction

Background: Most pregnancy associated anaemias are due to iron deficiency, which is explained by the greatly increased demands on iron. Anaemias occurring during pregnancy are known to increase maternal and perinatal morbidity and mortality and, therefore, it would be therapeutically important to be capable of selecting women who are iron deficient prior to their developing a frank iron deficiency anaemia. However, diagnosis of iron deficiency is difficult, even in non-pregnant women. A large overlap exists in the distribution of haemoglobin concentrations between normal individuals and those who are iron deficient .(1)

Anaemia in pregnancy has been defined by criteria from the Centres for Disease Control and Prevention (CDC) as a haemoglobin level of less than 11 g per dL during the first and third trimesters and less than 10.5 g per dL during the second trimester.(2) WHO defined anemia in pregnant females as haemoglobin levels of 11g/dl or less.Iron-deficiency anemia (IDA) is a public health problem in the developing and even industrialized countries. Pregnant women and children under 5 years of age are among the high-risk population.(3)

In children, the serum ferritin level was relatively constant from 3 years of age until adolescence, where the prevalence of exhausted iron stores was 13% in boys and 18% in girls. In post adolescent men, there was a gradual increase in serum ferritin levels until 30 years of age. Subsequently, serum ferritin remained relatively constant until old age. Among 30- to 70-year-old men, 9.4% had ample iron stores. The prevalence of depleted iron stores was 1.4%, and of iron deficiency anaemia 0.24%. In women, serum ferritin levels remained low from adolescence until the menopause. Among 30- to 50-year-old premenopausal women, the prevalence of ample iron stores was 0.49%, whereas 18% had exhausted iron reserves and 2.6% had iron deficiency anaemia. After menopause, serum ferritin gradually rose and approached male levels. Among 60- to 70-year-old post-menopausal women, 3.0% had ample iron stores, 2.3% had depleted stores and none had iron deficiency anaemia. In fertile women, the choice of contraception had a significant influence on the iron loss at menstruation. Hormonal contraception reduced iron loss, whereas the use of intrauterine devices increased iron loss. These effects were reflected in the serum ferritin levels of menstruating women.(4)

During pregnancy, diagnostic problems are even more complicated. The rate of iron metabolism increases in many ways during pregnancy. Enhanced absorption, increased mobilization of storage iron and elevated serum transferrin concentration accelerate iron turnover. Red cell mass is considerably elevated but because of a greater rise in plasma volume, a certain degree of haemodilution always occurs. This results in a fall of haemoglobin concentration and haematocrit values as well as in the red cell count, even though red cell mass actually increases, invalidating the diagnostic value of these conventional laboratory measurements. Knowledge about the amount of storage iron is therefore crucial for detecting iron deficiency during pregnancy. (1)

Ferritin water-soluble protein, which is a core of ferrihydrite crystal, within an apoferritin shell. Ferritin is multimeric protein, which concentrates and stores the excessive systolic iron and subsequently, donates the stored iron for cellular needs. (Herbert et al, 1997) Human erythroblasts contain much more ferritin than the cells of other haematopoietic lineage and mature erythrocytes. (Vaisman et al, 2000) In normal subjects, the majority of storage iron is present as ferritin, and haemosiderin occurs predominantly in macrophages of the reticulum-endothelial system rather than hepatocytes. (Hoffbrand et al, 2001)(5)

Serum ferritin has been shown to reflect the status of body iron stores although the mechanism by which serum ferritin is related to iron stores is somewhat obscure owing to the limited knowledge about the origin of circulating ferritin. However, its concentration is proportional to the amount of iron stored as ferritin or hemosiderin in the reticuloendothelial tissues such as bone marrow. We have shown that serum ferritin concentration reflects changes of body iron stores during normal pregnancy. (1)

Reduced amounts of Hb accompany an overall reduction in body iron in iron deficiency anaemia or acute blood loss. In other anaemias such as the megaloblastic anaemia, iron is redistributed from red cells to macrophage iron stores, with corresponding increase in marrow stainable iron and serum ferritin level. (Hoffbrand et al., 2001)(5)

Hypothesis

Red blood cell indices along with serum iron, serum ferritin, serum TIBC and serum transferrin parameters completely reflect the iron stores in pregnant females.

Alternate Hypothesis

Red blood cell indices and serum ferritin correlates with the iron stores in pregnant females.

Research Question

Do Red blood cell indices run parallel with changing values of serum ferritin in pregnant females?

Aim

To study red blood cell indices in context and correlation to serum ferritin levels.

Objectives

To measure the red blood cell indices in pregnant females expecting the women prior to expected date of delivery. To determine the frequency of iron deficiency anaemia in pregnancy by measuring Hb level and RBCs indices. To determine iron status of pregnant females by measuring serum ferritin.

Materials and Methods

The study was cross sectional type and carried out for two years January 2017 to January 2019 in 100 consecutive pregnant women reporting to the antenatal OPD of an Archarya Vinoba Bhave Rural Hospital at Sawangi Wardha. Institutional ethical clearance was be obtained.After informed consent, blood samples were collected 2 ml in EDTA and 3 ml in sterile vacutainer. The EDTA anticoagulated sample was used for estimation of Hb and the red cell indices on a sysmex Coulter Act 7part automated Haematology cell counter.

The red cell indices assayed were total RBC count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width coefficient of variation (RDW-CV%) by Horiba Automated analyser. A peripheral smear was seen to subtype the anaemia. The serum was separated from the sample in sterile tube and ferritin levels measured by fully automated bidirectionally interfaced Chemiluminescent Immuno Assay. The data of the red cell indices and ferritin levels were analysed by SPSS 16. Scatter plots were constructed between serum ferritin and RDW-CV%, RBC count, Hb, MCV, MCH and MCHC and between MCV and Hb. Non-parametric test was done wherever required. Receiver operator characteristic (ROC) curves were drawn to look at maximum sensitivity and specificity for Hb, MCV, MCH, MCHC and RDW-CV% to look for statistically significant correlation with serum ferritin and also to see which one gave maximum area under curve.

All the pregnant females with low Hb are included in the study excluding the pregnant females.

Observation and Results

The present study titled “Red blood cell indices along with hemoglobin and serum ferritin estimation at internal correlation in pregnant females” was conducted in Department of Pathology, Jawaharlal Nehru Medical College of Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha (Maharashtra). The study was conducted for a duration of two years i.e. from January 2017 to January 2019. The study was prospective, observational and analytical type.

The total 100 cases were taken for the study. These patients who had a complaint of weakness and fatigue. Samples from venous blood were collected with all aseptic precautions in EDTA contained vials. Hemoglobin as well as red cell indices like mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH), Mean Corpuscular Hemoglobin Volume (MCHC), Hematocrit, Red cell distribution width (RDW) along with serum ferritin was performed in all the pregnant females. Hemoglobin levels 11gm/dl or less is anemia in pregnancy according to WHO. Ferritin levels <12ng/ml is considered as gold standard for diagnosis of Iron deficiency anaemia. All the results of Horiba Seventh part differential coulter machine automated analysers were recorded and interpreted in tabulated form. Statistical analysis was implemented using descriptive statistics. Total 100 women was included in the study. The mean age of women is 22.46 years (SD 2.94). Most of women belonged to the age group of 20-30 years.

Table 1. Distribution of women according to age.

Age distribution	**Number of Patients**
21-30	64
31-40	36

Table 2. Distribution of women according to type of anemia.

Distrubution of women according to type of anemia	**Number of women**
Iron deficiency anemia(Hb≤11gm/dl, Ferritin <12ng/ml)	40
Anemia due to the other cause	18
Non-Anemic (Hb ≥11gm/dl) with normal ferritin >12ng/ml	20
Non-Anemic with Iron deficiency	22
Total	100

Table 3. Table showing Red cell indices and Serum ferritin levels in women.

Parameters	Mean ± Standard deviation
Hemoglobin (g/dl)	10.58 ± 1.62
MCV (fl)	78.82 ± 7.84
MCH (Pg)	26.31±2.91
MCHC (g/dl)	33.34±2.31
HCT (%)	31.43±3.50
RDW (%)	14.11±2.56
Serum Ferritin (ng/ml)	17.86±16.4

Analysis of the difference of means of various indices showed Hb, MCV, MCH, MCHC and total RBC to be significantly lower (p ¼ 0.000, 0.000, 0.000, 0.000 and 0.012, respectively) and RDW-CV% to be significantly higher (p ¼ 0.010) in the IDA cases. Serum ferritin was significantly lower in the IDA cases as compared to other pregnant women and 58% of non-anaemic had ferritin levels 12 ng/dL. This difference was statistically significant (p ¼ 0.000, Manne Whitney test). Correlation of red cell indices and Hb with serum ferritin was assessed for 40 IDA cases. The Hb, MCV, MCH and RDW-CV% showed significant correlation with serum ferritin levels in IDA cases (p ¼ 0.023, 0.021, 0.035, 0.013, respectively). Though MCHC and RBC count showed some correlation with serum ferritin (r ¼ 0.337 and 0.087, respectively) but it was not statistically significant.

Discussion

Anemia is one of the most complications related to pregnancy. All women during childbearing age are prone to develop ID but pregnant females are especially at risk. Pregnancy is a physiological condition and usually has no effect on general health of a pregnant woman. However, pregnancy results in hormonal, hemodynamic and hematological changes. These physiological changes need to be viewed as normal adaptations determined by nature. Increased total blood volume and hemostatic changes help to combat the hazards of hemorrhage at delivery. The increase is less in iron deficient women than in those with iron reserves. In some iron deficient women this inability to expand plasma volume may mask a decrease in hemoglobin concentration (6,7). Increased iron requirements during pregnancy are due to fetal growth and expansion of red cells mass(8).

In the present study there is a severe progressive decline in HbL, PCV, MCV, MCH and MCHC P-IDA compared with p-controls which confirm the values reported by some investigators [9,10]. As pregnancy proceeds, most women show hematologic changes suggesting iron deficiency. It is believed that the iron deficiency of the mother can not only influence fetal growth but also affect maternal well- being. Most iron transfer to the fetus occurs after 30 weeks of gestation which correspond to the time of peak efficiency of maternal iron absorption [11,12].

Maternal blood volume increases markedly during pregnancy with an increase in plasma and red cell volumes. A decline in the maternal HbL was once termed physiologic anemia of pregnancy. However, in many cases it is due to iron deficiency. During normal pregnancy, approximately 1000 mg of iron are required to meet metabolic demands. In the second half of pregnancy the daily iron requirement of the mother is 3 to 7 mg. Although in pregnant women the iron absorption rate is accelerated, only 2 to 3 mg can be absorbed daily from the average diet, which usually contains about 10 mg of iron. Therefore, even in women with sufficient iron reserves at the beginning of pregnancy, some degree of iron deficiency might be expected to develop (13). A wide variation of PCV throughout the pregnancy limits its usefulness as a parameter to assess the iron status (14). This disagrees with other studies (15,16). Furthermore, a key physiological change during pregnancy, which modifies the chemical constitution of blood, amplifies transfer of some haemopoietic micronutrients, and increases the utilization of some of these micronutrients as defense mechanisms against pregnancy induced oxidative stress may lead to maternal depletion and low hematological values(17). Also the superimposition of anemia on the adaptive hematological changes results in a limitation of red cell mass expansion and a more profound diminution of all hematological parameters when ID appears, so the effect of hemodilution becomes more sever if the pregnant woman has low iron stores(18). This is in agreement with other researchers' study (Babay*et al*) (19).

In the present study red blood cell distribution width is significantly higher in P-IDA compared to p-control as which agrees with the other studies. In this work a significant negative correlation is found RDW and MCV and between RDW and MCH correlation is found in P-IDA. RDW can give the idea of early ID before other tests. It gives the idea of red cell size variation which is the earliest morphologic changes in IDA. RDW helps in early detection of the ID and can detect even very small change in the size of the RBC prior than noted on MCV findings. A high RDW value is more significant in diagnosis of microcytic nature of the RBC. The rise in the RDW in the last trimester and near delivery is more significant than changes in MCV for diagnosis of IDA in pregnancy [45]. As anisocytosis is less prominent in pregnancy and also in early iron deficiency anemia, RDW appears to be a reliable and useful parameter for detection of ID during pregnancy [46]. Red blood cell distribution width is a numerical measure of anisocytosis. It may be useful in distinguishing certain causes of anemia, in particular, in distinguishing Iron deficiency, RDW raised from other disorder. Usually red blood cells are a standard size. Certain disorders, however, cause a significant variation in cell size. Higher RDW values indicate greater variation in size. If anemia is observed, RDW test results are often used together with MCV results to figure out what the cause of the anemia might be. It is mainly used to differentiate between IDA, in which RDW is elevated, and other microcytic anemias.

Conclusion

Several conclusions can be drawn from this study: The inclusion of the RDW in the complete blood count has made diagnosing certain anemia easier, especially those that are microcytic and the categorization of anemias based on the MCV and RDW. Serum ferritin level has not significantly changed and correlated with women with any biochemical in patients with iron deficiency anemia. In general, the results of this study revealed that RDW might provide additional and useful laboratory tests for the assessment of anemia caused by IDA.

In view of this, 58% of non-anaemic pregnant women had iron deficiency, we recommend that all pregnant women in India should get iron supplements unlike what is recommended in the developed countries where iron supplementation is based on serum ferritin levels.

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