EFFECT OF IRON REPLACEMENT THERAPY IN PREGNANT BETA THALASSEMIA CARRIERS WITH COEXISTING IRON DEFICIENCY ANEMIA

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Abstract

Background and Objective: Iron deficiency anemia (IDA) and β -Thalassemia trait are two prevalent etiologies of microcytic hypochromic anemia. Pregnant women with IDA face significant risk of short-term and long-term complications for mothers and newborns. The incidence of concurrent thalassemia trait and iron deficiency was reported to be quite high but despite the high prevalence of these two conditions, the diagnosis is often underestimated and not properly managed. The present study was conducted to determine effect of iron therapy in pregnant beta thalassemia carriers with iron deficiency anemia.

Methods: Study Group constitutes 60 beta thalassemia trait pregnant women with iron deficiency anemia (IDA) with Hb less than 11g/dl, HbA2 levels >3.5% on HPLC and low serum ferritin (<30 ng/mL). After the initial investigations, participants received iron supplementation as 60 mg elemental iron three times daily for duration of 8 weeks. After completing therapy, complete blood count and serum ferritin were performed.

Results: Iron replacement therapy results in effective increment in hemoglobin, red cell indices and Serum ferritin.

Conclusion: Pregnant women with beta-thalassemia minor combined with IDA can receive Iron replacement therapy for improvement in Hemoglobin effectively.

Keywords: β –Thalassemia Trait, Iron deficiency anemia, Haemoglobinopathies, HPLC.

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Anemia in pregnancy is a significant global health concern with varying incidences across different areas of world from 19% in developed countries to as high as 35-75% in developing countries. The World health organization WHO defines anemia in pregnancy as having hemoglobin below 11gm/dl in any trimester.[1,2] UK antenatal guidelines have defined slightly different cut offs for hemoglobin level in each trimester. The iron deficiency is most common cause of anemia in pregnancy worldwide. In Pakistan, different studies have shown anemia affecting 41.7% to 77.0% of women of reproductive age.[3,4] High prevalence of about 42% has been reported for Anemia in pregnancy in Pakistan. Anemia is particularly more common in peripheral areas of Pakistan and is associated with adverse outcomes such as preterm birth, low birth weight and postpartum haemorrhages.[5] This anemia is primarily attributed to Iron deficiency although it may also result from underlying hemoglobinopathies, predominantly beta thalassemia trait (β TT). Iron plays a pivotal role as essential element for pregnant mothers and in the growth and development of the fetus.[6]

In Pakistan both iron deficiency anemia (IDA) and β -Thalassemia trait are the two most prevalent etiologies of microcytic hypochromic anemia.[7] Iron mainly functions in transporting oxygen by red cells but its role in the immune and neuronal system is also well established. During pregnancy, iron demand increases due to multiple factors including the increase of blood volume, red blood cells, hematopoietic activity

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and growth of developing fetus. During early phase after birth, iron stores mainly fulfil newborn iron demands as breast milk is low in iron content.[8] Iron is an essential element for physiological processes in mothers and normal growth of the fetus, successful pregnancy outcomes and prevents iron deficiency anemia in both mothers and newborns.[9] Consequently, universal strategy to recommend iron supplementation during pregnancy for the prevention and rectification of maternal anemia and adverse fetal effects is being applied.[10]

IDA in Pregnancy can results in serious complications for mothers, fetuses, and newborns' wellbeing. According to International Federation of Gynecology and Obstetrics (FIGO), minimum prophylactic iron supplementation daily dose of 30 mg in pregnancy should be recommended in areas of high prevalence of anemia. Mothers with established iron deficiency anemia require daily doses of 100-200mg as therapeutic treatment.[11]

B-thalassemia syndrome is an autosomal recessive inherited disorder caused by a quantitative deficiency of functional β-globin chains.[12] Worldwide population carrier rate for β-thalassemia gene is approximately reported as 1.5%[13]. β-thalassemia is a heterogeneous disorder in genotype and phenotype. Homozygous and compound heterozygous cases result in transfusion dependent anemia. Heterozygous state are symptoms free but hematological parameters are often useful to provide evidence for further testing.[14]

In Pakistan reported carrier frequency of Beta thalassemia is around 5-7% with roughly 9.8 million people are estimated as carriers.[15] The diagnosis of BTT relies on levels of hemoglobin A2, which is increased in usual beta thalassemia trait more than 3.5% and remains typically low in individuals without beta-thalassemia gene. During pregnancy, Beta-thalassemia carrier patients face challenge as increasing iron requirement results in iron deficiency and progression of hypochromic microcytic anemia.[16] This study was designed to determine effect of iron supplementation in pregnant beta thalassemia minor patients with iron deficiency anemia.

METHODS

This study was conducted between March 2022-February 2023 at Pathology department, Post Graduate Medical Institute. All the reporting beta thalassemia carrier pregnant females during whole year were included in this study. Study Group constitutes 60 beta thalassemia trait pregnant women with iron deficiency anemia (IDA) with Hb less than 11g/dl, HbA2 levels >3.5% on HPLC and low serum ferritin (<30 ng/mL). Blood samples were collected in EDTA vials. Complete blood count of all the participants performed on Sysmex XN 1000 hematology analyzer. Chemiluminescence immunoassay was used for serum ferritin and thalassemia screening on HPLC were done before start of treatment. After the initial investigations, participants received iron supplementation for 8 weeks at dose of 180 mg elemental iron in three divided doses in a day. After completing for 8 weeks, complete blood count and serum ferritin were repeated. Statistical software package SPSS version 20.0 was used for data analysis. Mean and standard deviation were calculated for numerical values. A P value below 0.05 was regarded indicative of statistical significance. Paired t test was applied to determine mean difference before and after therapy.

RESULTS

Pregnant women mean age was 28.6 ± 3.3 ranging from 19 to 37 years. 11 (18.3%) women were primigravids. Mean Hemoglobin was 6.4± 1.02 (range 5.5 to 8 g/dl). Among 60 women 2 (3.3%) had mild anemia (Hb10–11 g/dl), 37 (61.6%) with moderate anemia (Hb7–10g/dl) and 21 (35%) presented with severe anemia (Hb <7g/dl) as shown in Fig 1.

Table I shows CBC parameter in pregnant females with iron deficiency before and after iron therapy. Mean Hemoglobin was 7.5±0.5 g/dl (range 5 - 10.2 g/dl) after replacement therapy. Mean serum ferritin values increased from mean 6.75 to 32.3 ng/ml.

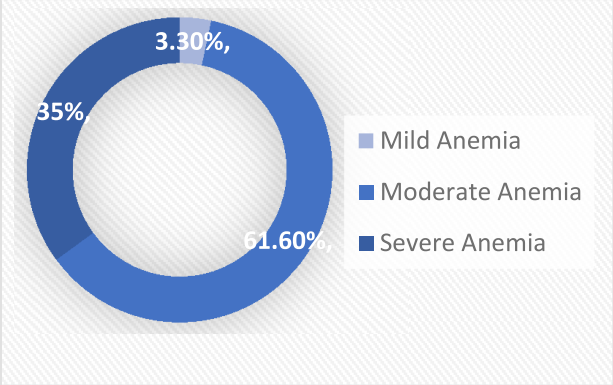

Fig 1; *Distribution of Degree of Anemia*

Table 1: *Thalassemia Trait Pregnant Women with Iron Deficiency Anemia*

Parameter	Pre iron therapy	Post iron therapy	P value
Hb (g/dl)	6.4± 1.02	8.5± 1.11	0.033
RBC (million/mm^3)	4.5±0.65	5.2±0.74	0.051
MCV (fl)	60.3±2.44	68.2±5.34	0.028
MCH (pg)	19±2.31	21±3.0	0.031
MCHC (g/dl)	30±2.03	31±3.1	0.047

DISCUSSION

Beta Thalassemia is among the commonest single gene disorders in world particularly in regions where gene mutations are more prevalent. Severity of disease can vary widely depending upon specific genetic mutations and involvement of one or both beta globin genes. Both β-Thalassemia trait and iron deficiency anemia (IDA) result in microcytic hypochromic anemia with high prevalence reported in our country. Pregnancy with IDA is at increased risk of complications for mothers, fetuses, and newborns due to increased demand. Short time complications include fatigue, infections, preterm birth and post-partum anemia for mothers. Fetuses may experience low birth weight, premature birth and neurodevelopmental delays and anemia. The incidence of concurrent thalassemia trait and iron deficiency was reported to be quite high but despite the high prevalence of these two conditions, the diagnosis is often underestimated and not properly managed due to lack of awareness for thalassemia by health care providers. We have conducted this study to determine effect of iron replacement in pregnant beta thalassemia minor patients with iron deficiency anemia and results showed improvement in Haemoglobin and serum ferritin level similar to previous studies. An Indian study included a total of 150 people to determine the prevalence of iron deficiency in β thalassemia minor. Both male and female participated with increased frequency of iron deficiency 29.67% in females as compared to lower prevalence in males 3.38% making beta thalassemia carrier females more susceptible to severe anemia in case of increased demand.[17]

Similarly Yousafzai et al reported decreased serum ferritin level in 18.8% thalassemia trait.[18]

In Verma et al study increment in mean hemoglobin level, serum iron levels and other parameters similar to other studies. HbF levels were also analyzed and reported no signifant change after iron therapy but HbA2 values showed significant rise after therapy as reported in literature.[19]

An Irani comparative study of 2020 showed analysis of pregnant women with iron deficiency anemia. β-thalassemia minor with coexisting IDA were also included in one of three group, comparison between all groups before and after receiving iron supplements did not find any significant difference between improved mean values of ferritin with conclusion of effective Iron replacement in therapeutic doses resulting in increased hemoglobin, and MCV among pregnant women in all three groups. It was emphasized by authors to check serum ferritin level in Beta thalassemia pregnant females to timely consider iron deficiency as a contributor of exacerbation of anemia with adequate replacement.[20]

Chen et al conducted a study in 2022 highlighting importance of iron replacement therapy in pregnant beta thalassemia carrier females in increasing haemoglobin, red cell parameters and serum ferritin. They also mentioned similar iron hemostastatic role of Hepcidin in iron deficiency anemia individuals without beta thalassemia genetic defect.[21]

Decreased intake of iron, especially haem iron found mainly in meat can result in iron deficiency anemia in pregnancy. It can be one of major contributory factor in developing iron deficiency in underdeveloped

countries like Pakistan. Beta thalassemia carrier pregnant females with decreased iron intake results in more significant anemia. Iron deficiency anemia can results in adverse effects for pregnant females and newborns. Our study highlights to consider iron deficiency as a cause of anemia in thalassemia carrier pregnant females. In case of finding of Hemoglobin less than expected for carrier state antenatal screening should include serum ferritin. Iron therapy at treatment dose should be started with follow up monitoring by serial CBC and serum ferritin at regular intervals to avoid worsening of anemia as well as improved maternal and neonatal outcome.[22]

CONCLUSION

This study provides evidence that pregnant women with beta-thalassemia minor combined with IDA can receive Iron replacement therapy for improvement in Hemoglobin effectively. Therefore, pregnant beta - thalassemia trait with documented iron deficiency should be given therapeutic iron doses with monitoring.

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