Frequency of Beta Thalassemia Trait in Pregnant Females Presenting With Microcytic Hypochromic Anemia in First Trimester

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***Abstract*- Background:** Anemia of pregnancy primarily affects women of low socioeconomic status. Globally, by WHO (World Health Organization) criteria, 52% of pregnant women from undeveloped or developing countries are anemic compared with 20% from industrialized nations. Heterozygous β-thalassemia (β-thalassemia trait; β-TT), caused by the inheritance of a single β-thalassemia allele, either β^0 or β^+, is an important cause of anemia. More importantly, however, its diagnosis is important for the prevention of beta thalassemia major.

Objective: To determine the frequency of beta thalassemia trait in pregnant females presenting with microcytic hypochromic anemia in first trimester.

Method and Material: This is a cross sectional survey and was conducted in Pathology department, King Edward Medical University, Lahore and all cases were selected from Lady Atchison Hospital and Lady Willingdon Hospital (affiliated with Mayo Hospital, Lahore, Pakistan). After telling the patients about pros and cons of the procedure and taking informed consent and ensuring their confidentiality.

The following investigations were carried out from Pathology department, King Edward Medical University, Lahore:

Complete blood count: Blood samples were collected in K_3EDTA vials and analyzed within 1-3 hours of collection by using a haematology analyzer Sysmex KX-21for Hb, total red cell count, MCV and MCH.

Peripheral blood smear: Blood films were made from each sample stained by Giemsa and examined for red cell morphology .i.e microcytosis, hypochromia, NRBCs and anisocytosis.

Hemoglobin Electrophoresis: Blood samples in K_3EDTA vials were subjected to cellulose acetate electrophoresis and Hb A_2 estimation done by elution.

Results: A total of 120 patients were included. Majority (39%) were between 26 and 30 years of age with a mean and SD 27.43±3.11 years. Mean ± SD of the quantitative variables of the patients with beta thalassemia trait were as follows; Hemoglobin 10.77±0.97 g/dL, MCV 62.07±4.26 fL , MCH 19.51±2.45 pg, MCHC was 28.08±2.16 g/dL and mean HbA2 was 4.29±0.37 %. Frequency of beta thalassemia trait in pregnant females presenting with microcytic hypochromic anemia in first trimester was 15.33% (n=19).

Conclusion: Beta thalassemia trait is one of the commonest causes of microcytic hypochromic anemia. Pregnant females presenting with microcytic hypochromic anemia should be investigated for beta thalassemia trait along with iron studies. Beta thalassemia trait detection in pregnant females can be an important step for prevention of beta thalassemia major.

***Index Terms*-** Beta thalassemia Trait, Microcytic Hypochromic Anemia, Pregnancy, First trimester.

I. Introduction

Anemia is defined as a reduction in the hemoglobin concentration of the blood according to age and gender, which is less than 13.5g/dL in adult males and less than 11.5g/dL in adult females. Anemia is classified as microcytic, hypochromic; normocytic, normochromic and macrocytic.(1) The causes of microcytic, hypochromic anemia include iron deficiency, anemia of chronic disease (chronic inflammation, malignancy), thalassemia trait and sideroblastic anemia.(2)

There are marked physiological changes in the composition of the blood in healthy pregnancy, mainly to combat the risk of hemorrhage at delivery. Plasma volume and red-cell mass increase by 50% and 18-25% respectively, resulting in delusional decrease in hemoglobin concentration called the physiological anemia of pregnancy, which is maximum at 32 weeks of gestation. WHO has recommended a cut-off value of 11.0 gm. /dl to define anemia at any time during pregnancy (3). Microcytic hypochromic anemia is very common and is found in 11.2% of pregnant females during first trimester, the common causes of which are iron deficiency and thalassemia trait(4). Out of these patients beta thalassemia trait has been found in 8.5% of pregnant females patients. (5) Beta thalassemia trait is one of the causes of microcytic, hypochromic anemia. Although it presents like iron deficiency anemia, it has significant genetic implications (6). Prevalence of beta thalassemia trait in Pakistan is 5% (7). A diligent approach is to rule out iron deficiency anemia first since Iron deficiency anemia can mask beta thalassemia trait in laboratory investigations.(8) Beta thalassemia trait can be diagnosed in laboratory with the help of RBC indices that show low MCV (<75 fL) and MCH (<25 pg.), peripheral

blood picture that shows microcytic hypochromic RBCs, hemoglobin electrophoresis for HbA_2 estimation (>3.5%) and confirmation can be done by PCR for the mutational analysis (9). Mild to moderate degree of microcytic hypochromic anemia is encountered in the carriers of beta thalassemia trait. In the absence of definitive diagnosis, many of these patients receive oral or parenteral iron therapy. This may go on intermittently or continuously for prolonged periods of time because the anemia persists. This sort of iron therapy is not only unnecessary but may be harmful because of iron overload. Beta thalassemia trait can be easily diagnosed and with the help of this study patients of microcytic hypochromic anemia will be assessed for the cause of this anemia thus categorizing them as iron deficiency anemia or beta thalassaemia trait. The current study will help in early identification of beta thalassemia trait patients and then subsequent referral to the antenatal units to confirm presence or absence of thalassaemia major fetus. This study will help the obstetricians and physicians to properly identify the cause of microcytic hypochromic anemia and thus ensuring proper management and strengthening the importance of antenatal checkup with special emphasis on beta thalassaemia trait. It will also help hematologists and physicians to consider judicious use of iron therapy. We only need to give beta thalassaemia trait a proper place in lists of differential diagnosis of microcytic hypochromic anemia, and thus appropriate management that comes with it. Once diagnosed to have beta thalassaemia trait, they can be referred for proper antenatal checkup and then determination of trait status of spouse becomes mandatory to determine the fetal chances of inheritance of thalassaemia major. If thalassaemia major is diagnosed termination of pregnancy could be offered to them. If thalassaemia major children's birth is not prevented then it will take a toll on country's finances. Conventional therapy of beta thalassaemia major is life-long transfusions and iron chelation or bone marrow transplant, and these treatment regimens do pose a significant load on the health sector blood transfusion services financially and demands a lot of time and resources. Prevention of birth of children with beta thalassaemia major would thus spare a lot of distress, effort and expenses for the families involved and for society. It is important that we diagnose them in first trimester as early termination of pregnancy is better tolerated. Such studies have been conducted in western countries but the exact frequency in pregnant female patients has not been established in our setup. According to a literature published in Maharashtra, India, the frequency of beta thalassaemia trait in pregnant females is 3.1% (10), whereas as previously it was reported to be 8.5%. In order to confirm / refute the discrepancy, this study will be of great help.

II. Results

A total of 120 cases fulfilling the inclusion criteria were enrolled to determine the frequency of beta thalassaemia trait in pregnant females presenting with microcytic hypochromic anemia in first trimester.

Table no 1: Age Distributions of the Patients (n=120)

Age (in years)	No. of patients	%
20-25	35	29.17
26-30	47	39.17
31-35	38	31.66
Total	120	100
Mean and SD	27.43±3.11	

Age distribution of the patients was done, which shows majority of the patients between 26-30 years of age i.e. 39.17 % (n=47) while 29.17 % (n=35) between 20-25 years and 31.66 % (n=38) were between 31-35 years of age, mean and SD was calculated as 27.43±3.11 years. (Table No.1)

Other quantitative variables

Table no.02: Quantitative Variables in Patients having Beta Thalassemia trait. (n=19)

Variables	Range	Mean and SD
Hemoglobin g/dL	11-15 g/dL	10.77±0.97
MCV fL	75-95 fL	62.07±4.26
MCH pg	25-34 pg	19.51±2.45
MCHC g/dL	29-35 g/dL	28.08±2.16
HbA_2	3.5-7%	4.29±0.37

Mean±SD of other quantitative variables of the patients with beta thalassaemia trait were calculated and presented in Table No. 2, where mean Hemoglobin was 10.77±0.97 g/dL, mean MCV was 62.07±4.26 fL, mean MCH was 19.51±2.45 pg, mean MCHC was 28.08±2.16 g/dL and mean HbA_2 was 4.29±0.37 % (Table No. 2).

TABLE No. 3Hemoglobin in Patients Having Beta thalassemia Trait and in Patients Not Having Beta Thalassemia Trait. (n=120)

Beta thalassemia trait	No. Of patients	Hemoglobin g/dL Mean±SD
Yes	19	10.77±0.97
No	101	7.93±1.29

Mean±SD of Hemoglobin of the patients with beta thalassaemia trait was 10.77±0.97g/dLwhileMean±SD of Hemoglobin of the patients not having beta thalassaemia trait was7.93±1.29g/dL (Table No. 3).

Table no. 4: RBC Indices (MCV, MCH and MCHC) In Patients Having Beta Thalassemia Trait and Patients Not Having Beta thalassemia Trait. (n=120)

Beta thalassemia trait	No. Of patients	MCV fL	MCH pg	MCHC g/dL
Yes	19	62.07±4.26	19.51±2.45	28.08±2.16
No	101	70.52±5.94	23.59±4.11	24.02±2.97

Mean±SD of RBC Indices of the patients with beta thalassaemia trait were calculated and presented in Table No. 4, where mean MCV was 62.07±4.26 fL, mean MCH was 19.51±2.45 pg and mean MCHC was 28.08±2.16 g/dL (Table No. 4).

Mean±SD of RBC Indices of the patients not having beta thalassaemia trait were calculated and presented in Table No. 4, where mean MCV was70.52±5.94fL, mean MCH was 23.59±4.11 pg and mean MCHC was 24.02±2.97g/dL (Table No. 4).

Table no. 5: HbA2 status in Patients having Beta Thalassemia Trait and patients not having Beta Thalassemia Trait (n=120)

Beta thalassemia trait	No. Of patients	HbA2 % Mean±SD
Yes	19	4.29±0.37
No	101	1.88±0.67

Mean±SD of HbA2 of the patients with beta thalassaemia trait was 4.29±0.37%whileMean±SD of Hemoglobin of the patients not having beta thalassaemia trait was 1.88±0.67% (Table No. 3).

Table no. 6: Frequency of Beta Thalassemia Trait in Pregnant Females presenting with Microcytic Hypochromic Anemia in First Trimester. (n=120)

Beta-Thalassemia Trait	NO.OF PATIENTS	%
Yes	19	15.83
No	101	84.17
Total	120	100

Frequency of beta thalassemia trait in pregnant females presenting with microcytic hypochromic anemia in first trimester was found to be 15.33 % (n=19) while 84.17 % (n=101) patients had no findings of the morbidity. (Table No. 6)

III. DISCUSSION

Beta thalassemia trait is caused by the inheritance of a single β-thalassemia allele, either β^0 or β^+. It is usually characterized by a mild anemia with hypochromic microcytic red blood cells, elevated levels of hemoglobin A2 (HbA2), variable increases of hemoglobin F (HbF) (up to 2.0%) and polypeptide globin chain biosynthesis showing an approximately twofold chain excess.(11) Carriers of β-TT are usually asymptomatic. However, they are at risk of having children with severe clinical outcomes if their spouses are also carriers of the same type of thalassemia or other haemoglobinopathies. Carriers of β-TT may be at risk of having β-thalassemia major children who have a lifelong dependency on regular blood transfusion for survival, if the partner has β-thalassemia as well.(12)

In our study 120 pregnant females presenting with microcytic hypochromic anemia in first trimester were taken. In Pakistan the frequency of beta thalassemia trait in general population is 8-10 %.(13) A study conducted by Nisa Q showed that the frequency of thalassemia trait in pregnant women was 8.5% (5), while my study showed 15.83% carrier rate. This great variation in result was due to selection of pregnant females with microcytic hypochromic red cells as the study population.

Generally, beta thalassemia trait patients have mild anemia.(14)(15)

In my study the results are coherent with the previous studies i.e. all the women with thalassemia minor are mildly anemic and mean hemoglobin was 10.77±0.97 g/dL.

It has been observed in different studies that the sensitivity and specificity of red cell count and red cell indices is very high for screening of beta thalassemia trait.(14)(16) The MCV & MCH values are reduced in beta thalassemia trait. The MCHC is normal or only slightly reduced (14).My study showed reduced MCV and MCH. And along with them the values of MCHC were also low. This could be because of iron deficiency anemia. Mean MCV was 62.07±4.26 fL (Mean±SD), mean MCH was 19.51±2.45 pg and MCHC was 28.08±2.16gm/dl. A study conducted by Nisa Q showed that the values of MCV, MCH and MCHC are reduced in beta thalassemia trait

The most consistent feature of beta thalassemia trait is an increase in HbA2. Raised level of HbA2 confirms significant number of patients with beta thalassemia trait (14). Mean HbA2 in our study was 4.29±0.38 % (Mean±SD). This increase in HbA2 level is coherent with previous studies (5).

Low mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) with an increased HbA_2 value identify an individual with increased probability of being a β - thalassemia carrier.

IV. CONCLUSION

- Beta thalassemia trait is one of the commonest causes of microcytic hypochromic anemia. Pregnant females presenting with microcytic hypochromic anemia should be investigated for beta thalassemia trait along with iron studies. Beta thalassemia trait detection in pregnant females can be an important step for prevention of beta thalassemia major.

REFERENCES

[1] Hoffbrand A, Moss P, Petit J. Erythropoesis and general aspcts of anaemia. In Essential Haematology. 6th ed. Lundon: Blackwell Publishing; 2011. p. 15-32.

[2] Hoffbrand A, Moss P, Petit J. Hypochromic anamia and iron overload. In Essential Heamatology. 6th ed. Lundon: Blackwll Publishing; 2011. p. 33-49.

[3] Awan M, Akbar M, Khan M. A study of anaemia in pregnant womens of Railway colony Multan Pakistan. Pakistan Journal of Medical and residency. 2004; 43: p. 11-4.

[4] Taseer I, Safdar S, Mirbahar A, Awan z. Anaemia in pregnancy and related risk factors in under developing area. Professional Medical Journal. 2011; 18(1): p. 1-4.

[5] Nisa Q, Habibullah , Rizwan F, Memon F, Memoon A. Frequency of thalassemia trait in pregnant women. Medical channel. 2011; 17(1): p. 56-9.

[6] Thein S, Rees D. Hemoglobin and the inherited disorder of globin synthesis. In Essenital Heamatology. 6th ed. Lundon: Blackwelly; 2011. p. 83-103.

[7] Ahmed S, Hassan K, Ikram N. Thalassemia in Pakistan. Rawalpindi:; 2009.

[8] American College of Obstetricians and Gynecologist ACOG Practice bulletin no 95 Anaemia in pregnancy. In Obstet Gynacol.; 2008. p. 201-7.

[9] Bakhtiyar U, Khan Y, Nasir R. Relation between maternal Hemoglobin and Perinatal outcome. Rawal Medical Journal. 2007; 32: p. 201-7.

[10] Satpute B, Banker M, Momin A, Bhoite G, Yadav R. The incidence of Beta thalassemia trait in pregnant women from south Western Maharashtra. International Journal of Health Sciences and Research. 2012; 2(1): p. 103-7.

[11] Skarmoutsou C, Papassotiriou I, Traeger Sj. Erythroid bone marrow activity and red cell heamoglobinization in sufficient beta Thalassemia hetrozygotes as reflected by soluble transferrin receptor and reticulocyte hemoglobin in content and correlation with genotypes and HbA2 Levels. Hematologica. 2003a; 88: p. 631-6.

[12] Law H, Chee M, Tan G, NG I. The simultaneous presence of Beta Thalassemia alleles: a pitfall Thalassemia screening. In.; 2003. p. 14-21.

[13] Anjum S, Tayyab M, Shah S, Choudry N. Detection of Thalasseima trait:A study of 50 families. Journal of Ayube Medical college Abbotabad. 2001;: p. 13-113.

[14] Zaidi A, Raziq F, Alam N, Haider K. Screening of Thalassemia trait using red cell indices and red cell count. Pakistan Journal of Pathol. 2004; 15(2): p. 54-9.

[15] Lukens J. The Thalassemia and related disorders:Quantitative disorder of Hemoglobin synthesis. In Wintrobe's Clinical Hematology. 9th ed. Philadelphia; 1993. p. 1102-33.

[16] Hussain Z, Malik N, Chugtai A. Diagnostic significance of red cell indices in beta Thalassemia trait. Biomedical Journal. 2005; 2: p. 129-31.

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