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ORIGINAL ARTICLE

Clinical and Hematological Profile of β-Thalassemia Minor

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ABSTRACT

Background: β-thalassemia minor is the most common inherited hemoglobinopathy worldwide. The defect lies in the beta globin chain synthesis as a result of mutations in beta globin chain genes. Clinical presentation is variable, ranging from normal hemoglobin to severe anemia. Haematologically, classically, there is microcytosis, hypochromia, raised red blood cell count, and elevated HbA2 on hemoglobin studies. But these findings considerably overlap with some added factor, such as, isolated or combine nutritional deficiencies.

Aims: To evaluate the clinical and hematological profile of β-thalassemia minor cases, and, to make a protocol to investigate the patients having microcytic hypochromic anemia for carrier state of hemoglobinopathies especially thalassemia.

Study Design: Descriptive study.

Place and duration of study: Hematology OPD, Faisalabad Institute of Cardiology, Faisalabad from 1st January 2018 to 31st December 2020.

Methodology: 3520 patients were referred to our clinic for workup of microcytic hypochromic anemia. CBC and HbA_2 testing was done on all cases. Out of those, 111 fell into our criteria of the diagnosis of β-thalassemia minor.

Results: Ninety one **(**81.9%) of the patients presented with pallor. Tachycardia and shortness of breath was a complaint in 46 (41.4%) and 30 (27%) respectively. The hemoglobin mean of 9.1 (range 2.7-14.5 g/dL). Red cell distribution width RDW-CV of RBCs was ≤18% in 48.6% of the patients. Mean MCV was 73.3fL (range 54-156), mean RBCs count was 4.75 (range 0.8-7.6). Hemoglobin on HPLC of Biorad Variant II Beta Thalassemia Short Program revealed a raised HbA_2 in 100% of the patients of β-thalassemia minor. Iron deficiency was found to be in 35% of the total diagnosed β-thalassemia minor patients with mean concentration of Ferritin 13.3 ng/mL (range 0.8-80).

Conclusions: All patients with microcytic, hypochromic anemia and raised RBC count should be screened on HPLC for demonstration of HbA2 to exclude β-thalassemia minor. Microcytosis (MCV <76fL), Borderline raised RBC count (RBCs >$5x10^{12}$/L), Borderline high or low RDW (<18), and a raised HbA_2 level are highly consistent with the diagnosis of β-thalassemia minor.

Keywords: β-thalassemia minor, Hemoglobin A2 (HbA2), Microcytic hypochromic Anemia, HPLC, Thalassemia minor

INTRODUCTION

Iron deficiency anemia (IDA) and thalassemia are common presentations of microcytic anemia in adults as well as in children [1]. Both type of thalassemia' is not considered in iron deficiency anemia comprising minor and major thalassemia.[2] Conversely present literatures suggest that iron deficiency anemia may occur alongside with β-thalassemia minor (BTM). Initial low level of hemoglobin is observed in patients with both IDA and beta-thalassemia minor patients in contrast to those patients only with β-thalassemia minor.[3] Possible explanation behind this differentiation is the deficiencies of hematopoietic nutrients due to IDA that put major impact on synthesis of globin chain synthesis.[4,5] Other erythrocyte parameters including ferritin, serum iron and total iron binding capacity protein also showed similar changes. Iron replacement therapy demonstrates adequate effect on these alterations. Iron therapy showed improvement in values of HbA2 which is lower in β-thalassemia minor and iron deficiency anemia coexisting patients.[5.6] On the other hand, considerable alteration in HbA2 levels. Concomitant of iron deficiency anemia and β-thalassemia minor mainly leads to misinterpretation or misdiagnosis of the later due to similar biochemical presentation.[5] Another finding also revealed that chances of child with β-thalassemia major escalate many times if both of the parents is β-thalassemia minor patient. Typical representation of β-thalassemia minor is elevated microcytosis, RBC count and normal level of RDW.[7] Clinically, BTM is diagnosed due to increase of hemoglobin A2 level (>3.4%) and RBC count. Hemoglobin A_2 normal chain consist of two alpha and beta chains which is found in low level in adults.[8] Symptoms of BTM includes tachycardia, pallor and difficulty I breathy. Severity of disease depends upon degree of anemia.[9,10]

In this study we evaluated the patients with microcytic hypochromic anemia, suspicion of having β-thalassemia minor, and analyzed their hematological parameters, consistent with the phenotype. The presence of signs and symptoms of anemia were also assessed. We documented iron status with ferritin. The purpose of this study was to evaluate the clinical and hematological profile of microcytic hypochromic anemias, and, to make a protocol to investigate these patients for carrier state of hemoglobinopathies especially thalassemia major.

MATERIALS AND METHODS

It was prospective study with convenient based sampling technique conducted at Hematology OPD, Faisalabad Institute of Cardiology, Faisalabad from from 1st January 2018 to 31st December 2020. The present study enrolled 3520 patients which required a workup for identifying β thalassemia minor in them. Prior research initiation an ethical approval for its conductance was attained from the review department. Written permission for the patients for being a study participant was taken. A 2cc blood for serum collection and 3cc whole blood was withdrawn from each participants for analyses for various tests. CBC was evaluated of each patient. Patients who were having microcytic-hypochromic anemia as suggested by their hbA2 levels (>3.4% but <10%) were included. High performance liquid chromatography was performed for analyzing conA, HbA2 and HbE values. Increased HbA2 plus HbE and high HbA2 plus HbS, in addition to escalated HbA2 plus HbC were excluded from the study. Automated cell-counter was used for analyzing RBC indices. The analyser was provided by company Abacus 5 of Seico diagnostic. The samples showing HbA_2 >3.5% were diagnosed as β-thalassemia minor. Serum Ferritin was determined by enzyme linked immune assay protocol using kits from Biocheck USA. Ferritin reference range was from 12 to 300 ng/mL males while as 12 to 150 ng/mL for females. The data was entered and analyzed through SPSS-22.

RESULTS

One hundred and eleven (3.15%) were diagnosed with β-thalassemia minor. There were almost equal number of males and females suffering from β-thalassemia minor (Table 1). Ninety one (81.9%) patients having β-thalassemia minor were pallor while 46

(41.4%) had tachycardia and 30 (27%) were suffering from shortness of breath (Fig. 1).

A normal RDW and a mean cell volume (MCV) less or equal to 76 fl, raised RBC count, anemia, decreases level of hematocrit in addition to HbA2 greater than 3.5 values proposed a β-thalassemia-minor presence. The mean hemoglobin level was 9.1 ranging between value of 2.7-14.5 g/dL. In addition to this it was also observed that distribution of red cell was ≤ 18% in around 48.6% of the affected patients. Iron deficiency was indicated by serum-ferritin levels and were found to altered showing iron deficiency in 35% of β-thalassemia-minor patients (Table 2)

Table 1: Frequency of enrolled patients (n=3520)

Gender	No.	%
Male	1795	50.99
Female	1725	49.00
β-thalassemia minor (n=111) 3.15%		
Male	56	50.4
Female	55	49.5
Non-effected	3409	96.85

Table-2: Hematological Parameters in β-thalassemia-minor patients (n=111)

Parameter	Range	Mean
Hemoglobin (g/dL)	2.7-14.5	9.1
MCV (fL)	54-156	73.3
RDW-CV (%)	11-43	20.4
Total RBCs $x10^{12}$/L	0.8-7.6	4.75
Hemoglobin A_2 (%)	3.41-6.2	4.7
Ferritin (ng/mL)	0.8-80	13.3

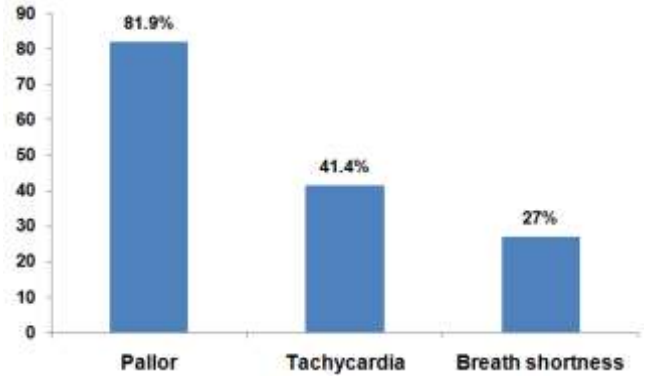

Fig 1: Clinical features of β-thalassemia minor patients

DISCUSSION

Health is one of the major concern of developing nations. β-thalassemia minor is one if the inherited blood disorder which lead to abnormal formation of hemoglobin, resulting into anemia and other medical ailments.[11] Asian countries are already facing major health challenges including iron deficiency anemia and β-thalassemia. In India, its estimated frequency is ranging from 3-8%[12] which give rise to ~40 million carriers in ethnically and culturally diverse nation. Few areas of India reported much higher prevalence upto 17%.[13,14] According to the recent statistics of thalassemia patients, approximately 10,000 β-thalassemia major children are inhabitants of India comprising 10% of the total number.[13-15]

Anemia is one of the daunting public health challenge especially for developing countries where malnutrition, inappropriate health-care system and poverty escalates the chances of this disease many time and also risk of affecting people.[16] Prevalence of different hemoglobinopathies comprising sickle cell anemia, β-thalassemia, HbD and HbE differ from region to region. Studies showed that, β-thalassemia minor is one the commonest hemoglobinopathies in India followed by Cooley's anemia.[17]

Primary diagnosis of β-thalassemia trait is the complete blood count and analysis of abnormal hemoglobins on HPLC. According to Dacie and Lewis, values of MCV and raised RBCs indicates high risk of β-thalassemia trait which would further be screened by HbA_2level.[18] Similar finding is reported by Linin 2011 in Taiwan.[19]

Limitations Of The Study:

1- Patients' relatives could not be screened due to financial issues of the majority of the people. As thalassemia runs in families, there should be awareness of testing all family members for the presence of β-thalassemia minor.

2- The patients with borderline HbA_2 (3.41-3.5%) should have been screened on PCRs for the presence of abnormal beta genes. We did not perform genetic analysis.

CONCLUSION

All patients with microcytic, hypochromic anemia and raised RBC count should be tested on HPLC for demonstration of HbA_2 to document the presence or absence of β-thalassemia minor. Microcytosis, slightly raised RBC count and borderline increased or decreased RDW with raised HbA_2 level are significantly constant with β thalassemia minordiagnosis.

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