ORIGINAL ARTICLE

β-THALASSAEMIA TRAIT: HAEMATOLOGICAL PARAMETERS

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Background: β-Thalassaemia syndromes are a group of hereditary disorders characterised by a genetic deficiency in the synthesis of β-globin chains due to a defect in β-globin genes. The objective of this study was to determine the haematological features of β-thalassaemia trait (BTT), and to determine the sensitivity of Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and Mentzer Index (MI) as a screening tool for β-thalassaemia trait. **Methods:** A descriptive study was conducted in Hayatabad Medical Complex, Peshawar from May 2009 to May 2010 with 203 subjects having BTT. Blood samples were collected in EDTA anti-coagulated tubes. RBC indices were taken as part of complete blood count (CBC) by haematology analyser, and Haemoglobin (Hb) electrophoresis was done to determine the HbA2 percentage. The data was collected and analyzed on statistical software for demographic details, RBC indices and HBA2 levels. **Results:** Out of 203 patients, 92 (45%) were males and 111 (55%) were females. Most patients tested were in the 15–45 year age group. One-hundred-sixty (79%) patients had anaemia. MCV was lower than 76 fl in all the cases. Mean MCV was 59.1 fl. MCH was low, the mean MCH being 19.3 g/dl. MCH <26 gave sensitivity of 99% in detecting BTT. We calculated MI for these cases and found out that it was <12 in 75% of cases and <15 in 197 (97%). **Conclusion:** β-thalassaemia traits present with a microcytic hypochromic blood picture, detected on simple haematology analysers as low MCV and MCH and MI which provide a useful screening tool for β- thalassaemia trait.

Keywords: β-Thalassaemia, Thalassaemia Minor, haemoglobinopathy

INTRODUCTION

β-Thalassaemia syndromes are a group of hereditary disorders characterised by a genetic deficiency in the synthesis of β-globin chains due to a defect in β-globin genes. The gene defect can involve both genes (homozygous) or one gene only (heterozygous).[1,2] Clinically β-thalassaemias are divided into β-thalassaemia major which is the homozygous state, and β- thalassaemia trait or minor, which corresponds to the heterozygous state. Other relatively uncommon forms are also present. In β- thalassaemia major there is severe transfusion dependant anaemia while in β- thalassaemia trait there is mild to moderate microcytic hypochromic anaemia. The diagnostic characteristic of β-thalassaemia trait is an elevated level of HbA2 on Haemoglobin electrophoresis.[3,4] PCR based diagnosis is done in difficult cases.

Thalassaemia poses a major problem in Khyber Pukhtunkhwa (KPK) with a high prevalence.[5] Screening of BTT is an important way of prevention of β-thalassaemia major in the following generations. Automated haematology analysers are in widespread use for the screening of BTT in KPK province of Pakistan. The purpose of this study was to describe the haematological parameters found in cases of BTT and review of literature.

MATERIAL AND METHODS

Children and adults, both males and females attending the Hayatabad Medical Complex Hospital as outpatients between May 2009 and May 2010 were recruited into the present study. Subjects of BTT were included in the study. Exclusion criteria included cases with concomitant other haematological conditions, recently transfused with blood or taking haematinics. β-Thalassaemia trait was defined as an HBA2 percentage of 3.5–6% on Hb Electrophoresis. Blood sample of 2.5 ml was taken in EDTA anticoagulated evacuated tube for CBC and RBC indices and for Hb Electrophoresis for diagnostic test of β-thalassaemia carrier. The laboratory techniques used in the study included: Haemoglobin (Hb), Red cell count (RCC), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Red cell Distribution Width (RDW), and Mentzer Index (MI) calculated by the formula: MCV/RCC.

HbA2 test: Cellulose acetate paper electrophoresis was done and reading for HbA2 percentage taken. Sensitivity of MCV, MCH and MI in predicting β- thalassaemia trait was calculated. Based on previous studies, the present study needed a sample size of at least 203 subjects with a confidence interval of 95%.

Statistical analysis included Categorical data presented as percentage, while numeric data presented as Mean±SD. Sensitivity was calculated with the formula: True positive/true positive + false negative.

RESULTS

During the present study, 204 subjects were enrolled, one was excluded, and the remaining 203 cases were analysed. One-hundred-forty-four subjects were between 15–45 years old (70.9%) with the mean age at diagnosis being 21 years. One-hundred-eleven

(54.7%) were females and the remaining 92 (45.3%) were males (Figure-1).

One-hundred-sixty (78.8%) people were anaemic for their age and gender. Mean Hb Level was 10.7±1.67 g/dl while minimum and maximum were 5.2 and 15.5 g/l respectively (Table-1). Mean MCV was 59.1 fl±4.86, no subject had MCV within normal limits and hence sensitivity of 100% was achieved. Mean MCH was found to be 19.3 g/dl. All but two patients had MCH below the reference range of 26.0 g/dl and hence the sensitivity was more than 99%. Mean RDW (CV) was 15.1%, being higher than reference range in most cases (66.5%) and normal in the rest (33.5%). Mentzer index (MCV/RBC count) was below 13 in 166 (81.8%) cases while it was below 15 in 197 (97%) cases. The mean of MI was 10.8. Mean HbA2 percentage was 4.1% (Table-2).

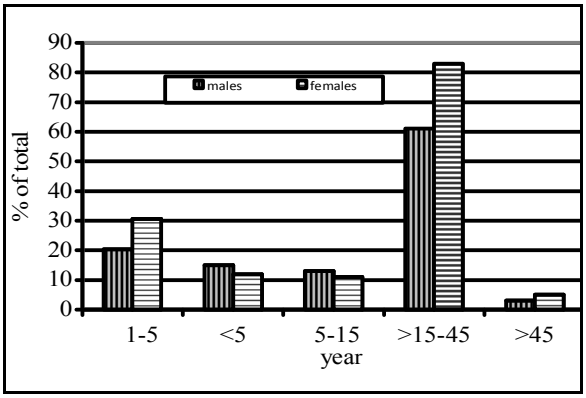

Figure-1: Distribution in age and gender in groups

Table-1: Demographic characteristic

	Mean±SD	Range
Hb (g/dl)	10.73±1.67	5.20–15.50
RBC count (×10^6/µl)	5.56±0.82	2.93–7.28
MCV (fl)	59.12±4.86	44.30–77.80
MCH (g/dl)	19.32±2.04	11.60–29.00
RDW (CV)	15.11±1.61	11.00–22.60
HbA2 (%)	4.13±0.38	3.5–6.0

Table-2: Sensitivity of MCV, MCH and MI

	Cut-off	Sensitivity
MCV	<76 fl	100%
MCH	<26 g/dl	99%
MI	<13	81.4%
MI	<15	97%

DISCUSSION

β-thalassaemia trait has a prevalence of about 7.96% in Pukhtun population.[5] Early screening and counselling is essential for prevention of β-Thalassaemia Major in the society. For an efficient screening program, it was necessary to determine different haematological parameters of β-thalassaemia trait in population of KPK province. Currently the screening tests include naked-eye single tube osmotic fragility test (NESROFT)[6] and RBC indices like MCV and MCH[7]. These methods have shown variable accuracy in different studies. The advantages of osmotic fragility test are ease and simplicity and disadvantages are lack of harmony between different laboratory procedures of NESROFT. RBC indices are machine dependant, and with variable sensitivity and specificity.[8,9] The indices are considered to be quick and easier method of screening in areas where facilities are available. Exclusion criteria in the present study were other haematological disorders or patients on haematinics or recently transfused. This was done to minimize confounding factors that may interfere with the result because these conditions have a direct effect on RBC indices measurement.

Normal range of HbA2 level in the general literature was 4–6%[2], but it can be varied according to laboratories. In our study, we used the reference range of 3.5–6% used in Hayatabad Medical Complex laboratory.

Previous studies have shown there has been significant degree of anaemia in BTT population compared to normal population. This may partially be due to the fact the study was done in hospital[10]. Our study showed anaemia in 160 (78.8%) subjects. The advantage in our hospital based study was that we had stratified different age and gender groups. The degree of anaemia in different ethnic groups has shown variation in previous studies. Red cell count may be normal but sometimes is very high. This is because of the fact that the RBCs produced are small and poorly haemoglobinized. The mean RCC in our study was 5.56±0.82 million/µl. MCV and MCH values are invariably low in BTT when counted with well calibrated haematology analyser. Our study showed a similar result with MCV low in all cases while MCH below the reference range in all but 2 cases. In one study on β-thalassaemia carriers, the MCV was 61±6.8 fl, the MCH was 20.27±2.4 ρg[11] while in our study, these variables were 59.1±4.86 fl and 19.3±2.0 g/dl. This shows that both MCV and MCH are sensitive screening tests for BTT. However, Since Iron deficiency Anaemia is also a common condition in our population with a low MCV and MCH, testing should be done to calculate the false positive rate and hence, the specificity of MCV and MCH in detecting BTT. RDW is said to be typically within a normal range in BTT,[12] and it has been used to discriminate between BTT and IDA.[6] In our study, mean RDW was 15.1±1.6, with 135 (66.5%) cases having RDW higher than normal. This showed a discrepancy from the previous studies. A case control study may be necessary to investigate this finding. MI is one of the common mathematical formulae used to discriminate BTT from IDA.[6] In a study the sensitivity of MI at the cut off of 13 was found to be 92%. This was raised to 96.4% when the cut-off of 15.2 was taken.[6] In our study, the sensitivity was 81.8% for MI

<13 and 97% for MI <15. Mean HbA2 level is generally stated to be between 5.0–5.3%.[11,13] In our study, the mean HbA2 percentage was 4.11±0.44%.

CONCLUSION

β-thalassaemia trait is frequently reported in Hayatabad Medical complex, Peshawar. Automated Haematology analyser proved to be a useful tool in the screening of β-thalassaemia trait. The haematological parameters are characterized by a low MCV and MCH, which were found to be more sensitive screening tool than MI. Most of the BTT patients diagnosed at the hospital were found to be anaemic. A population study needs to be done to further evaluate the status of anaemia in BTT population. Iron studies are also necessary to rule out concomitant iron deficiency as the latter is also a common cause of microcytic anaemia in our population. People with anaemia should be screened for β-thalassaemia trait to prevent thalassaemia major in proceeding generations.

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