ORIGINAL ARTICLE

PATTERN OF THALASSEMIAS AND OTHER HEMOGLOBINOPATHIES: A STUDY IN DISTRICT DERA ISMAIL KHAN, PAKISTAN

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ABSTRACT

Background: Thalassemia is used to describe disorders with a significant decrease in the rate of synthesis of a globin chain. The term hemoglobinopathy is used to indicate those disorders with structurally abnormal hemoglobin. The study was aimed to see the pattern of different hemoglobin disorders in referred cases of district Dera Ismail Khan and adjacent area.

Material & Methods: This study was carried out on 300 patients who were referred for the Hemoglobin electrophoresis from October 2009 to April 2013. Detailed clinical history regarding age, sex, cast, family history, blood transfusion history and physical findings like splenomegaly were noted. All blood samples were analyzed for Hb Electrophoresis in the Department of Pathology, Gomal Medical College Dera Ismail Khan, Pakistan.

Results: Out of total 300 referred cases, 227 (75.6%) were detected to have abnormal hemoglobin. Among hemoglobin disorders the most common disorder was Beta thalassemia major in 87(38.30%) followed by sickle cell disease 73(32.16%) and Beta thalassemia trait 42 (18.5%). Other hemoglobin disorders like Beta thalassemia intermedia, sickle cell trait, sickle cell/beta thalassemia, HbE disorder were collectively detected in 25 (11.0%) cases.

Conclusion: Hemoglobin disorders are still a problem for the different communities of Pakistan. Preventive measures like pre-marriage detection of carrier state must be considered as mandatory step to control the disease.

KEY WORDS: Hemoglobinopathies; Thalassemia; Sickle cell anemia.

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INTRODUCTION

The term hemoglobinopathy is used to indicate only those disorders with structurally abnormal hemoglobin (Hb). So these are qualitative disorders of hemoglobin. The term thalassemias are used to describe disorders with a significant decrease in the rate of synthesis of one or more globin chain; therefore these disorders are also termed as quantitative disorders of hemoglobin.[1]

Hemoglobinopathies are significant causes of morbidity and mortality throughout the world. They are not cured absolutely but can be prevented by genetic counseling and prenatal diagnosis.[2] Hemoglobinopathies are disorders of red blood cells formation that has a widespread prevalence extending from Mediterranean zone, Middle East, Indian subcontinent and parts of south Asia.[3]

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Hereditary disorders of hemoglobin synthesis e.g. thalassemias and hemoglobin structure e.g. HbS, HbC, HbD have a worldwide distribution. Thalassemias are probably present in every racial and ethnic group, whereas structural hemoglobin defects are distributed within certain geographic and racial limitations. Among hemoglobin disorder Beta thalassemia is probably the most common single gene disorder while other hemoglobin disorders like HbD, HbE and HbS alone or in combination also exist in our population.[4,5]

Beta thalassemia is major health problem in Pakistan. It is the most prevalent genetically transmitted disease with a carrier rate of 5 -8 %.[6] Sickle cell disease is the most common of the hereditary blood disorder in malaria endemic areas, affecting millions of persons globally. Sickle cell disorders are seen commonly in Sub-Saharan Africa but also occur in Mediterranean, India and Arabian Pninsula.[7] Alpha Thalassemia is a hemoglobin defect prevalent in

southern China and South East Asia. The diagnosis of alpha thalassemia cannot be made on peripheral blood or cellulose acetate findings.[8]

For the diagnosis of hemoglobin disorders, blood counts, peripheral film examination and red cells indices are the first line investigations. Then on the basis of hemoglobin electrophoresis a definitive diagnosis can be established.[9]

The present study was undertaken to evaluate the spectrum of hemoglobinopathies in population as referred cases to Gomal Medical College, Dera Ismail Khan and adjacent area.

MATERIAL AND METHODS

This was a cross-sectional study was conducted at the Department of Pathology, Gomal Medical College, D.I.Khan, Pakistan from October 2009 to April 2013. A sample of 300 patients was selected by convenience sampling. The study was carried out on the patients who were referred for the Hb electrophoresis. All anemic patients were included. Patients having blood transfusion in the last four weeks were excluded.

Detailed clinical history regarding age, sex, caste, family history, blood transfusion history and physical findings like splenomegaly were noted. Three ml of blood sample was collected in EDTA bottle. Automated Hematology Analyzer (Nihon Kohden, Tokyo) was used to determine peripheral cell count and red blood cell indices (RBC, HB%, HCT, MCV, MCH, and MCHC). Peripheral blood films were examined for red blood cells morphology and any other relevant findings.

Hemolysate was prepared by adding distilled water and carbon tetrachloride to the blood sample. Hb electrophoresis was performed on Wealtech, USA (Fig. 1). Current flow was adjusted according to the instruction manual. Cellulose acetate strip was used for application of hemolysate and different bands of hemoglobin were observed (Fig. 2). The results were reported after comparing the result with the normal control. In all the cases review of clinical notes and peripheral blood findings were kept in mind.

As HbD band appears due to HbD disease as well as sickle cell disease, therefore sickling test was performed to differentiate between these two diseases.

Gender was a demographic while type of hemoglobin disorders was a research variable and were analyzed as frequency (nubmer) and relative frequency (%).

RESULTS

Out of 300 patients, 227 (75.6%) were detected to have abnormal hemoglobin. Out of 227, male patients were 150 (66%) and female were 77 (34%).

Figure 1: Hb Electrophoresis machine with tank containing alkaline buffer.

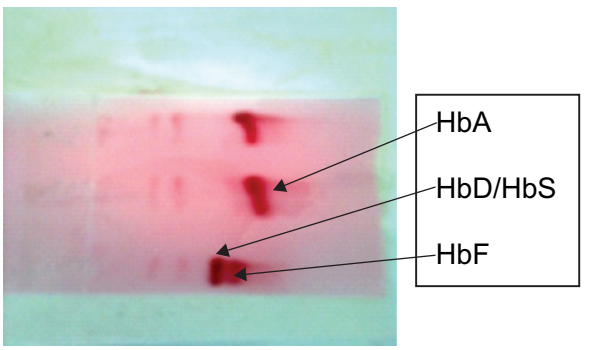

Figure 2: Cellulose acetate strip showing band at HbD position (lower 3rd case) which was proved to be sickle cell band by performing sickling test.

Table 1: Breakup of Hemoglobin disorders (n= 227).

S.No.	Type	Number	Percentage
1	Beta thalassemia major	87	38.30
2	Sickle cell disease	73	32.16
3	Beta thalassemia trait	42	18.50
4	Beta thalassemia intermedia	13	5.73
5	Sickle cell trait	6	2.65
6	HbE disease	2	0.88
7	HbD/Beta thalassemia	2	0.88
8	Sickle cell/Beta thalassemia	1	0.45
9	HbD trait	1	0.45
	Total	227	100

Among the hemoglobin disorders the most common disorder was Beta thalassemia major in

87 (38.3%) patients followed by sickle cell disease in 73 (32.16%) and Beta thalassemia trait in 42 (18.5%) patients. Beta thalassemia intermedia was diagnosed in 13 (5.73%) patients, Sickle cell trait in 6 (2.65%), HbE and HbD/Beta thalassemia in 2 (0.88%) cases each and Sickle cell/ Beta thalssemia and HbD trait in one (0.45%) case each. (Table 1)

In patients detected as Beta Thalassemia trait HbA2 was increased more than 3.5%, RBC count more than $5x10^9$/ litre and MCV was lesser than 70 fl. Peripheral blood film in these cases revealed microcytic hypochrmic blood picture with target shaped red blood cells.

All the patients of Beta thalssemia major had severe anemia, splenomegaly and history of blood transfusion before the age of 2 years; however 13 cases were diagnosed as beta thalassemia intermedia as their blood transfusion need was very less. The peripheral blood film of Beta thalssemia major cases revealed marked anisopoikilocytosis with red cells fragmentation and nucleated red blood cells. Hb electrophoresis in all these cases revealed high Hb F (fetal hemoglobin).

The cases of sickle cell disease presented with aches and pains in different parts and joints of the body. All of them were anemic but there blood transfusion need was much less as compared to Beta thalssemia major. Sickle cell disease is common mostly in three tribes named as Shirani, Ustrana and Baytani.

The cases of sickle cell trait had mild anemia and they were symptoms free except one case who complained aches and pains during exertion. The sickling test was positive in all the sickle cell disorders but the only difference between sickle cell disease and sickle cell trait was that this test showed sickling of the red blood cells a little bit late in carrier states. In peripheral smear sickle cells are frequently seen in case of sickle cell disease however in trait these cells are not commonly seen in the peripheral film. Oat type or boat type of red blood cells are commonly seen in sickle cell disorders.

The HbE disease, HbD/Beta thalassemia and Sickle cell/Beta thalassemia all presented clinically just like Beta thalassemia major but the sickle cell/ Beta thalssemia patients complained of body aches as well beside other symptoms. The HbD trait was asymptomatic however slightly low hemoglobin (10.5 g/dl) was noted on blood examination.

DISCUSSION

In Pakistan there is strong tendency to marry within own tribe or family. Cousin especially first cousin marriage with a background of family history of hemoglobinopathy results in homozygous state. The most common hemoglobinopathy in one setup is thalassemia. In Pakistan it is seen in all parts of the country and over 5000 homzygotes are born each year. Carrier frequency varies from 4.0% to 5.0% in different groups in various parts of the country. In a family having a patient of Beta thalassemia major, the prevalence of carrier is more than 30%.[10-14]

During routine workup of these cases it is important to differentiate beta thalassmia minor from iron deficiency. Advances in carrier diagnosis using hematological indices as a useful tool can make an early detection of carrier possible. Microcytic hypochromic morphology of red blood cells in proportion to degree of anemia, anisopoikilocytosis with presence of pencil shape red cells on peripheral blood, red blood cell count usually less than 5.0 million/ cmm and decreased MCV usually favors the diagnosis of iron deficiency anemia. Whereas , uniformly microcytic hypochromic blood picture more pronounces as compared to the level of hemoglobin, minimal or absence of anisocytosis, presence of target shape red blood cells, red blood cell count more than 5 million/ cmm and decreased MCV favors the diagnosis of Beta thalssemia trait.[15-17]

Although hemoglobinopathies are autosomal recessive disorders but male patients were referred more than females. Possible reason is probably more caring of male gender in the affected communities. In our study the affected males were 66% while female patients were 34%. In a study conducted by Balgir RS[18] among 667 patients 52.3% were male while 47.7% were female. The reason of preponderance of males over females is the same as given in our study i.e more health care taken for males over females.

In our study among hemoglobin disorders the most common disorder was Beta thalassemia major 38.3%, followed by sickle cell disease 32.16% and Beta thalassemia trait 18.5%, while study conducted by Amanat et al[9] in Rawalpindi (Pakistan) among hemoglobinpathies the commonest one was Beta thalassemia trait (50%), followed by Beta thalassemia major (37.5%) and HbD trait (6.35%). Similarly a study conducted by Mesbahudin et al[19] in Bangladesh the most common hemoglobinopathy was Beta thalassemia trait (21.3%), followed by E/ Beta thalassemia (13.5%) and HbE disease (9.2%).

In a study conducted by Balgir[18] in state of Orissa (India) sickle cell trait was the most common hemoglobinopathy (29.8%) followed by Beta thalassemia trait (18.2%), Sickle cell disease (7.6%), Beta thalassemia major (5.3%), Sickle beta thalassemia (1.7%). Our study is contrary to this. The best explanation is that referred cases were mostly severe anemic having a positive history of hemoglobinopathy and the defective gene responsible for Beta thalassemia major is more common in Pathans of KPK Province. In our study sickle cell disease is the second most common (32.16%) hemoglobinopathy

while other studies conducted in Pakistan do not show this prevalence rate. The reason is that sickle cell endemic areas are nearer to our study area i.e. Gomal Medical College, Dera Ismail Khan. All the tribes (Shirani, Ustrana, Baytani) suffering from sickle cell disease are living near district Dera Ismail Khan.

CONCLUSION

Hemoglobin disorders are still a big problem for the different communities of Pakistan. If the disease continues to pass vertically, it may take the form of epidemic. The only way to prevent the disease is carrier detection and awareness among the peoples. Instead of discouraging cousin marriages, preventive measures like pre-marriage detection of carrier state must be considered as mandatory step to control the disease.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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