DETECTION OF β-THALASSAEMIA TRAIT: ASTI DY OF FIFTY FEMALES

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***Background**:* his study was carried out to detect beta-thalassaemia frail in the siblings of beta thalassaemia major children by Hemoglobin (Hb) electrophoresis ***Methods**:* Subjects were divided into two groups Group I Mas the patterns group comprising 100-subjects siblings of beta- thalassaemia major children and Group 2 was the control group with 25-subjects *Results:* It was observed that 58% of the siblings of beta-thalassaemia major children had beta-thalassaemia trail Even in the control group 2 subjects had beta thalassaemia trait which shows that thalassaemia gene is very common in Hazara division of Pakistan.

INTRODUCTION

Thomas Cooley was the first person to recognize thalassaemia as a clinical entity. Thus the condition was labeled as Cooley's anemia. Later it was found to be an inherited disorder of hemoglobin synthesis Inherited disorders of human hemoglobin synthesis are extremely diverse but fall into three groups:

- There are structural hemoglobin variants which alter the function and stability of the Mb molecules e g HbC. HbS & HbD etc.
- The thalassaemia syndromes which are characterized by a reduced rate of synthesis of one globin chain leading to clinical manifestations due to an imbalance in globin chain production e g a and P-thalassaemia.
- Certain genetically determined conditions in which switch from HbF to HbA (adult Mb) does not occur, such as hereditary persistence of fetal hemoglobin <HPFH) in which there is abnormally elevated level of feta! hemoglobin.

The thalassaemias are a heterogeneous group of genetic disorders of human hemoglobin synthesis, characterized by imbalanced globin chain production which leads to ineffective erythropoiesis and anaemia'. Thalassaemias may be classified as α and β forms depending on the basis of deficiency of respective chain[1].

β-thalassaemia is also classified on the basis of clinical severity, thus they are divided into three categories namely

- Thalassaemia major.
- Thalassaemia intermedia.
- Thalassaemia minor

In the case of α-Thalassaemia major which is the classical homozygone β-Thalassaemia (a Iso called Cooley's anemia) there is marked reduction in the production of p chain and a relative excess of α chain. The disorder is associated with severe anemia, retarded growth hepatosplenomegaly. marked skeletal changes and skin pigmentation. The introduction of different transfusion (hypertransfusion and supertramfusion) improved the survival of these patients

In Thalassaemia major the patient remain.-. until 4-5 months of age i e. the time when the switch from HbF to HbA synthesis occurs. Thereafter the diagnosis is straightforward with a very loan hemoglobin The peripheral film shows severe microcytic hypochromic anemia along with marked anisocytosis, poikilocytosis target cells and many nucleated red cells The reticulocyte count is high, as is the serum bilirubin level. X-ray of skull is also characteristic with thinning of cortex and increased medullary area. The Hb electrophoresis shows raised HbF which may be 10-98% of the total Hb.

Thalassaemia intermedia comprises of an ill-defined group ranging in severity from a disorder similar to transfusion dependent Thalassaemia major to a symptom less anemia which is slightly more severe than that of heterozygous (3-thalassaemia* These patients have Hb in the range of 7.0 to 10 gm dl. They do not need regular blood transfusions,

It is heterozygous state which may present with chronic anemia along with splenomegaly or an almost symptom less state. Clinically these subjects may present with features of iron deficiency anemia and if iron is given they develop iron overload [7] The disease usually manifests itself during stress (e g. pregnancy in females) or they are diagnosed on routine blood examination. It is important to exclude iron deficiency anemia in which HBA2 is reduced *. On Hb electrophoresis these patients may present in one of the following three forms:

1. HbA2 is raised (more than 3 5%).
2. HbA2 is normal while HbF is raised in the range 3.5-36%[4]

In the developed countries much attention has been directed to the prevention of diseases by detection of thalassaemia carriers and marriage counselling* By using this prevention program in Sardinia the incidence of homozygous patients decreased from 1:250 live births to 4:1000 live births'[1] Similarly in Cyprus the incidence of Thalassaemia major cases dropped by 96%[1]

The present study was mainly designed to decrease the incidence of β-Thalassaemia major cases by marriage counseling

MATERIALS AND METHODS

The study was carried out in the Pathology Department of Ayub Medical College and Hospital Complex, Abbottabad. One hundred subjects were selected. They were the brothers and sisters of p-Thalassaemia major patients- The subjects were selected from the Ayub Medical College and Hospital and from the Thalassaemia major patients registered with Abbottonians Medical Association an NGO working for the welfare of thalassaemic children Twenty-five healthy controls were selected. In all these cases complete blood counts along with reticulocyte count, RBC morphology and red cell indices were performed. In all these cases Hb-electrophoresis was performed. The level of HbF was also seen by modified Betke's method The level of serum ferritin was also estimated in these patients and controls.

RESULTS

A total of 58 cases were seen with p-Thalassaemia trait. Maximum cases (58.63%) were detected in the 0-9 years of age group followed by 10-19 years of age group (31.00%) given in table-1.

In most (74.17%) HbA_2 was in the range of 3.6-6%. While 14.55% subjects of P-Thalassaemia Trait had an HbA_2 level 6.1-7%. Only 10.93% of these subjects had an HbA_2 level in the range of 7.1- 9.0%.
In the control subjects two persons out of 25 had an HbA_2 level of more than 3.6% and they were the P-Thalassaemia trait cases.
In most of the cases HbF was below 3% while only 10.34% subjects had HbF of more than 3%. In the control group all subjects had HbF level of less than 1%.

The pattern of family distribution was interesting. A total of 50 families were investigated out of them 23 families had one child affected while 14 families had no effected children other than the one having Thalassaemia major (Table-2).

Table-1: Age and Sex

Age	Sex		Total	Percentage
(Sex)	Male	Female		
0-9	17	17	34	58.63
10-19	7 .	11	18	31.03
20-29	2	4	6	10.34
Total	26	32	58	100

Table-2: Pattern of family distribution

No of Children effected	No of families effected	Total No of children	No of effected children	% of (Families
One effected	23	65	23	42%
Two effected	06	21	12	24%
Three effected	5	23	15	12%
Four children effected	2	12	8	2%
No children effected	14	32	0	32%
Total	50	153	58	

DISCUSSION

In the present study out of 100 siblings of Thalassaemia major children 58% were detected to have p-Thalassaemia trait. As the study was carried out in the siblings of β-Thalassaemia children thus both the parents were carriers. The incidence has closely followed the Mandelian pattern of inheritance which states that each offspring of a carrier couple at risk of having a child with Thalassaemia major has a 25% chance of being normal, a 50% chance of heterozygosity and a 25% chance of Thalassaemia major[11].

Thalassaemia is an autosomal recessive disorder. A child who inherits the abnormal gene from both the parents (homozygous) suffers from Thalassaemia major leading to severe intractable anemia and dependence on blood transfusion plus iron chelation therapy for all his life. Such cases can be prevented by identification of the carrier's subjects and advising them to avoid marrying another carrier.

Even in the healthy control subject (out of 25 subjects) two had HbA_2 more than 3.6% which indicates that Thalassaemia gene is very common in this part of the country. As seen in the section of results and observations, the detection of p-Thalassaemia trait cases is easy if an experienced person sees the Red Cell Indices and RBC morphology. The diagnosis is ultimately confirmed by hemoglobin electrophoresis.

Table – 3: The Hematological Parameters Were Characteristics in the Patients of β-thalassemia

HB Cm/dl	RBC^{x} 10^{12}/L	PVC	MCV	MCH	MCHC	Retie	HbA2	HbF	S. Ferritin
9.78 ± 1.50	4.79± 0.91	43.17 ± 8.02	89.05 ± 12.37	21.61 ± 4.67	23.47 ± 5.29	2.33 ± 1.5	5. 06 ± 1.29	1.28 ± 0.80	130. 82 ± 153.3
12.38 ± 1.75	4.99 ± 0.6	45.28 ± 9.6	92.12 ± 10.10	25.2 ± 3.6	27.78 ± 4.31	0.98 ± 0.64	2.67 ± 0.92	0.38 ± 0.10	96. 68 ± 52.0

As a result of present study it is recommended to have a mass-screening program for the detection of β-Thalassaemia trait carriers in the general population. Because marriage counseling to these carrier subjects is vital to induce the incidence of β-Thalassaemia major cases as has been carried out in the developed countries.

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