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THALASSEMIA- THE ERYTHROCYTIC SLAYER

Medical Science

Dr. Poonam Woike M.D, Demonstrator, Department Of Pathology, Government Medical College, Datia, M.P

Dr. Priya Gaur* Resident, Department Of Obstetrics And Gynaecology *Corresponding Author

Dr. Rajesh Gaur Dean, Government Medical College, Datia, M.P

ABSTRACT

Thalassemia is an inherited blood disorder in which the body makes an abnormal form of hemoglobin. Hemoglobin is the protein in red blood cells that carries oxygen. The disorder results in large numbers of red blood cells being destroyed, which leads to anemia. Thalassemia is inherited as an autosomal recessive disorder. Beta thalassemia is caused by deficient synthesis of beta chain with normal alpha chain synthesis. Alpha thalassemia is caused by deficient synthesis of alpha chain with normal beta chain synthesis. Defect may occur at different steps of beta chain synthesis such as splicing mutations, chain terminator mutations and promoter region mutations. The most common cause of reduced alpha chain synthesis is deletion of alpha globin genes. These defects causes ineffective erythropoiesis and destruction of red cells due to cell membrane damage and decreased deformability leading to extravascular hemolysis. Anaemia leads to several additional problems such as erythroid hyperplasia in bone marrow, skeletal deformities, iron overload, secondary haemochromatosis, cardiac failure, endocrine defieciency and even death. The aim of the study was to find out the incidence of thalassemia in different blood groups as well as various age groups. Total 128 diagnosed cases of Thalassemia were selected, their ABO blood grouping and Rh typing was done and the results were compiled into various categories. The disease was most commonly found in blood group B (39.77%) with predominance of males aged between 0-5 years (42.18%).

KEYWORDS

Thalassemia, Hemoglobin, Anemia.

INTRODUCTION

Thalassemia is a form of inherited autosomal recessive blood disorder characterized by abnormal formation of hemoglobin. The term thalassemia is derived from the Greek, thalassa (sea) and haima (blood). The abnormal hemoglobin formed results in improper oxygen transport and destruction of red blood cells. Beta-thalassemia is prevalent in Mediterranean countries, the Middle East, Central Asia, India, Southern China, and the Far East as well as countries along the north coast of Africa and in South America. The highest carrier frequency is reported in Cyprus (14%), Sardinia (10.3%), and Southeast Asia. [1] The α-thalassemias involve the genes HBA1[4] and HBA2,[5] inherited in a Mendelian recessive fashion. Two gene loci and so four alleles exist. It is also connected to the deletion of the 16p chromosome. α Thalassemias result in decreased alpha-globin production, therefore fewer alpha-globin chains are produced, resulting in an excess of β chains in adults and excess γ chains in newborns.

Underproduction of either alpha or beta globin chains causes accumulation of excess unpaired chains. This leads to destruction of developing red cells and premature removal of circulat ing red cells in the spleen. The anemia in thalassemia is therefore a combination of ineffective erythropoiesis and hemolsis in the spleen. Point mutations in or near the globin gene are responsible for the majority of beta thalassemias. More than 400 genetic alterations have been documented in beta thalassemia.

Haematological findings in thalassemia includes anisocytosis, target cells, pokilocytosis, basophilic stippling, microcytic hypochromic RBC's and fragmented RBC in peripheral smear examination. Bone marrow shows marked erythroid hyperplasia, reversed myeloid to erythroid ratio, increased bone marrow iron and dyserythropoiesis. Other findings shows decrease in MCV, MCH, MCHC and total iron binding capacity whereas increase in levels of serum ferritin, serum iron, percentage saturation and HbA_2 and HbF.

Beta Thalassemias are due to mutations in the HBB gene on chromosome 11,[6] Beta-thalassemia includes three main forms: Thalassemia Major, variably referred to as "Cooley's Anemia" and "Mediterranean Anemia", Thalassemia Intermedia and Thalassemia Minor also called "beta-thalassemia carrier", "beta-thalassemia trait" or "heterozygous beta-thalassemia". Thalassemia major occurs when a child inherits two mutated genes, one from each parent. Children born with thalassemia major usually develop the symptoms of severe anemia within the first year of life. They lack the ability to produce normal, adult hemoglobin and experience chronic fatigue. They may also fail to thrive.

Investigations include haemoglobin electrophoresis, NESTROF (naked eye single tube osmotic fragility test) and radiological survey of skull (shows crew cut appearance and hair on end appearance).

Having a single gene for thalassemia may protect against malaria and thus be an advantage.[7] People diagnosed with heterozygous (carrier) β-thalassemia have some protection against coronary heart disease.[8] Two major consequences of the genetic defect of thalassemia are severe anemia and expansion of the bone marrow in the body's effort to produce more red blood cells. This leads to poor growth, impaired physical activities, facial and other bone deformities, fragile bones and enlargement of the liver and spleen. Worsening anemia leads to intense erythropoietic drive, with expansion of bone marrow compartment and resumption of extramedullary haematopoiesis. Osteoporosis is frequent even in well transfused patients and spontaneous fractures might occur in them. If left untreated, it will lead to death within the first decade of life.

This selective survival advantage of carriers (known as heterozygous advantage) may be responsible for perpetuating the mutation in populations. In that respect, the various Thalassemias resemble another genetic disorder affecting hemoglobin, sickle-cell disease.[2][3] The only treatment to combat severe anemia is regular blood transfusions and iron chelation therapy.

MATERIALS AND METHODS

This is a one year prospective study. The patients suffering from Thalassemia were included in the study. The patients were thoroughly examined and complete personal and family history was noted. ABO blood grouping and Rh typing using haemagglutination method was done and their various parameters such as age, sex, blood group and diagnosis were summarized, compiled and tabulated in charts for further analysis. The results were obtained using frequency distribution and percentage proportion.

RESULTS

Total 128 diagnosed cases of Thalassemia were included in the study. Out of which 115 were suffering from Thalassemia Major, 11 from Thalassemia Intermedia and 02 associated with Sickle Cell Disease. The cases were further divided on the basis of different blood groups, male or female predominance and age groups to see the spectrum of disease in various aspect described in table 2, 3 and 4.

Table 1 – Distribution Of Types Of Beta Thalassemia.

Type	No. Of Cases	Percentage
Thalassemia Major	115	89.84%
Thalassemia Intermedia	11	8.59%
Thalassemia Minor	0	0
Sickle Cell Disease	02	1.56%

Table no 2. Spectrum Of Disease In Different Blood Groups.

Blood Group	Number Of Cases	Percentage
A +	30	23.43%
A -	02	1.5%
B+	44	34.37%
B-	07	5.4%
O+	32	25%
O-	05	3.9%
AB+	08	6.25%
AB-	0	0

Table No. 3. Male / Female Preponderance

Gender	Number Of Cases	Percentage
Male	86	67.18%
Female	42	32.81%

Table No 4. Age Wise Distribution

Age group	Number of cases	Percentage
0-5	54	42.18%
6-10	41	32.03%
11-15	18	14.06%
16-20	06	4.68%
20-25	05	3.90%
25-30	03	2.34%
>30	01	0.78%

DISCUSSION

Thalassemia is a genetic blood disorder. People with this disease are not able to make enough haemoglobin, which causes severe anaemia. Symptoms appear in the first two years of life and include paleness of skin, poor apetite, irritability and failure to grow. A blood sample sent for lab investigations proves to be very effective in it's diagnosis. Red blood cells will appear small and abnormally shaped when looked at under a microscope.

A complete blood count (CBC) reveals anemia, hemoglobin electrophoresis shows the presence of an abnormal form of hemoglobin, mutational analysis can help detect Alpha Thalassemia. In our study total 128 subjects were taken which were suffering from Beta-Thalassemia and they were further divided into various parameters.

Out of 128 patients 115 were suffering from Thalassemia major and 2 were having Thalassemia major associated with sickle cell disease. The study reveals number of males (67.18%) was more than females (32.81%) who suffered from the disease. Also, the disease was predominantly seen in blood group B, followed by group O, A and lastly AB. Maximum patients who suffered from the disease fell into the age group 0-5 years followed by 6-10 years, 11-15 years, 16-20 years, 21-25 years, 25-30 years and only one in the age group >30 years (patient was suffering from Thalassemia Intermedia). It is seen from the above data that with increase in age the number of patients suffering from Thalassemia major is reduced due to frequent blood transfusions, infections and other complications arising from disease.Hence, iron overload causes most of the mortality and morbidity associated with thalassemia (9). Nontransferrin-bound iron (low-molecular-weight iron) is a highly toxic state of iron formed when the iron-binding capacity of transferrin has been exceeded (10). Hence, long-term transfusion programs should be accompanied by therapy with iron-chelating agents within the first 3 years of life (11). Ferritin levels below 2500 mg/mL are associated with improved survival (12). To date, over 1000 bone marrow transplants have been performed in thalassemic patients at medical centers of excellence (13). Human globin genes have been transferred into mouse cells (14). Successful application of gene transfer for the treatment of thalassemia is experimental and will require that the newly introduced genes do not alter the growth properties of the bone marrow cells by the recombinant retroviral genome (15). As carrier states of the thalassemias are readily identifiable, affected fetuses can be diagnosed. Recent efforts have been directed to early diagnosis by fetal DNA analysis (46) carried out on amniotic fluid cells or by chorionic villus sampling. The harvesting of fetal cells from the maternal circulation is being explored for this purpose (47).

CONCLUSION

Thalassemia is a serious health problem worldwide. In this study the major blood group affected from Thalassemia was found to be B (39.77%), with an increased male> female cases and maximum patients were between 0-5 (42.18%) years of age with a decrease in subsequent age groups. Research work has to be done to explore why there's high prevalence of Thalassemia in blood group 'B'

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