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A STUDY OF ANEMIA IN BETA – THALASSEMIA CARRIER PATIENTS IN INDEX MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTER, INDORE (M.P.)

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Abstract

Background: This study was conducted at Index Medical College, Hospital and Research Center, Indore (M.P.) from June 2019- May 2020.

Material and Methods: Patients attending the department of haematology and referred from other periphery area after written consent (below and above 18 years patients of both gender) were included in the study. There haemogram and blood group, blood urea , serum creatinine, serum iron and vitamin B – 12 level, urine R/M and stool test for worm infestation and liver function were done bedside all relevant investigations. There blood sample for electrophoresis was done HbA1 and HbA2 and HbS who had criteria that showed thalassemia with a peripheral blood picture and electrophoresis with Hb less than 10 gm/dl were noticed and analysis done .

Exclusion Criteria: Patient who had more than 10 gm haemoglobin, pregnant women, patients who refused for written consent with other haematological disorder such as sickle cell anemia, patients who had undergone blood transfusion within 4 months, patients suffering from HIV and HBV – HCV infection , patients of tropical splenomegaly and cancer patients .

Results: In females, below 18 years, total patients were 13 out of which 12 patients needed blood transfusion and above 18 years, total patients were 27 out of which 25 patients needed blood transfusion.
In males, below 18 years, total patients were 22 out of which 19 patients needed blood transfusion and above 18 years, total patients were 13 out of which 9 patients needed blood transfusion.

Conclusion: Most of the carriers are asymptomatic but few of them had symptoms and may need blood transfusion also. Pre-marital counseling for genetic disorder through genetic counseling is good tool to lesson the burden of genetic transmitted disease and recurrent transfusion and iron - overloaded.

Keywords: Beta - thalassemia and its type, MCH (mean cell hemoglobin), MCV (mean corpuscular volume), MCH C (mean cell hemoglobin concentration), Hb A1 (adult hemoglobin), Hb A2(adult hemoglobin), HbF (fetal hemoglobin).

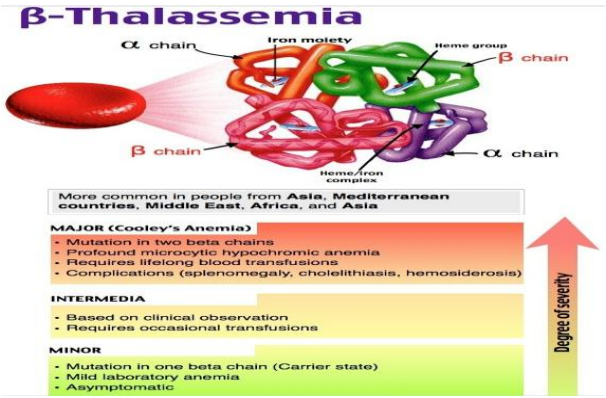
Introduction

Beta-thalassemias are a group of hereditary blood disorders characterized by anomalies in the synthesis of the beta chains of hemoglobin resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individuals.

Beta-thalassemias are caused by point mutations or, more rarely, deletions in the beta globin gene on chromosome 11, leading to reduced (beta+) or absent (beta0) synthesis of the beta chains of hemoglobin (Hb). Transmission is autosomal recessive; however, dominant mutations have also been reported. Diagnosis of thalassemia is based on hematologic and molecular genetic testing, electrophoresis genetic. Differential Diagnosis includes sideroblastic anemias, congenital dyserythropoietic anemias, and other conditions with high levels of HbF (such as juvenile myelomonocytic leukemia and aplastic anemia) and fetal haemoglobin. Genetic counseling is recommended and prenatal diagnosis limit the family may be offered.

Disease name and synonyms:

The term thalassemia is derived from the Greek, thalassa (sea) and haima (blood).



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".

Apart from the rare dominant forms, subjects with thalassemia major are homozygotes or compound heterozygotes for beta0 or beta+ genes, subjects with thalassemia intermedia are mostly homozygotes or compound heterozygotes and subjects with thalassemia minor are mostly heterozygotes.

Definition:

Beta-thalassemia syndromes are a group of hereditary blood disorders characterized by reduced or absent beta globin chain synthesis, resulting in reduced Hb in red blood cells (RBC), decreased RBC production and anemia.

Most thalassemias are inherited as recessive traits.

Beta-thalassemias can be classified into:

Beta-thalassemia

• Thalassemia major

• Thalassemia intermedia

• Thalassemia minor

* ATYPICAL CARRIER - very mild mutations associated with consistent residual output of Hb beta chains and with normal RBC indices and normal or borderline HbA2. The above reported groups of carriers are referred to as atypical carriers.

Epidemiology:

Beta-thalassemia is pervasive in Mediterranean nations, the Middle East, Central Asia, India just as different nations.

The most noteworthy transporter recurrence is accounted for in Cyprus (14%), Sardinia (10.3%), and Southeast Asia 1.

The high quality recurrence of beta-thalassemia in these locales is undoubtedly identified with the particular weight from Plasmodium falciparum intestinal sickness[1].

It has been assessed that about 1.5% of the worldwide populace (80 to 90 million individuals) are transporters of beta thalassemia,

In any case, precise information on transporter rates in numerous populaces are missing, especially in zones of the world known or expected to be vigorously influenced[2].

The most widely recognized mix of beta-thalassemia with anomalous Hb or basic Hb variation with thalassemic properties is HbE/betathalassemi which is generally predominant in Southeast Asia where the transporter recurrence is around half.

Clinical description:

The aggregates of homozygous or hereditary heterozygous compound beta-thalassemias incorporate thalassemia major and thalassemia intermedia.

Thalassemia intermedia incorporates patients who present later and don't need normal bonding.

Aside from in the uncommon predominant structures, heterozygous beta thalassemia brings about the clinically quiet transporter state. Transporters of thalassemia minor are typically clinically asymptomatic yet now and again have a mellow weakness. At the point when the two guardians are transporters there is a 25% danger at every pregnancy of having kids with homozygous thalassemia.

Blood bondings are only sometimes required.

Microcytosis and hypochromia are found for each situation.

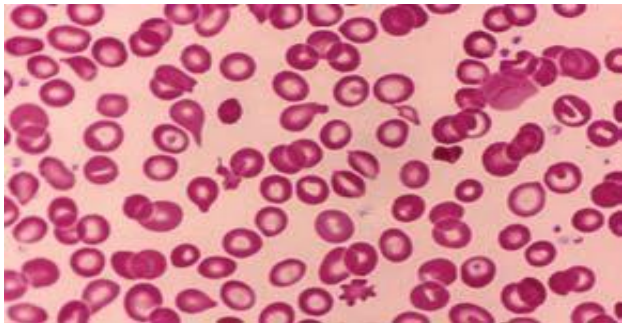
People with HbS/beta-thalassemia have a clinical course like that of Hb SS.

Etiology:

More than 200 mutations have been so far reported; the large majority are point mutations in functionally important regions of the beta globin gene [3,4].

Deletions of the beta globin gene are uncommon.

The beta globin gene mutations cause a reduced or absent production of beta globin chains. In India, 619 Beta gene mutation and is β^0 severity are recorded.



Picture courtesy to Williams Hematology

Histopathological diagram showing beta thalassemia carrier

Hereditary transmission:

The beta-thalassemias are inherited in an autosomal recessive manner.

The parents of an affected child are obligate heterozygotes and carry a single copy of a disease- causing beta globin gene mutation.

At conception, each child of heterozygotes parents has 25% chance of being affected, 50% chance of being an

asymptomatic carrier, and 25% chance of being unaffected and not carrier.

The parents of the proband have a 1 in 4 (25%) risk of having further affected children in each pregnancy.

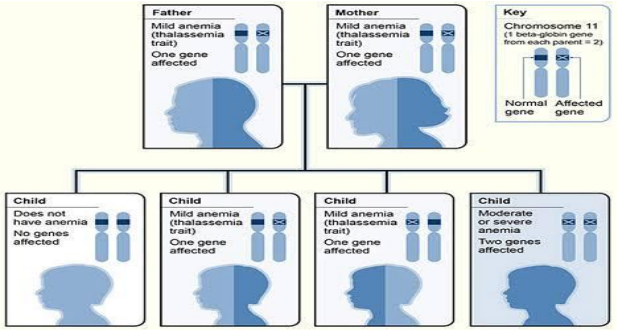


DIAGRAM SHOWING BETA THALASSEMIA

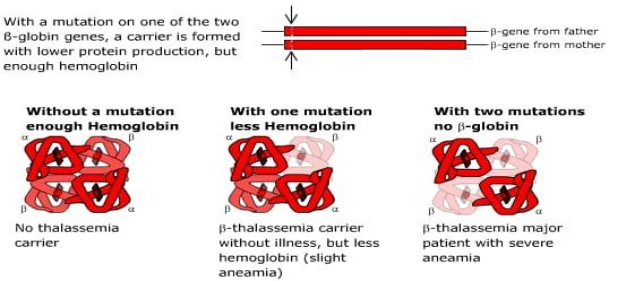


Diagram showing beta gene mutation

Dominant forms of beta-thalassemia, associated with mutations that result in the production of highly unstable beta globulin variants and leading to a clinically manifesting phenotype of beta-thalassemia in heterozygotes [5].

Genetic counseling and prenatal diagnosis :

Prevention of beta-thalassemia is based on carrier identification,genetic counseling and prenatal diagnosis [6].

Analysis of fetal cells in maternal blood and analysis of fetal DNA in maternal plasma for the presence of the father's mutation are currently under investigation [7,8].

Preimplantation genetic diagnosis may be available for families in which the disease-causing mutations have been identified.

Treatment of iron overload-related complications :

Iron preparation are taken by the patients advised by the practitioners and recommends iron treatment on the basis of iron levels and low ferritin levels and high total binding capacity.
Growth deficiency, delayed puberty, hypogonadism and difficulty in development of reproductive system are the complications.
If the annual red cell requirement exceeds 180-200 ml/Kg of RBC (assuming that the Hct of the unit of red cells is about 75%), splenectomy should be considered, if present.

ADIVCE:

Lifestyle and diet in beta thalassemia :

Patients with thalassemia should be discouraged from consuming alcohol, as it can facilitate the oxidative dam age of iron and aggravates the effect of HBV and HCV on liver tissue as it leads to cirrhosis portal hypertension which will further changed to haematopoisis[9,10].

There is no reason for patients with thalassemia to skip or delay standard recommended vaccinations.

It is currently generally perceived that thalassemia, as other ongoing ailments, has significant mental ramifications.

The manner by which the family and the patient deal with the infection and its treatment will critically affect the patient's endurance and personal satisfaction, and an overall acknowledgment by the patient of his/her own condition establishes the way to typical advancement from youth to adulthood[11].

A key function for treating doctors and other medical services experts is to support patients and families to look up to the troublesome requests of therapy, while keeping up a positive job.

Therapies under investigation:

It is under trial.

5-azacytidine, decytabine, and butyrate derivatives gave encouraging results in clinical trials [12].

The possibility of correction of the molecular defect in hematopoietic stem cells by transfer of a normal gene via a suitable vector or by homologous recombination is being actively investigated [13].

The most promising results in the mouse model have been obtained with lentiviral vectors [13,14] .

Prognosis:

Prognosis of thalassemia minor subjects is excellent.

If signs of iron overload are present then practitioners advised the patients to take iron chelators.

No iron therapy without serum iron levels .No other medication by self.

Material and Methods: This study was conducted at Index Medical College, Hospital and Research Center, Indore (M.P.) from June 2019- May 2020. Patients attending the department of haematology and referred from other periphery area after written consent (below and above 18 years patients of both gender) were included in the study. There haemogram and blood group, blood urea , serum creatinine, serum iron and vitamin B – 12 level, urine R/M and stool test for worm infestation and liver function were

done bedside all relevant investigations. There blood sample for electrophoresis was done HbA1 and HbA2 and HbS who had criteria that showed thalassemia with a peripheral blood picture and electrophoresis with Hb less than 10 gm/dl were noticed and analysis done .

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Results and Observations

Severity of anemia	Hb in g/dl
1. Mild	10–10.9
2. Moderate	9.9–7
3. Severe	6.9–4
4. Very severe	<4

Table 1: Socio-demographic distribution of study participants

Variables		Frequency	Percentage
Age	≤18 years	35	46.7
	>18 years	40	53.3
Total		75	100
Sex	Male	35	46.7
	Female	40	53.3
Total		75	100

Table 2: Haemogram of study participants

Variable		Frequency	Percentage
Grades of anemia	Mild	8	10.7
	Moderate	30	40
	Severe	22	29.3
	Very severe	15	20
MCV	Decrease	51	68
	Normal	22	29.3
	Increase	2	2.7
MCH	Decrease	70	93.3
	Normal	2	2.7
	Increase	3	4
MCHC	Decrease	35	46.7
	Normal	33	44
	Increase	7	9.3
HbA2	Decrease	0	0
	Normal	1	1.3
	Increase	74	98.7
HbF	Decrease	0	
	Normal	67	89.3
	Increase	8	10.7
HbA	Decrease	73	97.3
	Normal	2	2.7
	Increase	0	0
Blood transfusion given	Given	65	86.7
	Not given	10	13.3

Table 2 shows after application of chi square test statistically significant association was found between Severity of anemia and sex. Level of MCHC was found to be associated with sex of the participants & this association was also statistically significant as the p value for both was <0.05

Table 3: Association between severity of anemia & value of MCHC with sex

		Sex			df	Chi square	p value
		Male	Female	Total			
Severity of anemia	More severe (Very Severe + severe)	22	16	38	1	3.90	0.04
	Less severe (Mild +moderate)	13	24	37			
Total		35	40	75			
Normal MCHC	Yes	21	12	33	1	6.81	0.009
	No	14	28	42			
Total		35	40	75			

Discussion:

Modifier genes are characterized as hereditary variations that lead to contrasts in infection aggregate. In homozygous beta thalassemia,primary hereditary modifiers, influencing the clinical seriousness of the malady, incorporate hereditary variations ready to decrease the globin chain awkwardness, along these lines bringing about a milder type of thalassemia.

These components are the presence of quiet or gentle beta-thalassemia alleles related with a high remaining yield of beta globin, the coinheritance of alpha thalassemia or potentially of hereditary determinants ready to support a ceaseless creation of gamma globin chains (HbF) in grown-up life[15].

Some betathalassemia transformations (for example cancellation and non erasure delta beta-thalassemia, erasures of the 5' district of the beta globin gene) increment "essentially" the gamma globin gene yield.

Different transformations expanding HbF creation are those related with deletional and non-deletional HPFH connected to the beta globin gene group.

As of late, the genome-wide affiliation approach, especially considering quantitative characteristic loci (QTL) which cause raised HbF, have uncovered hereditary components inclusion.

The clinical aggregate of homozygous beta thalassemia may likewise be changed by the co-legacy of other hereditary variations planning outside the globin clusters.These auxiliary hereditary modifiers impact mostly the confusions of the thalassemia aggregate.

A few optional hereditary modifiers have been recognized in the ongoing years.

The presence of (TA)7 polymorphism in the advertiser area of the uridine diphosphate-glucuronosyltransferase gene,

which in the homozygous state is related with the Gilbert condition, is a danger factor for the advancement of cholelitiasis in thalassemia major and intermedia patients[16,17].

Other candidate genes for modification of the thalassemia phenotype are the apolipoprotein E ε4 allele and some HLA haplotypes, which seem to be genetic risk factors for left ventricular failure in homozygous beta-thalassemia [18,19].

Less consistent data have been reported for genes involved in iron metabolism (i.e. C282Y and H63D HFE gene mutations), probably because their effect on iron overload is hidden as a result of treatment (i.e. secondary iron overload from red cell transfusion and iron chelation), and for genes associated with bone metabolism [20,21,22,].

Most of these patients have excess functional alpha globin genes (alpha gene triplication or quadruplication) which increases the imbalance in the ratio of alpha/non-alpha globin chain synthesis [15,23,24].

Conclusion: Most of the carriers are asymptomatic but few of them had symptoms and may need blood transfusion also. Pre-marital counseling for genetic disorder through genetic counseling is good tool to lesson the burden of genetic transmitted disease and recurrent transfusion and iron - overloaded.

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References

1. Flint J, Harding RM, Boyce AJ, Clegg JB: The population genetics of the hemoglobinopathies. *Bailliere's Clinical Hematology* 1998, 11:1-50.
2. Vichinsky EP: Changing patterns of thalassemia worldwide. *Ann N Y Acad Sci* 2005, 1054:18-24.
3. Giardine B, van Baal S, Kaimakis P, Riemer C, Miller W, Samara M, Kollia P,Anagnou NP, Chui DH, Wajcman H, Hardison RC, Patrinos GP: HbVar database of human hemoglobin variants and thalassemia mutations: 2007 update. *Hum Mutat* 2007, 28:206.
4. Huisman THJ, Carver MFH, Baysal E: A Syllabus of Thalassemia Mutations. *The Sickle Cell Anemia Foundation, Augusta, GA* 1997.
5. Thein SL: Dominant beta thalassaemia: molecular basis and pathophysiology. *Br J Haematol* 1992, 80:273-277.
6. Cao A, Galanello R, Rosatelli MC: Prenatal diagnosis and screening of the haemoglobinopathies. *Baillieres Clin Haematol* 1998, 11:215-238.
7. Mavrou A, Kouvidi E, Antsaklis A, Souka A, Kitsiou Tzeli S, Kolialexi A: Identification of nucleated red blood cells in maternal circulation: a second step in screening for fetal aneuploidies and pregnancy complications. *Prenat Diagn* 2007, 27:150-153.
8. Lo YM: Recent advances in fetal nucleic acids in maternal plasma. *J Histochem Cytochem* 2005, 53:293-296.
9. Locatelli F, Rocha V, Reed W, Bernaudin F, Ertem M, Grafakos S, Brichard B, Li X, Nagler A, Giorgiani G, Haut PR, Brochstein JA, Nugent DJ, Blatt J, Woodard P, Kurtzberg J, Rubin CM, Miniero R, Lutz P, Raja T, Roberts I, Will AM, Yaniv I, Vermylen C, Tannoia N, Garnier F, Ionescu I, Walters MC, Lubin BH, Gluckman E: Related umbilical cord blood transplantation in patients with thalassemia and sickle cell disease. *Blood* 2003, 101:2137-2143.
10. Pinto FO, Roberts I: Cord blood stem cell transplantation for haemoglobinopathies. *Br J Haematol* 2008, 141:309-324.
11. Orofino MG, Argiolu F, Sanna MA, Rosatelli MC, Tuveri T, Scalas MT, Badiali M, Cossu P, Puddu R, Lai ME, Cao A: Fetal HLA typing in beta thalassemia: implications for haemopoietic stem-cell
12. Pace BS, Zein S: Understanding mechanisms of gamma globin gene regulation to develop strategies for pharmacological fetal hemoglobin induction. *Dev Dyn* 2006, 235:1727-1737.
13. Sadelain M, Boulad F, Galanello R, Giardina P, Locatelli F, Maggio A, RivellaS, Riviere I, Tisdale J: Therapeutic options for patients with severe β-thalassemia: the need for globin gene therapy. *Hum Gene Ther* 2007,18:1-9.
14. Puthenveetil G, Scholes J, Carbonell D, Qureshi N, Xia P, Zeng L, Li S, Yu Y, Hiti AL, Yee JK, Malik P: Successful correction of the human beta thalassemia major phenotype using a lentiviral vector. *Blood* 2004, 104:3445-3453.
15. Galanello R, Cao A: Relationship between genotype and phenotype.Thalassemia intermedia. *Ann N Y Acad Sci* 1998, 850:325-333.
16. Galanello R, Perseu L, Melis MA, Cipollina L, Barella S, Giagu N, Turco MP,Maccioni O, Cao A:Hyperbilirubinaemia in heterozygous b-thalassemia is related to co-inherited Gilbert's syndrome. *Br J Haematol* 1997,99:433-436.
17. Origa R, Galanello R, Perseu L, Tavazzi D, Domenica Cappellini M, Terenzani L, Forni GL, Quarta G, Boetti T, Piga A: Cholelithiasis in thalassemia major. *Eur J Haematol* 2009, 82:22-25.
18. Economou-Petersen E, Aessopos A, Kladi A, Flevari P,Karabatsos F,Fragodimitri C, Nicolaidis P, Vrettou H, Vassilopoulos D, Karagiorga-Lagana M, Kremastinos DT, Petersen MB: Apolipoprotein E epsilon4 allele as a genetic risk factor for left ventricular failure in homozygous betathalassemia. *Blood* 1998, 92:3455-3459.
19. Kremastinos DT, Flevari P, Spyropoulou M, Vrettou H, Tsiapras D, Stavropoulos-Giokas CG: Association of heart failure in homozygous beta-thalassemia with the major histocompatibility complex. *Circulation* 1999, 100:2074-2078.
20. Longo F, Zecchina G, Sbaiz L, Fischer R, Piga A, Camaschella C: The influence of hemochromatosis mutations on iron overload of thalassemia major. *Haematologica* 1999, 84:799-803.
21. Perrotta S, Cappellini MD, Bertoldo F, Servedio V, Iolascon G, D'Agruma L, Gasparini P, Siciliani MC, Iolascon A: Osteoporosis in β-thalassemia major patients: analysis of the genetic background. *Br J Haematol* 2000, 111:461-466.
22. Dresner Pollack R, Rachmilewitz E, Blumenfeld A, Idelson M, Goldfarb AW:Bone mineral metabolism in adults with β-thalassemia major and intermedia. *Br J Haematol* 2000, 111:902-907.
23. Origa R, Satta S, Matta G, Galanello R: Glutathione S-transferase gene polymorphism and cardiac iron overload in thalassemia major. *Br J Haematol* 2008, 142:143-145.
24. Sollaino MC, Paglietti ME, Perseu L, Giagu N, Loi D, Galanello R: Association of alpha globin gene quadruplication and heterozygous beta thalassemia in patients with thalassemia intermedia. *Haematologica* 2009, 94:1445-1448.