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Comparative study of Serum Bilirubin and A:G ratio in Thalassemia children with normal subjects

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Abstract

Thalassemia is a form of inherited autosomal recessive blood disorder characterized by abnormal formation of hemoglobin. The abnormal hemoglobin formed results in improper oxygen transport and destruction of red blood cells. Resulting destruction of RBC leads to produce bilirubin, which ultimately metabolized in liver for excretion. In thalassemia the rate of destruction of RBC is so rapid that it exceeds the liver capacity to metabolize the excess bilirubin.

A total serum protein measures total amount of protein in blood serum as well as the amount of albumin/globulin. Significant decrease in total protein of thalassemia major compared to minor was found, many studies had done and those results claim that decrease in serum total protein in due to secondarily decreased synthesis of protein by the liver. The A/G ratio of thalassemia patients were decreased furthermore, in thalassemia patients show high level of globulin in sera. Also significant higher increases in globulin in sera of major thalassemia patients were noticed compared to thalassemia minor patients.

Since very scanty literature is available regarding serum bilirubin and A/G ratio in thalassemia children and whatever results are available are having divergent reports hence this proposal work is selected.

Keywords: Serum Bilirubin, Albumin, Globulin, A/G ratio

Introduction

Thalassemia (Thallasa is Greek for sea, Haema is Greek for blood).[1] Thalassemia (also known as mediterranean anemia, cooley's anemia; Beta thalassemia or Alpha thalassemia) is an inherited blood disorder affected by an abnormal form of hemoglobin. This blood disorders is most common inherited single gene disorder in the world. Its characterized by anemia due to enhanced RBC destruction.[2] A decrease in the rate of production of a certain globin chain or chains (α,β,γ,δ) impedes Hb synthesis and creates an imbalance with the other, normally produced globin chains.[3] Because 2 types of chains (α and non-α) pair with each other at a ratio close to 1:1 to form normal Hbs, an excess of the normally produced type is present and accumulates in the cell as an unstable product, leading to the destruction of the cell. This imbalance is the hallmark of all forms of thalassemia.

The type of thalassemia usually carries the name of the underproduced chain or chains. The reduction varies from a slight decrease to a complete absence of production. For example, when β chains are produced at a lower rate, the thalassemia is termed β+, whereas β-0 thalassemia indicates a complete absence of production of β chains from the involved allele.[4]

The Thalassemia syndrome is classified according to which of the globin chains, α or β, is affected. These 2 major groups, α- and β-thalassemia, are sub classified according to absent (α° and β°) or reduced (α^+ or β^+) globin chain synthesis. In addition, where γ-chains together with α-chains compose fetal hemoglobin (HbF) in the fetus and δchains in combination with α-chains compose hemoglobin A_2 in adults, impaired synthesis of γ-globin or δ-globin chains can occur.

Worldwide, 15 million people have clinically apparent thalassemic disorders. Reportedly, disorders worldwide, and people who carry thalassemia in India alone number approximately 30 million. These facts confirm that thalassemias are among the most common genetic disorders in humans; they are encountered among all ethnic groups and in almost every country around the world.[5]

India accounts for 10% of the total world thalassemia populations and approximate 1 in 20 in the general population is carrier of the mutated gene. Every year about 15,000 infants are born with hemoglobinopathies in India.[6]

Thalassemia affects the value of serum bilirubin and A/G ratio. Bilirubin is a tetrapyrrole and a breakdown product of heme catabolism. Bilirubin is then removed from the body through the stool (feces) and gives stool its normal color.[7] Bilirubin circulates in the bloodstream in two forms: Indirect (or unconjugated) bilirubin and Direct (or conjugated) bilirubin

The Albumins (formed from Latin: albumen "(egg) white; dried egg white") are a family of globular proteins, the most common of which are the serum albumins.[8]

Some Globulins are produced in the liver, while others are made by the immune system. Globulins, albumin, and fibrinogen are the major blood proteins.Albumin Globulin ratio or A/G ratio is a blood test, where the albumin value is divided by the globulin value. The normal serum albumin concentration is 3.6-5.4g/dl and that of globulin is 1.8-3.6g/dl; therefore, the normal A/G ratio is 1.36 (mean) with a normal range of 1.2-1.6.

Materials and methods

The proposed study was conducted in department of Biochemistry, Sardar Patel Medical College, Bikaner. The present study was comprised of 40 thalassemia children and 40 healthy subjects between the age group 4-16 years of both sex.

Blood sample of thalassemia children was taken after the consultation by Pediatrician, Department of Pediatrics, PBM Hospital, Bikaner. About 5.0 ml blood of thalassemic children was drawn in a perfectly clean dry syringe preferably disposable and then transferred to clean dry centrifuge tube allowed to clot at room temperature for 30 minutes. Then blood was precautionaly centrifuged. The serum was separately by centrifugation at 3000 revolutions per minute (rpm) for 10 minutes. Samples with of sign hemolysis were discarded. Analytical grade chemicals, standard were used and the Serum bilirubin, A/G ratio were estimated using enzymatic kit method by auto analyzer.

Results and discussion

The mean serum total bilirubin was increased to 1.94±1.24 mg/dl with a range of 0.70 to 7.80 mg/dl in thalassemia children. The increase level of serum total bilirubin level was statistically highly significant as compared to that of normal healthy children (control group) as evident by p-value which

is less than 0.0001 (p<0.0001) as shown in Table I. These findings results in close collaboration with the results obtained by Ali M Malik et al. [9]

Serum Direct bilirubin concentration was found to be 0.92±0.10 mg/dl with a range of 0.20 to 4.40 mg/dl in thalassemia children. The increase level of serum bilirubin level was statistically highly significant as compared to that of normal healthy children as evident by p-value which is less than 0.0001(p<0.0001) as shown in Table-I. These results were closely related to the studies of Ali M Malik et al. [9] and N Sultan et al. [10]

The mean serum Albumin was decreased to 3.31±0.92 gm/dl with a range of 1.90 to 5.40 gm/dl in thalassemic children. The decrease was statistically highly significant as compared to that of normal children as evident by p-value which is less than 0.0001 (p<0.0001) as shown in Table II. These results of our study were closely related to the study of Israa G Zainal et al. and Robiul Hasan Bhuiyan et al. [11,12]

The mean serum globulin was raised to 3.13±1.22 gm/dl with a range of 0.80 to 7.00 gm/dl in thalassemic children. The increase was statistically highly significant as compared to that of normal healthy children as evident by p-value which is less than 0.0001(p<0.0001) as shown in Table-II. These results are in close collaboration with the results obtained by Ali M Malik et al [9] and Robiul Hasan Bhuiyan et al.[12]

The mean A/G ratio was found to be 1.55±0.79 gm/dl with a range of 0.60 to 4.00 gm/dl in normal healthy children and it was decreased to 1.38±1.30 gm/dl with a range of 0.30 to 6.70 gm/dl in Thalassemic children. The decrease was statistically highly significant as compared to that of normal healthy children (control group) as evident by p-value which is less than 0.0001(p<0.0001) as shown in Table –III. These results of present series of study resembles with the findings of Saboor et al.[13].

Conclusion

Family history of thalassemia was more common in muslims than in any other religion. This may be due to the fact that there is trend of consanguineous marriages in muslims and this may cause increased frequency of Genetic diseases like thalassemia in them.

Table I: Comparison of Mean Serum Total Bilirubin Concentration (mg/dl) and Direct Bilirubin (mg/dl) in Thalassemia Subjects with Controls.

S.No.	Values	Total Bilirubin		Direct Bilirubin	
		Control Subject (n=40)	Thalassemia Subject (n=40)	Control Subject (n=40)	Thalassemia Subject (n=40)
1	Mean	0.96	1.938	0.47	0.9175
2	Range	0.400-1.600	0.700 – 7.800	0.200-0.900	0.200-4.400
3	SD	0.2827	1.238	0.221	0.1033
4	SE	0.4469	0.1958	0.03494	0.1033
5	T	21.48	9.896	13.45	8.884
6	DF	39		39	
7	p-value	<0.0001		<0.0001	

Table II: Comparison of Mean Serum Albumin Concentration (g/dl) Globulin (g/dl) in Thalassemia Subjects with controls.

		Mean Albumin Concentration		Mean Globulin Concentration	
S.No.	**Values**	**Control Subjects (n=40)**	**Thalassemia Subjects (n=40)**	**Control Subjects (n=40)**	**Thalassemia Subjects (n=40)**
1	Mean	3.675	3.310	2.705	3.130
2	Range	2.800-4.800	1.900-5.400	1.200-4.900	0.800-7.000
3	SD	0.5108	0.9151	0.9538	1.218
4	SE	0.08076	0.1447	0.1508	0.1926
5	t	45.50	22.88	17.94	16.25
6	DF	39		39	
7	p-value	<0.0001		<0.0001	

Table III: Comparison of Mean A/G Ratio in Thalassemia Subjects with Controls.

S. No.	**Values**	**Control Subjects (n=40)**	**Thalassemia Subjects (n=40)**
1	Mean	1.554	1.383
2	Range	0.600-4.00	0.300-6.700
3	SD	0.7870	1.302
4	SE	0.1244	0.2059
5	t	12.49	6.714
6	DF	39	
7	p-value	<0.0001	

The prevalence of β-thalassemia major is especially high in countries where there are close family marriage. Proper Genetic counseling can help decrease frequency of disease in these communities.

Resulting destruction of RBC leads to produce bilirubin production which ultimately metabolized in liver for excretion. In thalassemia the rate of destruction of RBC is so rapid that it exceeds the liver capacity to metabolize the excess bilirubin.

Liver disease associated with chronic blood transfusions in thalassemic children is caused decrease protein synthesis.

The increase level in serum globulin level significantly elevation in β-globulin fraction was observed in both major and minor thalassemia compared to normal control group.

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