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Comparison of Various Lipid Levels in Patients with B-Thalassemia Major with that of Normal Individuals

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Abstract **Original Research Article**

Background: Thalassemia is the most common heterogeneous group of genetic disorders in which the production of normal hemoglobin (Hb) is partly or completely suppressed because of defective synthesis of one or more globin chains that vary widely in severity from asymptomatic forms to severe or even fatal entities. Aim of this study is to compare of various lipid levels in patients with b-thalassemia major with that of normal individuals. ***Methods:*** In this cross sectional study, 30 children (case) previously diagnosed as beta thalassemia major were evaluated for serum lipid levels who were admitted at the Department of Pediatrics in DMCH & Thalassemia center of Dhaka Shishu Hospital from January 2012 to December 2012. The control group included 30 ages & sex matched healthy participants. Serum lipids profiles (total cholesterol, triglycerides, LDL- cholesterol, and HDL cholesterol) as well as hemoglobin, MCV, MCH & MCHC were compared between the two groups. P value < 0.05 was considered statistically significant. Serum total cholesterol (TC), Triglycerides (TG) and HDL cholesterol concentrations were measured by using Photoelectric Colorimeter (ERMA INC, model no AE-30F, made in Japan) in clinical biochemistry department of Dhaka Medical College. ***Results:*** Hematological tests showed the mean haemoglobin level in thalassemia group was 7.23 gm/dl with standard deviation of 1.23 whereas in control group the mean haemoglobin level was 10.37 gm/dl with standard deviation of 1.22. There was significant differences between two groups (p=.001). Mean MCV, MCH and MCHC in thaiassemic group were significantly lower [69.83 fl (SD 8.34), 23.10 pgm (SD 3.57) and 28.03% (SD-2.58)] than those in their control counterpart [8323 fl (SD 4.97), 29.23 pgm (SD 2.43) and 31.20% (SD-1.83)] respectively (p = 0.001 in all parameters). Beta thalassemia major patients had significantly lower high-density lipoprotein (HDL) and low-density lipoprotein (LDL) compare with controls (p<0.001). However, serum triglyceride levels of beta thalassemic males and females patients (203 ± 37.23, 221.21± 36.13 gm/dl respectively) were significantly higher than in control males and females (129.33 ± 13.88-124.53±15.23 gm/dl respectively) [p value < 0.001]. But total cholesterol level was not statistically significant between case & control groups. (P value 0.428). ***Conclusions:*** From the findings of the study it can be concluded that there is significant difference of various lipid levels between children with beta thalassemia major and normal healthy control which may help physicians to design the therapeutic module in the treatment of such patients.

Keywords: Beta thalassaemia major, Total Cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL), Low density lipoprotein (LDL).

INTRODUCTION

Thalassaemia occurs throughout the world and is one of the major public health problems in the endemic regions such as Mediterranean countries, Middle East, North Africa and Asia. Beta thalassaemia is considered to be the most frequent blood disorder worldwide[1]. Patients with this disease need repeated blood transfusion for survival. This may cause oxidative stress and tissue injury due to iron overload, altered antioxidant enzymes and other essential trace element levels. Lipid abnormalities have been detected in

different types of thalassaemia and also in various haematological disorders including sickle cell disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, spherocytosis, aplastic anaemia and myelodysplastic syndrome [1].

Beta thalassaemia major is a very serious condition where individuals with it are unable to make enough healthy red blood cells and depend blood transfusions all their life. However, quality and duration of life of transfusion-dependent thalassaemic patients has been transformed over the last few years, with their life expectancy increasing well into the third decade and beyond, with a good quality of life. Nevertheless, cardiac symptoms and premature death from cardiac causes are still major problems since.in the absence of effective iron chelation therapy, many patients develop evidence of iron-induced myocardial damage with cardiac failure, cardiac arrhythmia, sudden death, or a distressing lingering death from progressive congestive cardiac failure [2, 3].

During the past years many scientific evidences have raised the adverse effect of abnormal blood lipid levels, like total cholesterol -and other lipids and lipoproteins on atherosclerotic disease [4, 5].

Beta thalassemia is commonly associated with the shortened erythrocyte life span & excessive destruction of erythrocytes. Therefore blood transfusion is needed every 2-5 weeks to maintain a pre-transfusion Hb level above 10 g/dl [6]. Frequent blood transfusion in term can result in iron overload in key organs such as liver, heart & endocrine glands, resulting in heart failure, arrhythmia, hypothyroidism, hypoparathyroidism, diabetes mellitus, delayed puberty, growth retardation and so on. Most of these complications occur slowly and appear in the 2nd decade of the patient's life [7]. Lipid abnormality has been frequently reported in thalassaemia, but its pathophysiology is not totally clear [8-11]. In a recent study conducted by AB Patne, observed that low total serum cholesterol, low HDL-cholesterol and low LDL cholesterol with elevation of triglycerides in beta thalassaemia major patients, as compared to control subjects [12]. This alteration is likely due to diminished hepatic biosynthesis as of anemia and iron overload, while a reduced extrahepatic lipolytic activity could account for the rise in circulating TG [13].

OBJECTIVES

General objectives

- To compare various lipid levels in patient with β-thalassemia major with that of normal. individuals.

Specific objectives

- To evaluate the serum total cholesterol level in patient with β -thalassemia major
- To evaluate the serum triglyceride level in patient with β - thalassemia major
- To evaluate the serum HDL (high density lipoprotein) level in patient with β- thalassemia major

METHODOLOGY

Type of study	Analytical cross sectional comparative study
Place of study	Department of Pediatrics in DMCH & Thalassemia center of Dhaka Shishu Hospital
Study period	January 2012 to December 2012
Study population	Both male and-female child from 5 to 15 years and fulfilling the definition of thalassemia.
Sampling technique	Purposive

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

- Children suffering from thalassemia, diagnosed by Hb electrophoresis
- Age in between 5-I5 years
- Received at least IO times blood transfusion

Exclusion Criteria

- Age less than 5 years and more than 15 years
- Patients who received, less than 10 times of blood transfusion
- Seriously ill patients
- Children having diabetes mellitus, hypothyroidism, hyperthyroidism, renal failure and
- hereditary hyperlipidemia
- Patients with other co morbid conditions (stroke, acute abdomen, peritonitis, etc.)

Procedure of data analysis

After collection all the data were checked and edited. Then data were entered into computer with the help of software SPSS for windows programmed version 17 & double checked before analysis. After frequency run, data were cleaned and frequencies were checked. An analysis plan was developed keeping in view with the objectives of the study. Descriptive statistical analysis was carried out in this study. Results on continuous measurements are presented on Mean±SD (Min-Max) and _results on categorical measurements are presented in number (%). Student t test has been used to find out the significance of the study parameters on continuous scale. Chi-squre and one way ANOVA test has been used to find the significance of the study parameters on categorical scale between two or more groups.

RESULT

Out of 60 children, 48.33% were female where as 51.67% were male (figure 2), total 14 (23.33%) had come from a family of consanguineous marriage while 46 (76.66%) children had come from family of non-consanguinous parents. In beta thalassemia major group 09 (30%) children came from family of consanguinity where it were only 5(16.6%) in the control group (Figure 1).

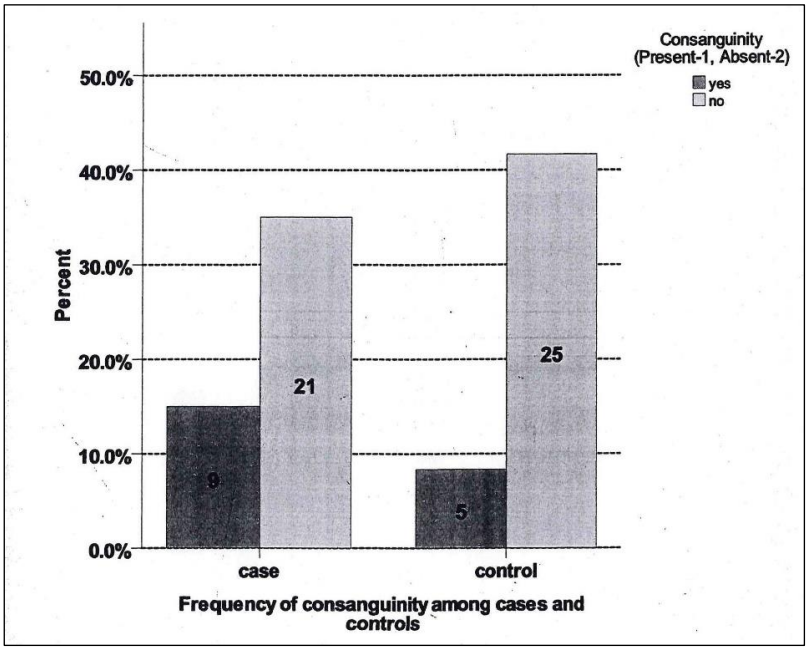

Figure 1: Status of consanguinity of the study population

Most common clinical characteristics are shown in Figure 4 & 5. Figure 4 shows degree of pallor between thalassemia group & the control group and in our study most of the thalassemic patient present with moderate pallor (60%) whereas most of control population was mildly pale (66.66%). Hundred percent children of thalassemia presented with spleenomegaly but only 16.66% (5 out of 30) presented with palpable liver (Figure 5).

Table 1 explains the status of family involvement where we can see 07 (.33%) of 30 children (case) had' affected family member & 10 (33.33%) had carriers of thalassemia in family.

Table 1: Status of thalassemia in family (n 30)

Parameters	Case (n=30)	
	Present	Absent
Thalassemia in family	07 (23.33%)	23 (76.66%)
Carriers of thalassemia in family	10 (33.33%)	20(66.66%)

Table 2 shows weight for age of the respondent & here was no significant difference between two groups (p=0.41) but significant difference of height for age between two groups (p=O.O l) were seen in Table 3. Among 30 thalassemia patients 2 patients were severely wasted and 5 patients (16.6%) were moderately wasted. In control group n-o children were severely wasted, 2 (6.6%) child were moderately wasted and rests are normal (Table 4). Six patients (20%) were severely stunted and 14 patients (46.6%) were moderately stunted in thalassemia group. Whereas no chil4 was severely stunted & only 2 (6.6%) child were moderately stunted in control group (Table 5).

Haematological parameters of both thalassemia group & control group are shown in Table 6. The mean haemoglobin level in thalassemia group was 7.23 gm/di with standard deviation of 1.23 whereas in control group the mean haemoglobin level was 10.37 gm/di with standard deviation of 1.22. There was significant differences between two groups (p=.001). RBC indices were statistically significant between thalassemia group & control group. The results of various lipid analyses of controls and thalassemic children are presented in Table 7. Beta thalassemia major patients had significantly lower high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) compared with controls ($p < 0.001$).

Table 2: Nutritional status of the cases (weight for age)

Group	Weight for age (%)				P (t - test)
	Mean	SD	Mini	Max	0.41
β thalassemia group	77.1%	7.85	60%	92%	
Control group	81.2%	4.2	75.5%	89.5%	

Table 3: Nutritional status of the cases (Height for age)

Group	Height for age (%)				P (t- test)
	Mean (%)	SD.	Mini	Max	0.01
Thalassemia group	88%	5.7	73%	96%	
Control group	91%	4.5	87%	97%	

Table 4: Nutritional status of the cases (Weight for Height-wasting)

Grading of wasting WHO Classification	Thalassemia group N=30'	Control group N=30	P value
Normal	23(76%)	28(93.3%)	NS
Moderate (-2.0 to -3.0SD)	5(16.6%)	2(6.6%)	
Severe (>-3.0)	2 (6.6%)	-	

Table 5: Nutritional status of the cases (Height for age - stunting)

Grading of stunting WHO classification	Thalassemia group N=30	Control group N=30	P value
Normal	10(33.3%)	28(93.3%)	<0.05
Moderate (-2.0 to -3.0SD)	14(46.6%)	2(6.6%)	
Severe (> -3.0SD)	6(2%)	-	

Table 6: Haematological parameters of the study population (n=60)

Haematological parameters	Thalassemic Group (n=30)				Control Group (n=30)				P Value
	Mean	SD	Mini	Max	Mean	SD	Mini	Max	
Haemoglobin (gm/dl)	7.23	1.23	4.4	9.5	10.37	1.22	8.0	12.5	.001
MCV(Fl)	69.83	8.34	54	88	83.23	4.97	74	92	.001
MCH(Pg)	23.10	3.57	17	7.23	29.23	2.43	25	33	.001
MCHC(%)	28.03	2.58	24	32	31.20	1.83	28	35	.001

Table 7: Serum Lipids (mean± SD) levels of male & female children with β- thalassemia major

Parameters (gm/dl)	Thalassemia Group (n=30)		Control Group (n=30)		p value
	Male (n=l6)	Female (n=l4)	Male (n=l5)	Female (n=l5)	
Total cholesterol	170.50 ± 22.83	173.14 ± 20.16	168.93 ± 17.81	166.13 ± 21.37	0.428
Triglyceride	2Q3 ± 37.23	221.21 ± 36.13	129.33 ± 13.88	124.53 ± 15.23	<.001
HDL-Ch	34.63 ± 5.43	36.0 ± 5.26	47.0 ±4.90	46.33 ± 5.37	<.001
LDL-Ch	71.13 ± 11.79	73.21 ± 13.27	94.33 ± 15.40	100.27 ± 11.30	<.001

DISCUSSION

In this study, total 51.67% children were male while 48.33% children were female. In thalassemia patients the male: female ratio was roughly 1:1, which is consistent with the study conducted in Bangladesh by Rahman & Jamal [14] where the same ratio was roughly 1:1. Mean age in the study group was approximately 100.85 months with standard deviation 24.1 months. The youngest and the oldest children were of 60 and 144 months respectively. These findings are almost consistent previous studies [15, 16].

Consanguinity seems to play an essential role in increasing the size of the problem in Mosul where 71.4% of the patients studied were the product of marriages between first and second cousins. Al-Haj [17] found higher results (88%) whereas a lower result (7%) was reported by Morshed. In our study out of 60 children, 23.33% children had come from a family with consanguinity of marriage while 76.66% had come from family of non-consanguinity of marriage. In β thalassemia group 30% children were from family of consanguinity while it was only in 16.66% in the control group. In the absence of local data about consanguinity of marriage & small sample size of our study, we cannot make any conclusion about it.

In our study out of 30 cases, twenty five had palpable liver and in 5 cases had not any palpable liver. In case of spleen, 100% cases were presented with palpable spleen. But in a local study nearly all patients had enlarged liver and spleen and 3 patients presented with previous splenectomy (n =126).

Hematological tests showed low Hb with a mean of 7.23 ± 1.23 gm/dl compared with ± 1.22 gm/dl in the control group. These results of low Hb among patients can be explained by the limited health education of the parents about the disease, so that, blood transfusion was used only when the patient showed clinical symptoms caused by severe anemia or simply just to sustain life [18]. Whereas reports from other countries focused on a super transfusion program (maintaining Hb le vel above 12 g/dl) or hyper transfusion program (where the Hb level never allowed dropping below 9 g/dl) [19].

Other haematological parameters of both groups were extremely variable. Mean MCV, MCH and MCHC in thalassemic group were significantly lower (69.83 fl, 23.10 pgm and 28.03%) than those in their control counterpart (83.23 fl, 29.23 pgm and 31.20 %). All three results were statistically significant (p =.0.001 in all parameters). These findings are favorably comparable with those of Vichinsky (Hb, MCV, MCH and MCHC were 7.8 gm/dl, 67 fl, 19 pgm and 28%) [20].

Beta thalassaemia major is one of t e most common genetic disorders worldwide. Lipid abnormality has been frequently reported in thalassaemia, but its pathophysiology is not totally clear. In this study, we observed low HDL-cholesterol and low LDL cholesterol with elevation of triglycerides in beta thalassaemia major patients, as compared to control subjects. We found, beta thalassemia major patients had significantly lower high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) compared with controls ($p < 0.001$). However, serum triglyceride levels of beta thalassemic males and females patients (203 ± 37.23, 221.21 ±36.13 gm/di respectively) were significantly higher than in control males and females (129.33 ± 13.88, 124.53 ± 15.23 gm/di respectively) [p value< 0.001]. But total cholesterol level was not statistically significant between case & control groups. (P value 0.428).

Our results agree with previous findings with regard to the above altered serum lipid. Pattern in patients with beta thalassaemia major. But we found no statistically significant difference of total cholesterol level between thalassemia group & control group which is not consistent with some studies but consistent with a study done by Ferdaus M Z, Hasan A. K.M. & Shekhar HU of Dhaka University [21]. This alteration is likely due to diminished hepatic biosynthesis as of anemia and iron overload, while a reduced extrahepatic lipolytic activity could account for the rise in circulating TG [22].

HDL cholesterol we observed that thalassaemic patients had very low values. Studies suggest that risk for myocardial infarction is high when HDL cholesterol is lows. The later may highlight the importance of total to HDL cholesterol ratio for the evaluation of blood lipids and the prevention of atherosclerotic disease. It has also been reported that the total cholesterol-to-HDL cholesterol ratio predicts coronary heart disease risk regardless of the absolute LDL- and HDL-cholesterol.51 We could suggest that thalassaemic patients are at much higher coronary risk than their matched controls, because of the low HDL cholesterol production, even if they are within normal values of total cholesterol.

CONCLUSIONS

In conclusion, our study revealed that there was significant difference of various lipid levels between children with beta thalassemia major and normal healthy control which may help physicians to design the therapeutic module in the treatment of such patients. Awareness to these findings is helpful to avoid unnecessary evaluation in patients with beta-thalassemia.

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