www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i7.71

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Study of Serum Lipid Profile in Beta-Thalassemia Major Patients

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Abstract

Objectives

1. *To assess the Serum Lipid Profile of patients with Beta-Thalassemia Major.*
2. *Comparison of the Serum lipid profile of Beta-thalassemia major patients with healthy children.*

Study Design: *This was a cross sectional case control study in which 100 diagnosed cases of Beta thalassemia major were enrolled. 100 healthy children of same age group consisted of control group. The blood samples of study and control groups were examined for lipid profile test and values were evaluated. The tests were done using Olympus AU400 Auto analyser and values were evaluated. Statistical analysis was done by using IBM SPSS version 20.*

Results: *Mean age of cases was 9.04 ± 4.11 years and of controls was 8.92 ± 4.0 years. The mean values of serum HDL-C, LDL-C, total cholesterol, TG and VLDL in cases were 26.5±8.9, 62.1±21.9, 111.8 ±26.7, 112.06±53.40, 25.58±21.15 mg/dl respectively. Moreover, the mean values of serum HDL-C, LDL-C, total cholesterol, TG and VLDL in controls were 47.6±4.3, 76.8 ±15.4, 76.8 ±15.4, 74.64±16.23, 22.63±6.6715 mg/dl respectively. Total-cholesterol to HDL-C ratio was4.57±1.55 and 2.66±0.39 in cases and controls respectively. Total cholesterol, HDL-C, LDL-C were significantly lower ($p<0.05$); triglycerides and total cholesterol & HDL ratio were significantly higher ($p<0.05$) compared with controls.*

Conclusion: *Beta thalassemia major patients have hypertriglyceridemia and hypocholesterolemia. This study concludes that children suffering from beta thalassemia major may possess increased risk of thrombotic and atherogenic complications. Early detection of these patients with deranged lipid profile is required to avoid these complications. It is also important to do routine periodical screening.*

Keywords: *Beta Thalassemia Major, Lipid Profile, Hypocholesterolemia, hypertriglyceridemia, Thromboembolism.*

Introduction

Beta-thalassemia is the commonest single-gene disorder in the Indian population [1-3]. Beta thalassemia major is caused by complete absence of beta globin chain production resulting from reduced synthesis of one or more globin chains which can be caused by different globin gene mutation resulting in ineffective hematopoiesis, increased hemolysis and early onset anemia [4]. Ten percent of the total worlds thalassemic are born in India every year. Certain communities in India, like Sindhis, Guajarati's, Punjabis, and Bengalis, are more commonly affected with beta thalassemia, the incidence varying from 1 to 17%

[3,5]. It has been estimated that the prevalence of pathological hemoglobinopathies in India is 1.2/1,000 live births, and with approximately 27 million births per year this would suggest the annual birth of 32,400 babies with a serious hemoglobin disorder [6].

Reportedly, there are about 240 million carriers of β-thalassemia worldwide, i.e. 1.5% of world population. [7,8]. A WHO update on beta-thalassemia in India indicated a similar overall carrier frequency of 3–4%, based on that the current national population would translate to between 35.6 and 47.5 million carriers of the disorder nationwide. The mainstay of treatment of thalassemia is regular blood (Packed Red Blood Cells) transfusions. The major complications of blood transfusion are those related to transmission of infectious agents or development of iron overload [9].

Over the past three decades, regular blood transfusions and iron chelation have dramatically improved the quality of life and transformed thalassemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life. Today life expectancy of these patients varies between 25-55 years, depending on the compliance with medical treatment. Despite increased life expectancy, complications keep arising [10].

Various endocrine, cardiac, and hepatic diseases may occur depending, on excessive iron-loading. Thalassemic patients are also subjected to peroxidative tissue injury [11, 12]. Variants of lipoproteins, cholesterol and triglyceride in thalassemic patients show marked oxidative modification due to free radical injury that could represent an event leading to pathogenesis [13]. Free-radical production is increased in patients with iron overload. Hypertryglyceridemia coupled with cardiac iron overload is responsible for many cardiovascular complications seen in these patients. Hence we intent to study the serum lipid profile in the beta thalassemic majorpatients The aim of the study is to assess the serum lipid profile of patients with beta-thalassemia major and compare the findings with healthy control participants.

Materials and Methods

A cross-sectional; case control study was done between Jan 2013 to Dec 2014 at a tertiary care hospital in a large Metropolitan city. In total;100 diagnosed Cases of beta-thalassemia major in the age group of 1 year to 18 years receiving regular blood transfusions; not suffering from any ailment or any other disease leading to deranged lipid profile were included. In controls; 100 normal healthy children were included. Approval of Institutional Ethical Committee was obtained. After explaining about purpose of study, outcome and explaining that respondent can refuse and withdraw from study at any time in local language an informed consent was taken. All details were recorded in a pre-tested pro-forma which included personal information, transfusion history, clinical examination and lipid profile of the patients. Lipid profiles were done using Olympus AU400 auto analyzer. Statistical analyses were performed by using IBM SPSS Statistics 20.

Results

Out of total 100 cases, 45 were female and 55 were male while out of total 100 controls 41 were female and 59 were male. Mean age of cases was 9.04 ± 4.11 years and of controls was 8.92 ± 4.0 years (Figure 1).

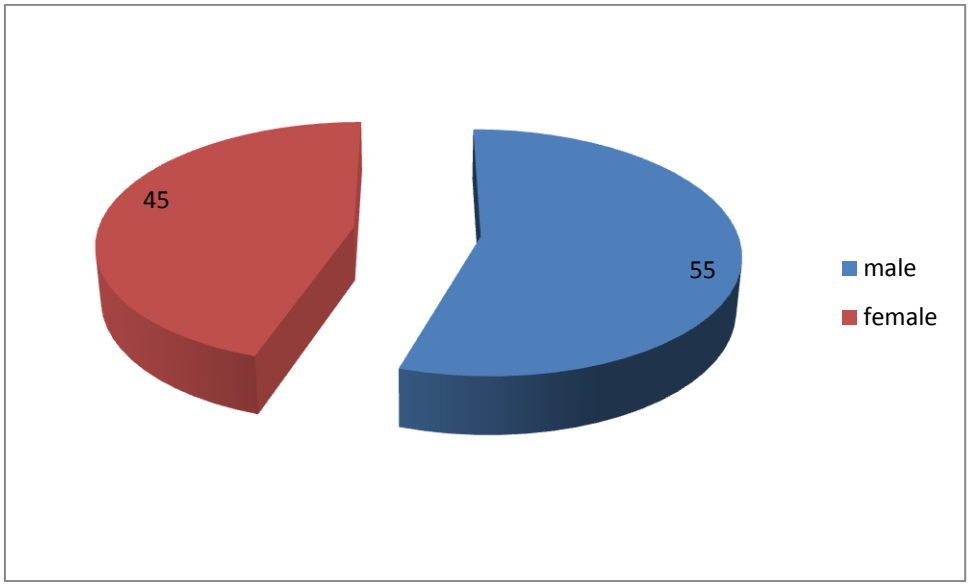

Figure 1: Gender Distribution of the studied cases.

Mean weight of cases were 21.59±8.08 Kgs with a mean height of 119.82±21.38 cms and 8.1±0.92 mg/dl Hb level. Mean weight of controls were 29.2±10.4 Kgs with mean height of 132.0±26.3 cms and 12.6±1.07 mg/dl Hb level. All cases had undergone regular blood transfusion.

Off the 100 cases, 91 patients (91%) were on Oral chelator therapy, eitherwith Defipirone or Deferasirox. 9 patients were not on any oral chelator therapy (Figure 2) ‘

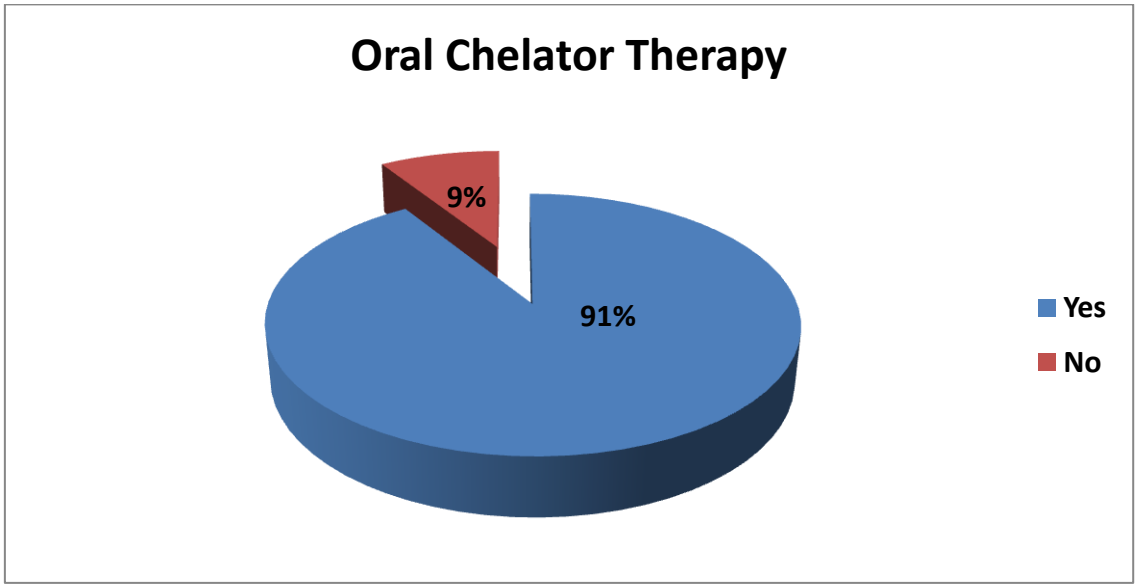

Figure 2 : Iron Chelation Status of Studied cases.

Study of cases revealed that amongst 100 cases, 99 were having Total Cholesterol within Normal range, while only 1 case showed Total Cholesterol above Normal range i.e. Hypercholesterolemia. Out of the 100 cases, 86 cases were having low HDL-C while remaining 14 cases were having HDL-C within normal range. Further analysis revealed that out of 100 cases, 98 cases were having LDL-C within Normal range, while only 2 cases were having High LDL-C values (Table 1).

Table 1 : Status of Cholesterol, HDL-C and LDL-C in studied cases.

	Frequency (n=100)	Percent
Total Cholesterol		
Normal	99	99.0
Hypercholesterolemia	1	1.0
HDL-C		
Low HDL-C	86	86.0
Normal	14	14.0
LDL-C		
Normal	98	98.0
High LDL	2	2.0

As shown in Table below (Table 2) out of 100 cases 87 were having normal values of VLDL-C while only 13 cases were having VLDL-C above normal range.

Table 2: VLDL levels in studied cases.

	Frequency (n=100)	Percent
Normal	87	87.0
High VLDL-C	13	13.0

Further when triglyceride levels were studied it was found that out of 100 Cases, 51 cases were having normal Triglyceride levels while 49 cases were having Triglycerides above normal range, i.e. Hypertriglyceridemia (Figure 3).

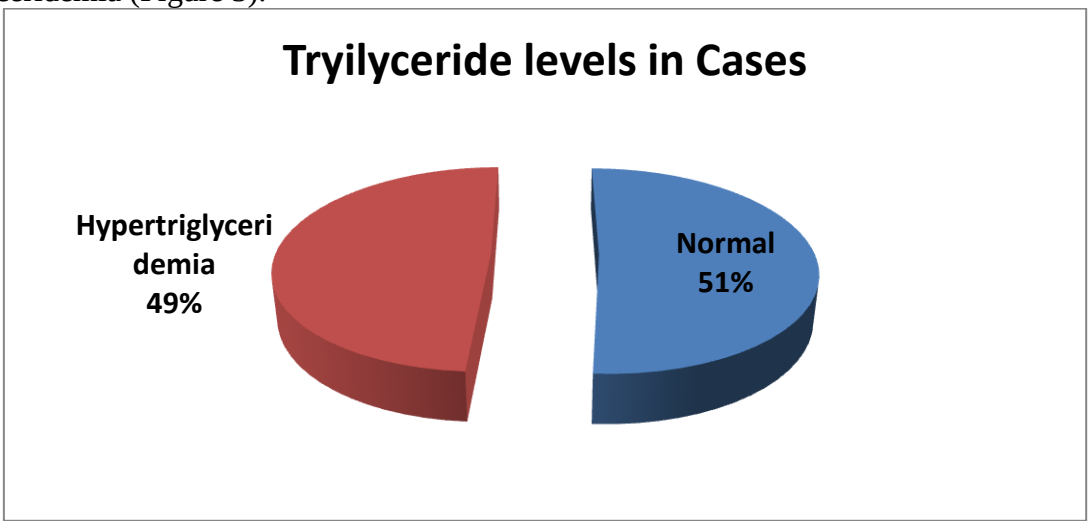

Figure 3: Triglyceride levels in studied cases

The mean values of the investigated blood lipids both in cases and controls are presented in Table-3 and Table 4 respectively.

Table 3: Analysis of Blood lipids in cases

Parameters	HDL-C (mg/dl)	LDL-C (mg/dl)	TC (mg/dl)	TG (mg/dl)	VLDL-C (mg/dl)	TC/HDL Ratio
Mean	26.55	62.11	111.89	112.06	25.58	4.57976
Median	26.00	62.50	113.50	99.50	22.00	4.57576
Std. Deviation	8.966	21.981	26.749	53.405	21.153	1.558721
Minimum	9	17	47	33	7	2.137
Maximum	53	115	174	345	191	10.143

Table 4 : Analysis of blood lipids in control group

Parameters	HDL-C **(mg/dl)**	LDL-C **(mg/dl)**	TC **(mg/dl)**	TG **(mg/dl)**	VLDL-C **(mg/dl)**	TC/HDL Ratio
Mean	47.66	76.84	126.12	74.64	22.63	2.66636
Median	47.00	77.50	128.00	74.00	23.00	2.60682
Std. Deviation	4.384	15.432	15.282	16.234	6.680	.398440
Minimum	41	50	100	50	12	1.906
Maximum	55	99	150	100	35	3.571

.Data analysis revealed, mean HDL-cholesterol levels were26.5±8.9 mg/dl in cases and 47.6±4.3 mg/dl in controls; mean LDL-cholesterol levels were 62.1±21.9 mg/dl in cases and 76.8 ±15.4 mg/dl in controls; mean total- cholesterol levels were 111.8 ±26.7 mg/dl in cases and 76.8 ±15.4 mg/dl in controls; mean triglyceride levels were 112.06±53.40 mg/dlin cases and 74.64±16.23mg/dl in controls; VLDL-cholesterol levels were 25.58±21.15mg/dlin cases and 22.63±6.67/dl in controls. Total-cholesterol to HDL-cholesterol ratios were 4.57±1.55 and 2.66±0.39 in cases and controls respectively.

Table 5: Comparison of various parameters of lipid profile in cases and control group

Parameters	Cases		Controls		Test value	p value
	Mean	SD	Mean	SD		
HDL-C	26.5500	8.96613	47.6600	4.38367	-21.151	.000
LDL-C	62.1100	21.98112	76.8400	15.43165	-5.485	.000
TC	111.8900	26.74908	126.1200	15.28205	-4.619	.000
TG	112.0600	53.40541	74.6400	16.23410	6.704	.000
VLDL-C	25.5800	21.15273	22.6300	6.67977	1.330	.185
TC/HDL-C Ratio	4.5798	1.55872	2.6664	.39844	11.893	.000

Above table (Table 5) shows the results of various lipid analyses of controls and thalassemic children. It is clear from the results that beta thalassemia major patients had significantly lower total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprsotein cholesterol (LDL-C) compared with controls ($p<0.05$).However triglycerides were significantly higher compared with controls ($p<0.05$). Very low density lipoprotein cholesterol (VLDL-C) were high in the beta thalassemia major patients but non-significant difference compared with controls ($p>0.05$). Total cholesterol & High-density lipoprotein cholesterol Ratio was significantly higher compared with controls ($p<0.05$).

Discussion

In this study lipid profile in beta thalassemia children were evaluated &compared it with a group of healthy children. In our study it was found that there is significant difference in between the values of cases and controls. It is seen that in beta thalassemia major Patient's serum levels of HDL-C, LDL-C and TC is low as compared to controls. In addition of that Triglyceride levels were substantially high. This appears because of many factors. The VLDL-C does not show any significant difference in the values, i.e. neither low nor high. Results of present study correlate well with previous study [14-19].

Most studies explain the mechanism of alteration in lipid profile of cases. This alteration is likely due to diminished hepatic biosynthesis as of anemia and iron overload, while a reduced extra hepatic lipolytic activity could account for the rise in circulating TG [14]. Iron-loading and the effects of repeated blood transfusions induce a hepatic acute-phase response, which could determine an LDL-class shift towards protein-rich, denser particles [14,17].

Some authors [15,20-24] suggested that accelerated erythropoiesis and increased uptake of LDL by macrophages and histiocytes of the reticulo endothelial system are the main determinants of low plasma cholesterol levels in beta thalassemia major.

Factors such as iron overload (high ferritin level), liver injury, and hormonal disturbances affects lipids pattern among patients with major form of beta-thalassemia, while some researchers observed that the lipid profile in thalassemia major patients is not influenced by age, sex, liver injury, and hemoglobin or ferritin levels [15]. The higher erythroid bone marrow activity with the enhanced cholesterol consumption could be the dominant mechanism implicated in the lipid abnormalities of thalassemia major patients [15, 25]. However other researchers did not find such differences.

Study comparing thalassemia major and intermedia demonstrated the lower concentrations of LDL-C found in with beta thalassemia major than with beta thalassemia intermedia patients could be related to the higher level of Hb and ferritin in patients with beta thalassemia major [26].

In thalassemia minor patients; Total cholesterol and LDL-C is lower, authors found nostatistically significant difference in TG, HDL and VLDL among thalassemia minor patients compared to control group [27]. The study also concluded the concentration of Total-C and LDL-C which in thalassemia carriers arebelow the normal levels, which can potentially reduce the risk of cardiovascular diseases. The Lipid-lowering effect of beta-thalassemia trait in minor thalassemiaraises the question as to whether this effect might slow down the progression of coronary diseases and delay the occurrence of myocardial infarction in these patients. This difference in finding is due to different trait studied; minor and major respectively.

Our findings of hypocholesterolemia and hypertriglyceridemia in patients of beta thalassemia major were supported by other studies [28, 29].

Finding of study shows that majority of the patients had blood lipid levels within the normal range, and consequently the prevalence of lipid abnormalities was much lower as compared to the general population of the same age this is contrary to other studies [30]. Same study gives exception of HDL-C which was below normal range. Also, the total-cholesterol to HDL-cholesterol ratio was high in patients, and may underline the importance of this index for the prognosis of future cardiac events in these patients which is in accordance with our study findings [30]. The importance of total-cholesterol to HDL-cholesterol ratio lies in prevention of atherosclerotic disease. The total-cholesterol-to-HDL-C ratio predicts coronary heart disease risk. Higher the ratio the higher is the risk for atherosclerotic and thrombotic complications.

Some study uses LDL/HDL ratio as a major of risk. Study found that LDL/HDL ratio was low which is suggestive of risk for atherosclerosis and thromboembolic events in beta Thalassemic children, which also supports our interpretation [31].

Beta thalassemia major patients have hyper triglyceridemia and hypocholesterolemia. No patient at present can be identified on the basis of clinical features of having a deranged lipid profile. Only way is by means of routine screening. Early detection of these patients with deranged lipid profile is required to avoid thrombotic and atherogenic complications. Patient with deranged lipid profile should undergo dietary and lifestyle modifications and may be started on lipid lowering agents like Statins or other agents if not controlled on dietary or lifestyle modifications. A regular follow up of these patients is to be carried out. It can be concluded that children suffering from Beta Thalassemia Major may possess increased risk of cardiovascular thrombotic disease and thrombotic complications in other organs. For better understanding and establishment of this cause effect relation, a longitudinal cohort study should be carried on lipid profiles in patients with beta thalassemia patients in relation to clinical features.

Conclusion

Lipid profile in Beta thalassmia patients show significantly low levels of total cholesterol, LDL-C and HDL-C. There was increase in triglyceride levels and total cholesterol/HDL-C ratio. VLDL-C levels were normal in these patients. From above observations it can be concluded that children suffering from Beta thalassemia Major may possess increased risk of cardiovascular thrombotic disease and thrombotic complications in other organs. Since it is impossible to predict these changes clinically hence a regular blood lipid profile should be regularly carried out in patients with beta thalassemia major.

Conflict Of Interest: None

References

1. Louis C.K. Low. Growth of children with beta thalassemia major. Indian J Pediatr 2005 Feb; 72:159- 160.
2. Verma IC, Choudhry VP, Jain PK. Prevention of thalassemia: A necessity in India. Indian J Pediatr 1992; 59: 649-654.
3. Agarwal, S., A. Gupta, U. R. Gupta, S. Sarwai, S. Phadke, and S. S. Agarwal. "Prenatal diagnosis in beta-thalassemia: an Indian experience." *Fetal diagnosis and therapy* 18, no. 5 (2003): 328-332.
4. Modell, Bernadette, and Matthew Darlison. "Global Epidemiology of Haemoglobin Disorders and Derived Service Indicators." *Bulletin of the World Health Organization* 86.6 (2008): 480–487. *PMC*. Web. 14 Dec. 2014.
5. Madan, N., Sharma, S., Sood, S. K., Colah, R., & Bhatia, (Late) H. M. (2010). Frequency of β-thalassemia trait and other hemoglobinopathies in northern and western India. *Indian Journal of Human Genetics*, *16*(1), 16–25. doi:10.4103/0971-6866.64941
6. Galanello R, Eleftheriou A, Traeger-Synodinos J, Old J, Petrou M, Angastiniotis M. In: Princeton of Thalassaemias and other Haemoglobin-opathies. 2003. Annex 1: Global epidemiological data tables; pp. 148–53.
7. Yaish HM. Thalassemia. http:// www.emedicine.com/PED/topic2229.htm Accessed as on date 6th August 2013.
8. Verma IC, Choudhry VP, Jain PK. Prevention of thalassemia: A necessity in India. Indian J Pediatr 1992; 59: 649-654.
9. Roberts D.J., Brunskill S.J., Deree C. Oral Deferiprone for Chelation in children with Thalassemia. National Blood Service, Systematic Review Initiative, UK OX3 9BQ.
10. Grow, Kirti, MinakshiVashist, PankajAbrol, Shiksha Sharma, and RituYadav. "Beta Thalassemia in India:

Current Status and the Challenges Ahead." *International Journal of Pharmacy & Pharmaceutical Sciences* 6, no. 4 (2014).

11. Arıca, Vefik, Seçil Arıca, CahitÖzer, and Murat Çevik. "Serum Lipid Values in Children with Beta Thalassemia Major." *PediatTherapeut* 2, no. 130 (2012): 2161-0665.
12. Shamshirsaz, Alireza A., Mir Reza Bekheirnia, Mohammad Kamgar, Nima Pourzahedgilani, NavidBouzari, Mohammadreza Habibzadeh, Reza Hashemi et al. "Metabolic and endocrinelogic complications in beta-thalassemia major: a multicenter study in Tehran." *BMC Endocrine Disorders* 3, no. 1 (2003): 4.
13. Omran, DakhelGhani. "Lipid Profile in Children with Beta–Thalassemia Major in Babylon."
14. Al-Quobaili, Faizeh A., and Imad E. AbouAsali. "Serum levels of lipids and lipoproteins in Syrian patients with beta-thalassemia major." *Saudi medical journal* 25, no. 7 (2004): 871-875.
15. Mansi, Kamal M., and Talal A. Aburjai. "Lipid Profile in Jordanian Children with ß-thalassemia Major." *International Journal of Hematology and Oncology* 18 (2008): 93-98.
16. Patne, A. B., P. J. Hisalkar, and S. B. Gaikwad. "Lipid Abnormalities in Patients of Beta Thalassaemia Major. "IJPBS, vol(2),issue 2,April-June(2012);106-112
17. Arıca, Vefik, Seçil Arıca, CahitÖzer, and Murat Çevik. "Serum Lipid Values in Children with Beta Thalassemia Major." *PediatTherapeut* 2, no. 130 (2012): 2161-0665.
18. Khubchandani, Asha, Viral Solanki, VijaysinhParmar, Meghana Solanki, Jaimin Patel, and SagarGangwani. "Estimation of Serum lipid profiles in patients with Beta-thalassemia major."
19. KhaleedJumaa K., Abeer A.A., MaysemM.Alwash, Nahi Y. Yaseen, Ahmed M.Hamza "*Biomarkers and trace elements in beta thalassemia major*." Iraqi Journal of Cancer and Medical Genetics.
20. Maioli, M., G. B. Cuccuru, P. Pranzetti, A. Pacifico, and G. M. Cherchi. "Plasma lipids and lipoproteins pattern in beta-thalassemia major." *Actahaemat-ologica* 71, no. 2 (1984): 106-110.
21. Maioli, Mario, Silvestro Pettinato, Gian Mario Cherchi, DomenicoGiraudi, Adolfo Pacifico, Giuseppe Pupita, and Massimo GB Tidore. "Plasma lipids in beta-thalassemia minor." *Atherosclerosis* 75, no. 2 (1989): 245-248.
22. Maioli, Mario, Giovanni B. Vigna, Giancarlo Tonolo, PatriziaBrizzi, MilcoCiccarese, Paola Donegà, MargheritaMaioli, and Renato Fellin. "Plasma lipoprotein composition, apolipoprotein (a) concentration and isoforms in β-thalassemia." *Ather-osclerosis* 131, no. 1 (1997): 127-133.
23. Christina C, Demosthenes B, Christos P. Distributionof serum lipids and lipoproteins in patients with beta thalassemia major; an epidemiological study in young adults from Greece.Lipids in Health and Disease 3: 328-334, 2004.
24. Goldfarb AW, Rachmilewitz EA, Eisenberg S. Abnormal low and highdensity lipoproteins in homozygous beta-thalassaemia. *Br J Haematol*. 1991;79:481-486.
25. Amendola, G., P. Danise, N. Todisco, G. D'urzo, A. Di Palma, and R. Di Concilio. "Lipid profile in β-thalassemia intermedia patients: correlation with erythroid bone marrow activity." *International journal of laboratory hematology*29, no. 3 (2007): 172-176.
26. Hartman, Corina, Hannah Tamary, Ada Tamir, Evelyn Shabad, Carina Levine, Ariel Koren, and Raanan Shamir.

"Hypocholesterolemia in children and adolescents with β-thalassemia intermedia." *The Journal of pediatrics* 141, no. 4 (2002): 543-547.

27. Hashemieh, M., M. Javadzadeh, A. Shirkavand, and K. Sheibani. "Lipid profile in minor thalassemic patients: a historical cohort study." *Bangladesh Medical Research Council Bulletin* 37, no. 1 (2011): 24-27.
28. Shams, Sedigheh, Mohammad TaghiHaghi Ashtiani, Maryam Monajemzadeh, Leili Koochakzadeh, HeshmatIrani, Fahimeh Jafari, and AmenehMohseni. "Evaluation of Serum Insulin, Glucose, Lipid Profile, and Liver Function in β-Thalassemia Major Patients and Their Correlation With Iron Overload." *Lab Medicine* 41, no. 8 (2010): 486-489
29. Zannos-Mariolea L, Papagregoriou-Theodoridou M, Costantzas N, et al.Relationship between tocopherols and serum lipid levels in children withbeta-thalassemia major. *Am J ClinNutr*. 1978;31:259–26332.Christina et al
30. Ferdaus, Mohammed Zubaerul, A. K. M. M. Hasan, and Hossain Uddin Shekhar. "Analysis of serum lipid profiles, metal ions and thyroid hormones levels abnormalities in β-thalassaemic children of Bangladesh." *JPMA. The Journal of the Pakistan Medical Association* 60, no. 5 (2010): 360.
31. Ragab, S. M., M. A. Safan, and A. S. Sherif. "Lipid profiles in β thalassemic children." *Menoufia Medical Journal* 27, no. 1 (2014): 66.