

Frequency of Diabetes Mellitus in Thalassemia Major Patients

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ABSTRACT

Objective: Aim of current study is to examine patients of major thalassemia and determine prevalence of diabetes mellitus among these cases.

Study Design: Cross-sectional

Place and Duration: DHQ Teaching Hospital Sargodha. Dec 2020-May 2021

Methods: Total 200 hundred patients of major thalassemia with ages 15-45 years were included. After obtaining written consent from the patient, demographic information such as age, sex, and body mass index were gathered. Fasting blood samples were used to estimate the FBS. Medical records were used to collect clinical and laboratory data, such as counts of red blood cells, Hb levels before transfusion, and five-year ferritin levels. Chi-square, student t-tests, and logistic regressions were used for statistical analysis. The whole set of data was analysed with SPSS 24.0.

Results: In major thalassemia patients majority of the cases were females 120 (60%) and 80 (40%) were total males. Mean age of the patients was 21.6±8.23 years and had mean BMI 20.5±9.19 kg/m². Frequency of DM among major thalassemia cases were 18 (9%). Mean five year ferritin among cases was 5214.3±2531 ng/ml. Among 18 cases of DM most of the patients were males 12 (66.7%) and 6 (33.3%) were females. Patients with ages >25 years and ferritin value >6000 ng/ml had increased risk of DM. Mean blood transfusion in DM patients was 2.9±3.66 U/mo with mean duration 15.8±4.17 years.

Conclusion: We found from this study that the prevalence of diabetes in major thalassemia patients was 9 percent, with the majority of cases being male. We believe this is attributable to older age, a higher mean five-year ferritin level, and a greater amount of blood transfused.

INTRODUCTION

T-thalassemia major is an autosomal recessive hemolytic disease that has an extremely severe form of the disease. After a decrease in the formation of α -globin chains, it causes severe anaemia. The eastern coast of the Mediterranean area, which includes the Arabian Peninsula, Turkey, Iran, India, and Southeast Asia, is becoming a thalassemia belt. Thalassemia major is one of the most common genetic illnesses in Iran, with more than 18800 individuals suffering from it. [2-3] In order to prevent consequences such as chronic anaemia and bone abnormalities, these people get blood on a regular basis. [4] Blood transfusions have significantly increased the life expectancy of people with thalassemia major in the previous two or three decades. [5] Increasing use of this medicine has also resulted in iron overload side effects. In the endocrine system, iron excess may cause problems. [6] DM is a severe endocrine problem in TM with prevalence of 20-30 percent [7]. Background pathophysiologic mechanism leading to DM in TM is unknown; some view the iron generated pancreatic cytotoxicity as the most important impact. While this was a common perspective, a fresh idea proposes the loss of beta pancreatic cells subsequent to a lengthy period of hyperinsulinemia could be implicated in development of DM in TM [8]. The later idea is further backed by study demonstrated a larger fasting insulin level and beta cell activity in TM patients [9]. Thalassaemia associated DM has been discovered to be especially more widespread in aged adults, and has been considered to be answerable for high frequency of morbidities. DM has been connected with increased prevalence of cardiac issues and heart failure in TM [10]. In fact, DM may lead to a continuing organ degeneration when applying chelation treatment in TM patients [11]. Regarding prevalence and comorbidities associated with DM, understanding of risk factors connected with the thalassaemia related DM is crucial.

Iron overload is a side effect of treatment, which requires regular blood transfusions. These patients' life expectancy and quality of life have improved significantly over the last two to three decades because to hyper-transfusion treatment [13]. As a result of the iron overload, there has been a rise in the occurrence of these therapeutic difficulties. Endocrine glands are one of the iron excess unfavourable effects. Growth retardation, hypogonadism, insulin dependent diabetes mellitus, hypothyroidism, and hyperparathyroidism may occur even in appropriately treated individuals. A lack of iron chelation may be the cause of widespread endocrine problems in severely thalassaemic

individuals living in less developed countries. A chelating drug called desferrioxamine has recently been shown to be effective in reducing tissue damage caused by iron buildup.

In the current study, we looked at the frequency of diabetes and its related variables in individuals with significant thalassemia.

MATERIAL AND METHODS

This cross-sectional study was conducted at DHQ Teaching Hospital Sargodha and comprised of 200 patients. After obtaining written consent from the patient, demographic information such as age, sex, and body mass index were gathered. Excluded patients were those under the age of 15 and those who had undergone fewer than eight units of blood transfusion.

The Hb level was kept above 10 g/dl and only went as low as 7 g/dl on rare occasions owing to patients being late for appointments. In addition, we meticulously examined the patient's medical records for any history of hepatitis C or B infection, pre-transfusion Hb and cell counts, and liver enzymes such as Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) (ALT). Using data from the three most recent times you received blood, we derived these metrics. Using blood receiving records from the previous year, an average amount of blood was computed for each occurrence. In addition, ferritin was determined as a mean value for the last five years. Samples of fasting blood were used to calculate FBS. If a patient's FBS level was below 126 mg/dl or if they had already had insulin treatment, they were regarded to have diabetes. When the FBS level was between 100 and 125 mg/dl, it was considered to be IFG, and the normal FBS level was set at less than 100 mg/dl. We used a chi-square test to see if there was any correlation between category factors and DM or IFG. Logistic regression was used to identify risk factors for diabetes mellitus (DM). The whole set of data was analyzed with SPSS 24.0.

RESULTS

Majority of the cases were females 120 (60%) and 80 (40%) were total males. Mean age of the patients was 21.6±8.23 years and had mean BMI 20.5±9.19 kg/m². (table 1)

Frequency of DM among major thalassemia cases were 18 (9%). (fig 1)

Among 18 cases of DM most of the patients were males 12 (66.7%) and 6 (33.3%) were females. (table 2)

Table 1: Characteristics of enrolled cases

Variables	Frequency	Percentage
Mean Age (years)	21.6±8.23	
Mean BMI (kg/m ²)	20.5±9.19	
Gender		
Female	120	60
Male	80	40

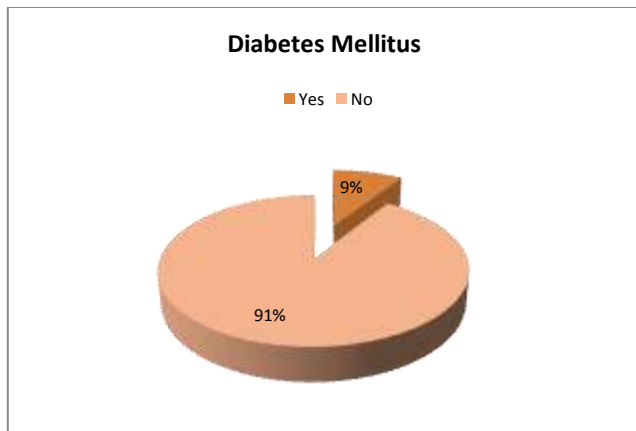


Figure 1: Prevalence of DM among major thalassemia patients

Table 2: Association of DM with gender

DM	Frequency (18)	Percentage
Gender		
Female	12	66.7
Male	6	33.3

Patients with ages >25 years and ferritin value >6000 ng/ml had increased risk of DM. Mean five year ferritin among cases was 5214.3±2531 ng/ml. Mean blood transfusion in DM patients was 2.9±3.66 U/mo with mean duration 15.8±4.17 years. (table 3)

Table 3: Risk of DM, ferritin level and blood transfusion

Variables	Frequency	Percentage
Mean five year ferritin (ng/ml)	5214.3±2531	
Mean blood transfusion (U/mo)	2.9±3.66	
Mean duration (years)	15.8±4.17	
Ferritin Value		
>6000 ng/ml	15	83.3
<6000 ng/ml	3	16.7

DISCUSSION

Autosomal recessive hereditary condition thalassemia is frequent in Asia and is caused by different mutations or deletions of the -globin gene on chromosome 11. There are mutations that result in less or no production of haemoglobin chains, which leads to an imbalance between the alpha and non-alpha globin chains, increasing erythrocyte fragility [16]. Extravascular hemolysis in Thalassemia increases iron absorption in the intestines and reduces iron bioavailability over time. Iron overload and a rise in iron ions might occur as a result of this phenomena in combination with repeated long-term blood transfusions [17]. Hypothyroidism, hypoparathyroidism and impaired glucose metabolism were among the most common endocrine diseases found in the patients. Patients with thalassemia might have problems with their pancreas and other organs. Type 1 diabetes is characterised by a lack of insulin production, whereas type 2 diabetes is caused by a lack of insulin resistance [18].

In this cross-sectional study 200 patients of major thalassemia with both genders were presented in this study. Majority of the cases were females 120 (60%) and 80 (40%) were total males. Mean age of the patients was 21.6±8.23 years and had mean BMI 20.5±9.19 kg/m². Our results were comparable to

the previous researches.[19,20] Frequency of DM among major thalassemia cases were 18 (9%). However, the incidence of DM was found to be 7.3% in an Iranian study of patients with similar ages to ours (10-22 years old) [21,22]. 10.5 percent of the United Arab Emirates [23], 6 percent of Saudi Arabia [24], 9.4 percent of Brazil [25], 18.6 percent of the U.S.A., and 41 percent of the United Kingdom [26] have also been found to have DM. At some point in the second decade, thalassemia major patients experience endocrine problems. Razavi has the highest rate of diabetes in the country (33.9 percent). [27]

Among 18 cases of DM most of the patients were males 12 (66.7%) and 6 (33.3%) were females. Patients with ages >25 years and ferritin value >6000 ng/ml had increased risk of DM. Mean five year ferritin among cases was 5214.3±2531 ng/ml. Mean blood transfusion in DM patients was 2.9±3.66 U/mo with mean duration 15.8±4.17 years. In 2004, Mehrvar's et al. [28] with a sample size of 407 thalassemia patients in Shiraz reported a prevalence of diabetes of 6.6%, which was similar with the current data. Male thalassemia major patients had a higher prevalence of diabetes (12.6 percent) than female thalassemia major patients (10.8 percent), although the difference was not statistically significant. The prevalence of diabetes in Iranian men and women was found to be 1.7 percent and 3.8 percent, respectively, in a review research conducted in the general population of Iran [29]. The iron excess in thalassemia patients has been established to have a function in the aetiology of endocrine diseases.

According to the same study, the prevalence of diabetes mellitus (DM) was considerably greater in TM patients who tested positive for anti-HCV antibodies (seropositive) (30). The presence of DM in TM has also been linked to cardiac dysfunction (reduced heart function) [31]. Patients with splenomegaly or splenectomy had a greater chance of developing IFG and DM, however. IFG patients exhibited higher AST hepatic enzyme levels, which suggests that liver problems may play a role in the development of aberrant glucose metabolism in the TM population.

CONCLUSION

We found from this study that the prevalence of diabetes in major thalassemia patients was 9 percent, with the majority of cases being male. We believe this is attributable to older age, a higher mean five-year ferritin level, and a greater amount of blood transfused.

REFERENCES

- Behrman RE, Kligman RM, Jenson HB, eds . Nelson textbook of pediatric. 18th ed. . Philadelphia: Saunders; 2007. pp. 2033–8.
- Haghi M, Pouladi N, Hosseinpour Feizi M, Hosseinpour Feizi A. B- Thalassemia in Iran. JSSU. 2010;18:127–33. [in Persian]
- Tabarsi B, Marbaghi A, Safavi M, Afkhami M. Comparative survey of problems in thalassemia major patients with regular and irregular follow ups of therapeutic principles. Sci J Blood Transfus Organ. 2007;4:33–40. [in Persian]
- De Sanctis V. Growth and puberty and its management in thalassemia. Horm Res. 2002;58:72–9.
- De Sanctis V, Tangerini A, Testa MR, et al. Final height and endocrine function in thalassaemia intermedia. J Pediatr Endocrinol Metab. 1998;11:965–71.
- Raiola G, Galati MC, De Sanctis V, et al. Growth and puberty in thalassemia major. J Pediatr Endocrinol Metab. 2003;16:259–66.
- Chatterjee R, Bajoria R. New concept in natural history and management of diabetes mellitus in thalassaemia major. Haemoglobin. 2009;33(Suppl 1):S127–30. [PubMed] [Google Scholar]
- Li MJ, Peng SS, Lu MY, Chang HH, Yang YL, Jou ST, et al. Diabetes mellitus in patients with thalassaemia major. Pediatr Blood Cancer. 2014;61(1):20–24. [PubMed] [Google Scholar]
- Hafez M, Yousry I, El-Hamed FA, Ibrahim A. Abnormal glucose tolerance in β-thalassaemia: assessment of risk factors. Haemoglobin. 2009;33(2):101–08. [PubMed] [Google Scholar]
- Pepe A, Meloni A, Rossi G, Caruso V, Cuccia L, Spasiano A, et al. Cardiac complications and diabetes in thalassaemia major: a large

- historical multicentre study. *Br J Haematol.* 2013;163(4):520–27. [PubMed] [Google Scholar]
- 11 Farmaki K, Tzoumari I, Pappa C, Chouliaras G, Berdoukas V. Normalisation of total body iron load with very intensive combined chelation reverses cardiac and endocrine complications of thalassaemia major. *British Journal of Haematology.* 2010;148(3):466–75.
 - 12 De Sanctis V. Growth and puberty and its management in thalassaemia. *Horm Res.* 2002;58 Suppl 1:72-9. Review.
 - 13 De Sanctis V, Tangerini A, Testa MR, Lauriola AL, Gamberini MR, Cavallini AR, Rigolin F. Final height and endocrine function in thalassaemia intermedia. *J Pediatr Endocrinol Metab.* 1998;11 Suppl 3:965-71. 14. Raiola G, Galati MC, De Sanctis V, Caruso Nicoletti M, Pintor C, De Simone M, Arcuri VM, Anastasi S. Growth and puberty in thalassaemia major. *J Pediatr Endocrinol Metab.* 2003 Mar;16 Suppl 2:259-66. Review.
 - 15 Gulati R, Bhatia V, Agarwal SS. Early onset of endocrine abnormalities in beta-thalassaemia major in a developing country. *J Pediatr Endocrinol Metab.* 2000 Jun;13(6):651-6. 1
 - 16 M. Casale, S. Citarella, A. Filosa et al., "Endocrine function and bone disease during long-term chelation therapy with deferasirox in patients with β -thalassaemia major," *American Journal of Hematology*, vol. 89, no. 12, pp. 1102–1106, 2014.
 - 17 M. H. Gozashiti, A. Hasanzadeh, and M. Mashrouteh, "Prevalence of metabolic syndrome in patients with minor beta thalassaemia and its related factors: a cross-sectional study," *Journal of Diabetes and Metabolic Disorders*, vol. 13, no. 1, p. 108, 2014
 - 18 V. De Sanctis, A. T. Soliman, M. Angastiniotis et al., "International network on endocrine complications in thalassaemia (I-CET): an opportunity to grow," *Georgian Medical News*, vol. 205, pp. 52–57, 2012.
 - 19 Bazi A, Sharifi-Rad J, Rostami D, Sargazi-Aval O, Safa A. Diabetes Mellitus in Thalassaemia Major Patients: A Report from the Southeast of Iran. *J Clin Diagn Res.* 2017;11(5):BC01-BC04. doi:10.7860/JCDR/2017/24762.9806
 - 20 Azami M, Sharifi A, Norozi S, Mansouri A, Sayehmiri K. Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in patients with thalassaemia major in Iran: A meta-analysis study. *Caspian J Intern Med.* 2017;8(1):1-15.
 - 21 Karamifar H, Shahriari M, Sadjadian N. Prevalence of endocrine complications in beta-thalassaemia major in the Islamic Republic of Iran. *East Mediterr Health J.* 2003;9(1-2):55–60.
 - 22 Belhouel KM, Bakir ML, Kadhim AM, Dewedar HE, Eldin MS, Alkhaja FA. Prevalence of iron overload complications among patients with β -thalassaemia major treated at Dubai Thalassaemia Centre. *Ann Saudi Med.* 2013;33(1):18–21
 - 24 El-Hazmi M, Al-Swailem A, Al-Fawaz I, Warsey A, Al-Swailem A. Diabetes mellitus in children suffering from β -thalassaemia. *Journal of Tropical Pediatrics.* 1994;40(5):261–66
 - 25 De Assis RA, Ribeiro AA, Kay FU, Rosemberg LA, Nomura CH, Loggetto SR, et al. Pancreatic iron stores assessed by magnetic resonance imaging (MRI) in beta thalassaemic patients. *Eur J Radiol.* 2012;81(7):1465–70.
 - 26 Noetzli LJ, Mittelman SD, Watanabe RM, Coates TD, Wood JC. Pancreatic iron and glucose dysregulation in thalassaemia major. *Am J Hematol.* 2012;87(2):155–60
 - 27 Chatterjee R, Bajoria R. New concept in natural history and management of diabetes mellitus in thalassaemia major. *Haemoglobin.* 2009;33(sup1):S127–S30.
 - 28 Karamifar H, Shahriari M, Sadjadian N. Prevalence of endocrine complications in beta-thalassaemia major in the Islamic Republic of Iran. *East Mediterr Health J.* 2003;9:55–60.
 - 29 Azami M, Nikpay S, Abangah G, Sayehmiri K. Evaluation of the incidence of splenectomy and frequency of regular iron chelation therapy in patients with thalassaemia Major in Iran: a meta-analysis. *Sci J Iran Blood Transfus Organ.* 2016;13:146–55
 - 30 Mowla A, Karimi M, Afrasiabi A, De Sanctis V. Prevalence of diabetes mellitus and impaired glucose tolerance in beta-thalassaemia patients with and without hepatitis C virus infection. *Pediatr Endocrinol Rev.* 2004;2(Suppl 2):282–84
 - 31 Ang AL, Tzoulis P, Prescott E, Davis BA, Barnard M, Shah FT. History of myocardial iron loading is a strong risk factor for diabetes mellitus and hypogonadism in adults with beta thalassaemia major. *Eur J Haematol.* 2014;92(3):229–36