

## Original Research Article

# Comparative study of serum ferritin and vitamin D in thalassemia patients with healthy controls

Shweta Gombar, Kiran Parihar, Mamta Choudhary\*

Department of Biochemistry, S.P. Medical College and Hospital, Bikaner, Rajasthan, India

**Received:** 15 December 2017

**Accepted:** 09 January 2018

**\*Correspondence:**

Dr. Mamta Choudhary,

E-mail: [mamtaasharad7@gmail.com](mailto:mamtaasharad7@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Thalassemia is the most common genetic disorder in humans; they are encountered among all ethnic groups and in almost every country around the world. Mostly occur in the regions surrounding the Mediterranean sea, hence the name. These are a group of hereditary haemolytic disorders characterized by impairment in the synthesis of globin chains of Hb. The present study aimed to find out the serum ferritin and vitamin D level in thalassemic children in the tertiary care hospital in Bikaner, western Rajasthan, India.

**Methods:** This study was conducted at Sardar Patel Medical College and associated hospital in Bikaner, Rajasthan. There were 40 cases and 40 controls in the age groups from 4 to 16 years. Fresh samples were taken and required tests were performed following standard protocol. Both ferritin and vitamin D were performed on Electrochemiluminescence (ECL).

**Results:** Level of serum ferritin was significantly high and vitamin D was significantly low ( $p$ -value < 0.0001 for both) in thalassemic children.

**Conclusions:** In this study the role of serum ferritin and vitamin D has been explored. The extremely high level of ferritin was found due to the regular blood transfusion and consequent iron overload and low vitamin D was found due to impairment in liver functions among thalassemic children.

**Keywords:** Ferritin, Vitamin D, Thalassemia

### INTRODUCTION

Thalassemia (British English: thalassaemia), also called Mediterranean anaemia, is a form of inherited autosomal recessive blood disorder characterized by abnormal formation of hemoglobin.<sup>1</sup>

Haemoglobin consist of four protein chains, 2  $\alpha$  and 2  $\beta$  chains. Four genes are needed to make enough alpha protein globin chain and two genes are needed to make enough beta globin protein chain. The two major types of thalassemia  $\alpha$  and  $\beta$  are named after defect in these protein chains.<sup>2</sup> A large number of thalassemic syndromes are currently known; each involves decreased production of one globin chain or more, which form the

different Hbs normally found in RBCs. The most important types in clinical practice are those that affect either  $\alpha$  or  $\beta$  chain synthesis.

#### *Alpha-thalassemia*

Several forms of  $\alpha$  thalassemia are known in clinical practice.

The most common form studied is Hb H disease: This condition, which results from the deletion or inactivation of 3  $\alpha$  globin genes ( $\alpha\alpha/\alpha\alpha$ ), represents  $\alpha$  thalassemia intermedia, with mildly to moderately severe anemia, splenomegaly, icterus, and abnormal RBC indices.<sup>3</sup>

### Beta-thalassemia

Similar to  $\alpha$  thalassemia, several clinical forms of  $\beta$  thalassemia are recognized; some of the more common forms are as follows: Thalassaemia intermedia: This condition is usually due to a compound heterozygous state, resulting in anaemia of intermediate severity, which typically does not require regular blood transfusions. Thalassaemia major (Cooley anaemia): This condition is characterized by transfusion-dependent anaemia, massive splenomegaly, bone deformities etc.<sup>4</sup>

Ferritin is a universal intracellular protein that stores iron and releases it in a controlled fashion. It has been the primary clinical measure of iron stores in thalassaemic patients undergoing transfusions. The clinical consequences of iron overload are varied and reflect the key sites of iron storage. In the liver, the formation of collagen and portal fibrosis has been shown to occur after about two years of transfusion therapy. Thus, many studies show a significant increase in ferritin level in it.<sup>5</sup>

Vitamin D is critical for calcium homeostasis and for mineralization of the skeleton. Vitamin D is transported to the liver and hydroxylated to 25-hydroxy vitamin D<sub>3</sub>. Regulated by parathyroid hormone, additional hydroxylation to 1,25-dihydroxyvitamin D<sub>3</sub> takes place in the kidney. Patients affected by thalassaemia major progressively develop iron overload, and a deficiency in liver hydroxylation of vitamin D. Thus, low vitamin D levels is found in most cases.<sup>6</sup>

### METHODS

This study was conducted at Sardar Patel Medical College and associated hospital in Bikaner, Rajasthan. There were 40 cases and 40 controls in the age groups from 4 to 16 years of both sex.

It was an institution based cross-sectional study, where clinically diagnosed thalassaemia patients those receiving regular blood transfusion were included. Very sick patients and those receiving calcium and vitamin D supplementations were excluded in the study.

Fresh samples were taken and required tests were performed following standard protocol. Both ferritin and vitamin D were performed on Electrochemiluminescence (ECL).

ECL is a kind of luminescence produced during electrochemical reactions in solutions. It is comprised of ECL cell. Serum Ferritin was analysed by sandwich principle and Serum Vitamin D was analysed by competitive principle.

### RESULTS

It is revealed from Table 1 that serum ferritin level with a range from 11 to 55 ng/ml with a mean as  $24.77 \pm 9.52$

ng/ml in normal control subjects was increased to  $2363.10 \pm 364.46$  ng/ml with a range of 1572 to 2920 ng/ml in thalassaemia children (study subjects).

It is revealed from Table 2 that serum vitamin D level with a range from 20 to 40 ng/ml with a mean as  $28.85 \pm 5.27$  ng/ml in normal control subjects was decreased to  $17.15 \pm 4.32$  ng/ml with a range of 10 to 27 ng/ml in thalassaemia children (study subjects).

**Table 1: Comparison of mean serum ferritin concentration in thalassaemia subjects with that of control.**

Values	Control subjects (n=40)	Thalassaemia subjects (n=40)
Mean	24.77	2363.10
Range	11-55	1572-2920
SD	9.52	364.46
DF	78	78
t	40.56	
P-value	<0.0001	

**Table 2: Comparison of mean serum vitamin D concentration in thalassaemia subjects with that of control.**

Values	Control subjects (n=40)	Thalassaemia subjects (n=40)
Mean	28.85	17.15
Range	20-40	10-27
SD	5.27	4.32
DF	78	78
T	10.85	
P-value	<0.0001	

### DISCUSSION

Beta thalassaemia is a single gene disorder requiring regular multi-blood transfusions which causes serious side effects and overload of iron in the form of ferritin. Excess or free iron can catalyze the formation of very toxic compounds such as OH- radicals through Fenton reaction which causes oxidative damage. Singh J et al observed that as the number of blood transfusions increased, the serum ferritin concentration was significantly increased.<sup>7</sup>

Serum ferritin levels in medically treated patients with  $\beta$  thalassaemia major was studied by Belhouli KM et al. The association between iron overload indices and pathology of the heart and liver in transfusion-dependent patients with  $\beta$  thalassaemia major has been extensively studied.<sup>8</sup>

The mean value of serum ferritin was increased and these results were in close collaboration with the results obtained by Mishra AK et al. These levels reflect inadequate chelation and vulnerability to develop iron overload related complications. There is an urgent need

to rationalize the chelation therapy and to create awareness about the consequences of iron overload in the patients. The study showed high levels of serum ferritin beta thalassaemia major patients which give an overall bleak view.<sup>9</sup>

The increased level of serum ferritin 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 ( $p < 0.0001$ ). The results of present series of study resembles with findings of Haghpanah S et al.<sup>10</sup>

Given the high prevalence of vitamin D deficiency in the general population and the added burden of increased metabolic demands, chronic medical care, and iron overload, it is not surprising that vitamin D deficiency is quite common in thalassaemia major patients. The results of mean serum vitamin D were in close collaboration with the results obtained by Wood JC et al.<sup>11</sup>

The decreased level of serum vitamin D level is statistically highly significant as compared to that of normal healthy children (control group) as evident by p-value which is less than 0.0001 ( $p < 0.0001$ ). The results of present series of study resembles with findings of Fahim M et al.<sup>12</sup>

Soliman A et al surveyed that the survival of patients with thalassaemia major has progressively improved with advances in therapy; however, osteoporosis and cardiac dysfunction remain frequent complications. Adequate circulating levels of vitamin D are essential for optimal skeletal health and reducing fracture risk.<sup>13</sup>

Low bone mass, a major cause of morbidity in patients with  $\beta$ -thalassaemia major is multifactorial. The prevalence of low vitamin D was found by Tzoulis P et al.<sup>14</sup>

## CONCLUSION

In this study the serum ferritin and vitamin D levels were explored. Ferritin serves to store iron in a non-toxic form, to deposit it in a safe form, and to transport it to areas where it is required. Multiple blood transfusions are needed to treat thalassaemia, which leads to hepatic iron overload and high levels of serum ferritin, thus many studies show a significant increase in ferritin level in it. In thalassaemia low vitamin D concentrations have been reported. The results were attributed to hepatic dysfunction which lead to defective hydroxylation of vitamin D and so decreased serum level. Family history of thalassaemia 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 thalassaemia in them.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Weatherall DJ, Clegg JB. Thalassaemia – a global public health problem. *Nature Med* 1996;2:847-9.
2. Weatherall DJ, Clegg JB. Inherited Haemoglobin Disorders: An increasing global problem. *Bull World Health Organ.* 2001;79:12-704.
3. Nathan DG, Gunn RB. Thalassaemia: the consequences of unbalanced haemoglobin synthesis. *Am J Med.* 1966;41(5):30-815.
4. Piomelli S, Karpatkin MH, Arzianian M, Zamani M, Becker MH, Geneiser N, et al. Hyper transfusion regimen in patients with Cooley's anaemia. *Ann N Y Acad Sci.* 1974;232(0):186-192.
5. Olivieri NF, Brittenham GM. Iron-chelating therapy and the treatment of Thalassaemia. *Blood.* 1997;89(3):739-61.
6. Holick MF, Mac Laughlin JA, Clark MB, et al. Photosynthesis of pre vitamin D3 in human skin and the physiologic consequences. *Science.* 1980;210(4466):203-5.
7. Jaidev S, Meena V, Sangeeta P. Study of serum ferritin level, SGOT, SGPT and hepatitis B status in multi transfused thalassaemia patients. *JARBS.* 2011;3(2):63-5.
8. Belhoul KM, Bakir ML, Saned MS, Kadhim AM, Musallam KM, Taher AT. Serum ferritin levels and endocrinopathy in medically treated patients with  $\beta$  thalassaemia major. *Ann Hematol.* July 2012;91(7):14-107.
9. Mishra AK, Tiwari A. Iron overload in beta thalassaemia major and intermedia patients. 2013;8(4):328-32.
10. Haghpanah S, Esmailzadeh M, Honar N, Hassani F, Dehbozorgian J, Rezaei N, et al. Relationship between serum hepcidin and ferritin levels in patients with thalassaemia major and intermedia in Southern Iran. *Iran Red Crescent Med J.* 2015;17(7).
11. Wood JC, Claster S, Carson S, Menteer JD, Hofstra T, Khanna R et al. Vitamin D deficiency, cardiac iron and cardiac function in thalassaemia major. *Br J Haematol.* 2008;141(6):891-4.
12. Fahim FM, Saad K, Askar EA, Eldin EN, Thabet AF. Growth parameters and vitamin d status in children with thalassaemia major in upper Egypt. *Int J Hematol Oncol Stem Cell Res. Haemoglobin.* 2013; 7(4): 10-14.
13. Soliman A, De Sanctis V, Yassin M. Vitamin D status in thalassaemia major: an Update. *Mediterr J Hematol Infect Dis.* 2013; 5(1).
14. Tzoulis P, Ang AL, Shah FT, Berovic M, Prescott E, Jones R et al. Prevalence of low bone mass and vitamin D deficiency in  $\beta$ -thalassaemia major. *Hemoglobin.* 2014 Jun;38(3):173-8.

**Cite this article as:** Gombar S, Parihar K, Choudhary M. Comparative study of serum ferritin and vitamin D in thalassaemia patients with healthy controls. *Int J Res Med Sci* 2018;6:693-5.