EVALUATION OF SOLUBLE TRANSFERRIN RECEPTORS AND FERRITIN LEVEL PATIENTS OF BETA THALASSEMIA MAJOR

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Abstract

Aim: The purpose of this study was to evaluate soluble transferring receptors (sTfR) and ferritin level in beta thalassemia major for diagnosis and management of iron chelating therapy.

Materials and methods: This study was conducted on 400 samples from β thalassemia major patients. ELISA technique was used for the detection of serum ferritin and sTfR according to the manufacturer's instructions.

Results: In male beta thalassemia major patients sTfR level was 89.2±20.1 nmol/l while in female patients mean sTfR was 97.4±23.3 nmol/l which were high on comparing with control. Serum ferritin level in male patient was 3013.35±914.08 ng/ml while in female patients was 3213.43±1014.08 ng/ml.

Conclusion: The concentration of sTfR, and ferritin level was increased in beta thalassemia major patients which indicate increased marrow activity and increased body iron.

Key words: soluble transferrin receptors, ferritin, beta thalassemia major, patient.

INTRODUCTION

Beta thalassemia is an inherited hemoglobinopathy with an autosomal recessive pattern of inheritance. It is caused by impaired synthesis of the β globin chain in haemoglobin(1) More than 200 mutation in beta globin gene have been associated most of which are point mutations. Deletion of beta gene is very rare in beta thalassemia(2). Mutations cause reduction of adult hemoglobin and excess production of alpha globin chain resulting ineffective erythropoiesis and apoptosis of erythroid cells. Clinical complication in beta thalassemia patients can be reduced by proper blood transfusion and iron chelating therapy(3). Complication related to transfusion of blood and blood product include, iron overload, transfusion transmitted disease, toxicities of iron chelation and bacterial infections(4). Worldwide, beta thalassemia is common single genetic disorder. In many developing countries most of children are affected with this lethal disorder(5). Its prevalence is increased around the Mediterranean, Indian subcontinent and in South-East Asia(6). It is also prevalent in southern parts of former USSR and People's Republic of China(7). Pakistan is one of the most affected countries having increase rate of beta thalassemia. Carrier rate of beta thalassemia trait in Pakistan is 5.4%(8). While in Khyber Pakhtun-Khwa the carrier rate is 5 to 8%(9).

Transferrin is a carrier protein for transporting iron into red cell precursors through specific receptor mechanism(10). Soluble transferrin receptor (sTfR) is monomeric form of TfR which lack its first 100 amino acids. Transferrin and its receptor circulate in complex form. Molecular weight of sTfR is 85 kDa. sTfR is produced by a proteolytic enzymatic activity. Enzyme responsible for cleavage is a serine protease. Breakdown occurs between amino acids Arg-100 and Leu-101(11). There is direct proportionality of sTfR and ferritin level to erythropoietic activity in the body. The proportionality increases in conditions where the erythropoietic activity of bone marrow increases like beta thalassemia major, beta thalassemia intermediate, sickle cells anemia, hemolytic anemia, megaloblastic anemia, congenital dyserythropoietic anemia and secondary polycythemia(12).

Ferritin is a storage form of iron in human. Serum ferritin reflects body iron store and its value are commonly elevated in patients with beta thalassemia. High level of ferritin leads to secondary hemochromatosis(13). Secondary hemochromatosis is frequently observed in beta-thalassemia major due to an increased rate of iron absorption by the gastrointestinal tract and frequent blood transfusions. In the beta-thalassemia trait, there is some degree of ineffective erythropoiesis, which intensify erythropoietic activity and increased iron absorption(14). Although bone marrow iron store is also a sensitive indicator but it is painful, invasive, expansive and sometime not suitable for everybody. For this reason soluble transferrin receptor and serum ferritin level are better option for determination of store iron, bone marrow erythropoietic activity and effectiveness of iron chelation(15). Serum ferritin level is also used for the differentiation of iron deficiency anemia from beta thalassemia major. Therefore, this study was conducted to evaluate soluble transferrin receptor and serum ferritin level in patients with beta thalassemia major for proper diagnosis and better management.

MATERIALS AND METHODS

The present study was conducted at Baqai Institute of Hematology, Baqai Medical University Karachi, Pakistan. In the present study 400 samples from known thalassemia patients were collected in which 200 samples were

form males and 200 samples from females. This study was conducted after the approval from ethical committee of Baqai Medical University, Karachi, Pakistan. Informed consent was taken from their respective guardians of the patients. For establishing reference ranges 50 samples from normal children were also collected. For determination of sTfR and ferritin level 8 ml of blood samples were taken in plan tube without anticoagulant. These samples were centrifuge on high speed and serum was separated. Serum ferritin was determined by ELISA method using point scientific, INC kit. Soluble transferrin receptors were determined by ELISA method using Quantikine IVD kit. The data were statistically analyzed using SPSS version 16. We include those patients who had no splenomegaly and had transfusion not more than 8 times.

RESULTS

We determined serum ferritin and soluble transferrin level on 400 samples from beta thalassemia patients and 50 samples from normal individuals. Mean sTfR level in normal male group was 37±7 nmol/l (Range 9.9-131.9 nmol/l), and in normal female group was 42±5nmol/l (Range 29.7-49.9 nmol/l). Beta thalassemia major male group had mean sTfR levels of 89.2±20.1 nmol/l (Range 115-191 nmol/l) while female group had mean 97.4±23.3 nmol/l (Range 106-182 nmol/l) as shown in table. Serum ferritin level of normal male control samples was 79±32 ng/ml while that of female control was 74±26 ng.ml. Serum ferritin level in male thalassemia patients was 3013.35±914.08 ng/ml, while that of female thalassemia group was 3213.43±1014.08 ng/ml.

Table Serum ferritin and sTfR results in control and patients samples

Parameters	Male (control)	Female (Control)	Male patients	Female patients
Age (months)	16.±3	17 ±4	9±2	12±4
Fer (ng/ml)	78.91±32.14	74±26	3013.35±914.08	3213.43±1014.08
sTfR(nmol/l)	37.51±7.27	42.19±5.50	89.2±20.1	97.4±23.3

DISCUSSION

In the present study we determined serum ferritin and soluble transferrin receptors on 400 children of beta thalassemia major. We observed that Serum ferritin level of male thalassemia major group was 3013.35±914.08 ng/ml while that of female thalassemia major group was 3213.43±1014.08ng/ml. A study at Rawalpindi, Pakistan in 2004 reported that mean serum ferritin level in beta thalassemia major patients was 3390 ng/ml which is similar to our results. Our results were different from the work done by Choudhry VP et al, at India which reported that the level of serum ferritin in beta thalassemia patients was 6723 ng/ml(16). This may due to poor management of iron chelation in these patients. For beta thalassemia patients proper iron chelation is essential to prevent major complication.

In the present study we determined that in β thalassemia major male group mean sTfR was 89.2±20.1nmol/l and in female group level of mean soluble transferrin receptor was 97.4±23.3mmol/l. We observed that the level of sTfR was increased both in male and female thalassemia children which indicate increased turnover of erythropoiesis and bone marrow activity. Aslam M et al, in 2014 at Pakistan, determined that the level of sTfR was increased in beta thalassemia which is helpful in diagnosing the cause of anemia and also help in evaluating the rate of erythropoiesis. A study conducted by Beguin Y in 2003 at Belgium reported that the level of sTfR are decreased whenever there is diminished erythropoietic activity, while its level increases when hemolysis or ineffective erythropoiesis stimulates bone marrow(11). Jayaranee S and Sthaneshwar P in 2006 at Malaysia reported that the level of sTfR was increased in condition having increased erythropoietic activity like beta thalassemia(17).

CONCLUSION

We determined that serum ferritin and sTfR was increased in patients of beta thalassemia major. Furthermore, serum ferritin level can be used for body stored iron and for chelating therapy. While, sTfR can be used for evaluating erythropoietic activity and early diagnosis of beta thalassemia major. In addition to this serum ferritin and sTfR can also be used as tool for differentiating beta thalassemia major from other microcytic hypochromic anemia.

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Conflict of interest

The authors declare no conflict of interest.

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