

## Hospitalization causes due to iron overload in beta-Thalassemia in Gorgan, Iran

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### ABSTRACT

**Objective:** To evaluate causes of hospitalization (due to complications of iron overload and other causes) in beta-Thalassemic patients.

**Methodology:** This study was performed on 244 patients with major beta-Thalassemia admitted in Taleghani hospital of Gorgan between 2000 and 2007. Causes of hospitalization (due to complications of iron overload and other causes) were evaluated. Data were analyzed with SPSS software.

**Results:** The most common causes of hospitalization due to iron overload were diabetes mellitus (31.6%) and heart failure (16.4%). The most common clinical findings were weakness and fatigue.

**Conclusion:** We perceive increased frequency of diabetes mellitus in this center compared to other studies in Iran and abroad. Therefore glucose tolerance test and genotypic research for IVS II nt 745 are recommended in Thalassemic patient in this area.

**KEY WORDS:** Thalassemia, Cardiac disease, Diabetes mellitus, Iron overload.

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### INTRODUCTION

Blood transfusion therapy significantly increases life expectancy of beta-Thalassemic patients by controlling anemia and its sequelae. But this treatment leads to progressive deposition of iron in tissues, posing significant risk of severe cardiac, endocrinological, and hepatic complications, which are fatal if not prevented.<sup>1</sup> Today many of the complications of Thalassemia seen in developed countries are the

result of iron overload. fibrosis and cirrhosis in the liver, diabetes mellitus in the beta cells of the pancreas, growth retardation and hypogonadotropic hypogonadism in the pituitary, testis, and ovaries, hypocalcaemia and osteoporosis in the parathyroid, and arrhythmias, myocarditis, and intractable cardiac failure in the heart.<sup>2</sup> Thus, iron overload, whether through increased iron absorption caused by erythropoietic activity or as a result of blood transfusion, constitutes the most important complications and major focus of clinical management in beta-Thalassemia.

Most of the pathologic processes develop slowly and usually are not apparent until the 2<sup>nd</sup> decade of life. In untransfused patients, these abnormalities develop more slowly. Diabetes mellitus is a frequent and often under recognized complication of Thalassemia, which is due both to pancreatic hypoproduction and (at least in some cases) to insulin resistance.<sup>3</sup>

Considering that Gorgan is a city located beside Caspian sea and is assumed as one of the prevalent areas of beta Thalassemia, statistical rendering of iron

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Table-I: Frequency of hospitalization of beta-Thalassemia with causes of iron overload in age groups.

Causes of hospitalization	Age (year)			
	< 2	2-5	5-15	>15
Diabetes mellitus	0	0	33.8	66.2
Heart disease	0	2.5	47.5	50
Hypocalcemia	0	0	62.1	37.9

overload is important information for developing facilities for patients.

### METHODOLOGY

The target population of this study was patients with beta-Thalassemia major admitted to Taleghani hospital of Gorgan (a city located in the north of Iran) between 21 March 2000 and 20 March 2007.

Causes of hospitalization due to complications of iron overload (diabetes mellitus, cardiac disease and hypocalcaemia) and other causes such as respiratory tract infection, gastrointestinal infection, arthritis, cellulites and reaction to transfusion, age and sex were evaluated. Data were analyzed with SPSS software (v: 13.0) and compared with other reports obtained from developing and developed countries.

### RESULTS

Of our 244 cases, 126 cases (51.6%) were female and 118 cases (48.4%) were male. The range of patients' age was between 2.5 months and 25 years. Diabetes mellitus was found in 31.6% of patients (77 cases); arrhythmia and heart failure were found in 16.4% of patients (40 cases) and hypocalcaemia was found in 11.9% of patients (29 cases) (Figure-1). None of patients were less than 5 years old had diabetes mellitus and hypocalcaemia and none of patients were less than 2 years old had cardiac disease

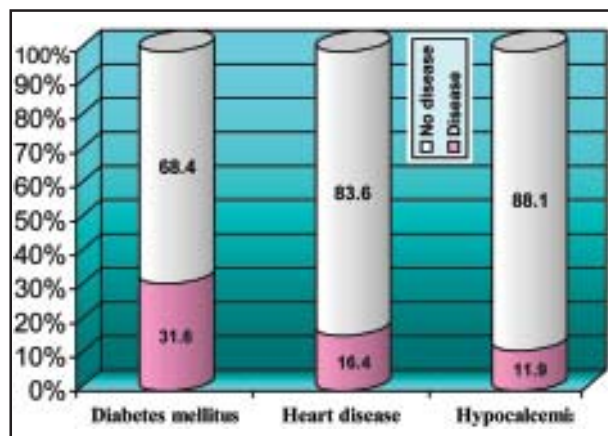


Fig-1: Frequency of hospitalization of beta-Thalassemia with causes of iron overload.

Table-II: Frequency of hospitalization of beta-Thalassemia without causes of iron overload in age groups.

Causes of hospitalization	Age (year)			
	< 2	2-5	5-15	>15
Respiratory tract infection	23.1	0	43.6	33.3
GI tract infection	9.1	18.2	57.6	15.1
Arthritis and Cellulitis	0	0	29.4	70.6
Reaction to transfusion	0	0	71.4	28.6

(Table-I). The youngest patient (2.5 months old) had pneumonia and the oldest patient (25 years old) had diabetes mellitus. Frequency of other causes of hospitalization is shown in Figure-2 and Table-II.

### DISCUSSION

The Thalassemias are common monogenic disorders of hemoglobin synthesis. Beta-Thalassemias are the most important among the Thalassemia syndromes and have become a world wide clinical problem due to an increasing immigrant population. Blood transfusion and increased gastrointestinal iron absorption result in iron overload and tissue damage.<sup>4</sup>

Patients with Thalassemia major have traditionally succumbed to the cardiac complications of iron overload. Recurrent pericarditis distinguished by characteristic pain, fever, and a friction rub may be initial manifestation of myocardial iron deposition and occasionally requires pericardectomy to relieve constriction, ventricular tachycardia and fibrillation or sever refractory congestive heart failure.<sup>3</sup>

Cardiac complication is one of the major causes of death in patients with Thalassemia major. Heart rate

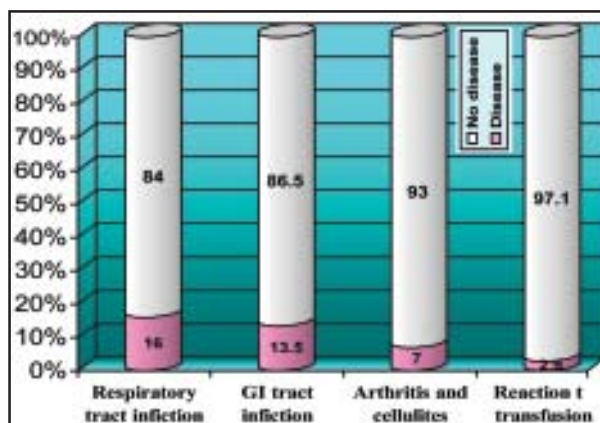


Fig-2: Frequency of hospitalization of beta-Thalassemia without causes of iron overload.

variability is a noninvasive index of neuronal modulation of heart rate.<sup>5</sup> Heart disease represents the main determinant of survival in beta-Thalassemia.<sup>6</sup>

Aessopas assessed clinically and echocardiographically 202 Thalassemia major patients aged 27.3±6.3 years and 75 age and sex-matched healthy controls. Overt cardiac disease was encountered in 14 patients (6.9%).<sup>7</sup> There were 211 patients included in study of "Durong" in Thailand. Their ages ranged from 2.6 to 18.2 years. Cardiac involvement was found in 26 patients (12.3%).<sup>8</sup> In our study cardiac involvement was found in 40 patients (16.4%). That is higher than world wide range. Although results of our study are similar to Hong Kong study.<sup>9</sup>

Cunningham performed a cross-sectional study in cancer institute and Harvard medical school on 342 patients in the registry of the National Institutes of Health-Sponsored Thalassemia clinical research network. None of patients were 15 years old or younger and 5% of patients aged 16-24 years had heart disease requiring medication.<sup>10</sup>

In our study none of the patients were 2 years old or younger, 6.2% of patients aged 2-5 years, 16.5% of patients aged 5-15 years and 22.2% of patients aged higher than 15 years had disease requiring medication. These finding may be results of poor disease control and management in early life in our center. Endocrine disorders commonly associated with Thalassemia in the United States today are generally thought to be secondary to the effects of chronic iron loading.<sup>3</sup> Fasting blood glucose levels are significantly elevated even in patients aged 5-10 years whose iron burden is 5 to 209. When glucose tolerance tests are performed as many as 50% of Thalassemic patients have chemical diabetes defined by glucose tolerance.<sup>3</sup>

Galati prospectively evaluated glucose tolerance in 84 patients over one year. 7.9% of patients had diabetes or impaired glucose tolerance.<sup>11</sup> In Hong Kong 232 patients were studied at a median age of 15.5 years (range 1.4-30.3 years). Cardiomyopathy and diabetes mellitus occurred in 15.1% and 8.6% of patients with Thalassemia major respectively.<sup>9</sup>

In Egyptian beta-Thalassemic patients the prevalence of diabetes was 10.4% (5 of 48).<sup>12</sup> To identify prevalence of endocrine dysfunction in Iranian with beta-Thalassemia, Karami assessed pancreatic function in 150 beta-Thalassemia patients aged 10-22 years at the pediatrics unit, Shiraz University of Medical Sciences. Type 1 diabetes mellitus was found in 7.3% with age 13.9±2.8 years.<sup>13</sup>

In our study diabetes mellitus was found in 31.6% of patients (77 cases); therefore, we perceive an increased frequency of diabetes mellitus in our center compared to other studies in Iran and abroad. The high frequency of diabetes mellitus in our study may be a result of poor disease control and management. On the other hand, glucose intolerance generally correlates with genetic predisposition and an association between diabetes and genotyping IVS II nt 745 has found. Therefore test of blood glucose and glucose tolerance every 6 months and genotypical research for IVS II nt 745 are recommended in Thalassemia patients in our center to detect early occurrence of diabetes.

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