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Prevalence of Articular Manifestations of Thalassemia Major: A Cross Sectional Single Center Study From Iraq

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Abstract
Objective:*To detect the prevalence of articular manifestations of thalassemia major and to evaluate its relationship to the duration of disease and the frequency of blood transfusion.*
Patients and methods:*This cross sectional study consisted of 70 patients with thalassemia major, 36 male and 34 female aged (2-18) years.All patients were assessed clinically for the presence of articular manifestations, which include(Joint pain, tenderness, presence of joint swelling, and limitation of movement).Laboratory investigations included biochemical tests for all of the patients. X-ray of the knee joint was performed for those with knee joint involvement.*
Results: *Articular manifestations were found in 38 out of 70 patients (54.3%). Nineteen patients (27.2%) had knee joint involvement (the knee joint most often involved). Six patients (8,6%) had ankle joint involvement, three patients (4.3%) had elbow joint involvement, one patient had ankle and elbow joints involvement (1.4%), four patients (5.7%)had knee and elbow joints involvement, five patients (7.1%) had knee and ankle joints involvement.There was significant correlation between number of joint involvement and: the duration of the disease (p=0.03, r=1.5) and the frequency of blood transfusion (p=0.01, r=1.2)*
Conclusion: *Thalassemia major is frequently accompanied by articular manifestations. The frequency of articular manifestations increases with the duration of the disease and with the number of blood transfusion.*
Keywords:*Thalassemia major, Articular manifestations, Hemoglobinopathy*

I. Introduction

Thalassemia is an inherited autosomal recessive blood disorder characterized by the underproduction of globin chains as a consequence of globin gene defects, resulting in malfunctioning red blood cells and oxygen transport [1]. In thalassemia major, there is failure of synthesis of beta chain and it is considered as the most common chronic, genetic blood disorder with significant emotional and behavioral problems [2]. The prolonged survival of these patients leads to the development of other health problems including degenerative diseases such as arthropathies, which require further attention since they have a significant impact on the quality of life [3].

Musculoskeletal manifestations of thalassemia major include osteoporosis, pathological fracture, and epiphyseal deformities which may results from expansion of erythroid marrow. None erosive synovitis without joint effusion has also been described [4]. Hyperuricemia and gout may develop in patients with thalassemia major because of the increased turnover or red blood cell precursor. [5]Thalassemia major may develop similar manifestations to sickle cell disease including hand foot syndrome and gout. Avascular necrosis of bone has been reported in both conditions. [6, 7]

In patients with beta-thalassemia who received multiple blood transfusions, septic arthritis should be considered especially viral hepatitis. Patient with repeated blood transfusions have experienced chronic iron overload and arthropathy with iron deposition in the synovium as occur in idiopathic hemochromatosis. [8]

Because of the scarce data and reports on articular manifestations of thalassemia major and up to our knowledge there was no study in Iraq.This study was designed to detect the prevalence of articular manifestations of thalassemia major and to evaluate its relationship to the duration of disease and the frequency of blood transfusion.

II. Patients And Methods

Study design and participants

This cross sectional study was conducted on 70 patients with thalassemia major attended to specialized center of blood disease in Al-Karama Teaching Hospital from May 2003 to April 2004.Patient diagnosis was based on the clinical presentation, the need for blood transfusion, and the level of hemoglobin F which was considered in this study between 60%-90%.Patient diagnosed as having osteoporosis with or without

pathological fractures were excluded from this study. A signed written consent was taken from all patients for inclusions in the study.

Clinical, laboratory, and radiological evaluation

Full history was taken from all patients studied and they were assessed clinically for the presence of articular manifestations of thalassemia major, which included joint pain, tenderness, the presence of joint effusion or limitation of movement. All patients were on regular vaccination regimen (especially hepatitis B vaccine). The correlation between joint complaints and blood transfusion regimen was reported. The following investigations were done for all patients: complete blood count (CBC), erythrocyte sedimentation rate (ESR) by Westergren method [9] and serum uric acid. Radiographs of the knees (antero-posterior view) were taken for the patients who had knee joint involvement.

Statistical analysis:

Statistical software SPSS version 10 for windows (USA, Chicago, Illinois) was used for analysis.Kolmogorov-Smirnov test was used to assess the normal distribution of continuous data. The normally distributed continuous variableswere presented as mean ± SD and categorical variables as number and percentages.The statistical significance, direction, and strength of linear correlation between 2 normally distributed continuous variables were measured by Pearson's correlation coefficient (r). P value < 0.05 was considered statistically significant.

III. Results

Of a total 70 patients with thalassemia major, there were (36)male, and (34) female, the age of patients included in this study ranged from 2-18 years (Mean 9.2 years). The duration of the disease ranged from 1.5-17 year (Mean 8.34 years) as in table 1. All the patients were blood transfusion dependent in which the patients received blood transfusion every 2 weeks as a minimal period and every 4-week as maximal period. The usual treatment of these children included blood transfusion regimen with chelation therapy (desferoxamine) and 5 mg per day folic acid. No splenectomy was done for any of our patients.

Arthropathy was found in (38) patients among (70)patients with thalassemia major studied.The pattern of joint involvement is shown in figure 1.

The knee joint was the joint most often involved. The joints involvement classified as following: Nineteen patients had knee joint involvement (27.2%), eleven had mild joint pain, six had moderate joint pain, thirteen had mild joint tenderness,three had moderate joint tenderness, no joint swelling or limitation of movement was detected.Six patients had ankle joint involvement (8.6%), one patient had mild joint pain, three had moderate joint pain, three had moderate joint tenderness, no joint swelling and no limitation of movement was reported.Three patients had elbow joint involvement (3.4%), all of them had moderate joint pain, moderate joint tenderness, no joint swelling or limitation of movement could be detected.

Five patients had knee and ankle joints involvement (7.1%), four patients had mild joint pain, four patients had mild joint tenderness, one patient had moderate joint tenderness, one patient had mild limitation of movement, four patients had no limitation of movement and no joint swelling.

Four patients had knee and elbow joints involvement (5.7%): Three patients had moderate joint pain, one patient had no joint pain, three patients had moderate joint tenderness, one patient had no joint tenderness, no joint swelling, and no limitation of movement.

One patient had elbow and ankle joints involvement (1.4%) the patient had moderate joint pain, moderate joint tenderness, no joint swelling, and no limitation of movement.

Serum uric estimation was within normal in all patients.No radiological abnormalities were detected among x-rays of patients with knee joint involvement.It has been found that frequency of joint involvement is more reported in patients with long disease duration (p=0.03, r=1.5), Also there were positive correlation between joint complain and the frequency of blood transfusion (p=0.01, r=1.5).There was no correlation between joint complaint and the level of HbF (p=0.28, r=0.13)

Table 1: Demographic distribution of thalasemic major patients

Variable	Value
Age(years)	
Range	2-18
Mean	9.2
Gender n.(%)	
Female	34(48.6%)
Male	36(51.4%)
Disease duration (years)	
Range	1.5-17
Mean	8.34

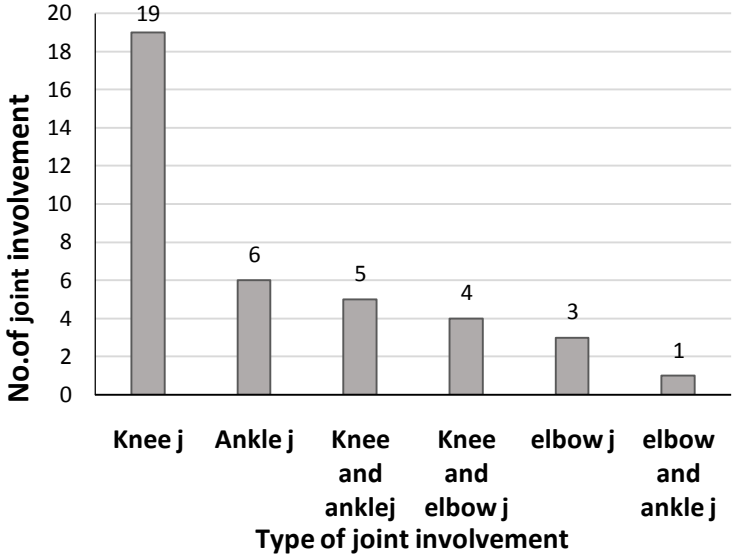

Figure 1: Pattern of joint involvement in 38 patients with thalassemia major

IV. Discussion

Several researchers have commented on the presence of joint manifestations in patients with thalassemia major [10, 11]. This study confirmed the frequent occurrence of joint abnormalities in (38) patients out of (70) patients with thalassemia major.The characteristic arthropathy had been reported less frequently among our patients when compared with previous reports described by other authors [12, 13].

In a series of 50 patients with thalassemia major aged (3-19) years, 25 patients had ankle pain that was exacerbated by weight bearing and relieved by rest, 3 patients had knee joint pain with mild tenderness and there is no effusion detected in any of these joints [12].Another study of 19 Turkish patients with thalassemia major aged (2-17) years had joint manifestations, the shoulder joints were predominantly involved [13].

In this study, the knee joint was prominently involved and there was no involvement of the shoulder joint .The ankle joint involvement was found in 6 out of 70 patients included in this study.

Asymptomatic hyperuricemia as well as gouty arthritis was reported earlier in patients with thalassemia major receiving multiple blood transfusion [5], asymptomatic hyperuricemia was not detected in this study (normal serum uric acid in all patients) and there was no evidence of gouty arthritis among our patients.

In this study we found that frequency of articular manifestations of thalassemia major increases with the duration of the disease and increases with the increase of the demand of blood transfusions.

The possible explanation of the skeletal changes in thalassemia may be related to the expansion and invasion of erythroid bone marrow, which widen the marrow spaces, attenuate the cortex, and produce osteoporosis and subsequently pathological fracture [14,15].

The limitations of this study aresmall sample size of the study and selection bias because our patients are selected group of patients referred to tertiary center care but these can be solved by a larger sample size study with multiple centers. However the strength of the study included: it is relatively inexpensive and took little time to conduct with strict inclusion and exclusion criteria and up to our knowledge it is the first study in Iraq that evaluated articular manifestations in patients with thalassemia major.

In conclusion, thalassemia major was frequently accompanied by articular manifestations. The frequency of articular manifestations increases with the increase in disease duration and the number of blood transfusion.

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Authors' contribution

All authors were involved in drafting the article and revising it for important intellectual content, and all authors approved the final version to be published. The authors participated in study conception and design, acquisition of data, and analysis and interpretation of data.

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