International Journal of Orthopaedics Sciences

ISSN: 2395-1958
IJOS 2016; 2(1): 29-32

www.orthopaper.com
Received: 14-01-2016
Accepted: 24-02-2016

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Prevalence of fractures among patients suffering from thalassemia

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DOI: https://doi.org/10.22271/ortho.2016.v2.i1a.3489

Abstract
Aim: The objective of this investigation was to ascertain the incidence rate of fractures among individuals affected with thalassaemia syndromes.
Methods: A retrospective study and patient interviews were undertaken involving one hundred hospitalized thalassaemia patients. The patient interview questionnaire comprised various sections, including inquiries pertaining to fractures, medical history (Including Orthopaedic and surgical procedures), tobacco and alcohol use, and demographic information. Using likelihood ratios, the risk factors for fracture were identified.
Results: 35.3 percent of patients with thalassaemia syndromes were affected by fractures. The incidence of fracture was found to be higher among patients with beta thalassemia (44.1%) compared to those with alpha thalassaemia (16%). Fractures most frequently occurred in the upper extremity, with falls and motor vehicle accidents being the leading causes, and casts or splints being the most frequently prescribed treatment. A total of 28% of the patients were found to have multiple fractures. Fracture risk factors among patients with thalassemia included low body mass index, male gender, beta thalassemia, splenectomy, and transfusion.
Conclusion: The incidence of fractures is significantly elevated in patients diagnosed with thalassaemia. It was determined that the aetiology was multifactorial.

Keywords: Interviews, patients, significantly

Introduction
Beta thalassemia is a prevalent monogenic hematological disorder that manifests on a global scale. Approximately 10–12,000 infants are born annually with thalassemia in India. An estimated 10% of the global prevalence of thalassemia is attributed to the country of India [1]. Thalassemia major is frequently associated with endocrinopathies; furthermore, bone health is a critical concern that may not receive adequate attention, particularly in developing nations. A component of thalassemia-related long-term morbidity and mortality is compromised bone health. The complex pathogenesis of bone disease associated with thalassemia is due to both the pathological and treatment-related effects of the disease [2, 3]. A variety of bone abnormalities, including osteoporosis, pain, fractures, and vertebral deformities, are among its manifestations [4, 5].
Homozygous beta-Thalassemia has historically been linked to significant osseous abnormalities, as Cooley *et al*. first documented in 1925 [6, 7]. Marked deformities of the long bone can be caused by pathological fractures as well as premature epiphyseal fusion [8, 9, 10]. The underlying enormous ineffective erythropoiesis, erythroid expansion of the medullary bone with thinning of the cortical bone, metabolic and endocrine dysfunction due to transfusional iron overload, have been proposed as the mechanisms underlying these abnormalities in thalassaemia [11, 12]. The correlation between homozygous beta-thalassaemia and severe osseous abnormalities has been documented in prior research [8].
Thalassemia patients experienced a significant incidence of fractures during the 1960s and 1970s due to suboptimal transfusion and chelation regimens [13]. A consequence deformity could potentially manifest itself throughout the course of healing the sustained fractures. Consistent transfusion and chelation procedures continue to be problematic in developing nations, resulting in a detrimental cycle of complications that can ultimately compromise bone

health and give rise to fractures. In the last thirty years, hypertransfusion therapy has significantly enhanced the management of patients with thalassemia by nearly restoring pre-transfusion hemoglobin levels to normal, halting the ineffectual erythropoietic process, and preventing bone deformities. Initiated in the mid-1970s, iron chelation via protracted subcutaneous infusions of desferrioxamine (Sc DFO) has been shown to increase survival and reduce endocrine complications associated with transfusional hemochromatosis [14].

Recent publications have provided evidence that bone disease in Thalassemia, specifically reduced bone mass, continues to be a prevalent, incapacitating, and inadequately comprehended issue, even among prepubescent and adult patients who are adequately transfused and chelated [15, 16]. The present evaluation of the incidence of fractures among individuals with beta-Thalassemia Major and the diverse Thalassemia syndromes is inadequate.

In this retrospective study, we aimed to establish the prevalence of fractures as well as to ascertain the predisposing factors for fracture among patients suffering from thalassaemia.

Methods

- All outpatient thalassemia patients who sought treatment were enrolled in this research. Patients who elected not to take part in the research were excluded from the study. Prior to the interview, written informed consent was obtained from all participants. The research was evaluated and granted approval by the Ethical Committee.
- The current study enrolled a group of 100 individuals diagnosed with thalassaemia; of these, 65 were classified as having alpha thalassaemia (Alpha-Thal) and 35 were classified as having beta thalassaemia (Beta-Thal).
- The medical history of the patient was acquired through a review of the patient interview and medical record. As general information, demographics, underlying diseases, transfusion regimens, and alcohol and tobacco use were documented.
- The patient's age, the location of the fracture, the etiology of the fracture, and the treatment modality were gathered as components of the fracture history.
- Fracture aetiology was categorized as follows: heavy object trauma, sports or recreational injury, motor vehicle accident, or fall.
- The treatment of fractures was categorized as cast/splint, surgery, hospitalization and no treatment.
- The sites of fractures were classified into the following categories: upper extremity (Including shoulder, arm, forearm, wrist and hand), lower extremity (Including leg, ankle and foot) and spine/back/pelvis.
- The documentation of transfusions and recent laboratory values (Serum ferritin level) were reviewed as part of the medical record review. Non-transfused patients were those who had not undergone blood transfusions prior to the commencement of this investigation. Transfused patients were individuals who had received an average of one transfusion annually.
- In addition, regular transfusion was defined as > 12 transfusions per year, or at least one transfusion every four weeks.
- The mean was used to express each value, with a standard deviation of SD. The statistical analysis was conducted utilizing version 5 of StatView for Windows. Chi-square tests were conducted on the categorical variables, descriptive statistics were computed, and an unpaired t-test was utilized to compare the values among patients with beta and alpha thalassaemia. A p-value less than 0.05 was considered to indicate statistical significance.

Table 1: Demographics, growth and iron status in thalassaemia patients

		No. of patients (%)		P-value
	All (n = 100)	Alpha-Thal (n = 65	Beta-Thal (n = 35)	
Age (Yrs)	33.7±11.4	41.7±12.7	31.5±9.7	< 0.002
Gender				
Male	30 (30%)	12 (18.5)	12 (34.2)	< 0.04
Female	70 (70%)	53 (81.5)	23 (65.7)	
Weight (kg)	50.3±7.9	50.8±7.6	50.0±8.0	> 0.05
Height (m)	1.56±0.06	1.54±0.08	1.56±0.09	< 0.04
Serum ferritin (ng/ml)	2,376±2,817	1,265±2,617	3,243±2,721	< 0.001

Table 2: Characteristics of fracture in alpha and beta thalassaemia patients.

Characteristic		No. of patients (%)		p-value
	All (n = 201)	Alpha-Thal (n = 65)	Beta-Thal (n = 136)	
Fracture prevalence	71 (35.3)	11 (16.9)	60 (44.1)	< 0.001
No. of fractures	1.39±0.79	1.27±0.55	1.53±0.92	> 0.05
Age at first fracture	18.8±13.4	28.0±22.7	14.8±10.1	< 0.01
Total no. of fractures	52 (52%)	14 (26.9)	38 (73.0)	
Site of fracture				
Upper extremity	32 (61.5)	21 (65.5)	11 (34.3)	
Lower extremity	12 (23.0)	4 (21)	8 (28.5)	
Spine/back/pelvis	8 (15.3)	1 (12.5)	7 (87.5)	
Cause of fracture				
Fall	22 (42.3)	7 (31.8)	15 (68.1)	
Recreation/sport	5 (9.6)	0	5 (100)	
Motor vehicle	19 (36.5)	5 (26.3)	14 (73.6)	
Heavy objects	6 (11.5)	2 (33.3)	4 (66.6)	
Treatment of fracture				
Cast/splint	31(59.6)	9 (29)	22 (70.9)	
Surgery	7 (13.4)	3 (42.8)	4 (57.1)	
Hospitalisation	6 (11.5)	1 (16.6)	5 (83.3)	
Not treated	6 (11.5)	1 (16.6)	5 (83.3)	

Results

Patients diagnosed with alpha thalassaemia had an average age of 41.7±12.7 years, whereas those diagnosed with beta thalassaemia had an average age of 31.5±9.7 years. Significant variations were identified in the alpha and beta thalassaemia groups with respect to age ($p< 0.002$), gender distribution ($p< 0.04$), height ($p< 0.04$), and serum ferritin ($p< 0.001$). Patients with beta thalassemia were younger and exhibited a significantly higher iron excess (up to three times) in comparison to those with alpha thalassaemia (3,243±2,721, $p< 0.001$). Patients with beta thalassaemia had a higher prevalence of fractures (44.1%) compared to those with alpha thalassaemia (16.9%); this difference was statistically significant ($p< 0.001$). The age at which beta thalassaemia patients experienced their initial fracture was significantly lower than that of alpha thalassaemia patients (14.8±10.1 vs. 28.0±22.7, respectively, $p< 0.01$). Fractures occurred most frequently in the upper extremity (61.5%). Falls constituted the predominant causes of these fractures (42.3%), followed by motor vehicle accidents (36.5%). Predictably, the majority of fractures (59.6%) were managed with the application of a cast or splint, whereas hospitalization or surgical intervention accounted for only about 16% (13.4%).

Discussions

A prevalence of fracture in thalassemia patients was determined to be 35.3% in the present study. The present fracture prevalence is considerable lower than the 50% rate documented in the 1970s and 1980s, although it is comparable to the high incidence rate documented by other researchers [12, 17]. Furthermore, our findings are in contrast with two recent studies conducted by Basanagoudar *et al*. [18] and Vogiatzi *et al*. [6], which examined transfusion-dependent beta thalassemia patients and reported an overall fracture prevalence of 12%. This may be attributed to the chelation and transfusion regimens being less effective [19]. Hence, it is advisable to enhance transfusion technique and chelation regimen in order to mitigate the incidence of fractures in patients with thalassaemia. Additionally, in these thalassaemia patients, antiresorptive medication is considered for the treatment of reduced bone mass; however, due to its high cost, it is not routinely prescribed. Constant endeavors to obtain government funding ought to be prioritized.

The findings of this research investigation revealed that individuals diagnosed with alpha thalassaemia experienced a reduced incidence of fractures in comparison to those diagnosed with beta thalassaemia. This result was consistent with a study published by the Thalassaemia Clinical Research Network of North America (TCRN), which found that patients with beta thalassaemia major (16.6%) and beta thalassaemia intermediate (12.2%) had a higher incidence of fractures than those with beta thalassaemia/Hb E (7.4%) and alpha (2.3%). 17, 6 The reduced incidence of fractures observed in individuals with alpha thalassaemia can be attributed to the relatively low disease activity and mild haemolysis, in contrast to the high disease activity and moderate to severe haemolysis observed in those with beta thalassaemia.

The high incidence of fractures in thalassaemia is associated with aging and reduced lumbar bone mass, according to the TCRN findings [6]. Our findings, in contrast to those presented previously, indicate that the epidemiology of fractures among patients with alpha and beta thalassaemia is quite distinct. A higher incidence of fractures was noted among adolescent patients who were diagnosed with beta thalassemia. This could potentially be attributed to either an elevated disease activity in Thai children with chronic thalassemia or inadequate parental protection. Fractures occurred most frequently in the upper extremity, with motor vehicle accidents and falls accounting for the majority of fracture-related incidents. A cast or prosthesis was the prevailing treatment modality. Comparable results were observed for the two varieties of thalassaemia.

Fung *et al*. [12] identified several significant predictors of fracture prevalence in thalassaemia, including age, masculine gender, hypothyroidism, and the type of thalassaemia. Analogous significant predictors were identified in the current investigation as they had been previously delineated. Fracture risk factors include male gender, beta thalassemia diagnosis, prior splenectomy, transfusion, and a low body mass index. Thus, the multifactorial etiology of fracture incidence in thalassaemia is evident.

Conclusion

Fractures were more prevalent among adults with thalassemia major, according to our findings. Our findings have significant clinical ramifications; therefore, we recommend that patients with thalassemia major, particularly those with inadequate transfusion and chelation, have their bone health routinely evaluated.

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