

Fractures in Transfusion Dependent Beta Thalassaemia – An Indian Study

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ABSTRACT

Aim of Study: To analyse the incidence of fractures in beta thalassaemia patients and to identify causative factors.

Methods: We examined all cases of transfusion dependent beta thalassaemia (TDBT) seen at our institute over a two-year period. The transfusion records, incidence of fractures, cause of fracture and Hb levels were recorded. Radiographs of the involved parts were taken in cases with fractures only.

Results and Conclusions: Amongst 105 cases of TDBT assessed, 14 sustained a total of 28 fractures. Seven patients sustained more than one fracture. Two thirds of these fractures were caused by trivial trauma. All fractures, except one, were of the closed type. Radiologically, fractures frequently showed minimal or no displacement. All fractures were successfully treated by closed modalities of treatment. Majority of the fractures healed within normal union time for a given bone. Permanent deformities and gross limb length discrepancies were uncommon. On reviewing the literature, we noted that the incidence of fractures in our series and in the latest reports was lesser than previously reported. We postulate that this is a result of better and earlier control of hemoglobin status by improved transfusion techniques, and earlier recognition of the disease. Difficulties arise due to inadequate blood transfusion facilities in developing countries.

Keywords: Beta Thalassaemia, fractures

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INTRODUCTION

Beta thalassaemia is a severe hemolytic anemia occurring as a result of deficient or absent synthesis of beta globin chain of hemoglobin A⁽¹⁾. It is characterized by severe anemia, growth retardation, skeletal disturbances, iron overload, cardiac and endocrine abnormalities which cut short the life of the affected

patients⁽²⁾. Beta thalassaemia is widely prevalent in southern Asian countries including India, and it accounts for 10,000 of the 100,000 patients of beta thalassaemia born world-wide every year⁽³⁾. Currently emphasis of treatment is on early hyper-transfusion regimen and effective iron chelation therapy⁽⁴⁾.

Musculo-skeletal problems in beta thalassaemia occur frequently due to anatomic proximity of bones and joints to the active centres of hematopoiesis⁽⁴⁾. These include fractures⁽⁵⁻⁷⁾, premature epiphyseal fusions⁽⁵⁾ and thalassaemic osteoarthropathy⁽⁸⁾.

One third^(5,7) to half⁽⁶⁾ of beta thalassaemia patients have been previously reported to sustain fractures of the long bones as a result of minor, direct or indirect trauma, especially in the more severe variety of beta thalassaemia major⁽⁹⁾. Quite commonly the fractures are solitary, though multiple and recurrent fractures have been described^(6,7).

Fractures in thalassaemia are not routinely treated operatively⁽¹⁰⁾; this is so because these fractures are commonly the result of minimal trauma, and are quite frequently undisplaced or minimally displaced^(5,6). Secondly, these patients are poor surgical risk cases in view of their cardiac decompensation, endocrinal abnormalities secondary to hemochromatosis and are more prone to intercurrent infections, especially if they have undergone splenectomy. Thirdly, severe osteoporosis and poor bone stock potentially prevents successful internal fixations. These fractures usually unite with conventional techniques like closed reductions and casts, braces or splints, although some studies in the literature report varying time to union^(1,6,7). Deformities and shortening have been observed as a sequel to these fractures but these are usually not gross^(5,7). The one exception to this rule is a fracture of the femoral neck, which due to the attendant risks of non union or avascular necrosis, is best treated by adequate reduction and multiple screw fixation.

A review of the recent literature shows only occasional references to fractures in beta thalassaemia⁽¹¹⁻¹³⁾. Improvement in transfusion therapy has prolonged the life span of beta thalassaemia patients enabling them to participate actively in their

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Fig. 1a-b AP radiograph of united fracture shaft femur (a) and Lateral radiograph of united fracture both bones forearm in the same patient.

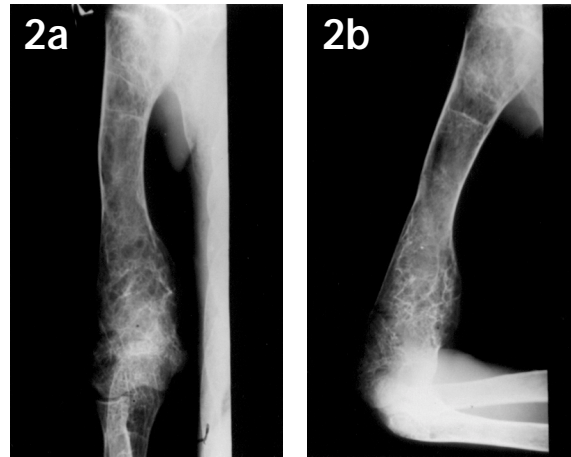


Fig. 2a-b AP and Lateral radiographs of an adult male who had sustained multiple fractures of the humerus. Note the severe osteoporosis and honey-combing of the humeral shaft, along with humeral head varus deformity due to premature epiphyseal fusion.

normal activities⁽⁶⁾. This may have altered the incidence of fractures and their characteristics. Hence we felt it necessary to analyse patients with transfusion dependent Beta thalassemia (TDBT) attending the thalassemia transfusion unit at our institute, for the occurrence of fractures and to study their characteristics.

MATERIAL & METHODS

A total of 105 TDBT patients requiring regular blood transfusions in the Thalassemia unit, Department of Paediatrics, PGIMER, Chandigarh between 1996-97 were evaluated on a one time basis for the occurrence of fractures. All patients above the age of five years of either sex were assessed. Mean age of the study group was 12.10 years. Out of 105 TDBT patients, there were 85 males and 20 females with a male to female ratio of 4:1. Ninety-five patients had been diagnosed as thalassemia major and 10 as thalassemia intermedia at the time of enrollment for blood transfusion. Sixty-three patients (60%) had maintained average pre-transfusion haemoglobin levels below 8 gm/dl and 42 patients (40%) had maintained levels above 8 gm/dl.

All patients and their parents were interviewed using a questionnaire regarding the onset, course and treatment of the disease. Patients sustaining fractures were further assessed by a detailed history, clinical and roentgenologic examination pertaining to the musculo-skeletal system.

OBSERVATIONS AND RESULTS

14 patients (13.3%) had sustained 28 fractures amongst the 105 TDBT study group. Four patients sustained fractures during the study period, whereas 10 patients had evidence of old healed fractures prior to the study period. Fractures were multiple in seven (Fig. 1), out of which two patients sustained multiple fractures during

the period of study. The highest number of fractures sustained by a single patient was six. There were no recurrent or intra-articular fractures.

Ten out of 85 males and four out of 20 females sustained fractures. The youngest patient to sustain a fracture was three years and the oldest was 15 years at the time of fracture. The mean age at fracture occurrence was 9.2 years. Twelve out of 95 patients with thalassemia major and two out of 10 patients with thalassemia intermedia sustained fractures. Eight of the 63 under transfused (Hb < 8gm/dl) and six of the 42 well-transfused cases (Hb > 8gm/dl) suffered fractures.

The oldest patient in our series was 25 years of age, and very few of the patients who were born before the advent of hyper-transfusion regimens reached this age. Most patients died in the later half of the second or the earlier half of the third decade of their lives. This was principally due to two factors; blood resources are scarce in our country, and repeated timely transfusions were not always possible. Additionally, a vast majority of the patients born prior to the advent of the cheaper oral chelator Deferiprone suffered from the complications of secondary haemochromatosis due to iron overload. They simply could not afford chelation therapy with Desferrioxamine, which has only become available in our country for the last five years.

The fractured bones in order of frequency were femur (8), humerus (6), forearm (6), tibia (5), phalanges (2) and one case had fracture of the clavicle. Nineteen fractures were caused by seemingly trivial trauma and the rest by relatively significant trauma. No significant difference in the fracture occurrence in upper limbs (15) and lower limbs (13) or the side involved (right side 15, left side 13) were seen. All fractures were of the closed type except one case of supracondylar fracture humerus, which was of the open

grade-1 type. Most long bone fractures commonly involved the diaphysis, except around the elbow joint where eight metaphyseal region fractures were seen (six supracondylar fractures and one each of the radial neck and proximal ulna).

Roentgenograms revealed minimal or no displacement in 23 of the 28 fractures. The fracture pattern was either transverse or short oblique with no comminution in all cases. Though the bones showed trabeculation and thin cortices in most fractures, severe osteoporosis was seen in patients with multiple fractures (Fig. 2) and in fractures around the elbow joint.

All fractures were treated by non-operative methods like posterior Plaster of Paris splints, closed reductions and casts, hip spica etc. Most fractures united within normal union times for a given age of the patient and site of the fracture. Shortening of the extremity was seen in five of 14 patients and in seven of 28 fractures. The shortening was more than an inch in two patients, one each in the upper and lower limbs, of which one required a shoe raise. Interestingly these patients had associated premature epiphyseal fusions of the proximal humeral and distal femoral epiphyses respectively. Fractures united with residual deformities in six patients and terminal restriction of joint movements in one. However significant deformities, posing difficulties in ambulation, were seen in two patients only. Two of the six supracondylar humeral fractures mal-united with resultant cosmetic deformities, one cubitus valgus and one cubitus varus; both of these had good functional results, which were acceptable to the patients. Two femoral shaft fractures had malunited in valgus out of which only one was severe enough to cause difficulty in ambulation.

Statistically there was no significant correlation of fractures with age, sex, thalassemia type or average hemoglobin status of the patients.

DISCUSSION

Musculo-skeletal manifestations of beta thalassemia that are commonly seen include fractures⁽⁴⁻⁷⁾, premature epiphyseal fusions⁽⁵⁾, thalassemic osteoarthropathy⁽⁸⁾ and of late, drug related side effects of patients on treatment with the iron chelator, deferiprone⁽¹⁴⁾.

This is one of the larger studies conducted on a thalassemic population for the occurrence of fractures, and maybe the first one of its type from a single centre in an underdeveloped country. In our experience, 14 patients sustained 28 fractures amongst 105 patients of TDBT studied for the occurrence of musculo-skeletal problems. The incidence of patients sustaining fractures in the present study was 13.3%.

As early as 1932, Baty reported the occurrence of fractures in thalassemic patients⁽¹⁵⁾. Caffey⁽¹⁵⁾ also observed these fractures infrequently in the femur of children and in the fibula, radius, metatarsals and spine of older patients. Fractures were also observed in 10 of the 21 patients with severe Cooley's anaemia and less frequently in the intermediate type of beta thalassemia by Erlandson⁽⁹⁾ et al. However the exact severity of the disease was not known. About a third of the patients in the previous studies by Exarchou⁽⁵⁾ and Dines⁽⁷⁾ and 50% of the patients in the follow up study by Finterbush⁽⁶⁾ had sustained fractures, in contrast to 13.3% of patients in the present study. In a multi-centric study on 977 transfusion dependent thalassemic patients, Ruggiero et al observed fractures in 193 patients with a prevalence rate of 19.7%. Children and adolescents sustained more fractures than adults did, and these fractures commonly followed mild to moderate trauma. The lower incidence of fractures observed by us was probably due to the fact that most patients in the present study maintained pre-transfusion haemoglobin levels greater than 9gm/dl in the early part of the disease, due to emphasis on hyper-transfusion regimen from a young age. However with increasing age, our patients could not maintain adequate haemoglobin status due to increasing demands for repeated transfusions and decreased availability of voluntary blood donors. This is a significant problem in developing countries, where cost and availability of blood for transfusion are important factors. Other reasons for the decreased fracture incidence could be the younger age of the patient population assessed (mean age 12.1 years) in our study and the exclusion of routine roentgenographic survey for the occurrence of asymptomatic vertebral fractures. The mean age of the patients analysed in previous studies by Exarchou et al⁽⁵⁾ and Finterbush⁽⁶⁾ was 16 years.

In all the previous studies, 40-60% of the fractured patients sustained multiple fractures⁽⁵⁻⁷⁾. Seven of our 14 patients (50%) had more than one fracture and all these patients had severe osteoporosis on radiographs. However recurrent fractures were not seen in the present study.

Dines et al observed that fractures were common in patients above the age of 10 years, with no sex predilection. Erlandson et al⁽⁹⁾ observed that fractures were more common in children above the age of six years, with severe Cooley's anaemia. Finterbush et al⁽⁶⁾ found that fracture occurrence was commonest between 5-12 years with an additional rise during growth spurt i.e. 14-17 years. In the present study, no specific age, sex, or thalassemia type related fracture pattern was seen, though the mean age at fracture occurrence was 9.2 years.

Fractures have usually been seen to unite with conventional techniques like closed reduction and casts, braces and plaster splints⁽⁶⁾. Time to fracture union was normal in all previous studies, except the one by Dines et al⁽⁷⁾ who noted that the fractures united slowly, frequently resulting in permanent deformities. All fractures in the present series united with conventional techniques like closed reduction and plaster slab, casts, and hip spica for femoral fractures. All fractures united within the expected time for the given age of the patient and site of the fracture.

Roentgenographically, little or no callus was seen after the healing of fractures in most of the cases. This could be attributed to minimal or no displacement of fractures seen in this disease, which usually occurred after trivial trauma in a majority of the cases. Such a fracture pattern and picture of healing is quite commonly observed in pathologic fractures.

Fractures were more common in under transfused patients than in well-transfused patients. This difference, however, was not statistically significant. The severe osteoporosis seen in all our patients with multiple fractures suggests that fractures could be related to severity of the bone disease, which is multi-factorial, rather than to the haemoglobin levels only.

We conclude that though the nature of injury causing fractures, their site, type, radiological pattern and methods of treatment have remained the same, the incidence of fractures in the cases being treated by modern methods has reduced as compared to previous reports in the literature. Our observations in this study suggest that an attempt should be made to achieve haemoglobin levels above 8-9 gm/dl (by more frequent and regular transfusions), at least

in the early part of the disease. We feel that this treatment policy brings down the incidence of fractures considerably in patients with transfusion dependent thalassemia. However, this maybe a problem in countries with scarcity of blood resources, but all efforts should be made to maintain optimum haemoglobin levels.

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