E:/Biomedica/Vol.23 Jan. – Jun. 2007/Bio-5 (A)

FREQUENCY OF COMPLICATIONS IN BETA THALASSEMIA MAJOR IN D. I.KHAN

F. UR. KHAN[1], M. H. KHAN[2], TARIQ AYUB[1], AND S. HUMAYUN SHAH[3]
Department of Paediatrics[1], Community Medicine[2] and Pathology[3], DHQ Teaching Hospital Gomal Medical Collage, D. I. Khan - Pakistan

This is a retrospective study performed to see the frequency and extent of complications in beta thalassaemia major patients in the region of D I Khan. It was carried out at the Department of Paediatrics, District Headquarter Teaching Hospital, Gomal Medical Collage (GMC), Dera Ismail Khan from, 1st January 2005 to 31st December 2005. The files of all the beta thalassaemia major patients admitted during the year 2005 were scrutinised for complications. All the patients had been investigated for the diagnosis and complications. Demographic and clinical data included age, sex, weight, geographical location, complications and splenectomy; and was gathered on a compilation sheet. Results were analysed by descriptive statistical methods. Beta thalassaemia minor and intermediate cases were excluded. A total of 123 patients with beta thalassaemia major were admitted for 295 times during the study period. Majority of the patients (95.9%) were from D. I. Khan. Majority were males (71.5%). Commonest complication observed was growth failure (52.8%). Next common was involvement of liver (21.1%). Other complications included heart disease (13.8%) and endocrinopathies (4.2%). It was concluded that the commonest complication of beta thalassaemia major in D I Khan was growth failure. Other complications were also not uncommon and involved liver, heart and endocrine glands.

Inherited haemoglobin disorders are amongst the most common single gene defects in human[1] and thalassaemias are the commonest of this group[2]. Beta thalassaemia represents a group of recessively inherited haemoglobin disorders[3] where beta globin chain synthesis is decreased resulting in an excess of alpha chains. This leads to increased synthesis of the haemoglobins without beta chains [e.g. Hb-F ($alpha_2$ $gamma_2$), Hb-A_2 ($alpha2delta_2$)]. Left over free alpha chains form tetramers ($alpha_4$), which are very insoluble and precipitate in red cells leading to increased fragility and early red cell death[1]. The estimated prevalence of beta thalassaemia is 16% in Cyprus, 3-14% in Thailand and 3-8% in India, Pakistan, Bangladesh and China. Prevalence is low in Afri-can blacks (0.9%) and northern Europe (0.1%)[4].

The combination of regular blood transfusions and chelation therapy has dramatically increased the life expectancy of thalassaemics into 4th & 5th decades of life. On the other hand, frequent blood transfusion has also led to iron overload with many complications including endocrinopathies, [2,3,5] behavioral and neurotic problems,[6,7] growth failure[8], cardiovascular problems[9-11] liver disease, [11-13] gonadal dysfunction and delayed puberty.[14] Frequent blood transfusion can also lead to increased chances of transfusion related infections.[12]

Present study consists of the analysis of ward record of beta thalassaemia major cases to determine the frequency and extent of complications.

MATERIAL AND METHODS

It is a retrospective audit of ward record from 1st January to 31st December 2005 and was conducted in the Department of Paediatrics, DHQ Hospital, GMC, D. I. Khan. The ward record of 2005 consisting of patient files was scrutinised for beta thalassaemia major and its complications. All new cases were investigated to confirm the diagnosis of beta thalassaemia major with Hb, peripheral smear, Hb-F assay and Hb-electrophoresis. Both new and old cases were investigated for complications using ECG, X-ray Chest, Echocardiography, S. Calcium, S. Ferritin and other investigations wherever relevant beside the routine investigations. Patients were labelled as having growth failure when their weights were below -2 standard deviations for age and sex. Beta thalassaemia minor and intermedia cases were excluded from the study.

Statistical Method

Results were analyzed by descriptive statistical methods, including percentage, mean etc.

RESULTS

A total of 123 patients were admitted during the study period for 295 times (mean 2.4 times/

patient) either for diagnosis, blood transfusion or complications. It accounted for 4% of total admissions to the Children Unit. Majority of the patients were from D I Khan District and its attached tribal area (118, 95.9%); three patients (2.4%) were from District Lakki Marwat and two (1.7%) were from District Tank. Male to female ratio was 2.5: 1 and majority were below 5 years of age (61.8%) (Table 1). Age of the youngest patient at diagnosis was 4 months and oldest patient of the study was 21 years old. The patients belonged to all ethnic, linguistic, geographical and racial groups living in D. I. Khan District, but Pathans were more than other racial groups (88, 71.5%). Twenty-five patients (20.3%) were newly diagnosed during the study period while 98 patients (79.7%) were already diagnosed and were admitted during the study period for blood transfusion and/or complications. Splenectomy had been performed in 22 (17.9%) patients, and all of them were above 5 years of age. Three patients died during the study period in the hospital due to cardiac complications. Other diseases present co-incidently in these thalassaemia patients were asthma in 5 patients (4%), Down's syndrome in 01 patient (0.8%) and VSD in 01 patient (0.8%).

Table 1: *Age and Sex Distribution.*

Age / Sex	≤ 05 years	05-10 years	≥10 years	Total
Male	52 (42.3%)	28 (22.8%)	08 (06.4%)	88 (71.5%)
Female	24 (19.5%)	09 (07.3%)	02 (01.7%)	35 (28.5%)
Total	76 (61.8%)	37 (30.1%)	10 (08.1%)	123 (100%)

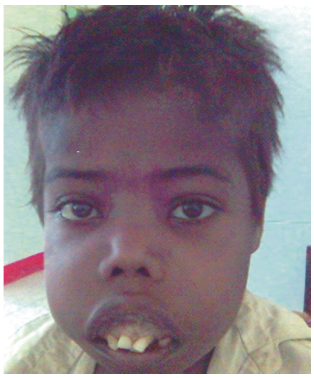

Fig. 1: *A case of beta thalassaemia major with typical thalassaemic facies.*

Table 2: *Complications.*

S. No	Complications	No	%
1.	Growth failure	65	52.8%
2.	Hepatic	26	21.1%
3.	Cardiac	17	13.8%
4.	Transfusion related infections (Hep B)	06	04.9%
5.	Endocrine	05	04.2%

Complications were observed in a total of 92 patients (74.8%). Some patients had more than one complication. Commonest complication was growth failure and was observed in 65 patients (52.8%). Next common were cardiac complications and were observed in 28 patients (22.8%). These included cardiomagaly on X-ray in 19 patients (15.4%), frank congestive cardiac failure in 9 patients (7.3%) and one patient (0.8%) of them had arrhythmia (supraventricular tachycardia). Hepatic enzymes were raised in 26 patients (21.1%). Six patients were positive for HBsAg, but none for anti HCV. Endocrine complications in-cluded delayed puberty in 02 patients (1.7%), hypoparathyroidism presenting as recurrent hypocalcaemic tetany in 02 patients (1.7%) and IDDM in 01 patient (0.8%).

Iron chelation therapy was inadequate in all patients (0-1 desferrol infusion only after each blood transfusion). S. Ferritin level was performed in 42 patients with complications and was found to be raised in all of them (>2000 ng/ml). All complications (except growth failure) were observed in children over 5 years of age.

DISCUSSION

Beta thalassaemia is a common problem in hospital practice, e.g. it accounted for 4% of hospital admissions in the present series. In our study complication rate is 74.8%. It is more than 50-70% of the incidence of complications reported in other studies.[2,3,8,12] The possible reasons are less frequent transfusions, low pre-transfusion haemoglobin and most importantly inadequate chelation therapy.

In our study commonest complication was growth failure (57.8%). It is due to growth hormone neuro-secretary disturbance and secondary growth hormone insensitivity.[3,8] Chronic anaemia, congestive cardiac failure, haemosiderosis and other endocrine and metabolic disturbances may also be contributory factors.[1,8] Similar figures have been reported by others as well[8]. Second common complication was raised hepatic enzymes (21.1%). All of them were negative for anti HCV, but 6 were positive for HBsAg. This is unexpected as Hepatitis C infection has been reported to be present in as many as 35-40% of thalassaemia patients.[12,13] The reason is not clear but may be due to better

pre-transfusion screening. Cardiac complications were noted in 17 patients (13.8%). This figure is higher than 4.8% reported from USA.[11] The reasons are multiple and include chronic anaemia, infrequent transfusions and inadequate chelation therapy. A recent study shows that presence of certain major histocompatibility antigens/alleles may protect (HLA-DRB1*1401), while others may predispose (HLA-DRB1*0501) to the development of congestive cardiac failure.[15] Therefore genetic, immune and infective processes may also be important in the causation of heart disease in beta thalassaemia major. Endocrine complications occurred in 5 patients (4.2%) and included delayed puberty, hypoparathyroidism and IDDM. This figure is lower than 57% reported by Satwani et al[2] and 88% reported by Shamshirsaz et al[3]. The reasons are not clear but may be due to lesser number of transfusions in our patients leading to less severe haemosiderosis and decreased number of endocrine complications.

The complication rate in the present study is higher than that in other studies.[16] The reasons are obvious – irregular/inadequate transfusions, lower pre-transfusion Hb levels and inadequate chelation therapy. Although the present study has the bias of a retrospective study it shows that the complication rate in beta thalassaemia is increasing. After increasing awareness in the public and rising number of blood transfusions, the life expectancy for beta thalassaemia patients is increasing,[17] and so will be the number of complications in future. Therefore regular transfusions/chelation and comprehensive care are mandatory to reduce the number of complications in future. Comprehensive care includes regular transfusions, chelation and monitoring (cardiac, hepatic, endocrine, transfusion related infections, eye and ear).[18]

It is **Concluded** that commonest complication of beta thalassaemia major in D. I Khan is growth failure. Other complications are also not uncommon and involve liver, heart and endocrine glands. Satisfactory cost-effective treatment for beta thalassaemia major as yet is not available, other than bone marrow transplantation. Therefore it is needed to put effort to eradicate or at least reduce the disease burden through preventive measures including pre-marital screening, genetic counseling and prenatal diagnosis. Until the achievement of this goal, establishing centers for palliative and curative treatment of beta thalassaemia is important.

REFERENCES

1. Sharada AS. Thalassemia and related hemoglobinopathies. Indian J Pediatr 2005; 72 (4): 319-24.
2. Satwani H, Raza J, Alam M, Kidwai A. Endocrine complications in thalassemias; Frequency and association with ferritin levels. P P J 2005; 29 (2): 113-9.
3. Shamshirsaz A, Bekheirnia MR, Kanger M et al. Metabolic and endocrinologic complications in beta-thalassemia major: A multicenter study in Tehran. BMC Endocrine Disorders 2003; 3 (4): 23-34.
4. Leung NT, Lau TK, Chung TKH. Thalassemia screening in pregnancy. Curr Opinion in Ob Gyn 2005: 17; 129-34.
5. Suvarna J, Ingle H, Deshmukh CT, Insulin resistance and beta cell function in chronically transfused patients of thalassemia major. Indian Pediatr 2006 May; 43 (5): 393-400.
6. Moorjani JD, Chithira I. Neurotic manifestations in adolescents with thalassemia major. Indian J Pediatr 2006; 73 (7): 603-7.
7. Zafeiriou DI, Economou M, Athanasiou-Metaxa M. Neurological complications in beta thalassemia. Brain Dev 2006 Sept; 28(8): 477-81.
8. Low Louis CK. Growth of children with beta thalassemia major (Editorial). Indian J Pediatr 2005; 72 (2): 159-64.
9. Ulger Z, Aydinok Y, Levent E et al. Evaluation of QT dispersion in beta thalassemia major patients. Am J Hematol 2006 August 21; 81 (8): 231-5.
10. Aessopos A, Samarkos M, Voskaridou E et al. Arterial calcifications in beta thalassemia. Angiology. 1998 Feb; 49 (2): 137-43.
11. Aessopos A Farmakis D, Deftereous S et al. Thalassemia Heat Disease. A comparative evaluation of thalassemia major and thalassemia intermedia. Chest 2005; 127: 1523-30.
12. Cunningham MJ, Macklin EA, Neufeld EJ, Cohen AR. Complications of beta thalassemia major in North America. Blood 1 July 2004; 104 (1): 34-39.
13. Perifanis V, Tziomalos K, Tsatra I et al. Prevalence and severity of liver disease in patients with beta thalassemia major. A single-institution fifteen-year experience. Hematologica 2005; 90: 1136-38.
14. Sanctis VD, Vullo C, Katz M et al. Gonadal functions in patients with beta thalassemia major. J Clin Pathol 1988; 41: 133-7.
15. Kremastinos D, Flevari P, Spyropoulos M et al. Association of heart failure in homozygous beta thalassemia with the major histocompatibility complex. Circulation 1999; 100: 2074-78.
16. Borgna-Pignatti C, Cappillini MD, De Stefano P et al. Survival and complications in thalassemia. Ann N Y Acad Sci Nov 2005; 1054:40-47.
17. Chern JP, Su S, Lin KH et al. Survival, mortality and complications in patients with beta thalassemia major in northern Taiwan. Pediatr Blood Cancer 2006 Sept 13; 45 (2): 53-6.
18. Medical Information. Thalassemia Comprehensive Care: More than just transfusions and chelation. Pamphlet. Cooley's Anemia Foundation, Inc. 2001.