Letters to the Editor

Evaluation of current management of homozygous β-thalassemia in Eastern Saudi Arabia

Sir,

β-thalassemia is common in the Kingdom of Saudi Arabia (KSA) along the coastal strip of the Red Sea and in the Eastern Province around Jubail, Qateef, Dammam, and Hofuf.[1] Although β-thalassemia disease has been known for many years in these areas and many of its manifestations are recognized, the details of actual incidence, the natural history of clinical course of the disease from early childhood to death are unknown. This is largely because of inadequate facilities for mass population screening, variable degree of severity, unavailability of national protocol treatment, inadequate supervision of management, poor health education and knowledge of the disease, variability of its manifestations and complexity of the interaction of the disease process with other health related events for example sickle cell disease.[2] There are at least 165 transfusion-dependent homozygous β-thalassemia patients who are receiving medical care at local hospitals in the Eastern Province of KSA. During the period, September 1998 to August 1999 a total of 165 patients with homozygous β-thalassemia were initially investigated from the participating hospitals. The hospitals involved in this study are King Fahd Hospital of the University (KFHU), Al-Khobar, the Maternity and Childhood Hospital, Dammam, King Fahd Hospital and Thalassemia Center, Hofuf and Qateef Central Hospital. The majority of the patients came from King Fahd Hospital and Thalassemia Center in Hofuf. Data from Qatif Central Hospital was incomplete and therefore was left out in the analysis. For each patient who visited the clinic a general history and physical examination were performed with particular reference to family history, weight, height, head, circumference, pallor, jaundice, splenomegaly, hepatomegaly, and cardiomegaly. Venous blood samples were also taken for routine hematology including complete blood counts, blood smear, reticulocyte counts, and where possible, levels of HbA2 (adult hemoglobin α_2d_2) (by micro chromatography), fetal hemoglobin and iron levels were estimated. All data (clinical, hematological and others) relating to each visit was recorded. The charts of all patients managed in these hospitals were also retrospectively reviewed to determine the demographic characteristics, duration of treatment, initial hemoglobin, transfusion trigger level and post-transfusion level, presence and degree of organomegaly, weight and height. The presence of complications was also assessed by extracting information regarding the results of the following tests: Serum iron, total iron binding capacity and ferritin, liver function test, fasting blood sugar, hepatitis profile, electrocardiogram (ECG), echocardiogram (Echo) and chest x-ray. Comparing the results between these patients and those who were not splenectomized also assessed the effects of splenectomy on these parameters. β-thalassemia major patients were identified in different hospitals of the Eastern Province (**Table 1**) suffering from the severe form of the syndrome. These patients were regularly seen in the inpatient and outpatient clinics at these hospitals. The signs and symptoms of the β-thalassemia major patients in the different areas were recorded. Differences in signs and symptoms were noticed in the results from the different areas, suggesting differences in the clinical presentation. This may be a consequence of different β-thalassemia genotypes resulting from different β-thalassemia mutations in the different areas. In the Eastern Saudi children investigated during our study, skeletal defects were a frequent finding. The most frequent were facial changes with bossing of forehead (58%) and maxilla hypertrophy observed in 52% of our subjects. The skeletal abnormalities were closely related to the age of onset and frequency of blood transfusion regimens. Patients adequately transfused had either no or mild abnormalities compared to patients with inadequate blood transfusion. During the follow-up of our patients, early growth failure was observed in 35%, 76% and 42% of the patients from Al-Khobar, Hofuf and Dammam. The frequency of hepatomegaly was high in the Saudi patients investigated during our study. Unlike the spleen, the liver showed a greater degree of enlargement. It was more than 5 cm below the costal margin in 60%, 67% and 70% of the patients from Al-Khobar, Hofuf and Dammam. The liver enzymes were high in 38%, 48% and 56% of the patients in Al-Khobar, Dammam and Hofuf.

Table 1 - Age and sex distribution of 165 patients with B-thalassemia major followed at different hospitals in Eastern Saudi Arabia.

Age	Al-Khobar n (%)	Dammam n (%)	Hofuf n (%)	Qateef n (%)
< 6 Years	3 (9)	7 (33)	27 (42)	20 (42.5)
6-12 Years	19 (57.5)	11 (52)	25 (39)	20 (42.5)
>12-15 Years	11 (33.5)	3 (15)	12 (19)	7 (15)
Total	**33 (100)**	**21 (100)**	**64 (100)**	**47 (100)**

Bilirubin level was elevated in the majority of our patients. Splenomegaly is a frequent finding in β-thalassemia major patients,[3] particularly in children who do not receive regular blood transfusion regimen. The complication of splenomegaly and associated hypersplenism includes physical discomfort due to large abdomen, anemia, severe thrombocytopenia and neutropenia. On the other hand, high transfusion regimen reduces the incidence of splenomegaly. The spleen was less than 5 cm enlarged in 27%, 57% and 50% but more than 5 cm in 24%, 29% and 31% of the patients in Al-Khobar, Dammam and Hofuf. Splenectomy was performed on 39%, 19% and 19% of the patients from Al-Khobar, Hofuf and Dammam.

Children on high transfusion programs have a considerably lower incidence of infection.[4] The most frequent encountered infection in our β-thalassemia patients are repeated upper respiratory tract infection and recurrent urinary tract infections. During the follow-up of our patients screening for hepatitis C virus was negative in 79%, 84% and 90% of the patients from Hofuf, Dammam and Al-Khobar respectively and human immunodeficiency virus was negative in all patients. Analysis of our data showed that 3 patients who are followed at our hospital, KFHU, died this year from cardiac complications. Another 3 patients of the surviving patients have incidence of congestive heart failure. Cardiac evaluation by chest x-ray, ECG and Echo revealed that 12% of the patients who are followed at KFHU have left ventricular global dysfunction. The cardiac evaluations of the patients with β-thalassemia major in other hospitals were unsatisfactory. Occasionally, Echo was carried out on a small number of the patients from other hospitals, despite the highly evaluated serum ferritin in some of these patients. Perhaps a more vigorous chelation therapy could reduce the serum ferritin. Patients are encouraged to use the Desfurroxamine (DF) with pump (infusion pump) 5-6 nights per week during sleep. Auditory, visual and bony abnormalities have been described, but these have only occurred with DF dose in excess of 60 mg/kg/day. Recently, a number of potential oral iron chelators have been developed in various laboratories. The results of bone marrow transplantation (BMT) in children without organ impairment are excellent and BMT must now be considered a real alternative to conventional treatment.[5] The outcome of our study shows that there are at least 165 transfusion dependent homozygous β-thalassemia patients who are receiving medical care at local hospitals in the Eastern Province. All private hospitals are not included. The thalassemia patients in these hospitals were previously (10-15 years ago) managed with blood transfusion on an irregular basis. They were transfused with blood whenever they came in with pallor and received DF intravenously in the hospital after blood transfusion. However, the management and follow-up of the thalassemia patients is now regular with blood transfusion given at 4 to 6 week intervals. At the same time, DF with pump both at the hospitals and at home became available. Each patient was encouraged to buy a pump while Desferral was provided on a regular basis from these hospitals. The management of these patients in the participating hospitals was not different from the basic standard treatment, which comprised blood transfusion, subcutaneous DF infusion and splenectomy, whenever indicated. Many of the patients followed in the participating hospitals were started on regular and aggressive blood transfusion (hyper-transfusion) to promote normal growth and avoid skeletal deformities. During the study period, we observed, although our older patients performed poorly with standard physical growth, abnormal facial appearance and very high serum ferritin due to their rejection of the appropriate methods of treatment, the younger patients who were diagnosed in the last 10 years, performed better. The mortality rate of the patients was 5.5% as 9 patients died, 6 of them from cardiac failure, and the importance of cardiac evaluation of these patients is stressed.

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