INVITED COMMENTARY

Complications in Transfusion-Dependent Thalassemia

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Thalassemia syndromes are one of the most common monogenetic diseases distributed worldwide. They are a group of hereditary blood disorders which result from a defect in the synthesis of either alpha or beta globin chains. Due to this defect, there is an imbalance in the ratio of alpha and beta chains resulting in ineffective erythropoiesis and a chronic hemolytic anemia. Based on the severity of the phenotype, beta-thalassemia is divided into two groups: transfusion-dependent thalassemia (TDT) and non-trans-fusion dependent thalassemia (NTDT) [1]. Although, the triad of chronic anemia, ineffective erythropoiesis and iron overload is seen in both the conditions, their clinical course and complications differ. Leg ulcers, gall stones, thrombosis and pulmonary hypertension are more common with NTDT [2]. With the advances in the understanding of pathophysiology and therapeutic modalities of beta-thalassemia, there has been a signi-ficant improvement in the management and the life expectancy of the patients with TDT. This has translated into new complications being identified that are associated with increasing age [3].

Endocrine complications are amongst the most common complications attributed to iron overload and inadequate chelation. These include hypogonadism, delayed puberty, growth retardation, hypothyroidism, hypoparathyroidism and adrenal dysfunction. In a study of 82 Malaysian patients with TDT, 65% had at least one endocrine dysfunction; short stature was the commonest problem (40.2%), followed by pubertal disorders (14.6%), hypoparathyroidism (12.3%), diabetes mellitus (5.2%) and overt hypothyroidism (4.9%) [4]. Subclinical hypothyroidism was seen in 13.4% patients. The authors suggested that early referral to endocrinologist aids timely recognition of endocrine complications which is important for optimal growth and chances of successful reproduction. Another study carried out among adole-scents with TDT revealed that normal or delayed onset of puberty with spontaneous progression was seen in 72.4% patients, while 27.6% patients had pubertal arrest or failure and were receiving hormonal replace-ment therapy (HRT) [5]. All patients on HRT had short stature. High serum ferritin was found to be significant deter-minant of delayed puberty. Low vitamin D levels and altered bone metabolism have also been observed in several studies. In a study of 32 patients on regular blood transfusion, 25(OH)D3 levels were significantly lower in older children compared to younger children. These patients also had higher ferritin levels. Authors suggested that hepatic iron overload may be associated with low 25(OH)D3 levels which may be an indicator of vitamin D deficiency and altered bone metabolism [6]. Another study on bone mineral density (BMD) in regularly transfused patients found that prevalence of suboptimal BMD was 86% at lumbar spine and 74% at femoral neck [7]. Regular monitoring of BMD and other biochemical parameters was advised in patients on regular transfusion [7]. Decreased BMD is major risk factor for the development of fractures and the prevalence increases with increasing age. Use of HRT and hypogonadism are additional risk factors [8].

This issue of the journal has two studies on the complications of TDT [9,10]. In the study by Handattu, et al. [9], children with TDT above the age of 5 years underwent comprehensive endocrine and metabolic bone disease evaluation – children older than 10 years also underwent *X*-rays of the thoracolumbar spine and dual energy *X*-ray absorptiometry (DEXA) scanning. Of the 37 patients studied, hypogonadism was found to be the commonest endocrine deficiency followed by short stature, abnormal glucose metabolism, subclinical adrenal insufficiency, hypothyroidism and hypopara-thyroidism [9]. Vitamin D insufficiency/deficiency was seen in 12 (60%) patients followed by hypocalcemia in two patients. Low bone mass and osteoporosis evidenced by vertebral fractures was also observed in four patients, all of whom had multiple endocrine deficiencies. The authors concluded that vertebral fractures can occur in the second decade of life in patients with TDT and are associated with endocrine abnormalities [9]. However, the correla-tion with any risk factors such as age, number of trans-fusions, and serum ferritin level was not assessed in the study [9].

In the second study, Kumaravel, et al. [10] have evaluated the risk of premature atherosclerosis in children with TDT. The carotid intima-media thickness (CIMT) was measured and correlated with clinical and biochemical parameters in children aged 2-15 years receiving regular blood transfusions. Significantly higher CIMT values were observed across all age groups compared to controls. Older age and higher serum ferritin values were significant risk factors for increased CIMT; dyslipidemia did not have a significant correlation with CIMT. The authors concluded that children with TDT are at increased risk of premature atherosclerosis [10]. In another study [11], 115 Egyptian children aged 5-18 years with TDT had significantly higher CIMT compared to controls. CIMT had a positive correlation with serum triglycerides. The study concluded that subclinical atherosclerosis started prematurely in children with beta thalassemia and CIMT can be used as a simple, accurate and non-invasive modality for early detection of athero-sclerosis.

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