ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue – 6, November - 2018, Page No. : 219 - 222

Growth and Endocrine Dysfunction in Children with Beta Thalassemia Major

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Endocrine dysfunction is common complication and a major contributor to morbidity and mortality in children with beta thalassemia major. Early detection and proper management is important for the improved quality of life in these children

Objectives: the study was undertaken to assess the growth and endocrine dysfunction in children with beta thalassemia.

Material and Methods: 51 children with beta thalassemia major were included in the study. Growth was assessed by anthropometric measurements. Blood samples were collected and various hormone levels were assessed.

Results and Conclusion: Growth and endocrine dysfunction is common in children with beta thalassemia major. As the age increases risk for endocrine dysfunction also increases.

Keywords: beta thalassemia, glycemic abnormalities, hypothyroidism, hypoparathyroidism

Introduction

Inherited haemoglobin disorders are amongst the most commonsingle gene defects in humans [(1)] and thalassemia is the commonest in this group [(2)]. Thalassemia refers to a group of genetic disorders of globin chainproduction in which there is an imbalance between the α-globin and β-globin chain production. Beta(β) thalassemia represents a group of recessively inherited haemoglobin disorders[(3)] where beta globin chain synthesis is decreased(β^+)or absent(β^0), resulting in a relative excess of alpha globin chains.β^0-Thalassemia syndromes are more severethan β^+-thalassemia syndromes, but there is significant variability between the genotype and phenotype. Beta-thalassemia major, first described by Cooley and Lee [(4)], refers to the severe β-thalassemia patient who often is homozygous for β^0 mutations and requires early transfusion therapy .When patients are homozygous for the β-thalassemia gene mutations (β^0 β^0),they cannot make any normal β chains.

The estimated prevalenceof beta thalassemia is 16% in Cyprus, 3-14%in Thailand and 3-8% in India, Pakistan, Bangladesh and China. Prevalence is low in African blacks (0.9%) and northern Europe (0.1%) [(5)]. The disease was previously considered fatal before 2nd decade of life[(6)]. But the combination of regular blood transfusions and chelation therapy has dramatically increased the life expectancy of children with thalassemia who can now live into their third and fourth decades.Though frequent blood transfusions have increased the life expectancy of these patients, iron overload and iron deposition in vital organs

secondary to multiple transfusions has also led to various morbidities. Many complications including endocrinopathies, behavioural and neurotic problems, growth failure, cardiovascular problems and liver disease has been documented.Apart from iron overload, other factors including chronic hypoxia due to anemia[8],viral infections, individual susceptibility, etc. has been pointed out in causing endocrine abnormalities and other organ damage.Many studies on endocrine aspects of thalassemia are available worldwide. But only few were done exclusively in paediatric population.In contrast to the western countries, life-long blood transfusions and iron chelation therapy that are considered as the cornerstone in the management of thalassemia may not be available always for the needy patients in developing countries like India.In such situations, the cost of chelation may preclude ideal therapy and the compliance with transfusion may not be optimal. Therefore, there is a high chance for increased prevalence as well as early onset ofseveral complications, includingendocrinopathies, in Indian population. Owing to these reasons, determining the magnitude of endocrine complicationsamong children thalassemia in India are needed and relevant.

Material and Methods

The present study was undertaken to estimate find out the prevalence of growth endocrine abnormalities in children with beta thalassemia major .51 children with beta thalassemia major attending haematology outpatient department in a medical college hospital in south India were included in the study. It was a hospital based observationalstudy lasted for one year.

Inclusion Criteria: Children with beta thalassemia major who has received at least 15 blood transfusions were included in the study.

Exclusion Criteria: Children with beta thalassemia major who has received less than 15 blood transfusions were excluded from the study.

The study was done after obtaining approval from institutional ethics committee. Demographic details and detailed histories were obtained from the mothers/ children themselves, through direct questionnaires and by reviewing of past medical records. Anthropometric details were recorded. Fasting Blood sugar; Serum free T_4, TSH Serum Parathormone levels and 25-OH vitamin D levels were estimated 2-3 weeks after their last blood transfusion. Obtained results were stratified as per standards and were entered in the proforma. PASW Statistics software was utilized for analysis..

Operational Definitions

Short stature - H/A < 3rdcentile; Underweight - W/A < 3rd centile - based on WHO growth charts (for 0-5 years) and IAP growth charts (for 5 – 18 years).Impaired FBS : FBS value of 100-125 mg/dL. Diabetes mellitus: FBS value ≥ 126 mg/dL. Hypothyroidism: Low free FT_4 and high TSH (overt cases) / normal FT_4, high TSH (subclinical cases) / Low FT_4 and normal or low TSH (due to central causes). Hypoparathyroidism : Serum PTH level <15 pg/mL .Serum 25-OH vitamin D – Normal level :>20 ng/mL.Vitamin D insufficiency: Serum 25-OH vitamin D levels 12-20 ng/mL).Vitamin D deficiency : Serum 25-OH vitamin D levels < 12 ng/mL

Observations & Results

51children who satisfied inclusion criteria were enrolled in the study. 45.1% children were <10years of age and 54.9% were ≥ 10 years of age. The mean age of the study population is 127.8 months.The study population had 58.8% males and 41.2% females. 88.2% childrenwere symptomatic before first birthday. 74.5% children were started on transfusion before 1 year of age.51% children were initiated on chelation therapy prior to 3 years of age. Out of 51 children, 25.5% had underweight. When height was measured 35.3% children had short stature. When endocrine abnormalities are considered, 7.9% children had glycaemicabnormalities,2% of them had diabetes

mellitusand, 5.9% ofthem had impaired glucose tolerance.Out of 51 children, 3.9% children had hypothyroidism and the rest normal thyroid function. 21.6% children had hypoparathyroidism. 19.6% had vitamin D insufficiency and80.4% children had normal vitamin D levels. None of them had Vitamin D deficiency. children in the age group of 10 years and more had higher proportion of growth retardation and endocrine abnormalities when compared to children < 10 years of age. 57.1% children had short stature, 14.3% children had glycaemic abnormalities, 7.1% children had hypothyroidism, 28.6% children had hypoparathyroidism and 33.1% children had vitamin D insufficiency in the older age group. Corresponding figures for short stature, hypoparathyroidism and vit.D deficiency were 8.7%, 13% and 4.3%respectively in younger age group. None of the children in less than 10 year age group has developed glycaemic abnormalities or hypothyroidism.

Discussion

The present study was conducted to estimate growth and endocrine dysfunction in children with beta thalassemia major. out of 51 children enrolled in the study 35.3% had short stature, 7.9 % had glycaemicabnormalities, 3.9% had hypothyroidism,21.6% had hypoparathyroidism and 19.6%) children had vitamin D insufficiency. Results obtained in the present study is comparable to studies conducted by De Sanctis V et al [9] and Altincik A et al[10]. As per his multicentre study De Sanctis V et al had reported that 30.8% of thalassemic children had short stature, 9.9% had glycemic abnormalities, 3.2% hadhypothyroidism, and 6.9% had hypoparathyroidism. Altincik A et al [10] reported 42% had short stature, 6.6 % had glycemic abnormalities and, 4.4% children had hypothyroidism. The prevalence of hypoparathyroidism in this study population is much higher when compared to the prevalence reported by De Sanctis V et al [17].

Present study showed higher occurrence of growth and endocrine problem in older children. In children who were aged ≥ 10 years, 57.1% had short stature, 14.3% had glycaemic abnormalities, 7.1% had hypothyroidism, 28.6% had hypoparathyroidism and 33.1% had vitamin D insufficiency. Only 8.7% of children had short stature, 13% developed hypoparathyridism and 4.3% developed Vit D insufficiency in the age group of 0-10 years. None of the children developed glycaemia abnormalities or hypothyroidism in less than 10 years age group. These figures clearly show that as age increases the risk for endocrine abnormalities also increases. De Sanctis V et al [17] also reported smilar trends.

Thalassemia international federation (TIF) guidelines for the management of transfusion dependent Thalassemia (TDT) actually recommends oral glucose tolerance test (OGTT) in every patient with thalassemia after 10 years of age (or earlier if needed); annual estimation of TFT right from 9 years of age (unless symptomatic hypothyroidism is observed earlier to this age) and screening investigations for hypoparathyroidism from 16 years of age[11].Finding of the present study emphasise the need of early screening for endocrine abnormalities at a younger age which will be helpful to detect subclinical cases before clinical manifestations.

Conclusion

The present study showed that significant number of children with thalassemia was developing endocrine complications including glycaemic abnormalities and hypothyroidism at an early age. As endocrine abnormalities further increases the morbidity and mortality in these children, early detection and proper management of these abnormalities are essential to ensure quality of life and to prevent early deaths. The Present study, suggests an early screening for endocrine disorders and TIF guidelines may not be overemphasized.

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Figure 1 :Proportion of thalassemic children with Short stature glycemic abnormalities, Hypothyroidism, Hypoparathyroidis , Vitamin D insufficiency.