www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i10.65

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

Epidemiological Clinical and Haematological Study of Beta Thalassemia (Homozygous) Pediatric Patients Treated In a Tertiary Care Centre in Odisha State

Authors
Bhagyalaxmi Das[1], Prafulla Kumar Mohanty[2], Rabindra Kumar Jena[3]
Dharma Niranjan Mishra*[4]
[1]Lecturer, Department of Zoology, Maharishi College of Natural Law, Bhubaneswar, Odisha, India
Email: *bhagyalaxmidas15@gmail.com*
[2]Professor, PG Dept. Zoology, Utkal University Vani Vihar, Bhubaneswar, Odisha, India
Email: *prafulla.mohanty3@gmail.com*
[3]Professor and Head, Dept of clinical Haematology S. C. B. Medical College Cuttack 753007, Orissa, India
Email: *rkjena@msn.com*
[4]Assistant Professor, Department of Anatomy S. C. B. Medical College Cuttack 753007, Orissa, India
Corresponding Author
Dharma Niranjan Mishra*
Assistant Professor, Department of Anatomy S. C. B. Medical College Cuttack 753007, Orissa, India
Email: *dharmaniranjan.mishra08@gmail.com*

ABSTRACT

Background: *Beta thalassemia is an autosomal recessive disorder that affects red blood cells both in the decreased as well as absence in production of adult haemoglobin (HbA) and characterized by severe anaemia, splenomegaly and bone deformities and require lifelong transfusion therapy, iron chelation and/ or bone marrow transplantation for successful control. The aim of the study is to evaluate the haematological and epidemiological parameters in relation to socioeconomic status and quality of life of the study group.*

Methods: *The blood samples were collected from 100 diagnosed cases of beta thalassemia. Haematological and epidemiological parameters were studied by asking research questionnaire developed for this purpose and analyzing various clinical complaints and laboratory data. The haemoglobin variants were analysed by fully automated capillary zone electrophoresis to confirm the diagnosis of homozygous state of beta thalassemia.*

Result: *In the present study majority of the patients (81%) were below the age of 10 years. The clinical examination showed anaemia in all the patients with hepatomegally and spleenomegally in 15% and 90% cases respectively. Blood transfusions were required in 90% cases as 1-2 units per month. In coastal districts of eastern and northern odisha 82(82%) patients were observed in comparison to 18 (18%) cases in western odisha. The mean haemoglobin was markedly decreased to 5.4±1.8 ranges 3-8 gm% followed by fetal hemoglobin (HbF) was raised up to 83.58 ± 9.30% ranges from 70.2% to 94.5% and adult haemoglobin (Hb A2) was decreased upto 2.63 ±1.09 ranges from 1.1 to 4.3%.*

Conclusion: *The incidence of beta thalassemia is common in costal districts without having any correlation with caste, religion and financial status. Anaemia and spleenomegally is seen in all and 90% patients respectively. The facilities of molecular diagnosis and comprehensive control programme should be available in Odisha state.*

Keywords: *Epidemiology, Anaemia, haemoglobin variants, β-Globin Gene.*

Introduction

Thalassemia is an autosomal recessive genetic disorder caused by the decreased or absent synthesis of one or more globin, the protein sub units of haemoglobin (Hb) A.[1] Two primary types of thalassemia are Alpha thalassemia with decreased alpha globin chain and β thalassemia with diminished or absent β globin chain in haemoglobin tetramer. Three clinical and haematological conditions of increasing severity are recognized i.e. β thalassemia carrier state (heterozygotes), thalassemia intermedia and thalassemia major.[2] The thalassemia major are homozygous characterized by severe anaemia, splenomegaly and bone deformities and require lifelong transfusion therapy and / or bone marrow transplantation for successful control.[3] The World Health Organization (WHO) recognizes thalassemia as the most prevalent genetic disorder and β thalassemia is the most common autosomal single gene disorder having a carrier population of more than 150 million and at least 2 million affected homozygous born annually (Cao and Galanello, 2002).[4] In India, about 5 to 15 percent of the population is carriers and around 1 million are born with β thalassemia major annually. The life expectancy of the patients is within 3 decades. Low income status, lack of awareness and other social factors such as preference to marry within same ethnic group and consanguineous marriages contribute to the increasing frequency of this disease (Sengupta-2008).[5] since there is no permanent treatment, screening of such patients and genetic counseling will help to fall in the number of affected births. The epidemiological data with anthropometric parameters and their relationship with human β globin gene mutation are still inadequate and to be studied. The facilities of molecular diagnosis and comprehensive control programme should be available in Odisha state.

Materials & Methods

Study Design: Cohort Study (Prospective Observational study) with asking research questionnaire developed for this purpose.

Study Location: This study was undertaken in the Out Patient Department Clinical Haematology S.C.B. Medical Collage Hospital, Cuttack from 2015 to 2016. Their family history, name, age, sex, caste, native place, pedigree chart and clinical sign symptoms were rerecorded after taking written consent.

About 3-4 ml intravenous (IV) blood samples were collected using EDTA as anti coagulant by disposable syringe from each patient. Clinical sign and symptoms related to haemoglobinopathy and laboratory investigations were done by automated blood cell counter and haemoglobin electrophoresis. The analysis of levels of haemoglobin variants i.e, HbA, HbF and HbA2 by electrophoresis and clinical data were diagnostic of beta thalassaemia. Sickling test was done by sodium matabisulphite solution as a reducing agent for the presence of sickle cell haemoglobin to rule out sickle cell disease..

Inclusion Criteria: All patients who diagnosed or suspected to have beta thalassemia and confirmed by negative sickling test and increased HbF level.

Exclusion criteria: Healthy people who suspected to have haemoglobinopathies with positive sickling test and normal HbF level.

Ethical issues

This study confirms to the ethical principles of medical research developed by the World Medical Association Declaration of Helsinki. Ethical clearance was given by the Research Committee Department of Skin and Venereal Diseases S.C.B Medical College Cuttack.

Data Analysis: All data obtained with questionnaire and biochemical analysis were analyzed using the Graph Pad's web site. Statistical significance was accepted when the two-tailed P value is less than 0.0001.

Results

The present prospective study was carried out in the Haematology Department S C B Medical College Cuttack from 2015 to 2016 with duly approved by IEC. Written informed consent was obtained after explaining the patients and their parents about the nature and type of study. One

hundred beta thalassemia patients were studied during this period. Following observations were made:

Table No 1. Distribution of thalassemia patients according to clinical severity

Type of Thalassemia	No of patients	Percentage
Thalassemia major	94	94%
Thalassemia intermedia	06	06%
Thalassemia minor	00	00%
Total	100	100%

The present study comprised of 94 thalassemia major patients and 06 thalassemia intermedia patients. We did not observe the thalassemia minor patients as they were irregularly attending the thalassemic out door due to mild signs and symptoms. Table No 1

Table No 2. Epidemiological data of the study group.

Parameters	Age group	No of patients	Percentage
Age in years	3-5	38	38%
	6-10	43	43%
	11-14	15	15%
	>14	4	4%
Sex: male/female	Male	61	61%
	Female	39	39%
Socioeconomic status	APL >Rs= 27000/annum	73	73%
	BPL Rs= <27000/annum	27	27%
Education	Literate- matriculation and above	63	63%
	Illiterate -below matriculation	37	37%
Geographical distribution	Northern odisha (coastal districts)	49	49%
	Southern odisha (coastal districts)	33	33%
	Western odisha	18	18%

In the present study majority of the patients (43%) were in the age group of 6-10 years followed by 38 % in the age group of 3-5 years, 15% of the patients in the age group 11-14 years and 4% were above the age of 14 years. The youngest patient was 3 years old and oldest was 14 years old. The mean age was 6.85±6.3 years. Among the total 100 cases, 63 % were metric and above but less than graduate and 37 % cases were illiterate. The family income of APL was 73% having monthly income above 27000/annum and BPL was 27% with monthly income below 27000/annum. Max 49 cases were diagnosed as beta thalassemia from northern odisha (coastal districts like Khurdha, Puri and Ganjam.) followed by 33 (33%) from Southern odisha in coastal districts especially in Cuttack, Jajpur, Kendrapara, Bhadrakh and Balasore followed by 18(18%) from western odisha.(Fig 1). (Table No 2 and Fig 1)

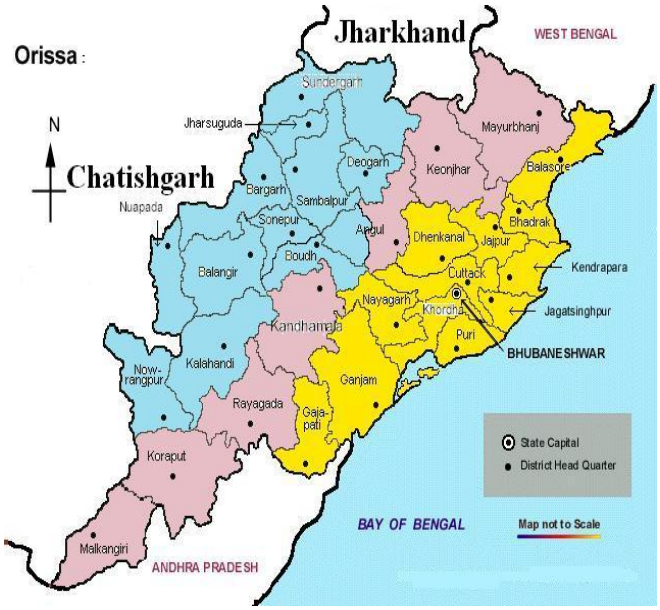

Fig 1. Showing the coastal districts of Odisha.

Table No 3. Clinical Profile of Study population

Clinical features	No of Cases=100	Percentage
Hepatomegally	15	15%
Spleenomegally	90	90%
Anaemia	100	100%
Icterus	20	20%
Growth retardation	7	7%
BT Requirement	1-2 unit per month	90%
BT Requirement	>2 units per month	10%
BT- Blood Transfusion		

The clinical examination showed anaemia in all the patients of the observed group. The hepatosplenomegally was seen in 15% and 90% cases respectively. There was clinical jaundice in 20% followed by 7% cases showed growth retardation. Blood transfusion requirement was observed in 90% cases as 1-2 units per month. Table No 3

Table No 4. Haematological Findings of Study population.

Blood test	Min	Max	Mean± SD	P. Value
Heamoglobin gm%	3 (%)	8 (%)	5.4±1.8	<0.0011
Reticulocyte count %	1(%)	7(%)	4±1.8	<0.0001
Serum bilirubin mg/dl	0.8 mg/dl	5.8 mg/dl	3.41± 1.83	<0.0001
LDH units per liter (U/L)	150(U/L)	730(U/L)	549 ± 116.98	<0.0001
AST (aspartate aminotransferase), which was previously called SGOT, ALT (alanine aminotransferase), which was previously called SGPT and ALP (alkaline phosphatase) was elevated in all the cases. Hb%- haemoglobin percentage RC- reticulocyte count. Lactate dehydrogenase (LDH)				

Coming to the haematological findings the mean haemoglobin was 5.4± 1.8 ranges 3gm% to 8gm% followed by reticulocyte count 4±1.8 ranges 1%-7 %, Serum bilirubin mg/dl 3.41± 1.83 ranges 0.8 to 5.8 and LDH units per liter (U/L) 549 ± 116.98 ranges 150-730. Table No 4

Table No 5. Haemoglobin electrophoresis data of study subjects

Hb Variants	N	Min	Max	Mean± Standard Deviation	P Value
HbA(%)	100	0 (%)	2.1(%)	1.51 ± 0.32	<0.0001
HbF(%)	100	70.2 (%)	94.5 (%)	83.58 ± 9.30	<0.0001
HbA2(%)	100	1.1 (%)	4.3 (%)	2.63 ±1.09	<0.0001
Hb- haemoglobin, SD-standard deviation, HbA-adult haemoglobin 1, HbF-foetal haemoglobin, HbA2 – adult haemoglobin 2, HbS- sickle haemoglobin					

Similarly the mean HbF% was 83.58 ± 9.30 ranges (70.2 to 94) which is markedly increased followed by HbA2 (%) 2.63 ±1.09 ranges (1.1% to 4.3%) and HbA 1.51 ± 0.32 ranges (0 to 2.1%) suggestive of beta thalassemia. Table No 5.

Discussion

Thalassemia major or beta thalassemia cases are found to be maximum in 90 (90%) cases and 10% are thalassemia intermedia patients. Though thalassemia minor patients were registered they were not attending the thalassemia OPD because of milder signs symptoms and occasional requirement of blood transfusions[5]. In the present study majority of the patients (81%) were below 10 years age. The youngest patient was 3 years old and oldest was 14 years old. The mean age was 6.85±6.3 years [6]. The children with thalassemia major do not survive the first decade of life, but with the availability of blood transfusion services and thalassemia screening service, most of these children are living longer[7]. Males were more in number comprising 61% of the patients and females were 39%. This is comparable with most of the studies conducted where male predominance has been seen. The male child is given priority over female, while seeking medical care and parents are ready to spend more for their male children[8]. The socio-economic condition of the most of parents/ guardians of Thalassemia patients were above poverty line and educational qualification were metric and above but less than graduation. As most of them were residing in rural area they were bound to travel towards transfusion center for the blood transfusion and medical treatment twice, thrice or even more than 3 times a month[9]. The socio-economic condition of the most of parents/ guardians of Thalassemia patients were above poverty line and educational qualification were metric and above but less than graduate.[10]

We observed an increasing trend of thalassemia major in coastal districts of eastern and northern odisha in comparison to western odisha[11]. All the patients are presenting anaemia with 20% having mild to moderate clinical jaundice. Ninety percent patients had splenomegaly at the time of diagnosis. We observed normal spleen only in 10 patients. Hepatomegally is seen in 15 (15%) cases only. As thalassemia syndromes are characterized by various degrees of ineffective hematopoiesis and increased hemolysis. The hepato-spleenomegally was due to extramedullary hematopoiesis results in enlargement of the liver and spleen[9]. Blood transfusions were required in 90% of the patients at the rate of 1- 2 units per month where as in10% cases, it was more than 2 units per month correlating with the fact that maximum number of patients were in the age group of 6-10 years. Thalassemia intermedia

patients were coming for blood transfusion usually after 2-3 months[13]. In the present study most of the cases presented with moderate to severe anaemia suggestive of decreased Hb production and increased reticulocyte count, increased serum bilirubin and Lactate dehydrogenase (LDH) were suggestive red cell destruction.[14]. There was increased foetal hemoglobin with mean value 83.58 ± 9.30 which is strongly suggestive decreased or absence of beta chain production. The level Hb A and HbA2 were compatible with the diagnosis of beta thalassemia major.[15]

Conclusion

Beta thalassemia cases are found to be maximum below the age of 10 years with male predominance. Its prevalence is more in coastal districts especially in Cuttack, Khurdha, Puri and Jajpur. Caste, education and financial status have no relation with the incidence and severity of the disease. All are presenting with anaemia with 90% cases having clinically palpable spleen. Socioeconomic and literacy do not have any significant difference in the study population. The anthropometric parameters and their relationship with human β globin gene mutation are still inadequate and it should be studied in further detail. All parents are unanimously agreed for a suitable policy for marriages counseling which is the reason of spreading Thalassemia. Molecular diagnosis for β-Globin Gene mutations in this state should be available for prenatal diagnosis of such disease in foetuses, which can prevent the incidence by selective termination of pregnancy and confirmation of the diagnosis in few cases of inconclusive parameters obtained by conventional haematological investigations.

Conflict of interest: None to declare

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