Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

# INCIDENCE AND CLINICAL PROFILE OF HEMOGLOBINOPATHIES IN CHILDREN: A HOSPITAL-BASED STUDY IN GAYATRI VIDYA PARISHAD HEALTH CARE AND MEDICAL TECHNOLOGY

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## Abstract

**Introduction:** The inherited disorders of hemoglobin are the commonest single-gene disorders in man. Hemoglobinopathies constitute a very important causative factor for anemia's of childhood. This is especially so in those regions where abnormal hemoglobin genes are prevalent in a frequency of high order. Sickle cell anaemia and thalassemia major can cause life-threatening situation and chronic ill health. They pose economical and psychological burden on the affected individual and his/her family, and the society as a whole.

**Materials and Methods:** Prospective hospital based observational study was conducted at the Department of Paediatrics, Gayatri Vidya Parishad Health Care and Medical Technology, Visakhapatnam from January 2021 to December 2022. Children aged 3 months to 12 years presenting with lethargy, generalized weakness and pallor to the Department of Paediatrics, Gayatri Vidya Parishad Health Care and Medical Technology, Visakhapatnam, O.P.D/I.P.D. My research protocol was approved by the Ethical Committee of the institution. Voluntary consent was obtained from the subjects and their parents of the study. Help from departments of Biochemistry and Pathology for laboratory investigations of hemoglobinopathies is taken. Thorough history was taken including History of presenting illness, past history, Family history. Anthropometry: Height and weight. Measured as per IAP Guidelines and compared to NCHS standards.

**Results:** Among 64 cases studied Beta thalassemia account for 50% (32)of cases of which 24 were beta thalassemia major, 8 were thalassemia intermedia, Rest 50%(32) were sickle cell hemoglobinopathies of which 22 are Homozygous Sickle cell anemia, 3 were sickle **β0** thalassemia, 4 were Sickle **β+** thalassemia, 3 were sickle cell Traits. 22 of 24(91.6%) Beta thalassemia major cases were diagnosed in 1st year of life, rest 2 were diagnosed in 2nd year of

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life. Earlist diagnosed case is at 5 months of age. 25% of thalassemia intermedia cases were diagnosed in 1st year of life and 75% were diagnosed in 2nd&3rd years of life. 6 of 22(27.2%) cases were diagnosed in 1st year of life ,among them one case was diagnosed in 4 months of age, 9(41%) during 2nd& 3rd years, 6(27.2%) during 4th& 5th years of life, one is diagnosed at 9 years of life. Sickle **β0** thalassemia 1 of 3 is diagnosed in 1st year and rest 2 during 2nd year. Sickle **β+** thalassemia all 4 are diagnosed in 2nd& 3rd years of life. Sickle cell trait cases 2 were diagnosed b/w 8-10 years and one is diagnosed at 12 years.

**Conclusion:** Haemoglobinopathies are a leading cause of child mortality worldwide, although with a variable geographical incidence. A reliable estimate of prevalence of the disease is necessary for reducing its burden. 3,000 ethnic groups in India still follow endogamy. Haemoglobinopathies are the commonest hereditary disorders in India and pose a major health problem. The data on the prevalence of β-thalassemias and other haemoglobinopathies in different caste/ethnic groups of India is scarce. Amongst the widely prevalent nutritional anemia, hidden is the problem of thalassaemia and abnormal hemoglobin

**Key Words:** anemia, Sickle cell anaemia, thalassemia, Haemoglobinopathies.

## INTRODUCTION

The inherited disorders of hemoglobin are the commonest single-gene disorders in man. Hemoglobinopathies constitute a very important causative factor for anemia's of childhood. This is especially so in those regions where abnormal hemoglobin genes are prevalent in a frequency of high order. Sickle cell anaemia and thalassemia major can cause life-threatening situation and chronic ill health. They pose economical and psychological burden on the affected individual and his/her family, and the society as a whole. [1]

The World Health Organization (WHO) has suggested that about 5% of the world population are carriers for different inherited disorders of hemoglobin. The UNICEF in 1996 estimated that there were 29.7 million carriers of beta thalassemia trait in India and about 10,000 infants with homozygous beta thalassemia born every year [3]. The general incidence of thalassemia trait and sickle cell hemoglobinopathies in India varies between 3-17% and 1-44% respectively [4], [5],[6].

Most of these children have a severe clinical presentation but are managed suboptimally due to lack of financial resources in majority of the families. Thus preventing the birth of affected children is the best option for India. A prerequisite for this is the knowledge of the prevalence of β-thalassemia and other haemoglobinopathies in different regions of the country and in particular in different ethnic groups. A few studies done earlier have shown that certain communities like the Sindhis, Kutchhi Bhanushalis and Punjabis from Western and Northern India have a high prevalence of β-thalassemia[5][6][7][8] and some population groups from the north eastern regions have a high prevalence of HbE (5-50 %)[9][10].

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However, there is not much information on the distribution of in the North coastal region of Andhra Pradesh.

GVPHC&MT, Visakhapatnam is tertiary hospital and acts as a referral center for most hematological cases from all 3 districts of North coastal AP. Facilities for hematological investigations and Blood bank were available at GVPHC&MT, Visakhapatnam. This study was carried out with objectives of creating a profile for cases of hemoglobinopathies coming at GVPHC&MT, Visakhapatnam and comparing the results obtained in present study with those of various studies done in India and abroad.

## AIMS AND OBJECTIVES

- To study clinical features and presentation of hemoglobinopathies (including Thalassemias) in children admitted to GVPHC&MT, Visakhapatnam.
- The study period was of two years from January 2021 to December 2022.
- To identify the children with hemoglobin disorders, using the history, clinical examination and available hematological and biochemical tests.
- To know their distribution in different age groups and both sexes, distribution in Tribal and Non-Tribal Patients.
- To know their clinical features and complication profile and compare between different hemoglobinopathies.
- To correlate the complication profile between children following Palliative and Moderate transfusion regimens.

## PATIENTS AND METHODS

**Study Design:** Prospective hospital based observational study.

**Study Period:** January 2021 to December 2022.

**Place of Study:** Department of Paediatrics, Gayatri Vidya Parishad Health Care and Medical Technology, Visakhapatnam.

**Study Population:** Children aged 3months to 12 years presenting with lethargy, generalized weakness and pallor to the Department of Paediatrics, Gayatri Vidya Parishad Health Care and Medical Technology, Visakhapatnam, O.P.D/I.P.D.

**Inclusion Criteria:**

- Children with severe anemia with haemolytic facies with or without jaundice features of CCF, hepatosplenomegaly and history of blood transfusion.
- Children with pallor and jaundice or associated bone pains, abdominal pain, chest pain with fever or hemiplegia.

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- Hemogram peripheral smear, HB electrophoresis/ HPLC suggestive of Hemoglobinopathy

**Exclusion criteria:** children with Non hemolytic causes of anemia and children with hemolytic anemia other than Hemoglobinopathy .

**Sample Number**: Total number of 64 cases were studied after considering inclusion and exclusion criteria.

My research protocol was approved by the Ethical Committee of the institution. Voluntary consent was obtained from the subjects and their parents of the study. Help from departments of Biochemistry and Pathology for laboratory investigations of hemoglobinopathies is taken. Thorough history was taken including History of presenting illness, past history, Family history. Anthropometry: Height and weight. Measured as per IAP Guidelines and compared to NCHS standards.

**Length/Height:** In children less than 2yrs length was measured on Infantometer. In children >2yrs Stadiometer was used. children were made to stand on bare feet flat on the floor with head, shoulder blades, buttocks and heels touching the wall, knees straight, child looking directly ahead with Frankfurt plane parallel to the ground. Measured in centimeters.

**Weight:** A balance beam table model was used for children <2yrs.older children were weighed on Floor model beam scale. All of them are weighed with minimum clothes. Each parameter was recorded by 3 separate individuals and average was taken. Heights and Weights Are compared to WHO-NCHS standards of Height for age and Weight for Height.

**Vitals:** Pulse rate, respiratory rate, Blood pressure and Temperature were recorded.

**General Physical Examination:**
Pallor, Icterus, edema, Haemolytic facies (frontal & occipital bossing, prominent malar bones, depressed nasal bridge, wide spaced eyes), clubbing were noted.

**Systemic Examination:**
Per abdomen: Liver span noted with upper border of liver delineated by percussion, lower border by palpation and measuring distance in between with measuring tape in centimeters.
Spleen palpated and Graded using Hackett's semi-quantitative assessment into 5 grades.
CVS: Heart sounds noted in mitral, aortic, pulmonary & tricuspid ares. Respiratory system, CNS examined. Laboratory investigations: 5 ml. of blood was collected in vacutainer tubes having EDTA as anticoagulant.

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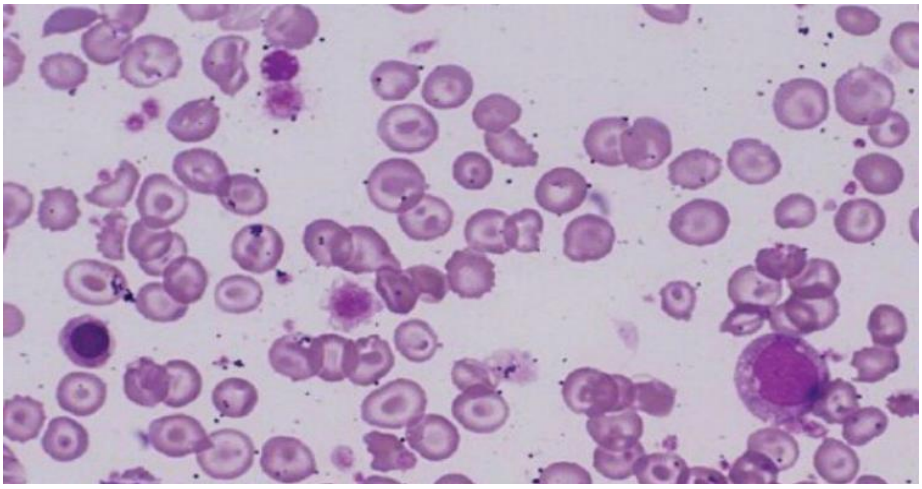

**Fig 1: Peripheral smear of Typical Thalassemia major showing anisopoikilocytosis & Target cells**

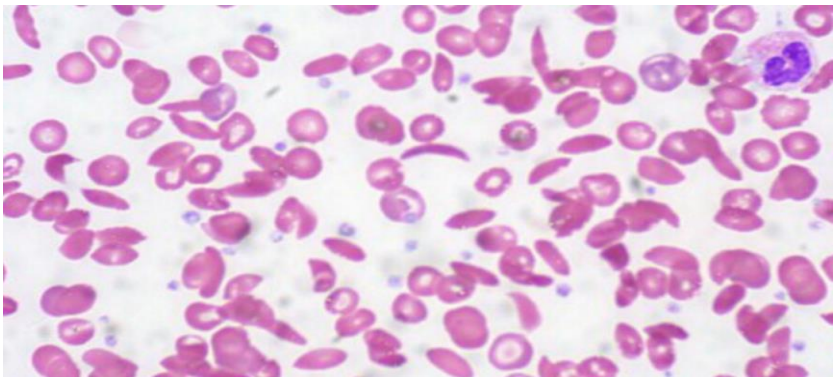

**Fig 2: Peripheral smear of Typical Sickle Cell Anemia showing sickle shaped RBC**

a) Hematological parameters: Hb, PCV, MCV, MCH, MCHC, RBC count and WBC count were measured using Sysmex cell counter.

Sysmex cell counter provides a high level of accuracy through the use of automatic floating discriminators. White Blood Cells, Red Blood Cells and Platelets - WBCs, RBCs and PLTs are counted using the direct current detection method with coincidence correction. Automatic discriminators separate the cell populations based on complex algorithms. The intensity of the electronic pulse from each analyzed cell is proportional to the cell volume.

The hematocrit (HCT) is directly determined based on the red cell count and volume detection of each individual RBC.

Hemoglobin Analysis - Hemoglobin analysis is conducted using a non-cyanide method.

b) Peripheral smear was evaluated for features of red cell Morphology.

Procedure: Blood films are made by placing a drop of blood on one end of a slide, and using a *spreader slide* to disperse the blood over the slide's length. The slide is left to air dry, after which the blood is fixed to the slide by immersing it briefly in methanol. Routine analysis of blood in

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medical laboratories is usually performed on blood films stained with Romanowsky, Wright's, or giemsa stain.
After staining, the monolayer is viewed under a microscope using magnification up to 1000x. Individual cells are examined and their morphology is characterized and recorded.

C)Reticulocyte Count: The reticulocyte is a non-nucleated immature red cell containing residual RNA. A supravital stain, new methylene blue, is used to precipitate the RNA into dark-blue filaments or granules to identify retics. An Reticulocyte Production index>/= 3 represents an adequate response to anemia by the bone marrow, whereas an RPI <2 is considered an inadequate response of erythopoiesis by the bone marrow to a state of anemia.
Sickling Test: Blood to be tested is mixed with freshly prepared solution of 2% sodium metabisulphate and sealed under a glass cover slip. Obseve under light microscope. Sickling ensues within few minutes to several hours.Cells with <40% HbS Sickle Relatively slowly and assume holly/mulberry leaf configuration.

Cells with >50% HbS SICKLE more rapidly within minutes & take filamentous shape.

**HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC):** was performed on an instrument, known as BIO-RAD 'VARIANT II'utilizes the principle of HPLC.The software delivers a printed report showing the chromatogram, with all the hemoglobin fractions eluted. The integrated peaks are assigned to manufacturer-defined "windows" derived from specific retention time(RT).This RT is the time that elapses from the sample injection to the apex ofthe elution peak, of normal hemoglobin fraction and common variantsTable. The "windows" are established ranges in which common variants have been observed to elute using the variant beta-thalassemia short program. The printed chromatogram shows allthe hemoglobin fractions eluted, the RT, the areas of the peaks, and the values (%) of different hemoglobin components.

**Normal hemoglobin pattern is taken as Hb A ≥95%, Hb A2 ≤ 3.5%, and Hb F < 2.5%**

Iron Studies were not done due to economic constraints and practical problems thus not included in present study. Microsoft Word software is used to type documents, and prepare tables. Microsoft Excel sheets to prepare pie diagrams and Bar charts.

## OBSERVATIONS AND RESULTS

In period of 2 years January 2021 to December 2022 among cases of Anemia presented to OPD/IPD Department of Paediatrics, Gayatri Vidya Parishad Health Care and Medical Technology, Visakhapatnam. 64 children with hemoglobinopathies aged 3 months to 12 years were studied after considering inclusion and exclusion criteria. In this present study of 64 cases of hemoglobiniopathies incidence, sex distribution, tribal and non tribal distribution, clinical features, height for age, weight for height, complications, children on different therapeutic modalities were analyzed.

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**Table 1: Distribution by Etiology**

| S.No | Hemoglobinopathy | No. of cases | Percentage |
|---|---|---|---|
| 1 | Beta thalassemia major | 24 | 37.5 |
| 2 | Beta thalassemia intermedia | 8 | 12.5 |
| 3 | Sickle cell anemia | 22 | 34.37 |
| 4 | Sickle **β0**Thalassemia | 3 | 4.68 |
| 5 | Sickle **β**+Thalassemia | 4 | 6.25 |
| 6 | Sickle cell trait | 3 | 4.68 |
| | Total | 64 | 100 |

Among 64 cases studied Beta thalassemia account for 50% (32)of cases of which 24 were beta thalassemia major, 8 were thalassemia intermedia, Rest 50%(32) were sickle cell hemoglobinopathies of which 22 are Homozygous Sickle cell anemia, 3 were sickle **β0** thalassemia, 4 were Sickle **β**+ thalassemia, 3 were sickle cell Traits.

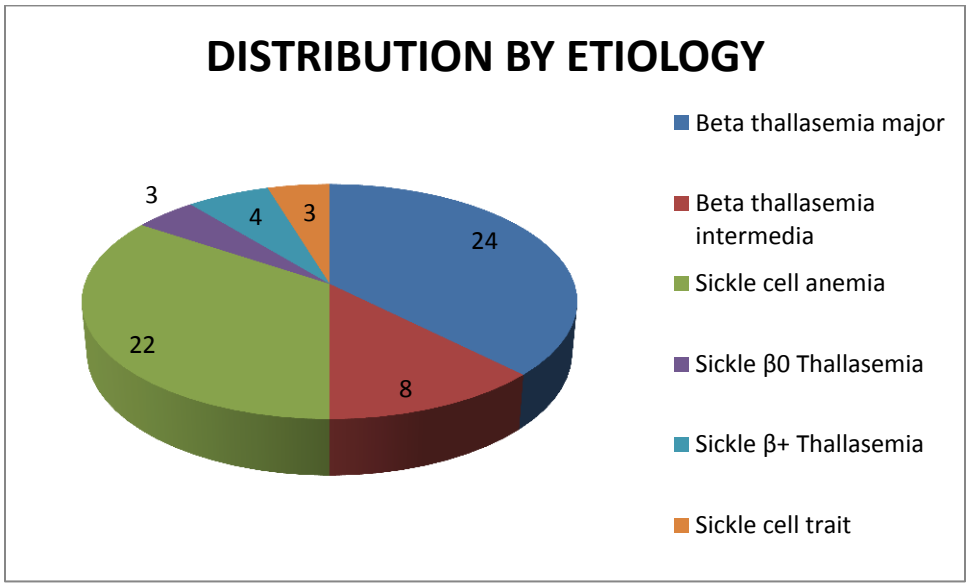
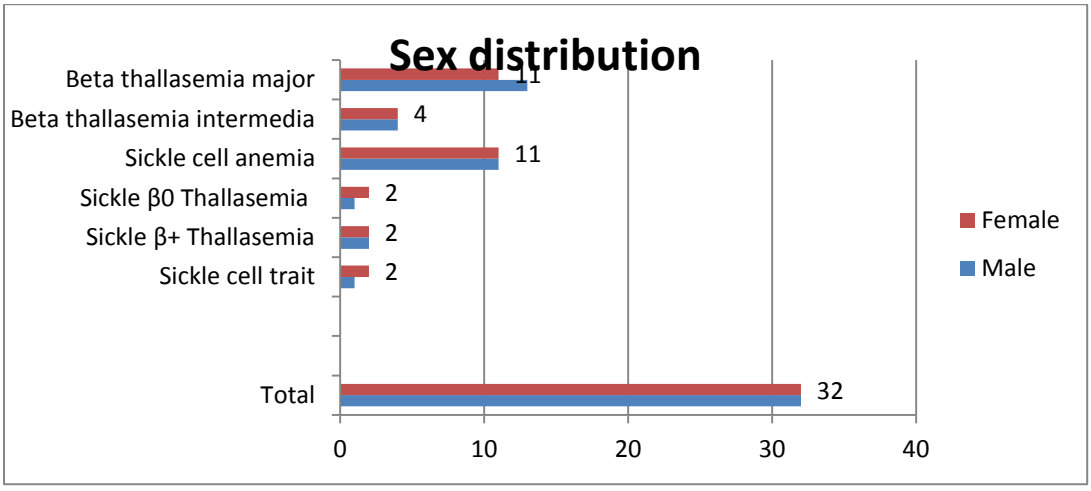
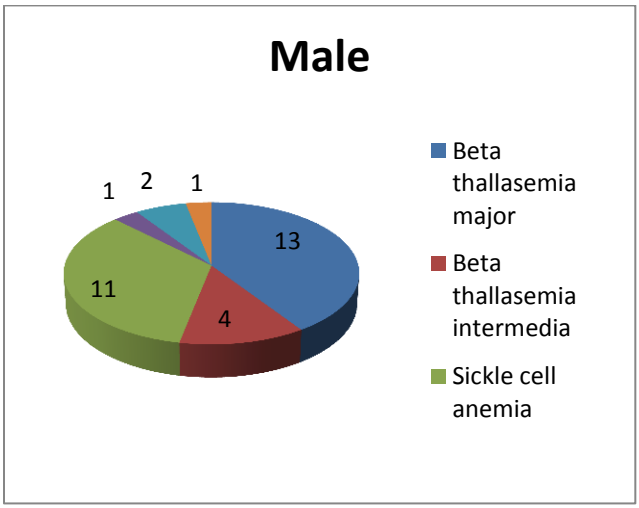



**Table 2: Sex distribution**

| S.No | Hemoglobinopathy | Male | Female |
|---|---|---|---|
| 1 | Beta thalassemia major | 13 | 11 |
| 2 | Beta thalassemia intermedia | 4 | 4 |
| 3 | Sickle cell anemia | 11 | 11 |
| 4 | Sickle **β0**Thalassemia | 1 | 2 |
| 5 | Sickle **β**+Thalassemia | 2 | 2 |
| 6 | Sickle cell trait | 1 | 2 |
| | Total | 32 | 32 |

Sex distribution for Thalassemia major is Male 54%, Female 46%. For thalassemia intermedia Male:Female is 1:1. Among cases of sickle cell anemia Male were 50% and Female were 50%. In sickle thalassemia cases Male were 43% and female were 57%. Among sickle cell trait Male:Female is 1:2. Overall Male:Female ratio recorded in this study among haemoglobinopathies is 1:1.



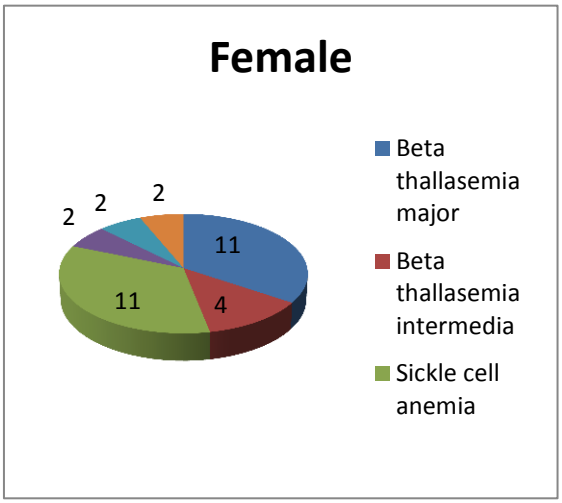




**Table 3: Tribal & Non Tribal distribution**

| S.No | Hemoglobinopathy | Tribal | Non Tribal |
|---|---|---|---|
| 1 | Beta thalassemia major | 7 | 17 |
| 2 | Beta thalassemia intermedia | 3 | 5 |
| 3 | Sickle cell anemia | 12 | 10 |
| 4 | Sickle **β0**Thalassemia | 2 | 1 |
| 5 | Sickle **β**+Thalassemia | 2 | 2 |
| 6 | Sickle cell trait | 2 | 1 |
| | Total | 28 | 36 |

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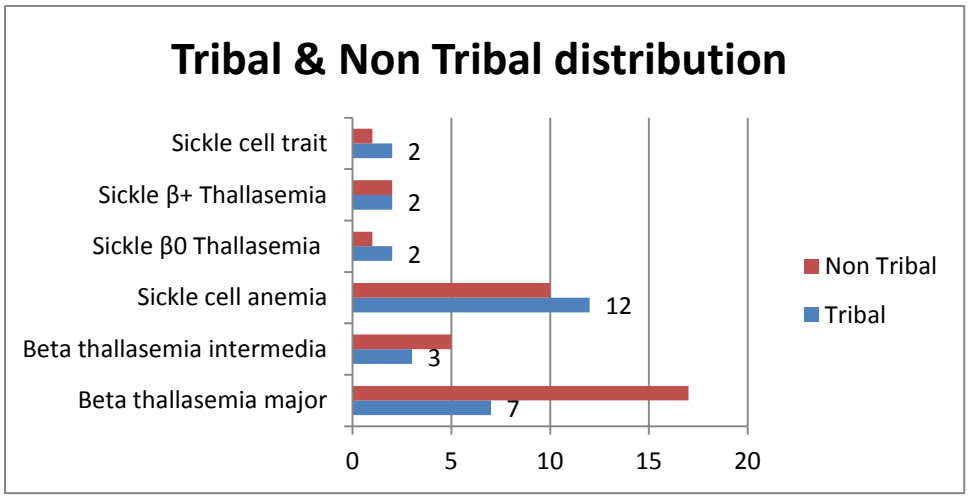
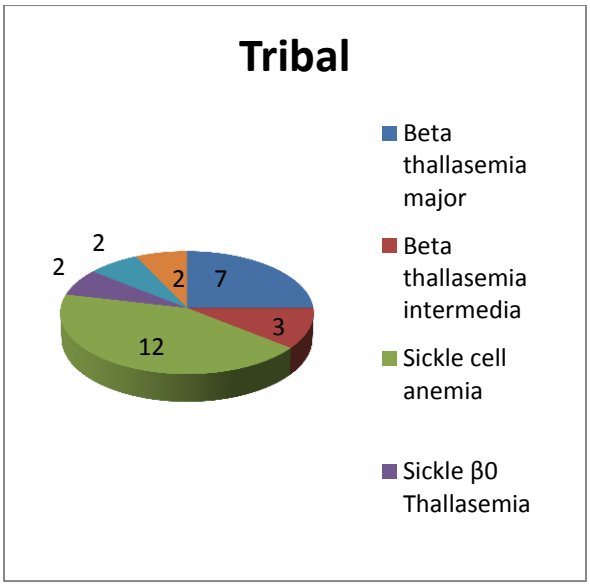
Among total cases in the study children belonging to Tribal ethnicity were 43.75%.(28)10 of 32 cases of Thalassemia major were Tribal which is 31.2%. Among Sickle cell anemia 12 of 22 i.e.. 54.5% were Tribal children. In Sickle thalassemia 4 of 7 cases were of tribal origin and in Sickle cell trait 2 of 3 cases were Tribal children.



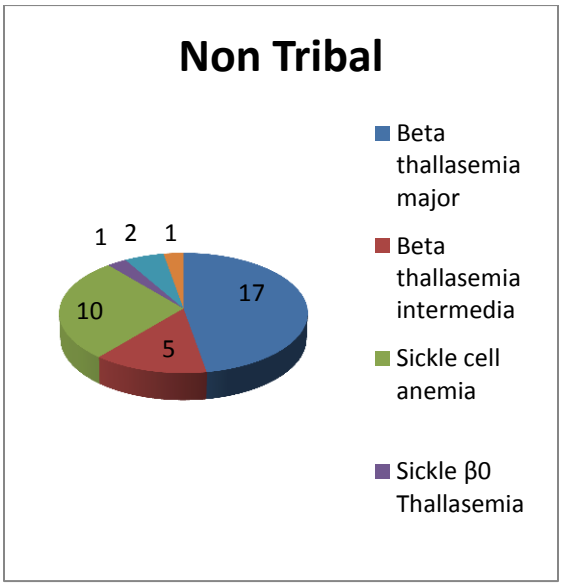




**Table 4: AGE at Diagnosis**

| S.No | Age | B thal Major | B thal Intrmedia | SCA | S. β0 | S. β+ | S.trait |
|---|---|---|---|---|---|---|---|
| 1 | 0-1yr | 22 | 2 | 6 | 1 | - | - |
| 2 | 1-3yr | 2 | 6 | 9 | 2 | 4 | - |
| 3 | 3-5yr | - | - | 6 | - | - | - |

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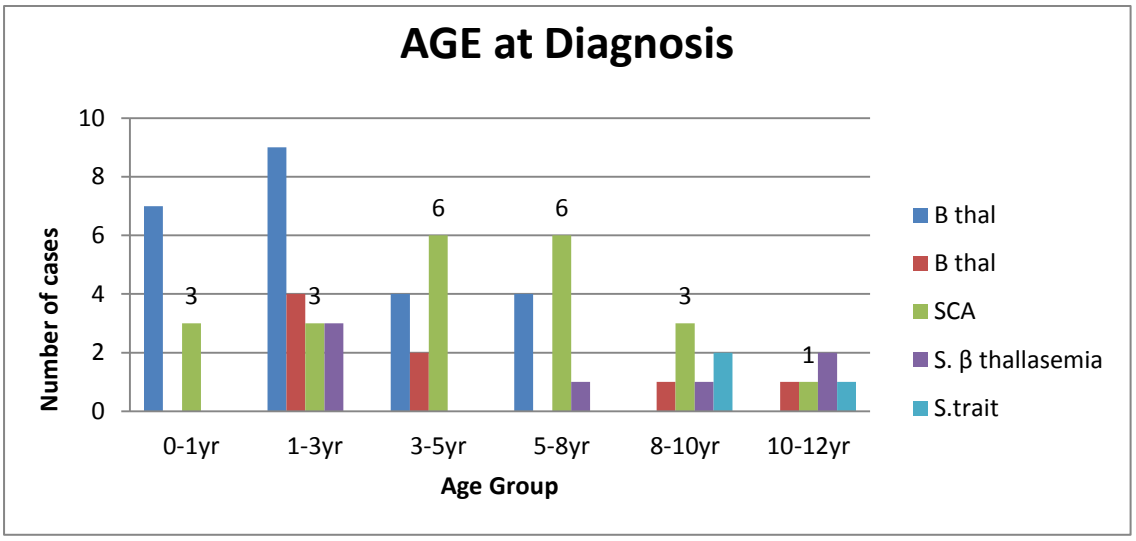
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 4 | 5-8yr | - | - | - | - | - | - |
| 5 | 8-10yr | - | - | 1 | - | - | 2 |
| 6 | 10-12yr | - | - | - | - | - | 1 |




22 of 24(91.6%) Beta thalassemia major cases were diagnosed in 1st year of life, rest 2 were diagnosed in 2nd year of life. Earliest diagnosed case is at 5 months of age. 25% of thalassemia intermedia cases were diagnosed in 1st year of life and 75% were diagnosed in 2nd&3rd years of life.

6 of 22(27.2%) cases were diagnosed in 1st year of life, among them one case was diagnosed in 4 months of age, 9(41%) during 2nd& 3rd years, 6(27.2%) during 4th& 5th years of life, one is diagnosed at 9 years of life. Sickle **β0** thalassemia 1 of 3 is diagnosed in 1st year and rest 2 during 2nd year. Sickle **β**+thalassemia all 4 are diagnosed in 2nd& 3rd years of life. Sickle cell trait cases 2 were diagnosed b/w 8-10 years and one is diagnosed at 12 years.

**Table 5: Age distribution at the time of the study**

| S.No | Age | B thal Major | B thal Intrmedia | SCA | S. β thalassemia | S.trait |
|---|---|---|---|---|---|---|
| 1 | 0-1yr | 7 | - | 3 | - | - |
| 2 | 1-3yr | 9 | 4 | 3 | 3 | - |
| 3 | 3-5yr | 4 | 2 | 6 | - | - |

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| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | 5-8yr | 4 | - | 6 | 1 | - |
| 5 | 8-10yr | - | 1 | 3 | 1 | 2 |
| 6 | 10-12yr | - | 1 | 1 | 2 | 1 |

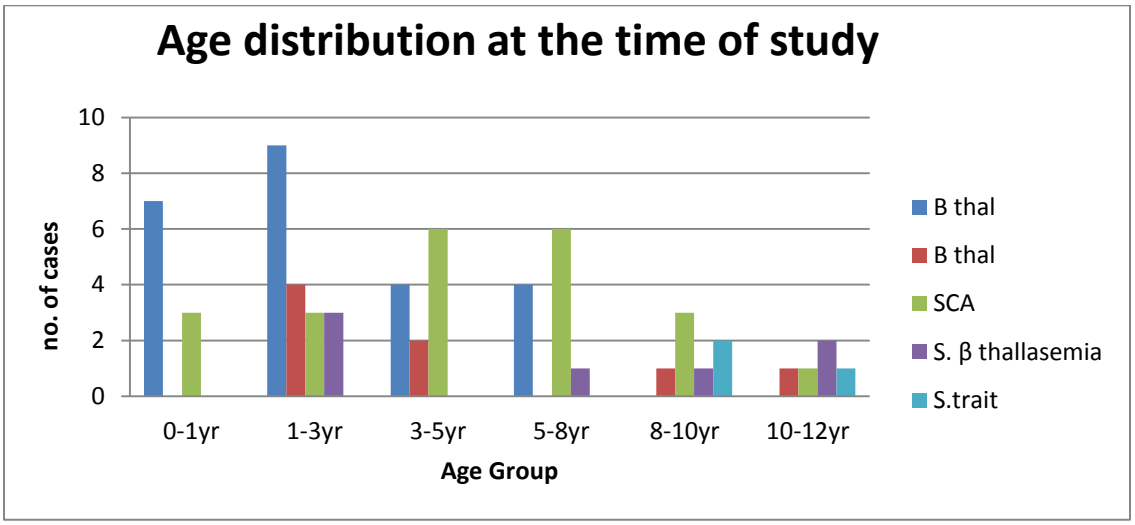


**Table 6: Transfusion requirement and frequency**

| Nature of disease | Total cases | Transfused cases | </=3 PA | 4-11 PA | > 11 PA |
|---|---|---|---|---|---|
| **Beta thalassemia major** | 24 | 18+6* | 6 | 6 | 12 |
| **Beta thalassemia intermedia** | 8 | 8 | 4 | 4 | - |
| **Sickle cell anemia** | 22 | 20 | 20 | - | - |
| **Sickle β0 Thalassemia** | 3 | 3 | - | 2 | 1 |
| **Sickle β+ Thalassemia** | 4 | 4 | 3 | 1 | - |
| **Sickle cell trait** | 3 | 0 | - | - | - |
| **Total** | 64 | 59 | 30 | 14 | 15 |

(*newly Diagnosed)

6 of 24 cases of thalassemia major had their 1st transfusion during this study. Among rest 18 cases transfusion frequency was 12 or more per year in 12 cases (66.6%). 2 cases had 16 transfusions per year. 8 of 18 are following Moderate transfusion Regimen and 10 are following palliative regimen. Thalassemia intermedia among 8 cases 3 are newly diagnosed. 2 are following Moderate regimen and 3 are following palliative regimen.

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SCA: Among SCA cases 20 of 22(90.1%) cases ever had a transfusion and none had transfusion requirement >3/year. Sickle β0 thalassemias 1 required >11 transfusions per year and 2 required b/n 4-11/year. Sickle β+ thalassemia 75% required </=3transfusions/year. Sickle cell trait children were not transfused.

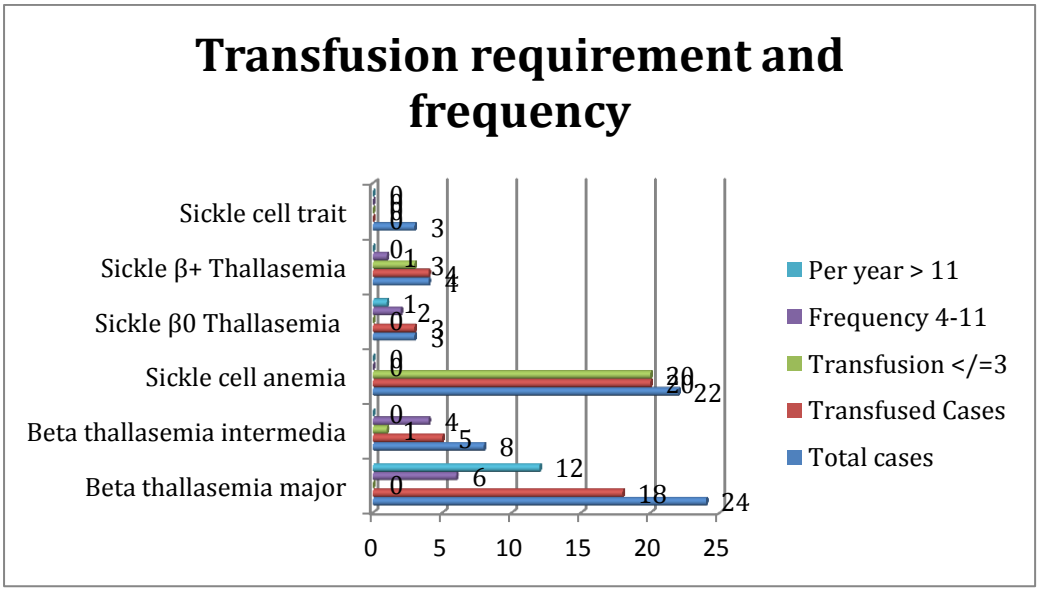


**Table 7: Effect on Growth (wasting & stunting according to WHO)**

| S.No | hemoglobinopathy | No. of cases with Wasting wt/ht<2SD | % | No. of cases with Stunting ht/age<2sd | % | No. of cases with both | % |
|---|---|---|---|---|---|---|---|
| 1 | Beta thalassemia major | 12 | 50 | 11 | 46 | 7 | 29 |
| 2 | Beta thalassemia intermedia | 3 | 37.5 | 3 | 37.5 | 0 | 0 |
| 3 | Sickle cell anemia | 9 | 41 | 10 | 45.5 | 3 | 13.6 |
| 4 | Sickle **β0**Thalassemia | 1 | 33.3 | 2 | 66.6 | 1 | 33.3 |
| 5 | Sickle **β**+Thalassemia | 0 | 0 | 1 | 25 | 0 | 0 |
| 6 | Sickle cell trait | 0 | 0 | 0 | 0 | 0 | 0 |
| | Total(64cases) | 25 | 39 | 27 | 42.1 | 11 | 17.1 |

50% of children with Beta Thalassemia major are wasted 46% stunted and 29% are both wasted and stunted. Thalassemia Intermedia 37.5% are wasted, 37.5% are stunted. Sickle cell Anemia 41% are Wasted 43.5% are stunted 13.6% were both wasted and stunted. Sickle **β0**thalassemia children 1 of 3 is stunted and wasted, 1 is stunted. Sickle **β**+ thalassemia 1 of 4 is stunted.

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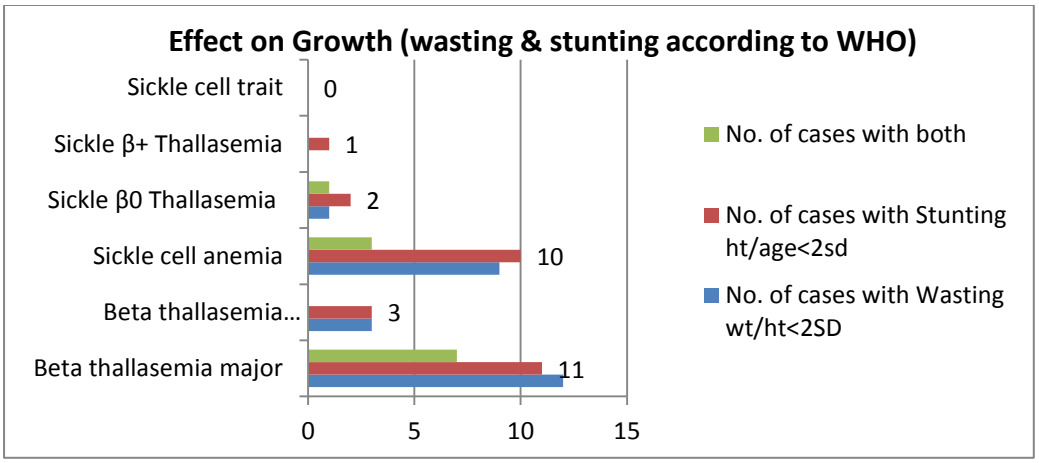


**Table 8: Clinical features and complications of Thalassemia**

| S.No | C/F or complication | Thalassemia major. No. of cases | % of cases (24) | Thalassemia intermedia No. of cases | % of cases (8) |
|---|---|---|---|---|---|
| 1 | Pallor | 24 | 100 | 8 | 100 |
| 2 | Fever | 5 | 21 | 2 | 25 |
| 3 | Jaundice | 6 | 25 | 0 | 0 |
| 4 | Haemolytic facies | 12 | 50 | 1 | 12.5% |
| 5 | CCF | 6 | 25 | 1 | 12.5% |
| 6 | HSM | 24 | 100 | 8 | 100 |
| 7 | Massive spleen Grade 4 & 5 | 5 | 20.83 | 0 | 0 |

Among T.Major and Intermedia Pallor was seen in all patients.

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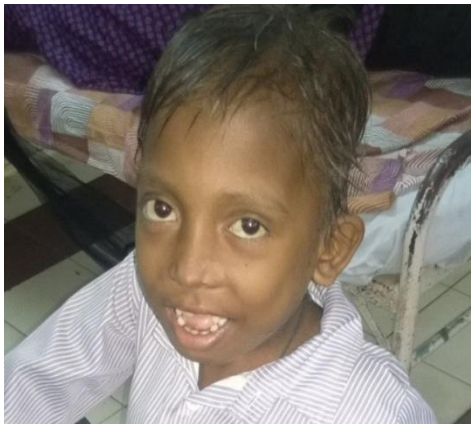

**Fig - 3: Child showing Hemolytic fascies with malocclusion of teeth**

**Fig -4 : Child showing typical hemolytic fascies with bossing of fore head, flat nasal bridge, malar prominance**

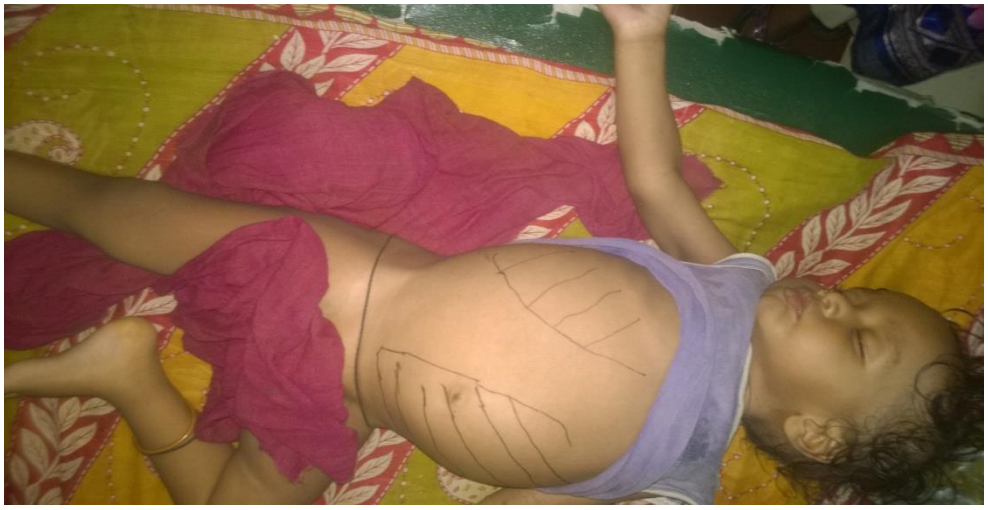

**Fig – 5 : Infant having massive hepatospleenomegaly due to thalassemia major**

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Fever was presenting complaint along with pallor in 21% of thallsemia major and 25% of intermedia. Jaundice was seen in 25%of T.MAJOR and none among T.intermedia. 25% of T.major presented with signs of Congestive Cardiac Failure. Haemolytic facies were noticed in 50% of the T.major case and 12.5% of T.intermedia cases. Hepatospleenomegaly is noticed in all cases of Thalassemia. Massive spleen of grade 4 according to Hackett's grading is noticed in 5 cases of thalassemia Major i.e. 20.83%.

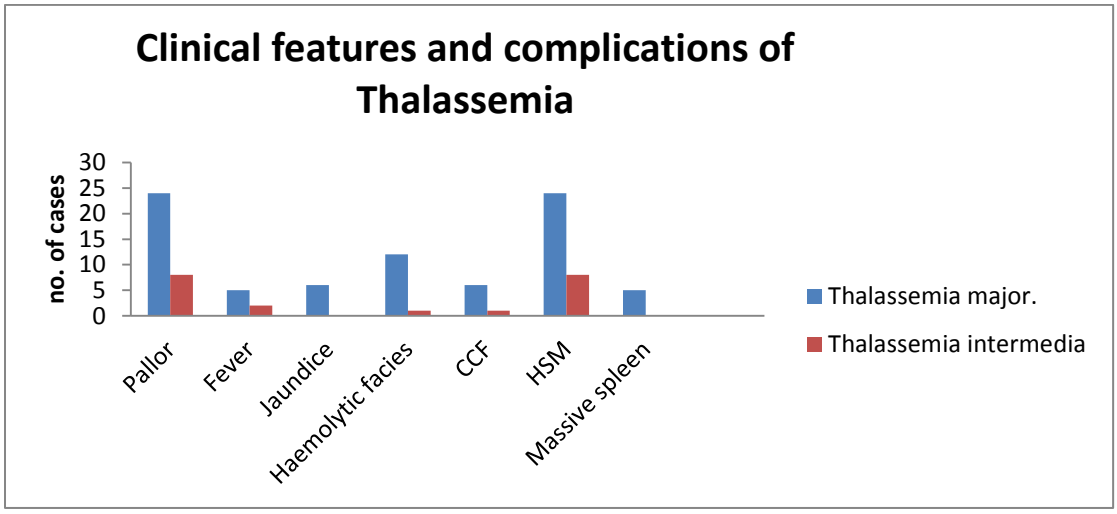


**Table 9: Effect of Palliative vs Moderate Transfusion Regimen**

| S.No | C/F or complication | T.major. cases On Palliative Regimen | % of cases (n=10) | T.major. cases On Moderate Regimen | % of cases (n=8) |
|---|---|---|---|---|---|
| 1 | Haemolytic facies | 8 | 80 | 2 | 25 |
| 2 | CCF | 3 | 30 | 0 | 0 |
| 3 | HSM | 10 | 100 | 8 | 100 |
| 4 | Massive spleen Grade 4 & 5 | 5 | 50 | 0 | 0 |
| 5 | Stunting | 9 | 90 | 1 | 12.5% |
| 6 | Wasting | 6 | 60 | 2 | 25 |
| 7 | Stunted & Wasted | 6 | 60 | 0 | 0 |

Haemolytic facies is seen in 80% (8) children following Palliative transfusion regimen and 25%(2) of children on Moderate transfusion. 30% (3) of children on Palliative regimen presented with CCF, non on Moderate regimen had CCF at presentation. Hepatospleenomegaly is present in all children in both groups, but Massive spleenomegaly is seen in 50% children on palliative regimen, none in moderate regimen. Wasting and stunting are seen in 60% children on palliative regimen and none on moderate regimen.

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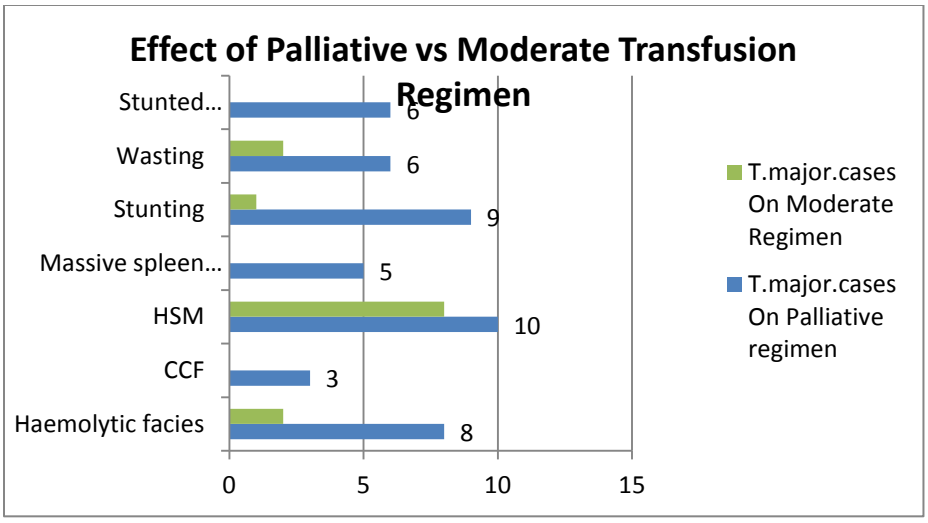


**Table 10: Clinical features and complications of Sickle Hemoglobinopathies**

| S.No | C/F or complication | Sickle cell anemia (22) | % of cases | Sickle thalassemia (7) | % of cases | Sickle trait (3) |
|---|---|---|---|---|---|---|
| 1 | Fever | 13 | 59 | 3 | 42.8 | 3 |
| 2 | Pallor | 22 | 100 | 7 | 100 | 2 |
| 3 | Jaundice | 17 | 77.2 | 5 | 71.4 | 2 |
| 4 | ACS(pulmonary) | 3 | 13.6 | 1 | 14.2 | 0 |
| 5 | Dactylitis | 3 | 13.6 | 0 | 0 | 0 |
| 6 | Bone pains | 7 | 32 | 2 | 28.5 | 2 |
| 7 | Abdominal pain | 2 | 9 | 0 | 0 | 1 |
| 8 | CNS/stroke | 1 | 4.5 | 0 | 0 | 0 |
| 9 | Aplastic crisis | 3 | 13.6 | 0 | 0 | 0 |
| 10 | Sequestration | 1 | 4.5 | 0 | 0 | 0 |
| 11 | Spleenomegaly | 10 | 45.5 | 7 | 100 | 3 |

Sickle Cell Anemia: 59% of SCA children presented with fever. Pallor was present in all cases and jaundice in 77.2% of cases. Vascular crisis is the reason for admission in 16 cases which is 72.72% of which Bone pains were most frequent complication with 7(32%) children presenting with this complaint. Acute Chest Syndrome is presenting feature in 13.6% of SCA cases. Dactylits/Hand Foot syndrome was presenting feature in 13.6% cases all of them are aged 1-2years. Aplastic crisis with severe anemia is presenting feature in 13.6%. Sequestration crisis is seen in 1 child with SCA. 1 child with SCA presented with stroke and right side hemiparesis. Splenomegaly is noticed in 10(45.5%) cases of SCA which is of grade 1 or 2. All case of sickle thalassemia had spleenomegaly. Grade 3 or 4.

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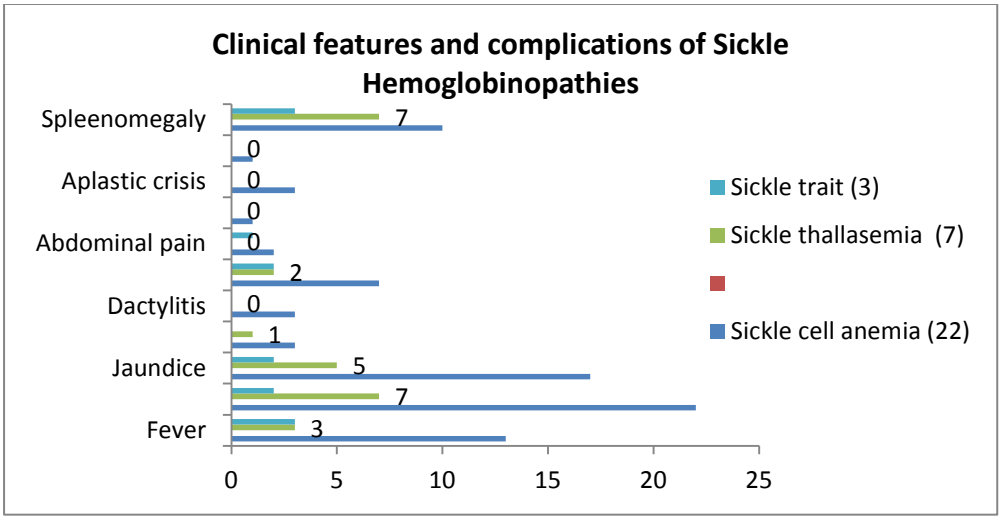


## DISCUSSION

Analysis of data: In period of 2 years January 2021 to December 2022 total 64 cases of hemoglobinopathies in children aged 3 months to 12 years were studied.

**1)Incidence:** Among 64 cases of hemoglobinopathies 50%were Sickle cell hemoglobinopathes and 50% were thalassemia. Among thalassemias Thalassemia major accounted for 24 of 32 cases which is 75% of thalassemia cases and Thalassemia Intermedia accounted for 25% of thalassemia cases and 12.5% of total cases of hemoglobinopathies. Sickle cell anemia accounts for 34.3% of total cases, sickle thalassemia accounts for 7 cases of which 3 are β0 sickle thalassemias and 4 are sickle β+thalassemias. Only 3 cases of sickle cell trait repoted to hospital during study period.

**Comparison with similar studies:**

a) A similar hospital based study on hemoglobinopathes conducted at NHL Medical college, Gujrath durig 2006-07 by Shah Sejal J with N=35.

b) A STUDY FROMS.D.M.College of Medical Sciences and Hospital, Dharwad,Karnataka With N=50,Shivashankara A.R et,al.

c) Multi center study by ICMR in 6 states in india Gujrath, Maharashtra, West Bengal, Karnataka, Assam, Punjab.

| Condition | Shah Sejal J et al Gujrath (n=35) | Shivashankara A.R et al Karnataka(n=50) | Present study (n=64) |
|---|---|---|---|
| **β**thalassemia major % of cases | 45.7% | 30% | 50% |
| **B**thalassemia intermedia % of cases | 5.7% | 40% | 12.5% |
| SCA % of cases | 20% | 2% | 34.3% |

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| | | | |
|---|---|---|---|
| Sickle βThalassemia | 11.4% | 2% | 11% |
| Sickle cell trait | 11.4% | 4% | 4.6% |

In India, average frequency of sickle cell gene is around 5%. The highest frequency of sickle cell gene in India is reported in Orissa (9%), followed by Assam (8.3%), Madhya Pradesh (7.4%), Uttar Pradesh (7.1%), Tamil Nadu (7.1%) and Gujarat (6.4%) [8-10]. The distribution of beta thalassemia is not uniform in Indian subcontinent. The highest frequency of beta thalassemia trait is reported in Gujarat (10-15%), followed by Sindh (10%), Punjab (6.5%), Tamil Nadu (8.4%) and Maharashtra.

Northern part of Coastal Andhra Pradesh comprising the districts of Visakhapatnam, Vizayanagaram, Srikakulam has unique population structure with high Tribal populatin, socio-cultural practices. Consanguinity in marriages is a well-accepted social norm irrespective of religion, caste, educational status and economical back ground. Thus the difference in Sickle cell Anemia cases can be explained by difference in demography and genetics in the population.

Incidence of Sickle cell trait is much higher but as they will have normal life and have few complications they usually present late or diagnosed during workup for other conditions. As this is a hospital based study the cases Sickle cell trait cases which presented with complications only have been diagnosed.

**2) Sex Ratio:** In present study of 64 cases 32 were male and 32 were female.sex distribution is almost similar in all types of hemoglobinopathies in study with 1:1 ratio between male & female. In Shah Sejal J et al Gujrath study ratio was Male:Female 3:1. As Both Thalassemia and SCA are Autosomal Ressesively inherited disorders equal incidence among both sexes is expected thus finding in the present study can be explained.

**3) Tribal and Non tribal distribution**: In our present study of 64 cases 28 cases were of Tribal ethnicity which is 43.75%. Among Thalassemia cases Tribal cases are 31.2%, where as in SCA cases they account for 54.5%.

GVPHC&MT Is tertiary centre for Visakhapatnam, Vizianagaram, Srikakulam districts in Andhra Pradesh and all cases in this study are from either of the 3 districts. These districts have unique demographics with high tribal population when compared to other districts. According to 2011 census and ITDA tribal Population of India is 8.2% of Andhra Pradesh is 6.63% where as Tribal population of Visakhapatnam-14.55%, Vizianagaram -10.05%, Srikakulam -6.5% which is higher than national average.

Among all cases reporting to GVPHC& MT, Pediatric department percentage of Tribal patients is around 20%. Tribal areas covered in present study are Paderu, Pedabayalu, Munchingput, Hukumpet, Dumbriguda, Arakuvally, G.madugula, G.K.Veedhi, Chintapalli, koyyuru, Ananthagiri, Parwathipuram, salur.

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Frequency of Hb*S in Tribal population has been found to vary from 7.3% to24.2% in different studies carried out in Andhra Pradesh (Negi 1976; Goud and Rao 1977; Babu et al. 1980)[33],[34][35][36]. However, the Tribal population of North coastal Andhra has not been explored so far for the distribution of β- globin gene cluster and its associated with Hb*S. Investigation of this aspect is important as the haplotypes are indicative of the severity of HbSS phenotype and can thus have prognostic value.

**Table 11: Distribution of different Hemoglobinopaties among Tribal cases in present study**

| S.No | Hemoglobinopathy | Tribal(n=28) |
|---|---|---|
| 1 | Beta thalassemia major | 25%(7) |
| 2 | Beta thalassemia intermedia | 10.71%(3) |
| 3 | Sickle cell anemia | 42.85%(12) |
| 4 | Sickle **β0**Thalassemia | 7.14%(2) |
| 5 | Sickle **β**+Thalassemia | 7.14%(2) |
| 6 | Sickle cell trait | 7.13%(2) |
| 7 | Sickle cell hemoglobinopathies | 64.28%(18) |

Among tribal cases sickle cell hemoglobinopathes are more common than Thalassemias compared to non tribal cases in Present study.

Inference can be drawn that Sickle cell hemoglobinopathes are more prevalent in Tribal population in this area.

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Spectrum of Hemoglobinopathies in the State of Orissa, India : A Ten Years Cohort Study RS Balgir.

**Table 2 : Age and sex-wise distribution of cases of different hemoglobinopathies**

| Age groups | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| 0-15 | 140 | 40.1 | 116 | 36.5 | 256 | 38.4 |
| 16-45 | 194 | 55.6 | 191 | 60.1 | 385 | 57.7 |
| 46+ | 15 | 4.3 | 11 | 3.4 | 26 | 4.9 |
| Total | 349 | 100.0 | 318 | 100.0 | 667 | 100.0 |

**Table 3 : Caste-wise distribution of cases of sickle cell disorders, β–thalassemia syndrome and other hemoglobinopathies in Orissa**

| Castes | Sickle cell disorders* N=396 %% | β–Thalassemia syndrome** N=248 % | Other hemo-globinopathies*** N=23 |
|---|---|---|---|
| General castes | 64.6 | 79.6 | 91.3 |
| Scheduled castes | 27.4 | 16.2 | 8.7 |
| Scheduled tribes | 8.0 | 4.2 | 0.0 |
| Total | 100.0 | 100.0 | 100.0 |

Compared to this study in present study Tribal cases are of higher percentage. Reasons can be Difference in Distribution of population and higher incidence of Abnormal genes in Tribal population in this area. According to 2014 Harithaet al The total prevalence of sickle cell gene has been found to be 9.71% among the studied sample of 4 tribal communities in Visakhapatnam. One more possible explanation is present study is Hospital based study and need not represent exact scenario in community.

**4. Age at Diagnosis:** Thalassemia: 22 of 24(91.6%) Beta thalassemia major cases were diagnosed in 1$^{st}$ year of life, rest 2 were diagnosed in 2$^{nd}$ year of life. Earlist diagnosed case is at 5 months of age. 25% of thalassemia intermedia cases were diagnosed in 1$^{st}$ year of life and 75% were diagnosed in 2$^{nd}$&3$^{rd}$ years of life. Depending on the mutation and degree of fetal hemoglobin production, transfusions in β-thalassemia major are necessary beginning in the 2nd mo to 2nd yr of life (Nelson).

Sickle cell Anemia: 6 of 22(27.2%) cases were diagnosed in 1$^{st}$ year of life ,among them one case was diagnosed in 4 months of age , 9(41%) during 2$^{nd}$& 3$^{rd}$ years, 6(27.2%) during 4$^{th}$& 5$^{th}$ years of life, one is diagnosed at 9 years of life.

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Thus Sickle cell Anemia can have variable age of presentation. In this study age at diagnosis varied from 4 months to 9years.This difference in age of presentation may be due to other co-morbid conditions and confounding factors like Malaria, High Altitude, other infections and neglect and local treatment without diagnosis. Therefore strong suspicion is necessary to diagnose early.

Clinical course of SCD has been described by a longitudinal study between 1977 and 1995 of nearly 5000 American patients (CSSCD). Child is usually asymptomatic until the second half of the first year of life.

All cases of Sickle thalassemia in this study are diagnosed in 1$^{st}$ 3 years of life. Sickle **β0** thalassemias have an earlier presentation.

Sickle cell trait cases 2 were diagnosed b/w 8-10 years and one is diagnosed at 12 years. As sickle cell trait cases are usually asymptomatic and only diagnosed accidently or when they had a complication their late age of diagnosis can be explained.

**5) Transfusion requirement and frequency:**

In the present study 6 of 24 cases of thalassemia major and 3 of 8 Thalassemia intermedia had their 1$^{st}$ transfusion during this study. 66.6% of Beta thalassemia major required >12 tranfusions a year of them two cases had 16/year. Thalassemia intermedia cases have transfusion requirement between 3-11/year.

This can be explained by nature of disease. As there is no beta chain production in B-Thalassemia major they will have no production of Hb A thus they are completely transfusion dependent. Where as in Thalassemia intermedia cases there is some production of Beta chain thus less dependent on transfusion.

SCA: Among SCA cases 20 of 22(90.1%) cases ever had a transfusion and none had transfusion requirement >3/year. Thus transfusion requirement in sickle cell anemia appears to be significantly less than thalassemias.

Sickle β0 thalassemias 1 required >11 transfusions per year and 2 required b/n 4-11/year. Sickle β+ thalassemia 75% required </=3transfusions/year.

Sickle β0 thalassemias similar transfusion requirement like B Thallsemia major and sickle β+ thalassemias have transfusion requirement like thalassemia intermedia.

Comparison with similar study: Shah Sejal J et al. NHL medical college, gujrath.

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| Nature of Disease | Total Cases | Transfused cases | Frequency of blood transfusion (in times) | | |
|---|---|---|---|---|---|
| | | | 2-5 | 6-10 | > 10 |
| Beta$^0$ Thalassemia Major* | 14 | 14 | 5 | 5 | 4 |
| Beta$^+$ Thalassemia Major* | 2 | 2 | 2 | - | - |
| Thalassemia Intermedia | 2 | 1 | 1 | - | - |
| Homozygous Sickle cell disease | 7 | 5 | 5 | - | - |
| Sickle cell trait | 4 | 0 | - | - | - |
| Sickle cell - B Thalassemia | 4 | 4 | 1 | 3 | - |
| HBE - Beta Thalassemia | 2 | 1 | 1 | - | - |

Present study Transfusions per annum(PA):

| **Nature of disease** | **Total cases** | **Transfused cases** | **</=3 PA** | **4-11 PA** | **> 11 PA** |
|---|---|---|---|---|---|
| **Beta thalassemia major** | 24 | 24 | 6(1$^{st}$transfusion) | 6 | 12 |
| **Beta thalassemia intermedia** | 8 | 8 | 4 | 4 | - |
| **Sickle cell anemia** | 22 | 20 | 20 | - | - |
| **Sickle β0 Thalassemia** | 3 | 3 | - | 2 | 1 |
| **Sickle β+ Thalassemia** | 4 | 4 | 3 | 1 | - |
| **Sickle cell trait** | 3 | 0 | - | - | - |
| **Total** | 64 | 59 | 30 | 14 | 15 |

Results in both studies are comparable with similar transfusion requirement in different Haemoglobinopathies.

**6) Effect on Growth:** Weights and Heights are measured and compared to WHO-NCHS standards of Height for age and weight for height. Weights and heights below 2 Standard Deviations of expected are noted. According to WHO Classification children weight for height <2SD are labeled Wasted and height for age <2SD are labeled Stunted. 50% of children with Beta Thalassemia major are wasted 46% stunted and 29% are both wasted and stunted. Thalassemia intermedia patients 37.5% are wasted, 37.5% are stunted.
Wasting and stunting are more prevalent in Thalassemia major compared to intermedia. It can be inferred that severity of disease has an impact on growth.

This is in accordance with study by Jhonson and Krogman.

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| Effect on growth in thalassemia major | Present study | Jhonson and Krogman |
|---|---|---|
| Wasting | 50% | 46% |
| stunting | 46% | 40% |

Growth impairment constitutes one of the significant problems of children with thalassemia major. Auxological studies (Erlandson et al., 1964; Johnston & Krogman 1964)[38] conducted on patients with beta-thalassemia in different parts of the world have shown not only compromised growth, but also great population-specific diversity in the pattern of their somatic growth. Short stature of thalassemia patients might be related to endocrine factors (Pintor et al., 1986; Vullo et al., 1990), zinc deficiency (Arcasoys Sc Cavador, 1975) or toxic effects of chelating tiierapy (Lederman et al., 1968; Peto 8c Thomson 1986), and has also been attributed to factors like chronic anemia, hypersplenism, folic acid deficiency, iron load etc by earlier workers (De Sanctis et al., 1991). Sickle cell Anemia 41% are Wasted 43.5% are stunted 13.6% were both wasted and stunted.

This is in accordance to study by Mukherjee and Ganga kedhar[39] which found that sickle cell anemia boys and girls have statistically significant lower weights and heights.

| Effect on growth in SCA | Present study | Mukherjee,GangaKedhar |
|---|---|---|
| Wasting | 41% | 44.5% |
| stunting | 43.5% | 46% |

Nikhar *et al*. [40] have reported the anthropometric and hematological data of SCD children from rural and urban areas of Wardha district, Maharashtra. The authors have shown a significant difference of body weight and BMI index between the rural and urban areas which indicates that SCD children from rural areas are underweight and undernourished. The BMI index is the body mass per unit per area and a measure of adiposity of an individual and found to be a good indicator of nutritional status. However, it is difficult to find out whether the inadequacy of nutrients is due to inadequate diet or poor absorption or defective metabolic utilization by an individual. In a population like India where sickle cell anemia is common along with iron deficiency anemia, [1] there is a possibility that low BMI seen in these children with SCD could have nutritional deficiencies which might have occurred due to inadequate food intake because of poor appetite especially during the vasoocclusive crisis. Dietary intake can significantly influence body weight. A number of studies have indicated that reduced stress levels (pain can be considered a specific type of stressor) are associated with improved dietary choices and nutritional status. The evidence in support of nutritional deficiencies in individuals with SCD has been increasing. A range of micronutrient deficiencies has now been identified in SCD patients, some of which can be corrected by supplements.

Another important factor to be investigated is socioeconomic status of the patients which has a direct implication on growth and nutrition and may be more prominent in the presence of chronic

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disease such as SCD. Poor socioeconomic status is known to have an adverse effect on the nutritional status and hemoglobin levels of SCD patients. The steady-state hemoglobin level may have a potential impact on growth of the patients because of its direct relationship with oxygen delivery to the tissues.

Phebus et al[41] found that height and weight deficit appear to begin as early as 2 years of age.

In present study Sickle **β0**thalassemia children 1(33%) of 3 is stunted and wasted, 1 is stunted. Sickle**β+** thalassemia 1(25%) of 4 is stunted.

Inference is Growth retardation is severe with Sickle cell anemia and Sickle **β0**thalassemia compared to Sickle **β+**thalassemia.

Hypoxia due to Anemia is main factor for growth Retardation. Low Socio economic status, Poor nutrition, High ferritin levels can further compound this problem.

## 7) CLINICAL FEATURES AND COMPLICATIONS:

**A) Thalassemia: A**ll children with thalassemia had pallor at the time of presenting to hospital.

Jaundice(Ictirus) is observed in 25%(6) case of T.major at time of admission and none of intermedia presented with jaundice.

Low incidence of jaundice in Thalassemia even it being a hemolytic anemia is due to ineffective erythropoisis rather than haemolysis is cause of anemia here.

Fever is seen in 21% of T.Major and 25% of T.intermedia cases at admission.

Fever in cases of thalassemia at admission have two inferences. 1)Fever can be due to any other infection but precipitating cardiac failure in already anemic child.

2)Thalassemia can cause immune deficiency which leads to infection and Fever.

Haemolytic Facies are seen in 50% of children with T.Major and 12.5% children with T.Intermedia.

6(25%) of T.Major presented with signs and symptoms of Congestive cardiac Failure.All of them have Hb <5gm% and 4 of 6 have fever at presentation. Fever in a anemic child can precipitate Cardiac failure by increasing oxygen demand. Thallasemic children have cardiac failure at lower Hb levels than normal children as their body is acclimatized to chronic anemia.

Hepato Spleenomegaly is seen in all cases of T.major and intermedia but Massive spleen which is Grade 4 or 5 According to Hackett's grading is noticed in 5 cases 20.08% but none of Intermedia. Chronic Hypoxia and increased Erythropoitin production leading to Extramedullary erythropisis is cause of Hepatospleenomegaly. Its severity depends on severity of anemia and

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chronicity of anemia. Therefore Massive spleenomegaly is seen in cases of T.Major only in this study.

**B)Clinical features and complications of Sickle Hemoglobinopathies:-**

Pallor is observed in all cases of Sickle cell Disease and trait in present study.

Jaundice is noticed in 77.2% cases of SCA and 71% of Sickle Thalassemias in the study. Cause of jaundice is Intra and Extra vascular hemolysis which leads to increased load on liver resulting in Unconjugated Hyperbilurubinemia. Most of the cases of SCA present to hospital due to some vascular crisis and Haemolysis occurs during this crisis.

Fever is seen in 59% of SCA at admission and 42.8% of S.Thalassemias during this study.Fever can be precipitating factor for crisis as raise in temperature causes hypoxia and Sickling .Fever can also be a result of some infection due to immune deficient status of SCA patients. In this study Fever is seen in 59% SCA patients at presentation but only 21% of Thalassemia cases at presentation.one possible Explanation can be due to Functional Aspleenia in SCA makes children more vulnerable to infection. But conclusion can not be drawn as data is limited and confounding factors need to be taken care of.

Vascular crisis is the reason for admission in 16 cases which is 72.72% of which Bone pains were most frequent complication with 7(32%) children presenting with this complaint. Dactylitis/Hand foot syndrome is presenting feature in 3(13.6%) cases.All 3 cases with dactylits are aged between 1-3 years. Explanation for this age relation can be maturation of short bones with age and change in angle of micro vasculature entering into short bones from acute to more linier with increasing age.

Acute Chest syndrome is diagnosed in 3(13.6%) cases.

Aplastic Crisis is seen in 3(13.6%) children . All these 3 children had fever followed by rapidly progressing severe pallor and Hb%<4gm%.reticulocyte counts are low. Aplastic crises are caused due to parvo virus B leading to death of erythroid progenators.

Sequestration crisis is noted in 1 child with sever pallor and grade 3 spleen.

Stroke is reported in one case during the study in a 8year old Tribal child with onset Right sided hemiparesis.

Complications like Leg ulcers,Megaloblastic crisis, are not noted in present study.

This is similar to Clinical course of SCD that has been described by a longitudinal study between 1977 and 1995 of nearly 5000 American patients (the Cooperative Study of Sickle Cell Disease, ***CSSCD***).[18]

COMPARISION OF C/F of hemoglobinopathies with previous study::

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| CLINICAL FEATURE | Shah Sejal et al.(n=35) | Present study(n=64) |
|---|---|---|
| Pallor | 100%(35) | 100%(64) |
| Icterus | 22.9%(8) | 46.8%(30) |
| Hepatomegaly | 71.4%(25) | 68.75%(44) |
| Spleenomegaly | 88.6%(31) | 81.25%(52) |

Even there is difference in percentage of cases with jaundice other features are of similar incidence in both studies.

In Sickle thalassemias fever and jaundice and ACS are noticed with similar frequency when compared to SCA , but hypothesis cannot be made as sample of sickle thalassemias is small and age matched controls need to be compared.

Other complications are not noted in cases Of Sickle thalassemia cases in present study.

One notable difference which is obvious between sickle thalassemia And SCA in this study is Spleenomegaly is seen in100% of cases of Sickle Thalassemia and only 45.5% cases of SCA.

**8) Effect of Palliative vs Moderate Transfusion Regimen in Beta thalassemia Major patients:**

Clinical features and complications of Thalassemia are either due to severe anemia or Excessive ineffective erythropisis .Moderate Transfusion regimen maintains pre transfusion Hb%>9.5 so that anemia is prevented and erythropitin production is suppressed.

In present study of 24 children with Thalassemia major 6 are newly diagnosed cases. Of remaining 10 patients were following Palliative transfusion regimen and 8 are following Moderate transfusion regimen.

Haemolytic facies is seen in 80% children following Palliative transfusion regimen and 25%of children on Moderate transfusion.30% of children on Palliative regimen presented with CCF,none on Moderate regimen had CCF at presentation.

Hepatospleenomegaly is presnt in all children in both groups,but Massive spleenomegaly is seen in 50% children on palliative regimen, none in moderate regimen. Wasting and stunting are seen in 60% children on palliative regimen and none on moderate regimen.

Possible explanation to this difference between two regimens is that maintenance of Hb.>9.5 prevents complications such as CCF directly and decrease the effects of ineffective erythropisis by suppressing Erythropoitin production .

Kattamis et al[42] found that Thallasemic patients with higher Hb levels grew at normal rates while growth is retarted in children with lower Hb.

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Growth was studied in 74 children with homozygous β-thalassaemia aged 1 to 11 years, treated with three different transfusion regimens.

In group I (38 cases) haemoglobin levels were maintained above 8 g./100 ml.; in group II (14 cases), pretransfusion haemoglobin levels ranged between 6 and 8 g./100 ml.; in group III (22 children), pretransfusion haemoglobin levels were below 6 g./100 ml.

Children in group I grew normally, both in weight and height; those in groups II and III were retarded, particularly those in group III.

Wolman 24 noted that patients treated with intensive transfusion therapy appear in better health and their growth was closer to normal than those who were under transfused.

Over the past years, the clinical picture of thalassemia patients has changed substantially with the improvement of treatment. A positive change in the management of children with thalassemia has been recorded after transfusion regimens of high hemoglobin levels (Wolman, 1964[43]) and also due to administration of subcutaneous chelating therapy as proposed by Proper (1986).

The beneficial influence of these treatment modalities in improving the growth status of β-thalassemia patients has been documented in the developed western world (Brook et al., 1969; Kattamis et al., 1970).

In these countries factors like chronic anemia and folic acid deficiency are no longer considered important causes of short stature as they are corrected with transfusions (De Sanctis et al., 1991), but this is not necessarily the case in developing countries like India, where intensive transfusions are not available to the majority of thalassemia patients, and patients remain under transfused.

The success of prevention programmers for the control of thalassemias in countries like Cyprus, Italy and Greece have shown that education and screening forms the most important part of these programme (Angastiniotis et al.1995; Caoet al.2002; Loukopoulos2011)[2][44]. It has also been emphasized that there is remarkable diversity in the frequency of the β thalassemias and carriers of other haemoglobin variants even within small geographic regions in different countries and hence accurate micromapping is important to estimate the disease burden (Weatherall 2011)[1].

## CONCLUSION

Haemoglobinopathies are a leading cause of child mortality worldwide, although with a variable geographical incidence. A reliable estimate of prevalence of the disease is necessary for reducing its burden. 3,000 ethnic groups in India still follow endogamy. Haemoglobinopathies are the commonest hereditary disorders in India and pose a major health problem. The data on the prevalence of β-thalassemias and other haemoglobinopathies in different caste/ethnic groups of India is scarce. Amongst the widely prevalent nutritional anemia, hidden is the problem of

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

thalassaemia and abnormal hemoglobin. In a developing country like India, where healthcare facilities in rural areas are less adequate, hemoglobinopathies can compound the burden on the families and also on the government as the treatment is very expensive. Implementation of mass screening programmes particularly in tribal areas will help in preventing the spread of the disease. Counseling for screening before marriage needs to be encouraged in order to avoid the psychological trauma and financial burden on the affected families. In already Affected Children with Beta thalassemia major it is better to Follow Moderate transfusion regimen which improves quality of life and allow growing normally.

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