

A TWO YEAR HOSPITAL BASED PROSPECTIVE STUDY OF SICKLE CELL DISORDERS IN CHILDREN AND COMPARISON WITH OTHER HOSPITAL BASED REGIONAL STUDIES IN INDIASunil Kumar Komanapalli¹, Siva Ranjan D², Vijaya Bhaskar P³, Krishna L⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT:: Various haemoglobinopathies are major health problem in east godavari district, andhra pradesh. Because of high prevalence of these disorders, we undertook limited hospital based study. **AIMS:** To study and to evaluate the sickle cell disorders in children who attended outpatient pediatric department, GGH, Kakinada **METHODS AND MATERIAL:** The present prospective study included 82 patients, referred for screening of hemoglobin disorders from October 2010 to September 2012, with Clinical history of anaemia, jaundice, splenomegaly and fever. Blood samples were collected into EDTA for testing parameters like hemogram, peripheral smear, reticulocyte count, Hb F(fetal hemoglobin) study, osmotic fragility test, Hb H Inclusion Bodies, hemoglobin analysis by HPLC (high performance liquid chromatography) and urine was collected for urobilinogen test. **RESULTS:** Total numbers of sickle cell disease and trait were 31 out of 82 screened cases with male predominance and six cases were sickle heterozygous conditions. The prevalence of sickle cell disorders is 37%. 54% of sickle cell cases were associated with iron deficiency anemia. Serum bilirubin levels are increased more in sickle cell disease compared to other abnormal Hb disorders. **CONCLUSIONS:** Our study indicates that sickle cell disease and trait were most common haemoglobinopathies. 93% of sickle cell cases had presented with Microcytic hypochromic anemia. The prevalence of sickle cell disease is 37%, although the present study is Hospital based which cannot represent any community or population, but it emphasizes the need of knowing the magnitude of this problem in this region.

KEY-WORDS: Sickle cell disease, Haemoglobinopathies, Prevalence, HPLC, Hospital based study.

INTRODUCTION: Sickle cell disease is a common hereditary hemoglobinopathy. It is caused by substitution of valine for glutamic acid in position six of beta globin chain. There are two main forms of Sickle cell disease. The homozygous state or sickle cell anemia (β genotype SS) and Sickle cell trait (β genotype AS), the heterozygous state.¹ In 1910, James Herrick, examined a 20 year old anemic patient with cough and fever, and stated that the RBC were only half of their normal number and were thin, elongated with crescent and sickle shape¹.

In India, it was reported by Lehmann and Cutbush in the aborigines at Nilgiri hills in 1952². Dunlop and Mozumdar in 1952 identified the gene in Assam in the tea garden workers, who had migrated from Orissa³. Reports of the gene in Uttar Pradesh (Bhatia.et.al.1955), west India (sukumaranet.al.1956)⁴, central India (Shukla & Solanki 1958)⁵, West Bengal (Choudury, Ghosh, Mukherjee 1964)⁶, and Andhra Pradesh were put forth later. In India, Hb S is mainly present in tribal and non-caste communities, with carrier prevalence of up to 40%.⁷ Extensive field studies in all the taluqs of East Godavari District, parts of Adilabad, Visakhapatnam, Warangal and the entire tribal

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belt in West Godavari District from 1978 to date, revealed Hb S, Rampa, Koyadora, Hofu and a new alpha chain variant, Hb Godavari [α 95 (G2) pro \square Thre] and also β thalassemia and α thalassemia interacting with HbS.⁸

The present prospective study included 82 patients; study was done on Children up to 18 years of age with Clinical history of anaemia, jaundice, splenomegaly and fever. Haemoglobinopathies are a part of abnormal hemoglobin's and recognized as a global problem. The most common is sickle cell disease, worldwide in distribution, causing severe disease and death in children and adolescence. The aim of this study was to know the prevalence and to evaluate the sickle cell disorders. As these disorders are common in Andhra Pradesh and it was conducted among children attended the Pediatric outpatient department (OPD) at Government General Hospital, Kakinada.

MATERIALS AND METHODS: The present prospective study included 82 patients, referred for screening of hemoglobin disorders from October 2010 to September 2012 from pediatric department, GGH-RMC, Kakinada. Children selected are of age group up to 18 years. Clinical history and physical findings were recorded as provided by the referring physician. We also examined clinically with special attention to anemia, splenomegaly and other relevant features noted.

Blood samples were collected into EDTA loaded bottles, for testing parameters like hemogram, peripheral smear, reticulocyte count, Hb F(fetal hemoglobin) study, osmotic fragility test, Hb H Inclusion Bodies, hemoglobin analysis by HPLC and urine was collected for urobilinogen test. Biochemical parameters like serum total bilirubin, serum ferritin values were also noted.

RESULTS: Fifty one (62%) patients out of 82 studied had hemoglobinopathy and 31 (38%) had Iron deficiency anemia (IDA). Among 51 patients who had disorders of abnormal Hb synthesis was described in [table 1].

Cases	Total
Sickle cell disease	19 (37%)
Sickle cell trait	12 (23%)
Sickle- thalassemia	4 (8%)
Sickle – hereditary persistence of fetal hemoglobin (HPFH)	2 (4%)
Other Hb disorders	14 (27%)
Table 1: Disorders of abnormal Hb synthesis (n=51)	

An age and sex distribution of Sickle cell disease (n-19) and trait (n-12) were showed male preponderance [figure 1].

Among 19 patients of sickle cell disease 17 had moderate to severe anemia and only two cases had mild anemia. Hb%, serum bilirubin and HPLC profiles of Sickle cell disease were showed in [table 2].

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Cases	Hb gm.%	Unconjugated Serum Bilirubin (mg/dl)	HPLC %
117/11	5	14.5	Hb S: 72 Hb A: 4.6
866/11	4.8	13.5	Hb S: 82.3 Hb A: 6.7
1399/11	5.2	8.8	Hb S: 81.9 Hb A: 0
282/12	6.2	6.8	Hb S: 57.2 Hb A: 32.4
127/12	2.8	11.5	Hb S: 72.9 Hb A: 7.5
151/12	5.3	3.5	Hb S: 77.3 Hb A: 3.1
520/12	5.6	14.8	Hb S: 63.3 Hb A: 15.7
356/11	9.2	8.5	Hb S: 69.8 Hb A: 4.9
1032/11	10.5	10	Hb S: 78.3 Hb A: 6.0
1033/11	9.8	3.3	Hb S: 79.7 Hb A: 4.8
1631/11	8.2	9.5	Hb S: 79.5 Hb A: 4.4
1913/11	10	8.5	Hb S: 79.4 Hb A: 1.8
1940/11	8.5	9.2	Hb S: 83 Hb A: 1.6
342/12	7.8	5.8	Hb S: 75.7 Hb A: 0
446/12	8	10.5	Hb S: 69 H b A: 10
945/12	9	2.8	Hb S: 72.1 Hb A: 4.5
948/12	6.8	6.2	Hb S: 74.3 Hb A: 4.5
990/12	7.5	3.6	Hb S: 71.8 Hb A: 0.9
996/12	9.5	3	Hb S: 54.7 Hb A: 21

Table 2: Hb%, serum bilirubin and HPLC profiles of Sickle cell disease

All the 12 cases showed moderate to severe anemia in sickle cell trait. Hb%, serum bilirubin and HPLC profiles of Sickle cell trait were showed in [table 3].

Cases	Hb gm.%	Unconjugated Serum Bilirubin (mg/dl)	HPLC %
1126/10	3.1	4.4	Hb S: 12.25 Hb A:86.4
1707/10	3.9	3.2	Hb S:22.5 Hb A: 68.0
423/11	7.1	2.2	Hb S: 27.9 Hb A: 64.5
803/12	6.5	3.2	Hb S: 34.1 Hb A: 61.2
1175/11	2.1	2.8	Hb S: 16.25 Hb A:78.8
1254/11	5.5	2.2	Hb S: 12.3 Hb A: 79
1790/11	5.8	4.1	Hb S: 11.1 Hb A: 83.7
1832/11	5	2.0	Hb S: 14.6 Hb A: 83
1860/11	4.5	2.1	Hb S: 5.33 H b A: 91.5
1861/11	6	2.9	Hb S: 40 Hb A: 56.7
705/12	9	2.6	Hb S: 22.2 Hb A: 58.5
331/11	9.1	5	Hb S: 15.5 Hb A: 82.9

Table 3: Hb%, serum bilirubin and HPLC profiles of Sickle cell trait

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Hb%, MCV, serum bilirubin and HPLC profiles of Sickle- β thalassemia cases was showed in [table 4].

Cases	Hb gm.%	MCV in(fl)	Unconjugated Serum Bilirubin(mg/dl)	HPLC
463/11	8.3	87	4.4	Hb S: 65.3% Hb F: 25.8% Hb A: 3.9% HbA2: 4.9%
1335/11	6.5	69	4.3	Hb S: 70.2% Hb F: 5.2% Hb A: 16.2% Hb A2: 6.1%
172/12	7	58	4.8	Hb S: 60.6% Hb F: 24.5% Hb A: 9.1% HbA2: 4.6%
180/12	9.2	76	2.1	Hb A: 41% Hb F: 28.4% Hb S: 28% HbA2: 3.7%

Table 4: Hb%, MCV, serum bilirubin and HPLC profiles of Sickle- β thalassemia cases

Two Sickle-HPFH cases showed mild anemia, Hb, MCV and unconjugated serum bilirubin values and HPLC profile was showed in [table 5].

Cases	Hb%	MCV(fl)	Unconjugated Serum. bilirubin(mg/dl)	HPLC %
1830/11	10.1	77	1.5	Hb S: 4.25% Hb A: 5.86% Hb F: 7.97% Hb A2: 1.91%
1978/11	10.9	82	2.2	Hb S: 26.09% Hb F: 29.54% Hb A: 43.01% HbA2: 1.34%

Table 5: Hb, MCV and unconjugated serum bilirubin values and HPLC profile

DISCUSSION: The cumulative gene frequency of haemoglobinopathies in India is 4.2%⁹. Hb S has been reported from various Indian states, community and ethnic groups with an average frequency of 4.3% (range 0-44%).¹⁰ The present study was mainly hospital based case study, which cannot be

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regarded as representative of any community or population. The study showed high prevalence of sickle cell disorders with male preponderance in concordance with the other hospital based regional studies. It was showed in [table 6].

Region	Prevalence
Western Maharashtra ¹¹	15.8 %
Orissa ¹²	16.5 %
Uttar Pradesh ¹³	3.2 %
Present study	37 %

Table 6: Prevalence of sickle cell disorders

Most of the sickle cell disease patients presented with fever, yellowish discoloration of eyes and few presented with splenomegaly and chest pain. Sickling with 2% sodium metabisulfite appeared after one hour in most of the cases and after six hours in a few cases. In all the cases, reticulocyte count and urobilinogen was increased and osmotic fragility was decreased. Seven (7/19) patients were above the age of 10 years, although they were symptomatic from childhood, indicating lack of awareness about the disease or tendency of the parents to seek advice of the doctors only as last resort. These cases had no splenomegaly, attributed to autosplenectomy. Four (4/19) patients were born of consanguineous marriage.

Out of 12 Sickle cell trait cases, most of them presented with fever and dyspnea. Sickling was positive in five (5/12) cases and negative in seven (7/12) cases, reason being low Hb S values (less than 20% in HPLC). Sickling test (sodium metabisulphite) is less sensitive in detecting these cases. Reticulocyte count and serum bilirubin are increased in only two (2/12) cases. Urobilinogen is increased in only one case. Three patients are born of consanguineous marriage.

Seventeen cases of sickle cell disease and all the cases of sickle cell trait had microcytic hypochromic (MCHC) anemia, in contrast to usual normocytic normochromic blood picture. These cases had low serum Iron & Ferritin values, indicating associated iron deficiency or alpha thalassemia trait. High incidence of IDA has been reported in patients with sickle cell disease from India¹⁴. Alpha thalassemia trait should be suspected with sickle cell disease or trait when Hb F is unusually low with typical blood indices and low Hb S.¹⁵⁻¹⁷ In present study 54% sickle cases were associated with MCHC anemia correlated with Gujarat study [table 7]

Studies	MCHC anemia in sickle cases
Gujarat ¹⁸	70 % (24/34)
South Orissa ¹¹	96.5% (272/282)
Present study	54% (17/31)

Table 7: Comparison of Sickle cases associated with microcytic hypochromic anemia with other regional studies

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When compared to sickle cell disease, thalassemia major cases had lower values of serum bilirubin, indicating that lysis of precursor cells liberates less bilirubin compared to that seen with lysis of mature erythrocytes as in sickle cases [table 8].

Cases	Unconjugated bilirubin average(mg/dl)
Sickle cases	8 (3.5-14.5)
Thalassemia major	3.4 (2.1-4.8)
Double heterozygous conditions	3.5 (2.1-5.4)

Table 8: Comparison of serum bilirubin values of sickle cell cases with other Haemoglobinopathies

Among four patients of sickle thalassemia, two were born of consanguineous marriage. Average age of presentation was 5 years. They presented with fever, recurrent respiratory tract infections. On examination they had mild to moderate splenomegaly. Hemogram revealed moderate anemia. In all these cases serum ferritin values were increased.

Sickle –HPFH cases presented with mild anemia, this can be due to high Hb F value protecting from sickling. Acid elution test revealed pan cellular distribution of Hb F.

CONCLUSION:

1. Total number of abnormal Hb disorders is 51 out of 82 screened cases with male predominance. Most of the patients belonged to the age group of 1-4 yrs. in sickle cell trait and 5-9 yrs. in sickle cell disease.
2. Fifty four percent of sickle cell cases are associated with iron deficiency anemia. Serum bilirubin levels are increased more in sickle cell disease compared to other abnormal Hb disorders.
3. Our study is a Hospital based study which cannot represent any community or population, but it emphasizes the need of knowing the magnitude of this problem in this region
4. Unlike many other genetic disorders where couple at risk cannot be easily diagnosed, sickle and abnormal hemoglobin give a tremendous opportunity for effective control of birth. There has to be only a political will to implement and achieve this.
5. Adequate measures and screening procedures should be adopted to reduce sickle cell disorders. Screening is affordable way to detect carriers and can be done in different societies like in high school, before marriage or in antenatal clinics.

REFERENCES:

1. Herrick JB. Peculiar elongated and sickle shaped red blood corpuscles in a case of severe anaemia. 1910. Yale J Biol Med. 2001; 74(3): 179-84.
2. Lehman H.and Marie Cutbush. Sickle cell trait in southern India. Br Med J. 1952; 1: 404-5.

3. Dunlop and Mozumdar UK: The occurrence of Sickle cell anemia among a group of tea garden labourers in upper Assam. *Indian Med Gaz.*1952;87:387-91
4. Sukumaran PK., Sanghavi LD., Vyas GN: Sickle cell trait in some tribes of Western India. *Current Sci.* 1956; 25:290.
5. Shukla RS, Solanki BR. Sickle cell trait in Central India. *Lancet* 1958; 1:297-8.
6. Choudary S., Ghosh J, Mukherjee B: Study of Blood groups and Hemoglobin variants among the Santral tribe in Midnapore District of West Bengal, India. *Am J Phys Anthrop.* 1967; 26:307-12.
7. Mohanty D, Colah R B, Gorakshakar A C, Nadkarni A H, Phanasgaonkar S P, Shetty S et al. Genetic disorders in haematological practice in India. *Community Genti.* 2002;5 (3): 197 -200.
8. Wajcman H, Kister J, Riou J, Galacteros F, Girot R, Maier-Redelsperger M, Nayudu NV, Giordano PC: Hb Godavari [α 95(G2)Pro \rightarrow Thr]: a neutral amino acid substitution in the alpha 1 beta 2 interface that modifies the electrophoretic mobility of hemoglobin. *Hemoglobin.* 1998 Jan;22(1):11-22.
9. Sarnaik SA. Thalassaemia and related haemoglobinopathies. *Indian J Pediatr* 2005;72:319-24.
10. Mohanty D, Mukherjee MB. Sickle cell disease in India. *Curr Opin Hematol* 2002;9:117-22.
11. Ambekar SS, M.A. Phadke, G.D. Mokashi, M.P. Bankar, V.A. Khedkar, V. Venkat D.G. Basutkar Pattern of Haemoglobinopathies in western maharashtra, *Indian Paediatrics* 2001; 38: 530-534.
12. Balgir RS. Spectrum of haemoglobinopathies in the state of Orissa, India: a ten year cohort study. *J Assoc Physicians India* 2005; 53: 1021-1026.
13. Vineeta G, Jyoti Shukla, Vijai Tilak, Baldev Bhatia. Spectrum of Haemoglobinopathies in Eastern Uttar Pradesh. *Indian J of Pedia.* 2009;76: 857.
14. Balgir RS. The burden of haemoglobinopathies in India and the challenges ahead. **Curr Sci:** 2000; 79:1536-1547.
15. WHO- executive board EB118/5, 118th Session Report by the Secretariat on Thalassaemia and other haemoglobinopathies: Prevalence of Haemoglobinopathies. 11 May 2006; p.1-8.
16. Varawalla NY, Old JM, Sarkar R, Venkatean R, Weatherall DJ. The spectrum of beta thalassaemia mutations on the Indian subcontinent; the basis of prenatal diagnosis. *Br J Haematol* 1991;78:242-247.
17. Das BM, Deka R, Das R. Haemoglobin E in six populations of Assam. *Ind J Anthrop Assoc* 1980;15:153-156.
18. Patel Ashwin P, Naik Madhuben R, Shah Nilam M, Sharma Narmadeshwar P, Parmar Prakash H. Prevalence of Common Haemoglobinopathies in Gujarat: An analysis of large population screening programme. *National Journal of Community Medicine*, 2012;3(1):112-6.

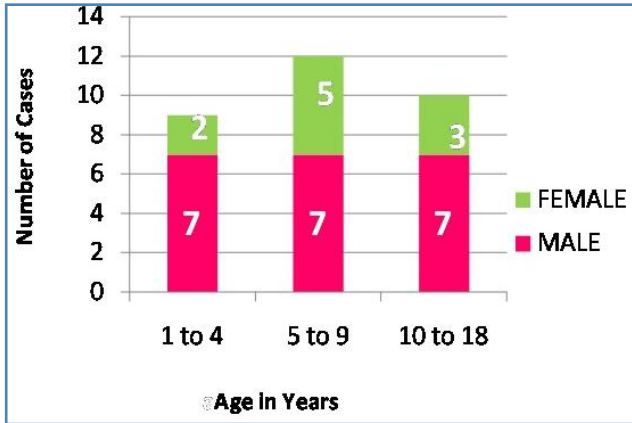


Fig. 1: Age and sex distribution of Sickle cell disease and trait

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