ISSN 2250-3153

Pedigree Analysis in Congenital Hemoglobinopathies

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Abstract- Hemoglobinopathies are a heterogeneous group of hereditary hemolytic anemias. Thalassemia and sickle cell anemia are the commonest hemoglobinopathies seen in our region. Aim ; to analyse the family members of hemiglibinopathies for carrier status. Material and methods ;Patients visiting our hospital with features of anemia, recurrent attacks of jaundice, splenomegaly were screened for evidence of hemolysis. Their siblings, parents, first cousins,grand parents are also screened for carrier status. Conclusion ;Thirty two people belonging to five families were screened over a period of one year. Of which three cases were sickle cell anemia, one case was thalassemia major, three cases were sickle thaslassemia, twelve cases were carriers, thirteen cases were normal.

Index Terms- hemoglobinopathies, hemolytic anemia, splenomegaly, sickle cell anemia, thalassemia.

I. Introduction

The frequency of total hemoglobinopathies in India was reported to be 4.2% [1,2] . Sickle cell anemia is due to replacement of glutamic acid by valine at the 6th position of globin chain. Thalassemia is due deficient synthesis of globin chains.Both sickle cell anemia and thalassemia are autosomal recessive conditions. If patients carry only one copy of the defective gene, they are carriers (heterozygous) and asymptomatic. If they carry two defective genes (homozygous), they manifest the disease. Few patients carry both sickle and thalassemia genes , they are called as double heterozygous cases.

II. Material and Methods

Thirty two cases were studied. Prior consent was taken from every individual before conducting the study.

Complete hemogram was done. Serum bilirubin levels were estimated.

Sickling test and osmotic fragility test were done wherever necessary.

After coming to a conclusion from these tests, samples were sent for High performance liquid chromatography(HPLC).

Reference ranges for HPLC were HbA 96-98%
HbA2 2.8-3.7%
HbF <2%
HbS 0%

III. RESULTS

Table ; depicting the values of various hematological parameters.

s.no	Age sex	MCV fl	MCH pg	Bilirubin	Rt %	sickling	Osmotic fragility	hplc				results
								HbA%	HbF %	HbA2 %	HbS %	
1	30F	86	29	N	0.5	+ve	N	50.3	0.9	3.7	40.4	Carrier
2	35M	85	28	N	1	_ve	N	80.3	2.2	4.8	-	Carrier
3	8M	83	26	raised	5	+ve	N	7.5	30.1	4.8	57.6	Disease
4	10M	85	28	raised	8	+ve	N	1.3	23.6	2.2	74.6	Disease
5	42F	85	28	N	1	+ve	Inconclusive	50	0.8	3.6	39.6	Carrier
6	48M	85	28	N	0.5	- ve	N	84.8	0	3.1	-	Normal
7	17M	86	28	N	0.2	- ve	N	71.5	1.1	2.8	-	Normal
8	33F	85	28	N	1	- ve	N	82.9	0	3.3	-	Normal
9	13M	88	29	N	1	- ve	N	82.7	-	3.2	-	Normal
10	40F	85	28	N	5	+ve	Inconclusive	52.1	0.4	4.1	37.8	Carrier
11	45MM	85	28	N	0.5	_ve	N	85.3	-	2.7	-	Normal
12	22F	86	29	N	0.2	_ve	N	87.5	-	2.5	-	Normal
13	17M	88	29	N	1	_ve	N	82.7	-	3.1	-	Normal

14	40M	85	28	N	0.5	_ve	N	84.8	-	2.2	-	Normal
15	15M	85	28	raised	8	+ve	N	4.2	22.5	6.7	63.1	Disease
16	30F	85	28	N	0.5	+ve	Inconclusive	60.3	0.8	3.1	38.2	Carrier
17	40M	85	28	N	2	+ve	N	50.4	1.1	3.5	38.9	Carrier
18	30F	85	28	N	0.5	+ve	N	49.4	1.2	3.6	38.9	Carrier
19	10M	85	28	raised	8	+ve	N	1.6	14.6	2.7	81.2	Disease
20	8F	85	28	raised	7	+ve	N	1.1	23.8	2.5	72.6	Disease
21	5F	85	28	raised	3	+ve	N	1.8	21.8	2.7	73.2	Disease
22	57F	85	28	N	0.5	_ve	Inconclusive	84.6	0.2	5.1	-	Carrier
23	72M	86	28	N	0	_ve	N	81.4	-	3	-	Normal
24	32M	88	28	N	0	_ve	N	87.7	-	2.8	-	Normal
25	47M	85	28	N	0.8	_ve	N	83.6	0.4	4.6	-	Carrier
26	37F	85	28	N	1.2	_ve	N	83.8	0.9	4.1	-	Carrier
27	14F	87	29	N	0	_ve	N	84.2	0.2	4.6	-	Carrier
28	10F	85	28	raised	7	_ve	Inconclusive	1.8	46.8	4.8	-	Disease
29	32F	85	28	N	0	_ve	N	83.8	0.9	4.1	-	Carrier
30	38M	89	30	N	0	_ve	Inconclusive	89.7	-	2.2	-	Normal
31	7M	85	28	N	1	_ve	N	81.4	0.4	3	-	Normal
32	5M	85	28	N	0.2	_ve	N	81.2	0.2	2.8	-	Normal

According to table three cases were sickle cell anemia with Hbs values from57% to 81%. Sickle carriers were showing HbS values from 37% to 40%. In thalassemia cases HbF was 22.5% to 46.8%. in thalassemia carriers Hb À was raised more than 3.7%.

IV. Discussion

The sequence of events that lead to the discovery of sickle cell anemia are quiet fascinating. In one Ghanian family, symptoms of sickle cell anemia were noted in 1670 itself but later in 1910 one Chicago cardiologist observed sickle cells in a west Indian student. Emmel in 1917, demonstrated sickle cells in vitro [3]. In India the first case of sickle hemoglobin was reported in the year 1952, by Dunlop and Muzunder in the garden labourers of Assam. At the same time by Lehman and Cutbush from the tribals of south India , [2] in 1925 , Cooley and Lee observed a peculiar syndrome with progressive anemia, jaundice, splenomegaly and pronounced erythroblastosis. These patients were from Mediterranean background, this syndrome was named as ‘ thalassemia” derived from the greek word for sea. In the previous days thalassemia was also called as cooley’s anemia after the founder.[4] According to the literature Thalassemia was brought to Asia by the Alexander the Great and his army.[5]

The cumulative frequency of total hemoglobinopathies in India was reported to be 4.2%. The frequency of beta thalassemia trait was reportedto be varying from 1-17%. In India 30 million carriers and 15,000 infants with major hemoglobinopathies have been reported.[1.6]

In the present study, out of 32 cases, 3 cases were sickle cell anemia,6 cases were sickle carriers,6 cases were thalassemia carriers. 1 case was thalassemia major,3 cases were sickle-thalassemia double heterozygotes. 13 cases were normal
Sickle cell anemia, thalassemia, sickle thalassemia were clinically very severe with gross anemia, recurrent attacks of jaundice and gross splenomegaly. All the patients succumbed to the disease before 17 years of age. Hemolytic facies like frontal bossing,malar prominence were seen in only 2 cases.All the carriers were asymptomatic.

In the present study patients hailed from Prakasam,Guntur and Krishna districts. Sickle cell anemia patients belonged to tribal community hailing from Kothapullareddy gudem near Macherla Town. All three children in one family died due to sickle cell anemia. Thalassemia and sickle thalassemia were seen in general population also. In the peripheral smear all the cases showed the classical findings but the MCV,MCH values were not correlating with the degree of anemia. Thalassemia carriers osmotic fragility was either within normal limits or inconclusive and peripheral smear showed no abnormality except for mild microcytic anemia in few cases. So, to detect a carrier status, HPLC or electrophoresis is a must.

Criteria for diagnosis by HPLC HbA>HbS – sickle carrier
HbS> HbA---- sickle cell anemia
HbA2----- >3.7% thalassemia carrier
HbA2 and HbF are raised--------thalassemia major HbA2, HbF,HbS are raised------sickle thalassemia disease.

In a pedigree chart square denotes male, circle female.single line joining denotes marriage,double line consanguinous marriage. Indicates death.

Half filled circle or squa carrier state, completely filled circle-diseased state.

V. Conclusion

In a developing country like India ,where healthcare facilities in rural areas are far from 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. Though the present study, is restricted to few families due to financial constraints, this is a small attempt to highlight the problem.

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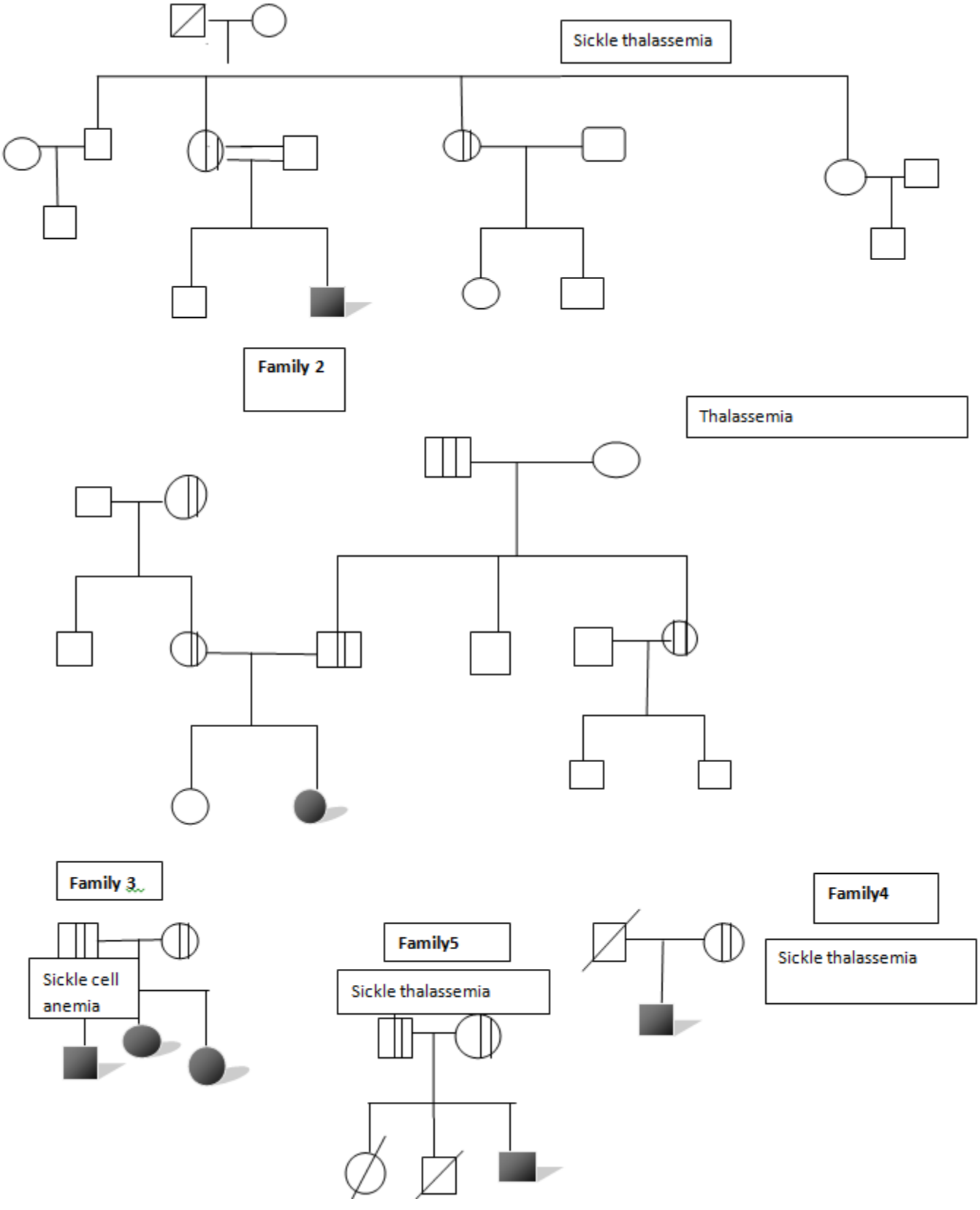
Pedigree charts family1


Sickle thalassemia
Family 2
Thalassemia
Family 3
Sickle cell anemia
Family5
Sickle thalassemia
Family4
Sickle thalassemia