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The Rising Double Heterozygous Cases of Haemoglobinopathies In Paediatric Population-A Hospital Based Cross Sectional Study

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Abstract: *In this study various abnormal haemoglobin fractions on HPLC were observed in 158 cases out of the total 300 screened paediatric anaemic cases. Of the 300 paediatric cases, samples analyzed on CE-HPLC for haemoglobinopathies, maximum 67 (22.33%) cases were diagnosed as S-β double heterozygous, 39(13%) as sickle cell trait, 27 (9 %) as β-thalassaemia major, 10 (3.33 %) as sickle cell disease, 05 (1.66 %) were diagnosed as β-thalassaemia trait, 03 (1%) were unknown haemoglobins , 02 (0.66 %) as Hb E-β-thalassaemia double heterozygous, 02 (0.66 %) as SCT + Hb D trait and 01 (0.3%) as Hb E trait.*
Keywords:-*Double heterozygous , paediatric haemoglobinopathies*

I. Introduction

The sickling disorders- HbSS, HbSD, HbSE, HbS β- thalassemia and other compound heterozygous hemoglobinopathies are all clinically significant, as these combinations present with different manifestations and degrees of severity, making precise identification important.[1]Majority of patients homozygous for β-thalassaemia or SCD; or double heterozygotes of β-thalassaemia with HbS or HbE have severe disease starting from infancy and require regular blood transfusion for survival and succumb eventually to myriad range of causes by adolescence or adulthood. Optimum management with adequate iron chelation or early hospitalization and treatment of infections, crisis as in a case of SCD is not available to vast majority[2,3].Automated cation-exchange High Performance Liquid Chromatography (HPLC) has emerged as an excellent screening tool for diagnosing these abnormal hemoglobins/ thalassemic states.[4,5]The simplicity of the automated system with internal sample preparation, superior resolution, rapid assay time, and accurate quantification of hemoglobin fractions makes this an ideal methodology for the routine clinical laboratory. [5]

The sparse literature available regarding haemoglobinopathies in children necessitated the need for the present study and early screening and detection of haemoglobinopaties will in turn help in early and better management of afflicted child, family counselling, planning for next child by parents. Understanding the actual rate or prevelance should facilitate the planning of public policies and other actions that can contribute towards the reducing homozygote's from the population and improving the quality of life of people with haemoglobinopathies.

II. Material And Method

This study cleared by institutional ethic commette of Government medical college NANDED Maharashtra, india. This is a hospital based cross sectional study in which a total of 300 anaemic paediatric patients (6months to 14 years of age) along with there parents blood samples were analysed for Hb variants who were referred from pediatric department of GMC nanded maharashtra,from various Primary health centre and rural health centre around nanded region of maharashtra. The study was conducted for 18 month from January 2013 to June 2014.patients were having clinical manifestation like anemia, hepatospleenomegaly, weakness, repeated infection, aches and pain, fever etc. Detail clinical history including ethnic origin, age sex, blood transfusion etc along with family history was taken.After consent from parents, 2 ml of venous blood collected in EDTA (Ethylene diamine tetra-acetic acid) coated vaccutainers from each patient and there parents wherever required. Patients transfused in last 3 months and age less then 6 month were not included in study. The Hematological profile of cases was done, which included PS, CBC including RBC Indices, reticulocyte count etc. The complete blood count was done by using orphee-mythic cell counter. With the help of Bio rad thalassemia short programme HPLC exact percentage of HbS, HbF, HbA_2 and HbA_0 was estimated to classify the cases.Then study of family members accompanying the cases was done to confirm the diagnosis and to determine ethnic background. The statistical analysis of all data was carried out using Microsoft Office Excel and SPS 16.

III. Results

During the study period of one year, a total of 300 paediatric cases were studied. The patient population age ranges from 6 months to 14 years. Out of 300 screened patients 158 cases were having abnormal haemoglobin. Out of abnormal Hb we found 71 cases of double heterozygous haemoglobinopathies that is very high.

The most common Hb abnormalirty detected was S β thalasaemia cases in 67 patients.The distribution of different pattern of Hb variant in study population has been shown in TABLE NO 1, Interpretation of results of HPLC was done on the basis of retention time , percentage of Haemoglobin, and peak characteristics. Eβ thalassaemia cases were 2 in number and SCT + HbD cases were also 2 in number.

Out of 71 double heterozygous haemoglobinopathis, there were 32 males and 39 female. Age wise distribution is shown in TABLE no 2, In which maximum 28nuber cases were under age group of 6-10 years, followed by 11-14 year in which cases were 24 and the minimum number cases were among 6month to 5years of age that is 18 cases.

Out of 71 cases of double heterozygous hemoglobinopathies cansanguinous marriage history was given positive in 26 cases. Caste wise distribution of double heterozygous cases shows maximum cases from boudha and banjara community i.e 35 and 16 cases .Table no 3 shows various caste and number of double heterozygous cases

Haematological profile in double heterozygous cases shown by table no 4. The average haemoglobin among 67 cases of S- beta thalassaemia cases was around 8.17±2.16 g/dl. The mean MCV level were found to be around 75.74±9.6 fl.The mean MCHC level was around 23.65±4.00 g/dl

Table And Figure

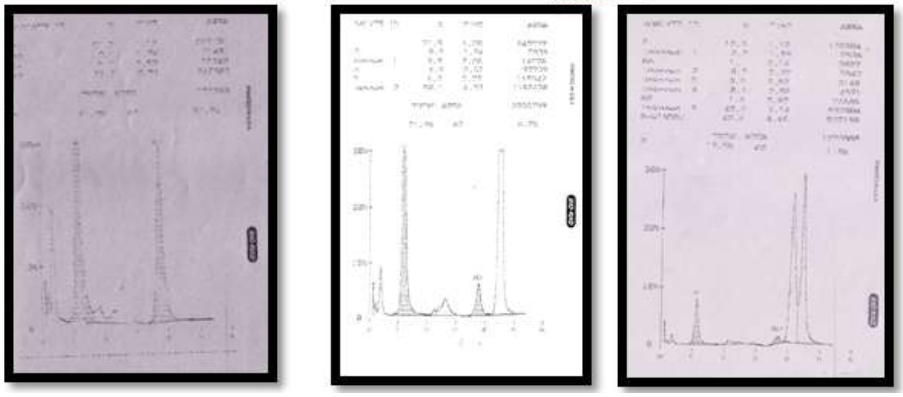

Fig 1 :-HPLC graph of showing double heterozygous haemoglobinopathies cases .Graph (a) showing HbE-Beta thalassaemia cases, graph (b) HbS-beta talassaemia case and Graph (c) showing HbS trait + HbD trait

Sr.no.	Haemoglobin Pattern	No. of Cases	Percentage %
1.	Normal	142	47.33 %
2.	Sickle cell trait	39	13 %
3.	Sickle cell disease	10	3.33 %
4.	β thalassaemia major	27	9 %
5.	β thalassaemiaintermedia	01	0.33 %
6.	β thalassaemia trait	05	1.66 %
7.	S β-thalassaemia	67	22.33 %
8.	E β-thalassaemia	02	0.66 %
9.	Heterozygous HbE	01	0.33 %
10.	SCT + HbD trait	02	0.66 %
11.	Alpha thalassaemia	01	0.33 %
12.	Unknown	03	1%
	Total	**300**	**100%**

Table 1- Haemoglobin patterns found during screening all cases.

AGE	Cases
0-5 yrs	**18**
6-10 yr	**28**
11-14yr	**25**

Table no 2:-Age sex distribution of double heterozygous cases double heterozygous cases.

CASTE	NO OF CASES
Boudha	**35**
Banjara	**16**
Muslim	**5**
Andh	**2**
Gond	**2**
Gowari	**2**
Kumbhar	**2**
Mahar	**2**
Sikh	**2**
Dhangar	**1**
Mang	**1**
Wadhar	**1**

Table no 3:-Caste wise distribution of various cases of double heterozygous haemoglobinopathies.

Variable (N)	**SB thal (67)**
Hb(g/dl)	8.17±2.16
RBC(10/ul)	3.9±0.90
PCV(%)	25.74±6.34
MCV(fl)	75.74±9.6
MCH(pg)	23.65±4.00
MCHC(g/dl)	28.65±4.12
HBA0(%)	24.90±10.67
HBA2(%)	6.11±2.27
HBF(%)	17.54±10.58
HBS(%)	52.74±16.94

Table no 4:-Haematological profile in double heterozygous cases.

No	Study		HbF	HbA0	HbA2	HbS
1.	S.S.Ambekar[67] 2001(IJHG) n=4	$S\beta^0$	25 %	5 %	5 %	68 %
		$S\beta^+$	28 %	19.8 %	3.5 %	61.7 %
1.	Rao Seema et al [46]2010 n=6		18.3 ±8.4	4.6 ± 1.8	4.5 ± 0.6	71.7 ± 5.8
2.	Dangi et al [45]2010 n=16		15.52 %	13.1%	4.19%	57.17%
3.	C.Vani et al [48]2011 th-60 n= 14		19.2%	-	-	65.6 %
5.	Present Study n=67		17.54±10.58	24.90±20.67	6.11±2.27	52.74±16.94

Table no 5:-Showing comparision of haemoglobin HbS,HbA0,HbA2 and HbF level in diagnosed cases of S-Beta thalassaemia cases in various study with present study**.**

IV. Discussion

4.1 Average age of presentation in present study was found to be 13.4 years which is comparable to the study conducted by Balgir et al[6] (13.5 years) in 2010 and Tyagi et al[7] (14.2 years) in 2003.

4.2 Incidence of double heterozygous cases in present study is 46.8% which is comparable to the study conducted by Dangi et al[8](45.7%) in 2010 and Tyagi et al[7](34.04%) in 2003. R.S Balgir et al[6]in(2010) reported the incidence rate of 32.11% of double heterozygous cases amongst the sickle disorder patients. This difference is may be due to regional variation. The probable cause for high detection of Sickle –Beta Thalassemia cases as compared to the other studies is that, family HPLC screening was done meticulously in the present study.

4.3 In the present study history of consanguineous marriage was the predominant cause for the occurrence of double heterozygous cases. It was found in 65 cases (55.55%). Patel D.K et al[9]and Tariq H.A et al[10]also stated that the main reason for increased incidence of double heterozygous cases in particular communities like SC and Muslims is consanguinity which is comparable to the findings of present study.

4.4 The caste wise distribution was carried out in Nanded and the nearby zone. It was found that the maximum number of double heterozygous cases were found in Boudha community i.e 29 cases (24.78%)

followed by Muslims 25 cases (21.37%). Banjara contributed to 12 cases (10.25%), Matang 12 cases (10.25%), Chambar 10 cases (8.55%), Teli9 cases (7.70%), kunbi 7 cases (5.99%) and others 13 (11.11%).

4.5 Table 5 shows comparision of various study and the present study in which the HbS levels were >50 %.

In all the studies the average HbF levels were high >15%, in present study it was (17.54±10.58)

The average HbA2 level in present study was (6.11±2.27).

In 67 cases out of 67cases,family HPLC study supported the diagnosis of double heterozygous Sβ Thalassemia.

V. Conclusion

Haemoglobinopathies form a significant proportion of hereditary disorders in paediatric population leading to a range of myriad complication , leading to mortality in large number of afflicted patients. Most common forms of these includes thalassaemia and sickle cell anaemia. Published literature includes various reports on screening patient using HPLC in adults as well as paediatric population .However , there is paucity of literature on studies on exclusive paediatric population. So we have performed this study with an aim to report the occurrence of double heterozygous cases in paediatric population attending tertiary hospital in our region.

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