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Epidemiology of Haemoglobin Disorders in East Midnapore District, West Bengal, especially from Haldia: A Report of 5-year study

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ABSTRACT

This retrospective, cross-sectional study was conducted to determine the prevalence of common Haemoglobin variants and abnormal haemoglobins in East Midnapore district of West Bengal over a period of 5 years. A total of 6904 blood samples were collected from subjects who were a) investigated for anaemia and suspected to suffer from hemoglobinopathy or b) willing for premarital or antenatal Haemoglobin variant analysis. High-performance liquid chromatography (HPLC) was performed on the samples with the instrument, D 10 dual Program of Bio Rad. Most of the subjects were from 18 to 35 year of age group and were from Haldia subdivision. Prevalence of hemoglobinopathy was found in 12.63% of cases, majority suffered from beta thalassaemia trait followed by Hb E trait.

Keywords: East Midnapore, Hemoglobinopathy, high performance liquid chromatography, Prevalence.

INTRODUCTION

Haemoglobin disorders are one of major health problems in India. This can be defined as a group of disorders in which there is abnormality in either production or structure of the haemoglobin molecule. Thus, they can be divided into two main groups. First, thalassemia syndromes, where production of either α chain or β chain is decreased. Accordingly, they are named as α- and β-thalassemia. The normal haemoglobin variants in adult population are HB A, Hb A2 and HB F. In thalassaemia, there is deviation in the normal proportion of these three normal variants. Second, structural haemoglobin variants where there are mutations in globin genes. These are also known as haemoglobinopathies as in these conditions abnormal haemoglobins are detected. The main structural haemoglobin variants are Hb S, Hb D, Hb E and Hb C [1]. Different screening programs undertaken in different regions have shown that many ethnic groups in Bengalees, have much higher prevalence rates of thalassaemia than the average ranging from 4% to 17% in India [2]. A study conducted in large rural population in West Bengal had reported that different types of hemoglobinopathies are prevalent in eastern part of the country [3]. However, extensive literature search on internet did not reveal any separate data from East Midnapore District of West Bengal. Though a software called Thalaman has been developed and

used to maintain records and assimilate the large screening and patient data from different locations of West Bengal under The West Bengal State Thalassemia Control Program, these patients included in this study did not give history of any such registration. Thus, this study may be considered as the first epidemiological study on a vast population from rural Bengal.

East Medinipore or "Purba Medinipur" as it is called in Bengali is divided into 5 sub divisions, Tamluk, Egra, Contai, Haldia and Purba Medinipur. The state of Odisha is at the southwest border, which has been reported to have high prevalence of hemoglobinopathy. According to the 2011 census Purba Medinipur district has a population of 5,095,875,[4]. Haldia in Purba Medinipur is an industrial Port city, which is a major river port and industrial belt. Under Haldia subdivision, there are 4 community Development Blocks, namely Nandigram, Sutahata, Mahishadal and Haldia. As of 2011 census, Haldia had a population of 200,762, out of which 104,852 were males and 95,910 were females. A lot of population migration takes place in East Midnapore, especially Haldia, regularly due to business and other purpose not only from other subdivisions but also from neighbouring states.

Under this backdrop, the primary objective of present study was to determine the prevalence of common Haemoglobin disorders in East Midnapore district of West Bengal.

The secondary objectives were as follows

a) The distribution of these disorders according to age and gender.

b) Geographical distribution of hemoglobinopathies in the study population.

MATERIALS & METHODS

This is a retrospective, cross-sectional study using secondary data from Record section of Micro Clinical Laboratory in Haldia, West Bengal. Micro Clinical Laboratory is a large NABL accredited laboratory which caters from patients of all subdivisions of East Midnapore.

No ethical permission was required as no human subjects were handled directly. Only secondary non identifiable data were used. The subjects were not identified by name but by the lab reference no. Thus, anonymity and confidentiality of the subjects were preserved. This is in accordance to Declaration of Helsinki guidelines.

The demographic and clinical details of patients were captured from July 2015 to June 2020. Epidemiological (Age, gender) and clinical data of all patients advised for HPLC of Haemoglobin within this time frame, was collected. History of pregnancy, any known maternal and paternal haemoglobin disorder and history of blood transfusion within past 1 month was also collected.

Data of the subjects who were advised for HPLC (high performance liquid chromatography) of haemoglobin by the clinicians were obtained. Patients investigated for cause of anaemia were suspected to suffer from haemoglobin disorder on the basis of red cell indices and were advised for HPLC. Subjects with suggestive family history of haemoglobin disorder and who were willing for premarital or antenatal Hb analysis were also advised for HPLC. Data of all these subjects were included in this study. Data of the subjects who had undergone blood transfusion within past 1 month were excluded from the study as blood transfusion may alter the chromatogram.

Data was generated by collecting approximately 2.5 ml of venous blood from each subject, in the tri-potassium EDTA vacuum container. The blood samples were tested by automated blood cell counter (sysmex XN 550) for red cell indices. Diagnosis of hemoglobinopathies was done by HPLC of Haemoglobin by the instrument,

D 10 dual program (Bio-Rad Laboratories). The instrument works on the principle of chromatographic separation of the analytes by ion exchange high performance liquid chromatography [5]. A sample report and a chromatogram were generated for each sample.

Following facts were considered to diagnose abnormal Haemoglobin [6]:

1. In Beta Thalassemia Carrier or trait, HbA2 remains high, (above 3.5% or more). However, a normal haemoglobin chromatogram does not rule out Beta Thalassaemia trait as rare carriers have HbA2 within normal range i.e., < 3.5%. Associated Alpha Thalassaemia inheritance will also

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mask Beta Thalassaemia trait. In Beta Thalassemia Carrier with severe anaemia, HbA2 may be low. So, if strongly suspected, chromatogram was asked to be repeated after correction of anaemia.

2. In Beta Thalassemia Major / Intermedia Hb F is high. Sometimes Hb F elutes with labile HbA1c (L HbA1C).
3. Hb S, Hb D, Hb C, etc, are abnormal haemoglobins and are eluted as separate windows on HPLC. These can be trait (Heterozygous) or disease (Homozygous) depending on percentage of abnormal haemoglobin.
4. Hb E is a variant of Hb A and is found in many patients in Eastern India. Hb E elutes with HbA2 in HPLC. HbA2 usually remains within 10% in Beta Thalassemia trait. So, if this band is above 10% it is interpreted as Hb E.
5. In severe iron deficiency anaemia, HbA2 level may be lower than normal range.
6. ~~In~~ some women, HbF was found to be more than normal and these cases were attributable to pregnancy. After parturition the level comes back within normal range.

Data were tabulated and analysed by applying formula of percentage calculation.

RESULT

A total of 6994 samples were analysed for Hemoglobinopathy from July 2015 to June 2020. (Table 1). Out of them 6904 were from East Midnapore and 90 were from other districts (49 from West Midnapore and 41 from 24 Parganas, Nadia and Hoogly District). Among 6904 samples, 6072 were found to be normal. Rest 872 samples (220 samples from male and 652 from female) showed some sort of abnormal Hb fraction. Age and gender distribution of study population with abnormal Hb fraction is given in Table 2. The age of the patients ranged between 1 year to 57 years. Most of the subjects were among 18 year to 35 year age group. The subdivision wise distribution of abnormal samples is shown in Table 3 (734 samples from Haldia, 32 from Egra, 74 from Tamluk and 32 from Contai). The samples from Haldia were from all Community Development Blocks in Haldia, namely Mahisadal, Sutahata, Nandigram and Haldia. Table 4 shows prevalence of haemoglobinopathy in study population and also types of different abnormal haemoglobin fractions in East Medinipore. Chromatograms of some haemoglobin disorders are presented in Figures 1, 2, 3a, 3b, 4, 5.

DISCUSSION

In this study, the prevalence of Haemoglobin disorder was found to be 12.63%. This is almost similar to the finding of Mondal et al, who reported prevalence of haemoglobin disorder as 11.43% [7]. Higher prevalence (25%) of thalassemia and hemoglobinopathies was reported from southern part of West Bengal [8], whereas study from north Indian population, reported hemoglobinopathy of 12.5%. [9].

Mutation of HBB gene cluster causes Thalassaemia. When one of β globin alleles bears a mutation, it is called beta trait, whereas when both alleles of the gene have mutations, it is called beta major. The most common Haemoglobinopathy found in this study was β thalassemia trait (11.07 %), a representative chromatogram of the condition is given in Figure 1. Almost similar prevalence of β thalassemia trait has been reported from rural Bengal in earlier study (10.38%.) [10]. Though the prevalence differs, almost all studies have reported that in most parts of India, β thalassemia trait is the commonest disorder of haemoglobin [2]. In comparison to beta trait, prevalence of beta major was found to be less (0.17%).

Hb S or sickle cell Hb is a condition where point mutation at β 6 results into change of glutamic acid to valine. This may be heterozygous (Hb S trait, Figure 2) or homozygous (Hb S Disease). In this study, the former prevalence was found to be 0.04% and 0.01% respectively. Orissa, which is very near to East Midnapore have high incidence of sickle cell trait [11]. For identification of Hb S, sickling test was done and was found to be positive in sickle cell disease. In sickle trait, the positivity depends upon several factors among which the percentage of sickle cells in the sample was most important.

Haemoglobin E (Hb E), results due to point mutation at β 26 resulting into change of glutamic acid to lysine. Hb E trait is the condition when the gene for

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haemoglobin E is inherited from one parent and the gene for haemoglobin A from the other. In case of Hb E disease, inheritance of the gene for Hb E takes place from both parents. In this study, Hb E trait was found in 0.54% cases (Figure 3a) and E Disease was found in 0.08% cases (Figure 3 b). A study conducted in the rural areas of West Bengal reported the prevalence of Hb E trait to be 3.86% which is higher than our finding [12].

Other variants detected in the present study included Hb D-Punjab, Hb J-Meerut, Hb Lepore, Eβ Thalassaemia (Figure 4), sickle-β thalassemia and Hereditary Persistence of Foetal Haemoglobin (HPFH, Figure 5) All these variants were identified as they were eluted in respective assigned windows.

CONCLUSION

Identification of Haemoglobinopathy has epidemiological importance as they do not have any treatment. They can be only be prevented if identified by population screening before marriage, and thus only way to stall the forward march of the disease. This study reflects the status of haemoglobinopathy in East Midnapore District of West Bengal. Beta Thalassaemia Trait and Hb E trait are found to be most prevalent abnormalities in this region. PCR and other molecular biology tools are necessary to identify mutation in Beta Globin gene cluster and to detect Alfa Thalassemia, which were not done. and can be considered as limitation of the study.

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TABLES

Table 1: Year wise Distribution of Study Population

Study period	East Midnapore	Other Districts	Total
July 2015 to June 2016	1027	20	1047
July 2016 to June 2017	1117	16	1133
July 2017 to June 2018	1451	18	1469
July 2018 to June 2019	1653	17	1670
July 2019 to June 2020	1656	19	1675
Total	6904	90	6994

Table 2: Age and Gender Distribution of hemoglobinopathies in East Midnapore

Age Group	Male	Female	Total
Upto 1 yr	20	10	30
>1 yr to 5yr	30	17	47
>5 yr to 10yr	10	15	25
>10 yr to 18 yr	12	77	89
>18 yr to 35 yr	118	489	607
>35 yr to 50 yr	20	27	47
> 50 yr	10	17	27
Total	220	652	872

Table 3: Sub Division wise Distribution of hemoglobinopathies in East Midnapore

Sub Division	Number of patients
Haldia	734
Egra	32
Tamluk	74
Contai	32
Total	872

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Table 4: Distribution of Types of abnormal Haemoglobin fraction in East Midnapore

Types of different Haemoglobin fraction	Number	Percentage
Normal	6032	87.37%
Abnormal	872	12.63 %
Beta trait	764	11.07 %
Beta Major	12	0.17 %
E trait	37	0.54%
E Disease	04	0.08 %
S trait	03	0.04 %
S Disease	01	0.01 %
Others	49	0.72 %
Total	6904	100%

Figure 1: Chromatogram of beta trait

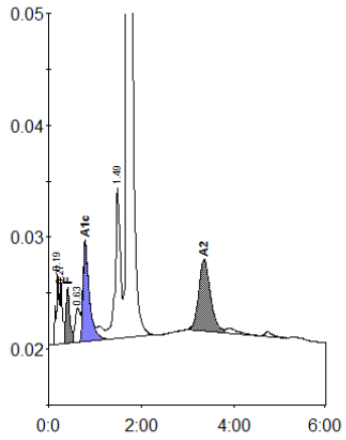

Figure 2: Chromatogram of Hb S trait

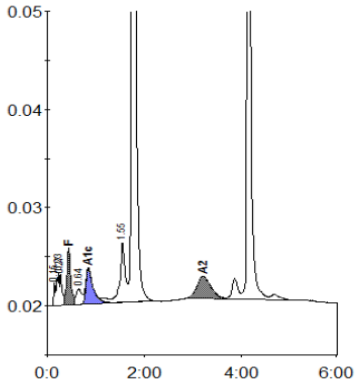

Figure 3a: Chromatogram of Hb E trait

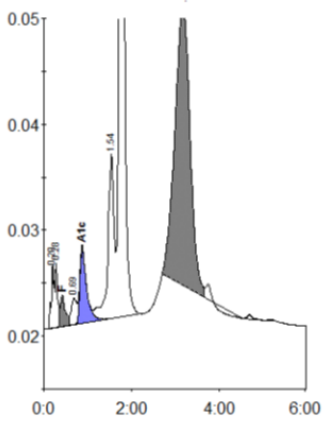

Figure 3b: Chromatogram of Hb E Disease

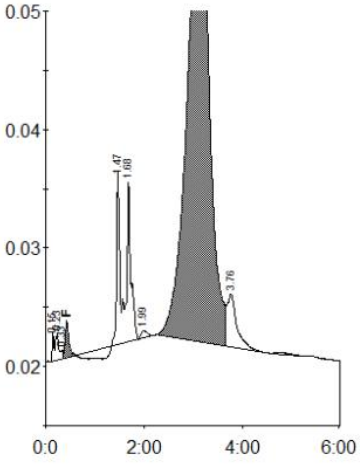

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Figure 4: Chromatogram of Hb Eβ

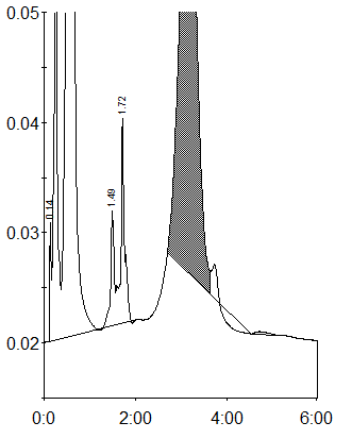
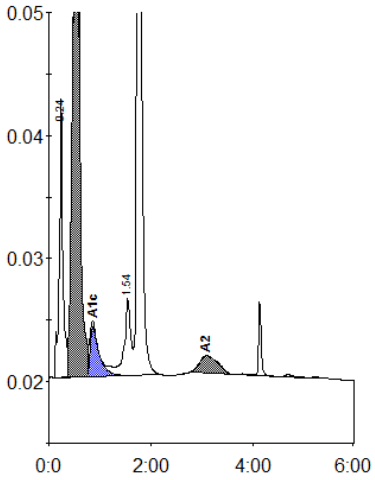


Figure 5: Chromatogram of HPFH



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