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Genetic Hemoglobin Disorders Among the People of Assam-A Tertiary Care Hospital Based Study

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ABSTRACT

Background: *Genetic hemoglobin diseases like hemoglobinopathies and thalassemia are prevalent worldwide. In India also, among the people of Assam, there is a high prevalence rate of these genetic blood disorders like HbE, HbS, beta thalassemia minor, beta thalassemia major, and compound HbE-beta-thalassemia. Assam is a hot spot for homozygous and heterozygous HbE. Also, beta thalassemia is encountered among the people of this region of India. With such knowledge of prevalence, the study was done to get more knowledge about the scenario of genetic hemoglobin disease.* ***Methodology:*** *Blood samples were collected from suspected anemic cases attending the tertiary care hospital within 2 years. The diagnosis of the Hb variants was done using a High-Performance Liquid Chromatography (HPLC) based Hemoglobin typing machine and the Complete Blood Count (CBC) was estimated using the automated Cell Counter.* ***Results:*** *It was observed that out of the total 1118 cases tested, 698 (62.43%) were positive for Hb variants like β-thalassemia minor (16.99%), β-thalassaemia major (2.32%), Hb E heterozygous (22%), Hb E homozygous (6.62%), Sickle cell trait (3.04%), Sickle cell disease (1.69%), Compound Hb E-β thalassemia (9.66%) and Compound Hb S-β thalassemia (0.1%).* ***Conclusion:*** *In Assam, the HbE variant is mostly prevalent among the Ahoms, Boro, and Kachari individuals, and sickle cell cases are mostly found among the people from the tea garden community. With such a high prevalence rate in the Assamese population of Assam, steps should be taken to curb this genetic disease. The prevalence of this inherited hemoglobin disease can be reduced by implementing awareness programs, imparting genetic counseling, and conducting screening programs. Properly designed community-based studies are required as a health priority to curb genetic blood disorders.*

Keywords: Hemoglobin, Genetic, Hemoglobinopathies, Thalassemia, Assam

INTRODUCTION

Hemoglobinopathies and thalassemia are genetic hemoglobin diseases and are prevalent worldwide. Southeast Asian countries have a high prevalence of these Hb variants. The Northeast region of India is a hot spot for these hemoglobinopathies and thalassemia. The majority of variant hemoglobins differ from the normal in that a single

amino acid has been substituted for another [1]. Also, double heterozygosity cases have been reported earlier like *HbS-HbE* but are rare. A case of Hb S-beta thalassemia was reported from Assam [2]. The most frequently encountered structurally variant hemoglobins are Hb S, Hb C, Hb D Punjab, and Hb E [3].

Thalassemia is a form of severe anemia occurring early in life and associated with splenomegaly and bone marrow changes [4]. The thalassemias are found in a broad belt extending from the Mediterranean basin to India and the orient [5]. Nearly 200 different mutations have been described in patients with β-thalassemia. Among them, about 28 mutations have been documented in Indian patients. Six mutations, 619 bp deletion at 3' end of a *β-Globin* gene, IVS1-5 (G→C), IVS1-1 (G→T), frame-shift mutations codon 8/9, codon 41/42 and nonsense codon 15, account for 90%-94% of the beta-mutations in India [6].

Hemoglobin E trait is the third most common hemoglobin disorder in the world and Southeast Asia, its prevalence is estimated to be 30%. Although the Hemoglobin E trait is associated with no morbidity, the offspring of individuals who carry this hemoglobin variant may exhibit clinical manifestations like β-thalassemia major (Compound hemoglobin E- β-thalassemia) if the other parent has β-thalassemia trait and contributes that gene. This combination is the most common cause of transfusion-dependent thalassemia in areas of Southeast Asia [7].

Hemoglobin D Punjab is found with the greatest prevalence (2%) among the Sikhs of Punjab in India as well as in nearby Gujarat (1%). About 5% of the world's population is a carrier of a potentially pathological hemoglobin gene [8]. The β-thalassemias are widespread throughout the Mediterranean region, Africa, Middle-east, the Indian sub-continent, and Burma, Southeast Asia. Estimates of gene frequencies vary from 3%-10% in some areas [9]. About 3% of the world's population (around 150 million people) carries β-thalassemia genes [10].

The inherited disorders of the blood include hemoglobinopathies one of the major public health problems in India [11]. The cumulative gene frequency of the three most predominant variant hemoglobins i.e. Sickle cell, HbD, and HbE has been estimated to be 5.35% in India. Thus, there is a tremendous amount of burden of hemoglobinopathies in India [12].

The Bodo-Kachari has a gene frequency of 0.50 for Hb E, the highest anywhere in the world [13]. HbE mutation among the Bodo-Kachari of Assam is found to be the highest observed frequency in the world followed by the tribes of adjoining Tripura [14].

β-thalassemia is detectable in almost every Indian population; however, it is seen with the highest frequency in the northwest and far east. Sindhis, Gujaratis, Bengalis, Punjabis, and Muslims account for most of β-thalassemia. The carrier state for β-thalassemia in India varies from 1%-17% with an average of 3.2%. α-thalassemia is most widely prevalent in the tribal population with a frequency of 1%-40% in Andhra Pradesh and Gujarat. Subsequently, Hb S has been reported from various Indian states, communities, and ethnic groups with an average frequency of 4.3% (range: 0%-44%). The sickle gene in India is mostly found among Dravidian and pre-Dravidian tribes. Hb D is predominantly seen in Punjab, Uttar Pradesh, Gujarat, Jammu, and Kashmir. It is most prevalent in Punjabi, Sikh, and migrant Sindhi populations [15].

The presence of HbE in all of the five examined members of an Assamese Tibeto-Burman group, the Kachari was unexpected because of the virtual absence of HbE in the Tibeto-Burmans of Tibet, Nepal [16]. Researchers in South East Asia provided further pieces of evidence of α and β thalassemia. The frequencies of HbE were determined in many groups living in the northeastern part of Thailand [17]. A subsequent larger survey in upper Assam proved the high frequency of HbE among the Kachari and documented a frequency of 0.5 [18]. Similarly, high frequencies of HbE were found in other Bodo Tibeto-Burman groups in Assam, e.g. the Bodo-Kachari of lower Assam, the Garo, the Rabha, and the Tiwa [19]. Earlier it was reported that the Hindu caste population of Assam shows the lowest prevalence of HbE, and within this group, the frequency of HbE is significantly lower in the Brahmin. The Muslim group largely of Assamese stock has a similar frequency of HbE [20]. Previously the only report on β thalassemia in Assam showed a 1.5 frequency of 5.5% among 182 Indeed Assamese, 1.5% among 129 Ahom, and 2.9% among 140 Khasis. HbE mutation among the Bodo Kachari population of Assam (North-East India) has been reported to be 64.5%, the highest observed frequency of this mutation in the world [21].

A high incidence of hemoglobinopathies and thalassemia has been detected in the Northeast region of India and their combination is unique for this part of the country [22]. In a hospital-based study, the occurrence of hemoglobinopathies and thalassemia in Northeast India was reported to be around 50% [23]. There is a high

occurrence rate of hemoglobinopathies and thalassemia in Assam. Hb E is the most common Hb variant found in Assam, India followed by beta thalassemia, Compound HbE-Beta Thalassemia, and Hb S [24].

The most effective approach to reducing the burden of society is to reduce the incidence by implementing a screening program, offering genetic counseling, prenatal diagnosis, and selective termination of pregnancy of the affected fetuses in India. Health education is an important component of preventive genetic programs [25].

Studies related to these types of genetic disorders help in putting forward the real scenario of the disease which is prevalent in society and help the Government to take up and put forward new programs which may help in curbing the disease.

METHODS

Ethical Clearance was taken from the Institutional Ethical Committee to carry out this hospital-based study. The necessary details of patients were filled up in a proforma and blood samples were collected in EDTA-coated vacutainers after taking written informed consent.

Blood samples were collected from the suspected Anemic patients attending the Out Patient Department of Gauhati Medical College and Hospital, a tertiary care hospital within 2 years. Patients with Anaemia were included in the study while patients who had a history of blood transfusion in the last 3 months were excluded from the study. A total of 1118 patients from the tertiary care hospital were screened for these Hb (Hemoglobin) variants. The complete blood counts were analyzed in an automated Hematology analyzer (*pocH- 100i, SYSMEX*). The CBC of the samples was analyzed using an automated cell counter (SYSMEX) within 24 hours of blood collection. The Hb variants were diagnosed using the Hemoglobin Typing Machine (D 10, BioRad). The chromatograms were analyzed and Hb variants were identified and diagnosed.

RESULTS

The Hematological parameters varied depending on the Hb variants the individual was diagnosed with. Most cases with Hb variants were Anemic with variations in Mean Cell Volume (MCV), Mean Cell Hemoglobin (MCH). The Hematological features of the study subjects are shown in Table 1. The Hemoglobin typing test was done and it was observed that out of the total 1118 cases tested, 698 (62.43%) were positive for Hb variants like β-Thalassemia minor (16.99%), β-thalassemia major (2.32%), Hb E heterozygous (22%), Hb E homozygous (6.62%), Sickle cell trait (3.04%), Sickle cell disease (1.69%), Compound Hb E-β Thalassemia (9.66%) and Compound Hb S-β-Thalassemia (0.1%) (Table 2). The rest 37.57% were not detected without any Hemoglobinopathies or Thalassemia.

Table 1 Mean ± SD of the Hematological features of the study subjects

VARIABLE	β-THAL MINOR-190	β-THAL MAJOR-26	HBE HETERO-ZYGOUS-246	HBE HOMO-ZYGOUS-74	SICKLE CELL TRAIT-34	SICKLE CELL DISEASE-19	COMP HBE-β-108	COMP HBS-β-1
HGB (g/dl)	10.89 ± 1.97	4.5 ± 1.53	10.94 ± 2.81	9.07 ± 2.3	11.75 ± 1.6	6.35 ± 2.17	5.24 ± 2.36	3.4
RBC(10^6/µl)	5.14 ± 0.99	1.87 ± 0.80	4.39 ± 1.02	4.59 ± 0.96	4.53 ± 0.79	2.33 ± 0.8	2.84 ± 1.03	1.17
MCV (fl)	66.27 ± 7.99	67.43 ± 4.19	74.69 ± 9.52	59.5 ± 6.47	78.07 ± 9.57	85.08 ± 8.57	61.69 ± 5.43	91.5
MCH (pg)	21.33 ± 2.93	25.03 ± 4.73	27.09 ± 22.33	19.58 ± 2.76	26.26 ± 3.73	27.13 ± 4.23	18.3 ± 2.89	29.1
MCHC(g/dl)	32.36 ± 1.26	37.06 ± 6.17	33.41 ± 22.33	32.83 ± 1.96	33.22 ± 1.46	31.77 ± 2.53	29.69 ± 3.31	31.8

*Data are Mean ± SD. Compound Hb S-β is a single case, so no SD values were calculated.

Abbreviations: HGB: Hemoglobin, RBC: Red Blood Corpuscles, MCV: Mean Cell Volume, MCH: Mean Cell Haemoglobin, MCHC: Mean Cell Hemoglobin Concentration.

Table 2 Total number of various Hb variants

HB Variants	No. of cases
β-thalassemia major	26
β-thalassemia minor	190
Hb E heterozygous	246
Hb E homozygous	74
Sickle cell trait	34
Sickle cell disease	19
Compound Hb E-β Thalassemia	108
Compound Hb S-β Thalassemia	1

DISCUSSION

It is seen that with a prevalence rate as high as 62.43%, Hemaglobinopathies and Thalassemia is a serious issues among the people of Assam, India. Though previously the HbE and beta Thalassemia were confined to only a few tribes and restricted to a few populations, our study suggests that these Hb variants occur in other populations too nowadays. These may be because of the non-adherence to strict intra-caste marriage norms and the migration of people worldwide.

Beta Thalassemia and Compound Hb E-beta Thalassemia are more serious because the patients are mostly transfusion dependent. The transfusion-dependent patients are a burden to their families and society too. But a lack of knowledge regarding the prevalence of these types of genetic Hemoglobin disease, the inability to carry out genetic counseling, and the presence of only a few centers for prenatal diagnosis have failed in community control of the birth of these preventable genetic disorders.

CONCLUSION

In Assam too, there are very less community-based screening schemes, and only a few awareness programs are held. So people are unaware of these genetic diseases. There are only a very few centers that assist in prenatal diagnosis. As we know that transplantation can be done to cure, but it is not affordable for everyone. So, with a more than 50% occurrence rate, more studies related to genetic Hemoglobin diseases should be conducted for comparison and better assessment of the scenario.

As an urgent need, to curb this genetic Hemoglobin disease, our Government should take more steps to establish programs. The most effective approach to reducing the burden of society is to reduce the incidence by implementing a carrier screening program, offering genetic counseling, prenatal diagnosis, and selective termination of pregnancy of the affected fetuses in India. As like in other countries, in India also, we can diagnose early, and treat and cure genetic Hemoglobin disease, with health awareness programs and counseling.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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