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Original Research Article

Study of Hemoglobin E Disorders in College Students

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ABSTRACT

Introduction: HbE is very common among the ethnic groups of the North East India having cultural and linguistic affiliation with the people of South east Asian countries. HbE occurs in three forms, heterozygous (HbAE), homozygous (HbEE) and the double heterozygous (HbE- β-thalassemia) form. The heterozygous (HbAE) and homozygous (HbEE) forms may be asymptomatic or mildly anemic with red cell indices showing microcytic and hypochromic type but the double heterozygous (HbE- β –thalassemia) presents with various severity from complete lack of symptom to transfusion dependent. Thus, study of HbE variants by Hb typing is of crucial importance to prevent these inherited blood disorders.
Materials and Method: In the present study a total of 50 subjects both male and female in the age group of 18-24 years of under graduate students of Silchar Medical College, Silchar were included in the study. Hb typing was done by electrophoresis at alkaline pH 8.5 using cellulose acetate membrane and complete hemogram analysis done by Sysmex 5 part hematology analyzer.
Results & Observation: A total of 50 subjects studied showed 15 subjects abnormal hemoglobin and 35 subjects normal Hb type. Out of that abnormal hemoglobin, 13 subjects were HbE variants. HbAE being the most common variety with incidence of 9(18%) followed by HbEE 3(6%) and HbE- β -thalassemia 1(2%).
Conclusion: HbE variants were very common among the students of Silchar Medical College. As it is an inherited blood disorders identification of the healthy carries is very important to prevent occurrence of more serious hemoglobinopathies in the future generation.

Key Words: hemoglobinopathies, HbE, electrophoresis, red cell indices, anemia.

INTRODUCTION

Hemoglobinopathies are the mostly encounter single gene blood disorders, which affect the globin chain of hemoglobin molecule. It can be abnormalities in globin structure (like Hb S, C, D, E etc) or inefficient synthesis of globin chain (thalassemia), leading to production of chronic and severe anemia.

These inherited groups of blood disorders affect many of the Indian population, where the gene frequency of hemoglobinopathies is 4.2%. [1] HbE placed the second most prevalent Hb variant in the world and that in India being the third most prevalent variant after Hb S and β-Thalassemia. [2] Hb E is the most common Hb variant among the autochthonus inhabitants of Assam, having cultural and linguistic affiliation with the people of South East Asian countries. [3] The incidence of HbE in Assam is very high with frequency of 52%. [4]

Itano, Bergren and Sturgeon in the year 1954 first discovered HbE in a person of Guatemalan origin with Spanish and Hindu ancestry. [5] It is an abnormal hemoglobin, with abnormalities in globin structure where there is substitution of glutamic by lysine at position 26(α2 β2 $^{26Glu\rightarrow Lys)}$of β –chain due to single point mutation, which results in activation of a cryptic mRNA splice site, resulting in reduced synthesis of β E chain leading to a thalassemic phenotype. [6] HbE can be heterozygous (AE), homozygous (EE) and double heterozygous (may co-inherit with thalassemia and other Hb variants). [7] HbAE forms occur where one copy of mutated gene is inherited from one parent, and a normal copy of healthy gene from another parent, thus, the red cell contain both normal Hb(HbA) and the variant(HbE) of 25-35% [8] but HbEE forms occur when a copy of mutated gene is inherited from both parents and has more than 90% of HbE. [8,2] The heterozygous (AE) and homozygous (EE) states are usually asymptomatic and have hematological findings similar to thalassemia minor with microcytic and hypochromic RBC. Whereas, double heterozygousity of HbE (HbE- β - thalassemia) produces complete lack of symptoms to severe anemia leading to long term transfusion therapy. [8]

Hemoglobinopathies are serious public health problems, as it causes lots of burden to the patients, their families and even the communities. So, it is important to study these genetic disorders in order to prevent occurrence of more serious hemoglobinopathies. Since the community of students comprises of different ethnic groups from various parts of the northeast region. The present study was undertaken to find the prevalence of Hb E among the undergraduate students of Silchar Medical College, Assam.

MATERIALS AND METHODS

This is a hospital based cross-sectional type of study conducted in the department of Physiology in collaboration with Pathology department in Silchar Medical College after it was approved by the Institutional Ethical Committee. A total of 50 subjects both male and female from undergraduate students of Silchar Medical College were included in the study. The subjects with recent blood transfusion were excluded from the study.

About 4ml of venous blood was collected under aseptic condition from the antecubital vein in EDTA vial after written inform consent was obtained 2ml of blood was used for complete blood count. The complete hemogram analysis was done in Sysmex 5 part hematology analyzer. The principle of the analyzer is based on impedance and optical methods. The following parameters were taken for the study- Hb %, RBC HCT, MCV, MCH, MCHC and RDW-CV). WHO criteria was used to classified anaemic groups with Hb <13gm/dl, MCHC< 34% in males and HB <12gm/dl and MCHC <34% in female non pregnant. [9] Another 2ml of blood was used to prepare hemolysates. Electrophoresis was performed with the hemolysates in horizontal electrophoresis pherotank by using cellulose acetate membrane dipped in Tris buffer at p^H 8.5. Hemoglobin is being a negatively charged protein will migrate towards the anode at alkaline pH will separate from HbA. Hemoglobin variants that have an amino acid substitution that is internally sited may not separate and those that have an amino acid substitution that has no effect on overall charge will not be separated by electrophoresis. Slides were prepared from cellulose acetate membrane after electrophoresis was done. The prepared slides were then analyzed by Scanion densitometer.

The statistical analysis of all data were done by using Microsoft excel and SPSS version 12. Statistically significant was considered at p-value<0.05.

RESULTS

Out of total 50 subjects studied, 15 subjects shows abnormal hemoglobin and 33 subject

shows normal hemoglobin type as shown in table 1.

Table 1: Incidence of abnormal hemoglobin

Incidence of hemoglobin	No.of subject	Percentage
Abnormal	15	30
Normal	35	70
Total	50	100

Figure 1 shows normal Hb type(HbA) in 70% of subject, HbE trait in was the most common type of Hb variant with incidence of 9(18%) of subject, followed by HbEE in 3(6%) of subject, 2(4%) subjects of β – thalassemia trait type and HbE/ β – thalassemia in 1(2%) subject.

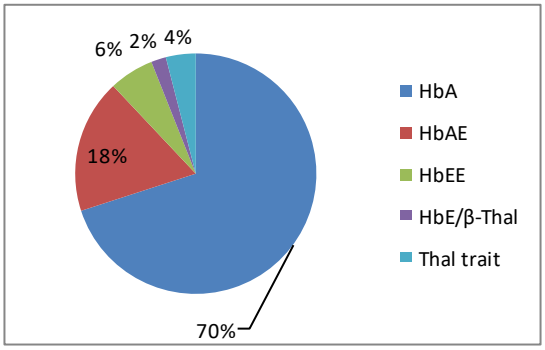

Table 2. Table 2 showing distribution of HbE variants in anemic and non-anemic

Group	HbAE	HBEE	HbE/ β –thalassemia
Anemic	3	2	1
Non-Anemic	6	1	0

Table 2 shows that 3 subjects with HbAE were anemic and 6 were non-anemic. 2 subjects with HbEE were anemic and 1 was non-anemic. The only subject with HbE/ β – thalassemia was anemic.

As shown in table 3 among the HbAE group the mean RBC count was 5.310^6/µL, Hb was 12.4 gm/dl, HCT was 36.1%, MCV was 72.5fl, MCH was 22.9 pg, MCHC was 32.6% and RDW was 15.4% Among the HbEE group the mean RBC count was 5.410^6/µL Hb 11.2 gm/dl, HCT was 33.6%, MCV was 62.0 fl, MCH was 20.5 pg, MCHC was 33.2% and RDW was 17.9%. Among HbE/ β-thalassemia the group the mean RBC count was 5.410^6/µL Hb 10.2 gm/dl, HCT was 31.8%, MCV was 58.9 fl, MCH was 18.9 pg, MCHC was 32.2% and RDW was 17.6%.

Table 3. Mean distribution of hematological parameters in HbE variants

Hemoglobin type	RBC 10^6/µL	Hb gm/L	HCT %	MCV fl	MCH pg	MCHC %	RDW CV
HbAE	5.3±0.7	12.4±1.3	36.1±3.5	72.5±4.9	22.9±2.01	32.61±1.6	15.4±1.8
HBEE	5.4±1.2	11.2±1.9	33.6±3.9	62.0±6.2	20.5±0.8	33.2±2.1	17.9±2.3
HbE/ β –thalassemia	5.40	10.2	31.8	58.9	18.9	32.1	17.6

DISCUSSION

Hemoglobinopathies are group of autosomal recessive abnormal hemoglobin synthesis, where the globin chain is affected resulting into structural hemoglobin variants and inefficient synthesis of globin chain (thalassemia). It constitutes the most important group of blood disorders affecting large number of population worldwide, including India, where the gene frequency is about 4.2%. With endogamous norms of marriages hemoglobinopathies were mainly confined to certain areas, religions, castes and tribes, but now it is widely prevalent all over the world, which is the results of migration and mixing of population through marriages.

Amongst the hemoglobinopathies, HbE is the mostly encounter Hb variant in the Northeastern states of India [1] (West Bengal, Assam, Andhra Pradesh, Nagaland, Manipur, Tripura, Meghalaya) with average frequency of 10.9%. [10] It has also been sporadically reported from other states of India like- Bihar, Orissa, Goa, Kerala, Tamil Nadu, Delhi and Chandigarh. In Assam the frequency of HbE is 50-80%. [10] The highest incidence is being reported among the ethnic groups of Bodo-Kacharis speaking the Tibeto-Burman languages even though it has been detected among the other ethnic groups of Assam like the Ahom, Koch, Chutia, Muttock, Deori, Sonowal and Mishing. [3] Conforming to the previous studies, our studies shows that 15 subjects out of 50 were abnormal Hb type, of which 13 subjects were HbE variants. The types of HbE variants detected in our studies were

the heterozygous (HbAE), homozygous (HbEE) and double heterozygous (HbE/ β - thalassemia) type with incidence of 18%, 6% and 2% respectively. Urade et al [3] in their study also reported high frequency of HbE among the Gallong tribe in West Siang district of Arunachal Pradesh.

Anemia was the most common presentation of individuals with HbE variants as reported by various authors. [3,7,8,11] Similarly our studies show that 3 subjects out of total HbAE was anemic, 2 subjects out of 3 subjects of HbEE was anemic and the only 1 HbE/ β-thalassemic individual was anemic. However, 6 subjects with HbAE and that of 1 HbEE subject were non-anemic. It shows that these individual were without any clinical symptoms and anemia. These findings are in agreement with previous findings. [10,12-14] So, identification of these individuals by Hb typing is of crucial importance as they may transmit their abnormal genes to their progeny and resulting in various combinations of hemoglobinopathies and thalassemias.

In our studies, the mean RBC count of individuals with HbE variants was normal but it showed microcytic hypochromic type of anemia showing decreased mean value of Hb, MCV, MCH and MCHC. These findings were in accordance with the previous studies of Patne, [1] Baruah et al, [3] Machumi Saikia et al, [7] Shah et al, [15] Das et al. [5]

RDW was found to increase in all the subjects with HbE variants. This is in contrast to previous findings, where RDW is within normal range in thalassemia minor and increase in pure nutritional anemia. [12] However, Baruah et al, [3] Sharma et al, [6] Ujwala Maheswari et al [16] found increase in RDW which is similar to the present study.

Thus, a microcytic hypochromic type of anemia with increase RDW in HbE variants may have been associated with Iron deficiency anemia the most common type of nutritional anemia in these regions though Iron studies was not done in our subjects. This was beyond the scope of our studies.

Red cell indices studies can give valuable information in the diagnosis of Hb variants even though it is difficult to set the cut off values. [3]

CONCLUSION

HbE variants were the most common type of hemoglobinopathy among the undergraduate students of Silchar Medical College. These inherited blood disorders can be prevented by population screening, genetic counseling, prenatal diagnosis and premarital counseling. These studies was undertaken to screen out the Hb variants among the students so that the silent carriers can be detected to prevent occurrence of more serious hemoglobinopathies in future generation.

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