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Screening for Haemoglobin E in the Ethnic Groups of East Sikkim a Hospital based Study

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Abstract

Background: Haemoglobin E (HbE) is the commonest haemoglobin variant in South East Asia and second most common globally. In India, high prevalence has been reported from the North eastern states and from Bengal. Data regarding the same from Sikkim is scarce. *Methodology:* After approval from the Institutional Ethics Committee, a hospital based observational cross sectional study was carried out for a period of two months in the Department of Medicine and Department of Pathology of a tertiary care hospital of East Sikkim, Gangtok. The objective was to screen patients of ethnic groups suspected to have HbE (those presenting with haemoglobin less than 10.5 gm/dl and having Red Cell Diffusion Width more than 15 and Mean corpuscular haemoglobin less than 27 pg). Patients with anaemia due to blood loss or iron deficiency were excluded. *Results:* Out of 1739 patients screened, 46 fulfilled the inclusion criteria. After obtaining informed consent from the participants, Complete Blood count and electrophoresis was performed in these cases. The mean age was 31.5+3.9 yrs, 26 were females and 20 were males. No case of HbE was detected. Except for the haemoglobin level, all other indices did not show any significant difference between the two sexes. *Conclusion:* This was a hospital based pilot study and as HbE maybe asymptomatic, cases might have been missed. A larger population based screening is required to know the actual burden of HbE in Sikkim.

Keywords: Ethnic groups; HbE; Sikkim.

Introduction

Haemoglobin E (HbE) is an important mutation and one of the commonly encountered one. It is the commonest haemoglobin variant in South East Asia and second most common globally [1]. In India it is prevalent in Bengal and the North eastern region but relatively rare in rest of the country [2]. A frequency of 52% in Assam, 7% in Manipur and 3.33% in West Bengal has been reported [3]. It has also been documented in residents from Orissa, Uttar Pradesh, Rajasthan, Bihar & Punjab. Sikkim is a landlocked state with a heterogeneous population of Bhutias, Lepchas, Nepalese and some immigrants from plains. No definitive reporting on presence or absence of Haemoglobin E disorders in Sikkim is present in literature Search. Haemoglobin E is the most frequent haemoglobin variant in the autochthonous mongoloid population of North east [4]. Sikkim has no direct communications with the other states of the North-east however it did have historical strong link with Tibet.

HbE is the result of substitution of glutamic acid by lysine at codon 26 of the β globin chain. A cryptic mRNA splice site is activated as a result of the mutation. The resultant effect is reduced synthesis of the β–E chain and this results in a thalassaemia phenotype. In HbE there is instability during conditions of increased oxidant stress due to the weakened α/β interface. HbE results in a range of disorders, varying from asymptomatic to life threatening. Though HbE trait has no significance clinically, yet it is essential to distinguish HbE disorders diagnostically as different genotypes leads to variable clinical course. Haemoglobin electrophoresis and high pressure liquid chromatography (HPLC) are the screening tests.

The main aim was to do a pilot study on anaemic patients with suspicion of HbE and screen them for HbE through gel electrophoresis, so that it can be included in the differential diagnosis of patients presenting clinically like thalassaemia intermedia or thalassaemia major.

Methodology

After approval from the Institutional ethics committee a hospital based observational cross sectional study was carried out for a period of two months in the Department of Medicine and Dept of Pathology of a tertiary care hospital of East Sikkim, Gangtok. The objective was to screen patients of ethnic groups suspected to have HbE (those presenting with haemoglobin less than 10.5 gm/dl and having Red Cell Diffusion Width (RDW) more than 15 and Mean Corpuscular Haemoglobin (MCH) less than 27 pg). Patients with anaemia due to blood loss or iron deficiency were excluded. During the study period a total of 1739 patients were screened of which 46 fulfilled the inclusion criteria. After obtaining an informed written consent, demographic data was collected, complete haemogram and gel electrophoresis for HbE was done. The primary outcome was to look for presence of HbE and the secondary outcome was to determine if HbE correlates with other RBC indices like MCV, MCH, MCHC and RDW. The data collected was analyzed using primary descriptive analysis. Mean with SD were calculated for MCV, MCH, MCHC and RDW.

Results

Out of the 46 participants, the mean age was 31.5±3.9 yrs, 26 were females and 20 were males. Age group 20-29 years had the highest number of females (77%) and age group 30-39 years had the highest number of males (35%). Red cell indices between the sexes were compared and are depicted in Table 1. There was no significant difference in the indices, except for the haemoglobin level. Electrophoresis was done for 46 samples; no case of HbE was detected among the eligible patients.

Discussion

In the present study 1739 patients were screened and 46 fulfilled the eligibility criteria. WHO cut off value for anaemia is haemoglobin <13 gm/dL for males and <12 gm/dL for females but there were very few patients also fulfilling the criteria of RDW greater than 15 and MCH less than 27 pg which is also taken into account in our study along with this haemoglobin cut off values. So the haemoglobin cut off value was reduced to less than 10.5 gm/dL for both sexes.

As there were no cases of HbE in our study, so no correlation could be made. The MCH values less than 27 pg is suggestive of haemoglobinopathies including beta-thalassaemia and Hb E syndromes. Hinchliffe et al. [5] in their review observed high values of MCHC in patients with HbC, D, S and E traits.

Balgir's review [2] on Burden of Haemoglobinopathies in India gives a map of India showing presence of Hb E in Sikkim but no reference was mentioned. Ambedkar et al. [6] mentioned a frequency of 0.7% in Sikkim but the reference given had no data of Sikkim.

Sikkim is home to people with an assortment of socio- cultural, linguistic and ethnic diversity due to the migration of various races. Predominance of HbE with a variable gene frequency in ethnic groups affiliated to Tibeto Burman linguistic families has been observed in North East India. In a study by Sharma & Mahanta [4] in which they evaluated the relationship of haemoglobinopathies

Table 1: Summary of the Red Cell Indices of the Patients

Parameters	Female (n=26) Mean (SD)	Male (n=20) Mean (SD)	Statistical Analysis
Hb%	7.35 (2.4)	8.7 (1.2)	t=2.502, df=44 p=0.01(significant)
MCV	72.6 (10.8)	70.61 (13.2)	t=0.548, df=44 p=0.59(not significant)
MCH	22.5 (6.8)	23.9 (3.3)	t=0.91, df=44 p=0.36(not significant)
MCHC	30.7 (7.4)	33.2 (1.3)	t=1.02, df=44 p=0.31(not significant)
RDW	15.9 (I.8)	16.1 (2.9)	t=0.1047, df=44 p=0.91(not significant)

SD=Standard deviation: df=degree of freedom

particularly HbE and Plasmodium Falciparum Malaria in North East India, concluded that HbE was predominant with a variable gene frequencies in ethnic groups affiliated to Tibeto – Burman linguistic families residing in malaria endemic North east India. Sikkim has a strong historical link with Tibet.

There is a genetic, ethnic and regional diversity of the haemoglobin variants as well as of the mutations in India which emphasizes to tackle the problem at a regional level. There is dearth of information from this area of India. It is the symptomatic cases who come to hospital and seek medical advice and are further investigated. Thus the information obtained from hospital based study is of limited utility.

Conclusion

A hospital based screening pilot study did not reveal any HbE in Sikkim but due to geographical continuity with Bengal and China and historical links with Tibet, there is a high likelihood of presence of HbE in Sikkim. A population based screening is required to estimate the burden. Marked difference in the clinical course and reduced awareness among the patients as well as the doctors might be the reason for patients not attending the hospital and doctors not including mild microcytosis without anaemia in the screening for HbE. Frequent inter current infections often lead to high morbidity in most patients with haemoglobinopathies. The cost of treatment is a cause of emotional, physical and psychological stress, not only to the patient but also to the caregivers. Implementation of an effective carrier screening programme is the most cost effective way of reducing the burden of haemoglobinopathies.

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