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Short Communication

Distribution of Thalassemia and Hemoglobinopathy in the koch Rajbanshi ethnic group of Jhapa, Nepal

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Abstract

Thalassemia and haemoglobinopathies are the most frequent monogenetic haemolytic disorders worldwide. Beta-thalassemia is an emerging global health burden. The study in the different ethnic groups of Nepal regarding incidence of various types of thalassemia is scarce, despite Nepal being included in the World Thalassemia Belt. The current study was done in the Koch Rajbanshi ethnic group of eastern Nepal to determine different varieties of thalassemia and haemoglobinopathies present in them. Three hundred (300) individuals were randomly selected for screening. The screening was done by complete blood count test and microscopical study of peripheral blood smear. The positive samples were further analysed by haemoglobin electrophoresis. Out of total 300 cases 57 cases (19%) showed abnormal red cell indices. Based on the level of haemoglobin A2 and haemoglobin E levels, 26 cases with HbE heterozygote/trait and 31 cases with HbE homozygote/ disease were diagnosed. Hence it was deciphered that haemoglobin variants are a common genetic problem in the Koch Rajbanshi ethnic group.

Keywords: Thalassemia, Haemoglobin E, haemoglobin disorders, electrophoresis, Koch Rajbanshi.

Introduction

Haemoglobinopathies, the common autosomal recessive single gene disorder worldwide, fall into two main categories, the thalassemia syndrome and structural variant haemoglobin[1]. As per an estimated data by the World Health Organisation (WHO), 7% of the people in the world were carriers of various haemoglobinopathies, and 300,000 to 500,000 of the paediatric population were born with significant disorders of haemoglobin on a yearly basis and majority of them belonged to the developing nations[2].

Among the hemoglobinopathies, beta thalassemia is an emerging global health problem. The clinical manifestations of beta thalassemia are highly variant. At one end of the spectrum there area symptomatic cases with mild (silent) mutations, while at the extreme end there are cases with severe lifelong transfusion-dependent anaemia and multi-organ involvement. The treatment of affected individuals presents substantial disease burden.

In North East India, Bangladesh and South-East Asia, HbE is the most prevalent haemoglobin variant[3]. This could be a logical explanation for its high prevalence in Nepal, as India and China border Nepal. According to a WHO report on Global distribution of haemoglobin disorders there are 0.2 to 0.99 births per 1000 infants with a major haemoglobinopathy[4]. This study is the first to report the prevalence of HbE in Rajbanshis of Nepal. Rajbhanshis are an indigenous group of people that migrated to Nepal from adjacent states of West Bengal and Assam in India about 250 years ago. Anthropologists suggest them to be kith and kin of the peripheral Koch people of North East India.

Materials and methods

Study sites: The study design is cross-sectional, observational study and was conducted at three districts of eastern Nepal: - Jhapa, Morang and Sunsari. Jhapa is the easternmost district of Nepal, it lies between $26^0$48' to $27^0$47'06'' latitude and $85^0$19'14'' to $87^0$85' longitude. Morang lies between $26^0$39'59'' latitude and $87^0$29'59' longitude. Sunsari lies between $26^0$38'29'' and $26^0$50' latitude and $87^0$07'44.76'' longitude. These districts lie in the Terai belt bordered by Assam and West Bengal of the northeastern parts of India.

Methods: Priorethical consent from Health and Research Council, Kathmandu and informed consent from the participants was taken. Samples were collected randomly from both males and females between 6 to 80 years with a median age of 23 years. Samples were not collected from individuals with a history of blood transfusion within the last 1 month.

Complete Blood Count: Three hundred (300) samples comprising of 192 females and 108 males were screened for beta thalassemia. About 3-5mL intravenous blood was collected

in EDTA (ethylene diamine tetra acetic acid) vials and analyzed with Sysmex, United States of America (USA) automated cell counter for complete blood counts. The blood samples were stored at 4^0C for further investigations. The presence of microcytic hypochromic anaemia, screened positive for Thalassemia and these were further subjected to Haemoglobin Electrophoresis for confirmation of the type of haemoglobinopathy. On the other hand those with normocytic normochromic anaemia ruled out the presence of Thalassemia.

Peripheral Blood Smear: Peripheral blood smear (PBS) of each patient was prepared on spot, stained with Leishman stain and the red cell morphology was microscopically observed for supportive diagnosis of hemoglobinopathies. Based on the presence of target cells Capillary electrophoresis was performed to confirm the type of haemoglobinopathy.

Haemoglobin Electrophores: Capillary electrophoresis (Sebia Minicap flex piercing) of all the cases with low MCV and target cells were performed to confirm the Hb variant. This is widely accepted as an important diagnostic tool for the quantification of HbA in the detection of thalassemia and haemoglobinopathies[4]**.**

Results and discussion

A total of 300 cases was studied, of these 243 cases showed normal red cell indices and 57 had lowered haemoglobin concentration and MCV with presence of target cells. The haemoglobin concentration was below cut-off level (<15 dL). On the basis of this 19 (33.3%) patients had mild severe anemia (Hb 6-10g/dL) and 38(66.7%) had mild anemia (10-16g/dL) with statistical significance (Table-1). The mean haemoglobin concentration 10.56 +/- 1.019 (mean +/- SD) was observed. In these 57 cases microcytic hypochromic anemia was also evident. The mean corpuscular volume (MCV) was 70.47 +/- 11.7 (mean +/- SD) (Table-2). Target cells were seen in peripheral blood smear.

Heamoglobin electrophoresis of all 57 cases performed, confirmed haemoglobinopathy. These 57 abnormal electrograms included 2 types of cases, HbE homozygotes and HbE heterozygotes (Table-3). On the basis of the level of HbA, HbA2, HbE and HbF obtained through capillary electrophoresis, 31 HbE homozygotes and 26 HbE heterozygotes were diagnosed (Figure-1, 2,3).

Table-1: Distribution of patients on severity of anemia.

Group, Hb g/dL	No of patients	Percentage (%)
Mild severe (6-10)	19	33.3%
Mild (10 – 15)	33	66.7%

Table-2: Haematological parameters of Koch Rajbanshi Ethnic Group.

Variables	Hb g/dL	MCV fL	MCH pg	MCHC g/dl	RDW-SD
Minimum	9.0	31.0	19.0	27.0	28.0
Maximum	14.0	91.0	72.0	36.0	48.0
Range	5.0	60.0	53.0	9.0	20.0
Mean	10.561	70.474	23.123	31.667	36.696
SD	1.0180	11.6988	6.8636	3.3452	5.8120

Table-3: Haemoglobin pattern and quantification in normal adult, HbE homozygote and HbE heterozygote case.

No of cases	HbE	HbA2	HbA	HbF	Haemoglobinopathy
243	……	2.2- 3.2	96.8 - 97.8	……..	Normal
31	>90 %	>3.2 %	……	O.7 – 5.9 %	HbE homozygote
26	24 25 %	3.0 - 4.0 %	< 71%	0.3 – 0.8%	HbE heterozygote

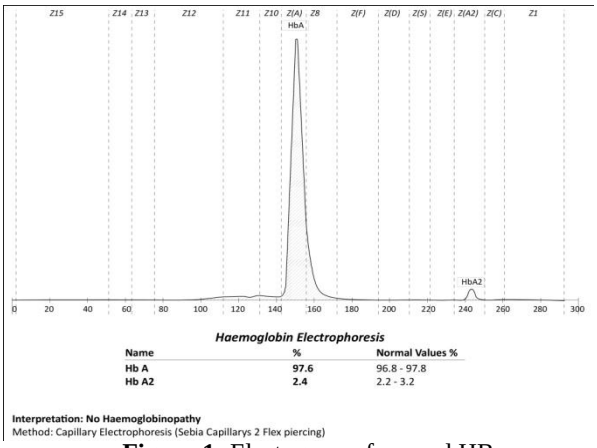

Figure-1: Electogram of normal HB.

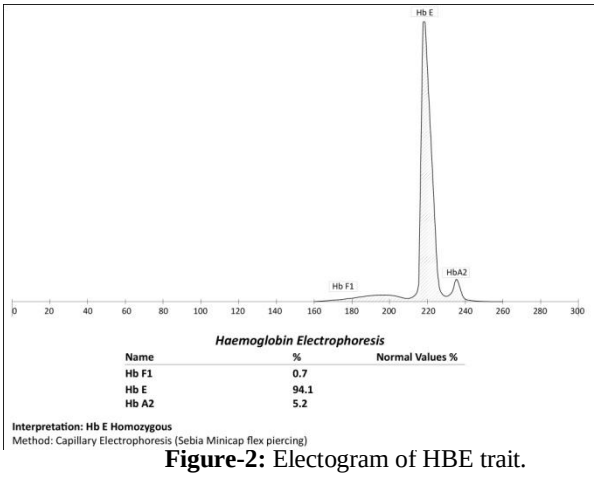

Figure-2: Electogram of HBE trait.

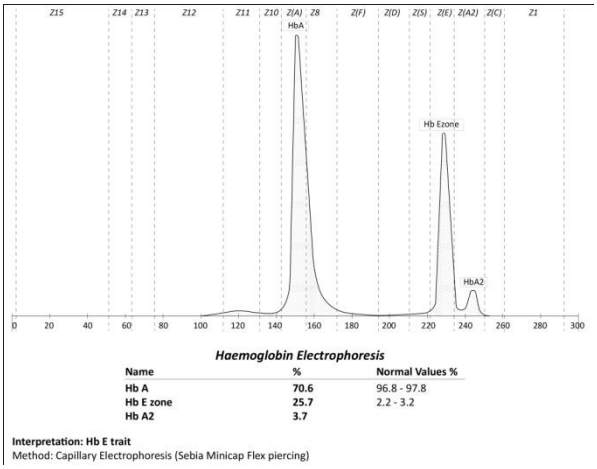

Figure-3: Electogram of HBE disease.

Discussion: The presence of thalassemia and HbE in Nepal has been reported earlier[7-9], but due to the lack of any screening programme, population based data regarding haemoglobin disorders in Nepal is scarce. In a study done by Sakai et al, thalassemia was found to be prevalent in the Danuwar and Tamang ethnic groups of Nepal. Jha et al further reported thalassemia in the Tharu community of western Nepal (prevalence of 37%). The current study done in the Koch Rajbanshi ethnic group of eastern Nepal is the first of its kind to be conducted in this geographical region. Studies done in India by Goswami et al[10] reveals that the presence of hemoglobinopathy was highest among Rajbanshis (72%) followed by Muslims (54%). In the Santhal and Oraowo, Bengali/Hindu and Marwari/Bihari approximately equal percentage (34%) of hemoglobinopathies was observed, whereas the least percentage was found in the Mongoloids like Nepali and other Hill-men populations (17.4%)[11]. Similarly in Nepal too, thalassemia is more prevalent in the Terai ethnic community as compared to the Mongoloid and Hill-men population. The similarity in the distribution amongst various communities is attributed to migration and constant mixing of people from different regions of India.

HbE the commonest structural variant in South East Asia is the second most prevalent worldwide. Das et al.[12] has reported a variable incidence of HbE in different states of north-eastern regions of India ranging from 16.2% to 47.3% reported.Others have reported an average HbE gene frequency of 10.9% in North Eastern India[13] and 25.48% in upper Assam[14]. However the frequency of HbE trait in Western India and North India was reported to be < 0.2% and 1.1% in Delhi, north India and 3.92% in Assam and 23.9% in West Bengal[15]. HbE thalassemia is a rare finding amongst the Nepalese, so far three cases have been reported in the Danuwars by Sakai et al, while two cases were reported in a district hospital in Pokhara by Bastola et al, however, in the current study 57 cases of HbE (HbE homozygote10.33% and HbE heterozygote 9%) was reported in the Koch Rajbanshis, which is a significant finding considering that the study was limited to East Nepal and Koch Rajbanshi of this area.

Conclusion

The findings of HbE gene in the Koch Rajbanshi of Nepal is being reported for the first time. This study suggests a high prevalence (19%) of Haemoglobin disorders in the study population. These findings can be applied as baseline data for future preventive measure programmes. A wider community based initiation for carrier detection and awareness generation must be seriously considered to prevent the transmission of haemoglobinopathies.

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