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Original Article

Genetics Section

β-Thalassaemia and its Co-existence with Haemoglobin E and Haemoglobin S in Upper Assam Region of North Eastern India: A Hospital Based Study

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ABSTRACT

Introduction: β-Thalassaemias are common genetic disorders in the Indian subcontinent and its status has not been well studied in the Upper Assam region of North Eastern India.

Aim: The aim of the study was to show the prevalence of β- thalassaemias and its co-existence with Haemoglobin E and Haemoglobin S in the Upper Assam region of North Eastern India.

Materials and Methods: A total of 1200 anaemic patients were investigated for β- thalassaemias. Complete Blood Count (CBC) and High Performance Liquid Chromatography (HPLC) were done for screening.

Results: Out of 1200 patients screened, 5.83% β-thalassaemia trait, 2.33% compound Hb E/β-Thalassaemia, 1.33% β-thalassaemia major and 0.42% compound Hb S/β- thalassaemia were detected. A high incidence of thalassaemia is found among the people of Upper Assam region of North Eastern India.

Conclusion: The only way to prevent the disease is carrier detection and awareness among the people about it.

Keywords: Anaemia, Complete blood count, HPLC

INTRODUCTION

β- Thalassaemia is a monogenic single gene disorder characterized by defective synthesis of the β-globin chain. In India β-thalassaemia is prevalent in almost every population; however the prevalence is high among the Sindhis, Gujaratis, Bengalis, Punjabis and Muslims [1].

Among the common Hb variants, Hb E is commonly found in the North-Eastern states of India and the average allele frequency of Hb E in North-East region is 10.9% [2]. Co-existence of β-thalassaemia with Hb E develops a condition which is very much similar to thalassaemia major and mild form of thalassaemia intermedia [3]. Interaction of β-thalassaemia with Hb E and Hb S is becoming a major health problem in India [4]. It should, however, be noted that the calculated numbers of β-thalassaemia heterozygotes in India assumed a carrier frequency of 3–4% [5].

AIM

This study was planned to show the status of β-thalassaemia along with its co-existence with Hb E and Hb S in the Upper Assam region of North East India.

MATERIALS AND METHODS

The present study was carried out among the patients sent to the Healthcare Clinical Biochemistry Laboratory of Assam Medical College & Hospital, Dibrugarh, Assam, India by clinicians as a work up for anaemia and for confirmation of β-thalassaemia. All the patients were from different districts of Upper Assam region of North East India [Table/Fig-1]. Due clearance was obtained from Institutional ethics committee for this study. This study was carried out from January 2012 to June 2015.

A total of 1200 patients who were between 1-65 years of age were studied. Detail clinical histories including ethnic origin, age, sex, blood transfusion etc. along with family history were recorded.

4 ml of venous blood was collected in EDTA vials after obtaining informed consent from each individual. Complete Blood Count (CBC) was done in cell counter (SYSMEX XS- 800i, Japan) using standard procedure. The screening of β- thalassaemia was done by a High-Performance Liquid Chromatography (HPLC) – based D10 Haemoglobin Testing System (BioRad Laboratories, USA). HPLC is one of the best methods used for accurate detection of various haemoglobin variants and β-thalassaemia trait [6,7]. HbA2 level of >4.0% was used as a cut-off for diagnosis of β-thalassaemia trait. After analysis of the samples, parents and siblings of patients found to have β-thalassaemia trait, compound Hb E/β-thalassaemia, β-thalassaemia major and compound Hb S/β-thalassaemia were called for investigation for β-thalassaemia and follow-up for counseling if required.

STATISTICAL ANALYSIS

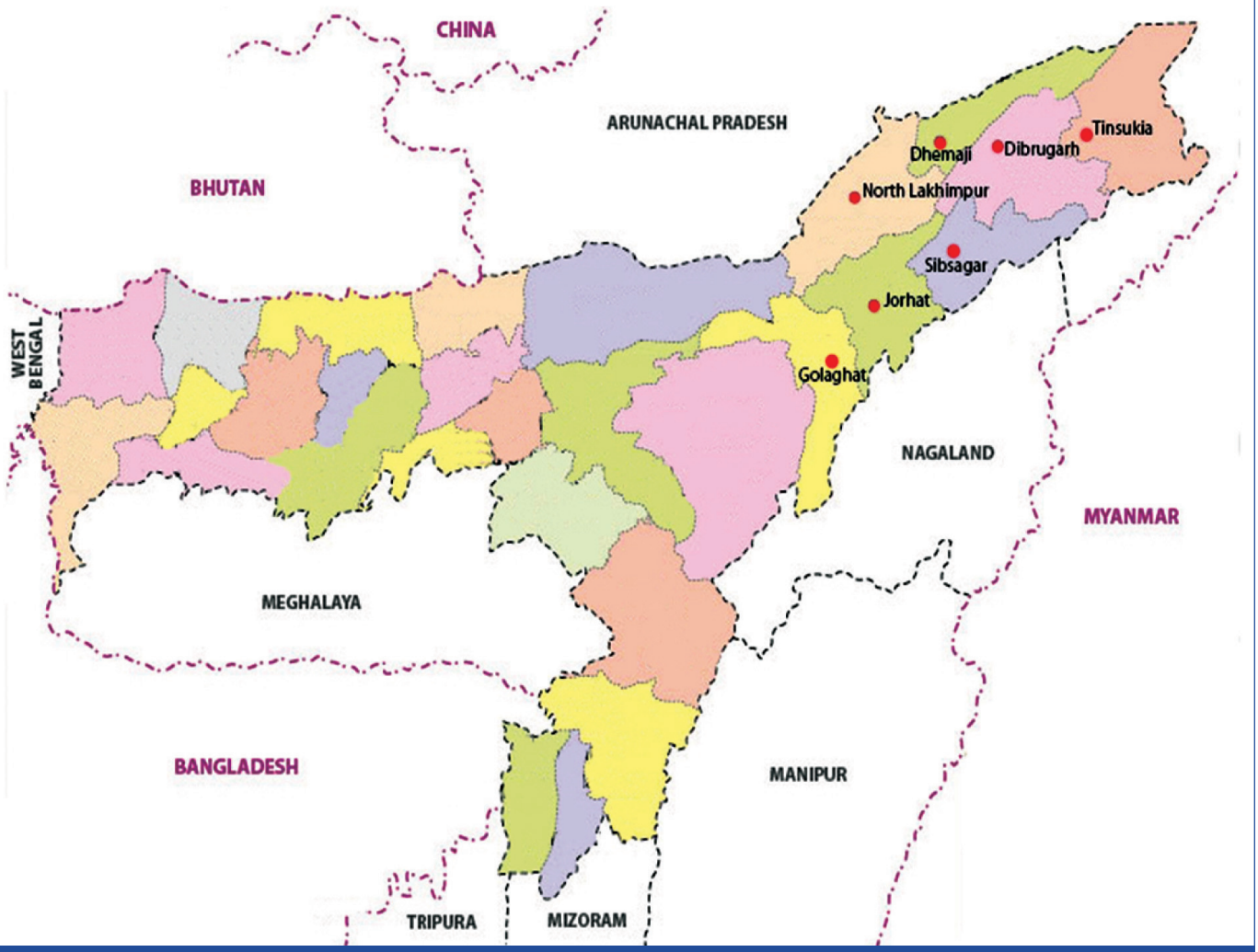
Statistical analysis was done by using SPSS 21. The Mean and SD were calculated by this software.

RESULTS

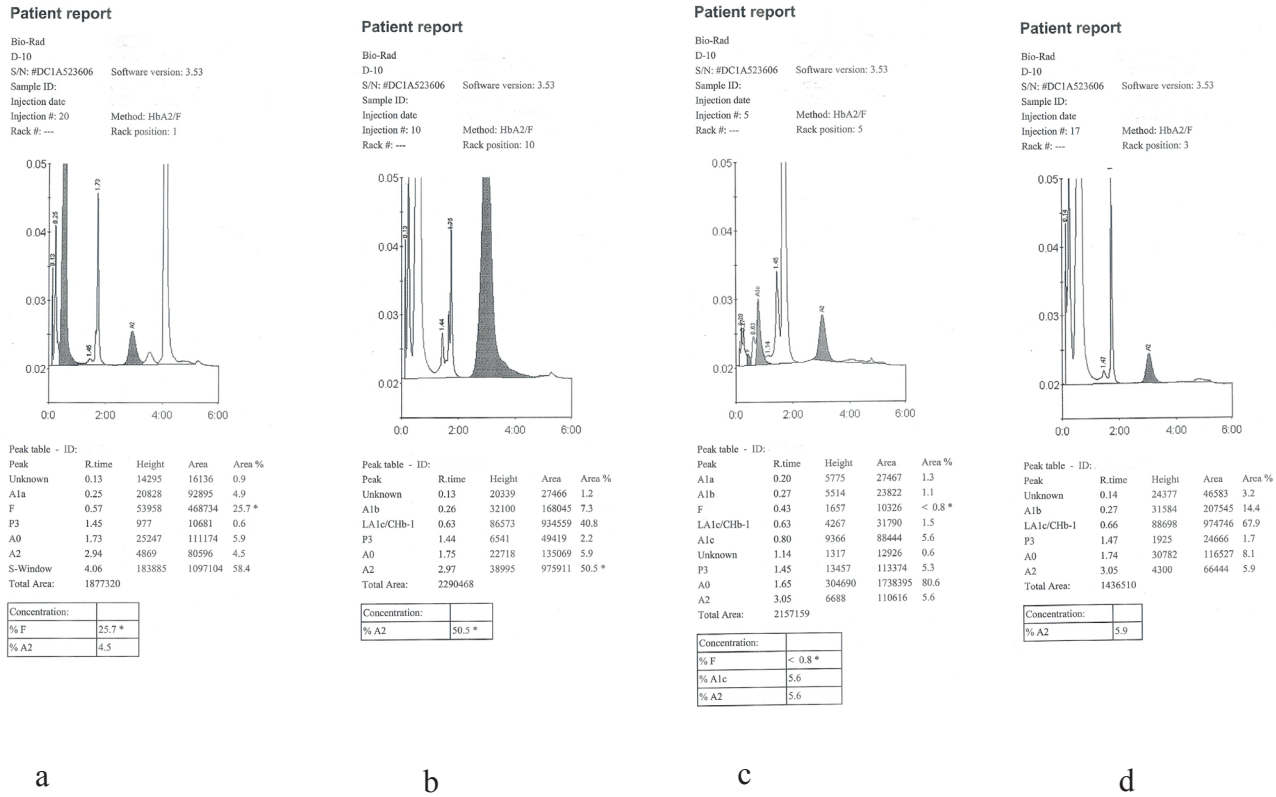
Among the 1200 studied patients males had a mean Hb of 8.36 ± 3.46 g/dl while females had a mean Hb of 7.18 ± 3.1 g/dl. In our study 5.83% β-thalassaemia trait (70 patients), 2.33% compound Hb E/β-thalassaemia (28 patients), 1.33% β-thalassaemia major (16 patients) and 0.42% compound Hb S/β-thalassaemia (5 patients) were detected. The types of chromatograms of the patients were shown in the [Table/Fig-2]. [Table/Fig-3] shows the haematological data [Mean ± SD] of the patients. Anaemia is the most common sign observed in all these patients. All the clinical signs found among the patients are shown in the [Table/Fig-4]. In this study β-thalassaemia trait is the commonest abnormality encountered. The haematological data shows mean Hb of 9.232 g/dl. The patients of Hb E/β-thalassaemia shows moderate to severe anaemia (mean Hb 5-7g/dl) [8]. In our study the mean Hb concentration among the Hb E/β-thalassaemia patients is 6.362 g/dl. The patients of β-thalassaemia major shows severe anaemia (mean Hb 4.678 g/dl). The patients with Hb S/β-thalassaemia shows mean Hb of 5.4 g/dl.

DISCUSSION

Thalassaemia is an inherited autosomal recessive blood disorder. Previously it was confined to certain areas, religions, castes and tribes but the prevalence has increased globally due to the



[Table/Fig-1]: Map of Assam showing the study sites.



[Table/Fig-2]: Chromatograms of the patients of: (a) Hb S/β-thalassaemia; (b) Hb E/β-thalassaemia; (c) β-thalassaemia trait; and (d) β-thalassaemia major detected during the study

Group	RBC(×10⁶/ µl)	Hb (g/dl)	MCV (fl)	MCH (pg)	MCHC (g/dl)
β- thalassaemia trait	4.468 ± 1.1564	9.232± 2.6436	71.242± 13.7913	21.656±3.3932	29.895±2.6782
β-thalassaemia major	3.342 ± 2.1758	4.678± 3.7285	69.111±9.3420	20.989± 2.5042	30.522± 4.1505
Hb E/β-thalassaemia	2.957 ± 1.2456	6.362± 2.7703	69.793± 16.2261	20.407± 5.2068	29.300± 3.2711
Hb S/β- thalassaemia	2.133 ± 1.2097	5.400± 2.6907	89.600± 5.1740	25.767± 1.6166	28.733± 1.2702

[Table/Fig-3]: Haematological data (Mean ± SD) of the patients of β-thalassaemia trait, β -thalassaemia major, Hb E/β-thalassaemia and Hb S/β- thalassaemia detected during the study.

Clinical signs	β-thalassaemia trait	Hb E/β-thalassaemia	β-thalassaemia major	HbS/β-thalassaemia
Anaemia	80%	42.86%	100%	100%
Splenomegally	7.14%	39.29%	62.5%	-
Hepato-Splenomegally	-	14.29%	25%	40%
Weakness	41.43%	35.71%	100%	80%
Fever	1.43%	-	-	-
Stomach Pain	-	7.14%	-	-
Gall stones	4.29%	3.57%	-	-

[Table/Fig-4]: Clinical signs observed among the patients of β-thalassaemia trait, β -thalassaemia major, Hb E/β-thalassaemia and Hb S/β- thalassaemia.

migration of people from one place to another and inter-community marriages [9].

It is evident from the present findings that β-thalassaemia is in abundance in endemic form in the present population. The prevalence of β-thalassaemia trait and sickle cell in India varies between 3-17% and 1-44% respectively because of consanguinity and caste and area endogamy [10,11]. It is interesting to note that the proliferation of abnormal Hb S and β-thalassaemia in Assam is due to caste and area endogamy. These many aspects are the root causes for increasing complexities of Sickle Cell Disease and β-thalassaemia in Assam. The Hb S/β-thalassaemia patients have more severe disease with lower Hb level, MCV and MCH than their counterparts having Hb SS [12]. The red cell count was relatively higher among Hb S/β-thalassaemia patients in relation of the haemoglobin and MCH in carriers of the thalassaemia may be due to production of extra microcytes.

Globally among the patients with severe β-thalassaemia, about 50% of them are affected by Hb E/β-thalassaemia genotype [13-20]. The prevalence rate of Hb E/β-thalassaemia is highest in India, Bangladesh and Southeast Asia [18,19,21].

In this study, the prevalence of Hb E/β-thalassaemia was 2.33% of the overall study population. The previous reports showed that the prevalence of Hb E/β-thalassaemia in northeast India is 9% [22], in upper Assam region is 1.26% [23] and in Dibrugarh it is 1.44% [24]. In this study all the patients with Hb E/β-thalassaemia were found to be severely anaemic. [Table/Fig-5] shows the comparison of the prevalence data of β-thalassaemia between this study and the other studies from India [22-26]. Patient with Hb E/β-thalassaemia carries one gene for β-thalassaemia from one parent and one gene for Hb E from the other parent and hence shows clinical manifestation similar to β-thalassaemia major or Hb E disease. In our study, the numbers of Hb E/β-thalassaemia patients are more than the number of β-thalassaemia major patients.

To estimate the disease burden of β-thalassaemias and other haemoglobin variants micromapping is important because the frequency of the disease varies widely even within small geographic regions in different countries [25].

Sl. No.	Study Site	Number Screened	β- Thalassaemia Trait (%)	Hb E / β-Thalassaemia (%)	Hb S / β-Thalassaemia (%)	β - Thalassaemia Major (%)	Study
1	Upper Assam	1200	5.83	2.33	0.42	1.33	Present study
2	Assam/Meghalaya/ Arunachal Pradesh	800	18.12	9	0.13	2.12	Pathak et al., [22]
3	Upper Assam	9000	3.48	1.26	0.59	0.36	Baruah et al., [23]
4	Bangalore	9981	2.16	0.01	0.06	-	Mohanty et al., [24]
5	Kolkata	9990	3.64	0.09	-	-	Mohanty et al., [24]
6	Dibrugarh	6816	1.48	1.44	0.04	-	Mohanty et al., [24]
7	Ludhiana	9991	3.96	-	-	-	Mohanty et al., [24]
8	Mumbai	10011	2.55	-	-	-	Mohanty et al., [24]
9	Vadodara	9991	2.68	0.01	-	-	Mohanty et al., [24]
10	South India	543	37.9	4.6	2.5	2.3	Chandrashekar [26]

[Table/Fig-5]: Comparison of the prevalence data of β-thalassaemia between this study and the other studies from India.

LIMITATIONS

Hb electrophoresis is not performed in this study which is another method for detection of β-thalassaemia and other Hb variants.

CONCLUSION

This study provides a comprehensive data on the status of thalassaemia in Upper Assam region of North Eastern India. The study shows that the prevalence of β-thalassaemia is high and it is causing a severe public health problem in this region. Since there is no effective treatment for this disease, so carrier detection and awareness programmes have to be conducted at community level for its control and prevention. Advance molecular techniques like polymerase chain reaction (PCR), direct sequencing should be used followed by genetic counseling of the patients.

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