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CASE REPORT Open Access

Compound heterozygosity for hemoglobin S and hemoglobin E in a family of Proto-Australoid origin: a case report

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Abstract

Background: Hemoglobin S and E are commonly occurring hemoglobin variants among distinctly separate tribal populations of Central and Northeast India, respectively. Combined heterozygosity for hemoglobin S and E or hemoglobin SE disease is a benign clinical condition with rare incidence. Reports of approximately 46 hemoglobin SE cases are available worldwide. We conducted a screening program to study the prevalence of hemoglobin variants among the tribal population working in the tea estates of Northeast India. A total of 551 subjects were screened, and complete blood count was performed. Based on their hematological profiles, hemoglobin typing was done for 218 subjects.

Case presentation: We describe a case of an adolescent male of Munda tribe diagnosed as double heterozygous for hemoglobin S and E. On screening of the nuclear family of the subject, the mother was found to have hemoglobin E disease and father as hemoglobin S trait. Both siblings of the subject were diagnosed as hemoglobin E trait.

Conclusion: This is the first case of compound heterozygous for hemoglobin S and E to be reported from the tea tribes of Assam, India.

Keywords: Proto-Australoid, Hemoglobinopathy, Hemolytic anemia, Sickle cell disease, Tea tribe

Background

Hemoglobinopathies are monogenic disorders characterized by abnormal hemoglobin structure [1]. Among the hemoglobin variants, the most commonly occurring and clinically significant variants are hemoglobin S (Hb S), hemoglobin C (Hb C), hemoglobin E (Hb E), and thalassemia [2]. In context to its occurrence, Hb E is the second most common abnormal variant of hemoglobin in the world and most common variant in Southeast Asia [3]. Central-West Africa, East Asia, and India experience higher occurrence of sickle cell disease in comparison with other parts of the world. Hemoglobinopathies are a cause of both economic and psychosocial burden [4]. Sickle cell disease shows an autosomal recessive inheritance resulting from A > T mutation in the sixth residue of the β-globin chain. Hb E results from a Glu→Lys mutation in the 26th amino acid.

Among the different types of hemoglobinopathies, prevalence of Hb S and Hb E in India is 4.3% and 10.9% respectively [5]. The burden of hemoglobinopathies in India is so high that it has become a major public health issue in some parts of the country [3]. In India, prevalence of Hb S among the tribals of central, southern, and western part has been reported [6]. In the eastern and northeastern part, Hb E is prevalent [7]. Sickle cell disease, particularly, has turned into a major health concern in states such as Chhattisgarh, Maharashtra, Gujarat,

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Research Article

PREVALENCE AND ALTERATION IN HAEMATOLOGICAL PARAMETERS OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENT PROTO-AUSTRALOID POPULATION OF MALARIA ENDEMIC HIMALAYAN BELT OF ASSAM, INDIA

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ABSTRACT: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common genetic disorder in malaria endemic regions and high among tribal population. To address the issue, the present study was framed to find out the prevalence of G6PD deficiency among the Proto-Australoid tribal population of malaria endemic Himalayan belt of Indo-Bhutan border areas of Assam and haematological changes in the target population. Screening for G6PD deficiency was done in 1436 normal individuals, out of which 6.62 percent (n=95) were found as deficient. Prevalence was higher in males (68.4%) compared to the females (31.6%). Complete Blood Count (CBC) was done in all samples. Further, analysis was performed to study the changes in the mean values of haematological parameters (both RBC and WBC indices) of G6PD normal and deficient subjects as well as between severe G6PD deficient and intermediate subjects. Subsequently association of haematological parameters with G6PD as well as between G6PD deficiency and gender was also studied. RBC indices *viz.*, Hb, RBC and MCHC showed significant positive correlation with G6PD. No significant correlation was seen with WBC parameters.

Key words: Glucose-6-Phosphate Dehydrogenase, Proto-Australoid population, Malaria, Haemolytic anemia, Hematology.

INTRODUCTION

The enzyme Glucose-6-Phosphate Dehydrogenase (G6PD) is a catalyst in the conversion of glucose-6-phosphate into 6-phosphogluconate, a rate limiting step of pentose phosphate pathway (Stanton 2012). The NADPH produced in this step controls the supply of reduced glutathione (GSH) to the Red Blood Corpuscles (RBC). This in turn saves the RBCs from oxidative stress (Au *et al.* 2000, Eferth *et al.* 2005). More than 400 million people of the world are affected by the deficiency of this enzyme (Nkhoma *et al.* 2009). G6PD deficiency causes premature breakdown of RBCs which results in haemolytic anemia. Generally, G6PD deficient individuals do not show any symptoms or suffer from any harmful effects, but exposure to certain factors like consumption of fava beans or certain anti-malarial drugs may trigger haemolytic anemia (Mehta *et al.* 2000). More than 400 mutants of G6PD have been reported on the basis of biochemical characterization and about 220 mutations are identified at DNA level (Gomez-Manzo *et al.* 2016). These mutations may result in changes in the protein structure thereby causing a decrease in its activity (Gomez-Manzo *et al.* 2014). The World Health Organization (WHO) has classified these mutations as Class I, II, III, IV and V based on the severity of the deficiency. Both class I and class II mutations show less than 10% enzyme activity causing chronic haemolytic anemia and periodic haemolysis respectively, and class III mutations exhibits 10-60% enzyme activity. The other two classes *i.e.*, IV and V show mild effect on the enzyme activity (WHO 1989).

The World Health Organization has established a population specific prevalence of G6PD deficiency in India ranging between 0-10%, with a higher prevalence among the tribal population (Tripathy and Reddy 2007). It has been estimated that a minimum of 3,90,000 children

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Carrier identification of Hemoglobin disorders among adolescents of Northeast India: Necessity of genetic counselling intervention

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ABSTRACT

Among hereditary hemoglobin disorders, Sickle cell disease and β-thalassemia requires serious considerations since lifelong blood transfusion is required for management of such patients. Certain advanced interventions are developed; however, such interventions are very costly and require strict observance, thereby generating the need of low cost but effectual strategy. Carrier screening and genetic counselling for these disorders have been proven to be effective in certain countries. Thus, the present work was carried out to understand the burden of carriers of Hb disorders among the adolescents of Assam, Northeast India. We attempt to highlight the need for introduction of genetic counselling to minimize the genetic load in future generations. Hemoglobin S and hemoglobin E were the major hemoglobin variants encountered in the study population. Prevalence of hemoglobin disorder carriers was observed to be 10.7% out of the total population. Among the total carriers, 20.2% were sickle cell carriers while 76.06% were Hb E carriers. Others were β thalassemia and compound heterozygous S and E. Thus, an extensive carrier screening program in the region is much needed to identify the carriers among the pre-marital age group population and to educate them through genetic counselling about the risks associated with such diseases.

KEYWORDS

Hemoglobinopathy, thalassemia, carrier screening, genetic counselling, Northeast India.

I. INTRODUCTION

Hemoglobinopathies and thalassemias are the most commonly occurring monogenic disorders that affect a person's hemoglobin. This group of disorders exhibit autosomal recessive pattern of inheritance [1]. Every year around 0.3-0.4 million children are born with such disorders in both low and middle-income countries [2]. These

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Correspondence/Letter to the Editor

Asymptomatic hemoglobin SE compound heterozygous hemoglobinopathy in an Aryan male from Northeast India

Dear Editor,

Hemoglobin S (Hb S) is a commonly encountered hemoglobinopathy among the tribal of anthropologically distinct Proto-Australoid population of Central, Southern and Western part of India.[1] The tea estate employees of Assam were from mainland India, who were brought by the British rulers during the last part of the nineteenth century. Again, Hemoglobin E (Hb E) is common among the Mongoloid population of northeastern India.[2] Compound heterozygosity for Hemoglobin S and E (Hb SE) is a clinically rare, silent, and benign condition; such cases have lower chances of being diagnosed. They are detected occasionally when the person is being tested for other complaints. Although rare, the Hb SE cases may suffer from intravascular sickling, vaso-occlusion, bone necrosis, and sudden acute chest syndrome. The clinicians involved in sickle cell disease management and pathologists engaged in clinical forensic medicine services may take these rare cases and symptoms into consideration for referral etc. To the best of our knowledge, the case presented here is the first report revealing the existence of compound heterozygosity for Hb S and E (Hb SE) in a person of Aryan origin.

During a screening program for different types of hemoglobinopathies among the tea estate daily wage laborers of Udalguri district, Assam of Northeast India, we detected the case of Hb SE trait in a clinically normal 45-year-old male of the Aryan race (Fig. 1a). We screened all members of the nuclear family. His wife and 21-year-old daughter were detected with Hb S trait, and his 13-year-old son was detected with transfusion-dependent Hb S disease (Fig. 1b, c, and d). Hematological profiles, namely Hb%, MCV, MCH, and MCHC of all members of the family, are presented in Table 1. Earlier generations of the case had natural death without any recorded medical history of hemoglobinopathies. As per the records from the District Marriage Registry Office, there was no racial intermarriage of both the parents and their earlier three generations. Since the present family members could not provide information about the presence of hemoglobinopathy among their earlier generations, we could not prepare the family pedigree.

We could not find any report on the occurrence of Hb SE from the Aryan community. The Hb SE case presented here was of Aryan stock and was asymptomatic. The hematological profile revealed normal Hb% and MCV, raised RBC count, and lower MCH and MCHC. Hb typing showed 2.9% Hb F, 4.5% Hb A_2, 68.6% Hb S, and 24.0% Hb E. A few earlier cases reported from India also had normal Hb%, MCV, MCH, and MCHC levels.[3] Although Hb SE is a clinically benign condition, sudden death after exercise was reported in a 12-year-old American Hb SE patient. In this case, approximately after 1 h and 45 min of exercise, the patient collapsed; hemodynamic instability and cardiac arrest were reported as per postmortem report, which is assumed to be due to tissue ischemia caused by intravascular sickling. He also had records of ventricular septal cardiac defect at birth, mild asthma, and fractures of the radius and ulna 17 months prior to death.[4] Earlier, another case of Hb SE in a 15-year-old *Teli* community male was reported from central part of India. He was suffering from recurrent upper respiratory tract infections, weakness, and tiredness.[5]

Again, a marriage between Hb SE trait father and Hb S trait mother had Hb S disease son and Hb S trait daughter. The subject's wife was from Proto-Australoid race (tea tribe). She had normal Hb% and RBC, lower MCV, MCH, and MCHC levels. The son was dependent on periodic blood transfusions. He had low Hb%, RBC count, and MCHC levels. The daughter had low Hb%, RBC, MCV, MCH, and MCHC levels, which is indicative of microcytic hypochromic anemia due to borderline low serum iron (65 microgram/dl). This may be due to multiple factors, including menstrual loss, low dietary intake, etc.

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Indian J Hematol Blood Transfus
https://doi.org/10.1007/s12288-023-01686-7

CORRESPONDENCE

The First Report of Three Glucose-6-Phosphate Dehydrogenase (G6PD) Variants: Mediterranean, Orissa and Kalyan-Kerala from Northeast India

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Dear Editor.

The most common enzymopathy prevalent in malaria-endemic regions is glucose-6-phosphate dehydrogenase (G6PD) deficiency. This deficiency affects over 400 million people worldwide. The global prevalence of G6PD deficiency is geographically associated with malaria endemic areas. The Northeastern region of India is malaria endemic, accounting for a large proportion of India's malaria incidences each year [1]. G6PD deficiency is a result of mutations in the DNA encoding G6PD enzyme. The significance of this enzyme lies in its involvement in the generation of NADPH, an antioxidant, during the process of the pentose phosphate pathway. Through subsequent processes, NADPH provides protection to the RBCs against oxidative damage. Mutations in the G6PD gene cause the G6PD enzyme to lose its stability and activity, thereby making deficient RBCs more prone to oxidative damage. G6PD deficiency is widespread across Africa, Asia, the Mediterranean, and the Middle East. Approximately 7.5% of the world population is carriers of G6PD deficiency, and 2.9% are deficient according to the World Health Organization (WHO) report. Moreover, a higher frequency of G6PD deficiency (5.5%) was reported among the tribal/scheduled caste population of India [2, 3]. Molecular genetic analysis has revealed about 220 different mutations in the G6PD gene. In India, the most commonly occurring variant is G6PD Mediterranean, followed by G6PD Orissa, and Kalyan-Kerala. However, these variants have not been reported earlier from the Northeastern region of India, which is predominantly inhabited by Mongoloid and Proto-Australoid population and few from Aryan stock. On the other hand, variants like G6PD A^+, Mahidol and Acores are previously reported from this part of the country [4, 5].

This is the first report to document the evidence of G6PD Mediterranean, Orissa, and Kalyan-Kerala from the tribal population of Northeast India. The variants were detected in a study conducted in four districts of Assam viz., Kokrajhar, Chirang, Baksa and Udalguri which form the Bodoland Territorial Region (BTR) and share its boundaries with Bhutan. The tribes included in the study were Bodo, Rabha, Garo and the tea tribe. G6PD deficiency was detected in 6.2% of the total population with highest number of cases from the tea tribe population. The variants were detected using Polymerase Chain Reaction–Restriction Fragment Length Polymorphism (PCR–RFLP) technique. Restriction endonucleases MboII, HaeIII and MnlI were used for Mediterranean, Orissa, and Kalyan-Kerala respectively [6, 7]. India has a diverse population admixture of various ethnic groups each of which differs in their physical, cultural and genetic background. Approximately 8.6% of the country's population is tribal. The Northeast India alone has more than 200 different ethnic groups belonging to Mongoloid and Proto-Australoid origin. Individuals of Mongoloid and Proto-Australoid descents were found to harbor the variants described in this report. G6PD Mediterranean and Kalyan-Kerala variants were detected in both Mongoloids and Proto-Autraloids. While G6PD Orissa was observed exclusively in the Proto-Australoids. All the detected cases of G6PD deficiency were asymptomatic.

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Case Report

A Case Report of Co-occurrence of Hemoglobinopathy EE and Glucose-6-phosphate Dehydrogenase A+ Variant

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Abstract

Hemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency are two genetic disorders prevalent in malaria-endemic regions. There are conflicting reports on the co-occurrence of G6PD deficiency and hemoglobinopathies. The present study was conducted to explore the co-occurrence (if any) of the two disorders among ethnic populations of Proto-Australoid and Mongoloid origin races. Out of 2310 subjects screened, only one case was detected with both disorders. The case described here is an asymptomatic female of 52 years detected with both hemoglobinopathy EE (HbEE) and G6PD A+ variant. Lower levels of hemoglobin (Hb) %, mean corpuscular hemoglobin (MCH), MCH concentration, platelets, and white blood cell count, and high red cell distribution width and fetal Hb% were recorded. Family screening revealed both daughters as HbAE and normal G6PD. The husband had HbAA and normal G6PD. Out of six siblings of the case subject, two were detected as HbEE and four as HbAE; G6PD was normal.

Keywords: Glucose-6-phosphate dehydrogenase A+, glucose-6-phosphate dehydrogenase deficiency, hemoglobinopathies, hemolysis, polymerase chain reaction–restriction fragment length polymorphism

Introduction

Hemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency are two genetically inherited disorders prevalent in malaria-endemic regions of the world. Although generally asymptomatic, G6PD-deficient individuals may experience hemolytic anemia when exposed to certain factors that act as hemolytic triggers.[1] Among these triggers, primaquine, an antimalarial drug, induces severe hemolysis in G6PD-deficient people.[2] Hemoglobin E (HbE) is a nontransfusion-dependent form of hemoglobinopathy, caused by Glu→Lys replacement at the 26th codon of the β-globin gene. Homozygous HbE is characterized by mild anemia with hypochromic microcytic red blood cells. HbE is the most prevalent Hb variant in North-east India.[3] Although there are limited studies on G6PD deficiency from this region, the prevalence of G6PD deficiency is reported to be 5.4%.[4] There are two schools of viewpoints on the association between G6PD deficiency and hemoglobinopathies. According to one school, a greater co-occurrence of G6PD deficiency and hemoglobinopathies was observed in regions with high frequencies of both genes. The second school of workers reported that G6PD deficiency and hemoglobinopathies are genetically independent disorders that assort independently.[5]

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DOI: 10.4103/bbrj.bbrj_228_23

Methods

Ethical consideration

Ethical agreement and approval for the study were obtained from the Institutional Ethics Committee of Bodoland University, Kokrajhar, Assam, India, vide Reference No.: IEC/BU/ICMR/2019-2 dated May 10, 2019.

Type of sampling and reasons for selection

Random sampling was done using STANDARD G6PD Analyzer (SD Biosensors) for identification of subjects with abnormality in either Hb or G6PD value, or both.

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Identification of glucose-6-phosphate dehydrogenase variants by utilizing polymerase chain reaction – Restriction fragment length polymorphism based method

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ABSTRACT

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a widespread genetically inherited enzyme disorder caused by mutation in the *G6PD* gene located in X chromosome. Although sequencing of the gene is considered as the standard method for detection of mutations, but the process is expensive, laborious, time-consuming and not possible to perform in low resource settings. Thus, the present work was aimed to identify the G6PD variants using Polymerase Chain Reaction – Restriction Fragment Length Polymorphism (PCR-RFLP) based method among the ethnic groups of malaria endemic Northeastern part of India. STANDARD G6PD Analyzer was utilized for screening to identify the G6PD deficient malarial patients. Molecular analysis of the deficient samples was done using PCR-RFLP technique. A total of 17 variants were explored using different restriction endonucleases. Five variants viz., Orissa (63.8 %), Kalyan-Kerala/Jamnagar/Rohini (9.02 %), Mediterranean (8.3 %), A^+ (11.8 %) and Mahidol (1.38 %) were detected among the patients. G6PD Orissa was the major variant among the study population. In malaria endemic regions like Northeast India, a mass screening program for identification of G6PD variants needs to be adopted.

1. Introduction

Malaria is one of the infectious diseases that cause high morbidity and mortality rates in the world's tropical regions. According to the World Health Organization (WHO), there were an estimated 249 million malarial cases worldwide in 2022 (WHO, 2023). In India, various species of malarial parasites such as *Plasmodium malariae*, *P. vivax*, *P. ovale* and *P. falciparum* are prevalent. In case of *P. vivax* infection, the persistent liver stages of the parasite (hypnozoites) may lead to disease relapse weeks or months after the initial infection (White, 2011). To prevent such relapses, the only way is inhibiting the reactivation of hypnozoites. The 8-aminoquinolines, including primaquine, stands as the sole anti-malarial drug that can prevent reactivation of the hypnozoites (von Seidlein et al., 2013). However, its use poses haemolysis risk, especially in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency (Baird et al., 2016). As per the WHO, a recommended safe dose of primaquine is 0.75 mg base/kg body weight weekly for eight weeks to prevent *P. vivax* and *P. ovale* malaria relapse in G6PD deficient patients, requiring close medical supervision. Again, in situations where the G6PD status is unknown and testing is unavailable, prescribing primaquine should involve a careful evaluation of risks and benefits of administering primaquine (WHO, 2016).

G6PD deficiency, the most common hereditary enzyme disorder in malaria-endemic regions, impacts over 400 million people of the world (Nkhoma et al., 2009). While G6PD deficient patients are partially protected against malaria, experiencing lower susceptibility to the disease, they face a significantly higher risk of haemolysis upon treatment with anti-malarial drugs like primaquine (Peters and Van Noorden, 2009). The presumed mechanism behind the protection is the reduced replication of the malarial parasite in the G6PD deficient red blood cells (RBCs). Due to either being phagocytozed or a shortened lifespan of G6PD deficient RBCs, the malarial parasite is unable to complete its life cycle within them. This observation of malaria protection, however, is not uniformly consistent across all G6PD defective genotypes (Guindo et al., 2007; Badoum et al., 2019; Johnson et al., 2009). G6PD deficiency occurs as a result of mutations in the G6PD enzyme encoding gene, *G6PD*

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Eurasian Conference on
'Science, Engineering & Technological Innovations'

Date: 20 & 21 November, 2021. (Online mode)

Jointly organized by

Kryvyi Rih National University, Ukraine, Europe
Automation, Computer Science and Technology Department
Research Culture Society
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Certificate of Participation and Presentation

Ref.No: RCS/ECSETI-21/CPP/006

This is to Certify that

Noymi Basumatary

has participated and presented a Paper titled

A study on acceptability of genetic counselling intervention for hereditary hemoglobin disorders among adolescents of Northeast India

in the 'Eurasian Conference on Science, Engineering & Technological Innovations' dated 20 - 21 November, 2021.

Prof. Natalia Morkun
ECSETI-2021 Conference Chair
Head, Automation, Computer Science and Technology Department, Kryvyi Rih National University, Ukraine.
www.knu.edu.ua

Dr. C. M. Patel
ECSETI-2021 Conference Chair
Director, Research Culture Society.
President, Scientific Research Association.
www.researchculturesociety.org

CERTIFICATE
OF APPRECIATION

International Conference on
BIOTECHNOLOGY FOR ENVIRONMENT & HEALTH

This certificate is presented to

Noymi Basumatary

from

Bodoland University

for the best oral presentation for the paper titled "**Prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency and comparison of hematological parameters among G6PD deficient and normal Proto- Australoid tribal population of malaria endemic Indo-Bhutan border areas of Assam**" in the **International Conference on Biotechnology for Environment & Health (ICBEH),** organized by School of Bio Sciences and Technology, Vellore Institute of Technology along with Association of Biotechnology and Pharmacy, from 25 - 27 November 2021.

K M Gothandam
Convenor, ICBEH

V Pragasam
Chairperson, ICBEH

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आज़ादी का अमृत महोत्सव

Certificate of Presentation

Azadi Ka Amrit Mahotsav

This is to certify that

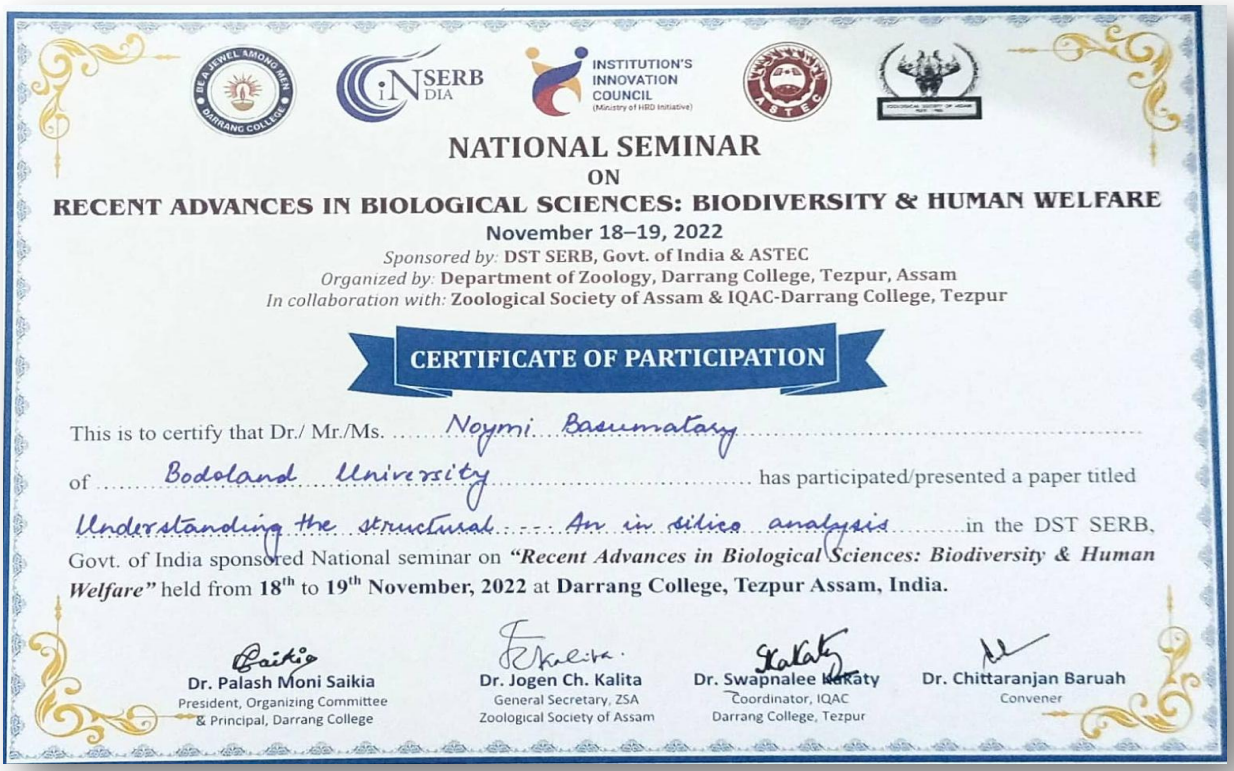
Miss. Noymi Basumatary

of

Bodoland University, Kokrajhar

has presented a paper entitled "*Global burden of Glucose-6-phosphate dehydrogenase (G6PD) deficiency- a lesser known asymptomatic genetic disorder: a pilot study from Bodoland Territorial Region (BTR), Assam.*" in the National Conference on "**Science & Technology for Sustainable Development (STSD-2022)**" held on 9th-10th September, 2022 at Science College, Kokrajhar, Assam, India.

Principal, Science College, Kokrajhar | President, Vijnana Bharati, NESM | Chairperson, National Conference STSD-2022 | Convenor, National Conference STSD-2022 | Convenor, National Conference STSD-2022 | Organizing Secretary, National Conference STSD-2022



NATIONAL SEMINAR

ON

RECENT ADVANCES IN BIOLOGICAL SCIENCES: BIODIVERSITY & HUMAN WELFARE

November 18–19, 2022

Sponsored by: DST SERB, Govt. of India & ASTEC

Organized by: Department of Zoology, Darrang College, Tezpur, Assam

In collaboration with: Zoological Society of Assam & IQAC-Darrang College, Tezpur

CERTIFICATE OF PARTICIPATION

This is to certify that Dr./ Mr./Ms. Noymi Basumatary

of Bodoland University has participated/presented a paper titled

Understanding the structural An in silico analysis in the DST SERB, Govt. of India sponsored National seminar on *"Recent Advances in Biological Sciences: Biodiversity & Human Welfare"* held from 18th to 19th November, 2022 at Darrang College, Tezpur Assam, India.

Dr. Palash Moni Saikia, President, Organizing Committee & Principal, Darrang College | Dr. Jogen Ch. Kalita, General Secretary, ZSA, Zoological Society of Assam | Dr. Swapnalee Hakaty, Coordinator, IQAC, Darrang College, Tezpur | Dr. Chittaranjan Baruah, Convener

APPENDICES

Appendix – I

Ethical clearance certificate

INSTITUTIONAL ETHICS COMMITTEE
Bodoland University,Kokrajhar, Assam, India.
PIN-783370.Phone No:-03661-277183

Ref. No:-IEC/BU/ICMR/2019-2 Date:-10.05.2019

CERTIFICATE

The Meeting of the Institutional Ethics Committee was held on 10th May, 2019. The Committee considered the research proposal entitled **"A study on Glucose-6-Phosphate Dehydrogenase (G6PD) variants in Sickle Cell Anaemic subjects among the tea tribes of malaria endemic Indo-Bhutan border districts of India"** submitted by Dr. Jatin Sarmah, Associate Professor, Department of Biotechnology under Faculty of Science and Technology, Bodoland University, Kokrajhar, Assam and presented by his research scholar Miss Noymi Basumatary for her research work leading to Ph. D. degree in the Department of Biotechnology, Bodoland University. **The study is sponsored by Lady Tata Memorial Trust Scholarship to Miss Noymi Basumatary**.

The committee did not find anything objectionable / unethical *vis-a-vis* human subjects in this research proposal. The proposed research work is, therefore, awarded ethical clearance.

(PRADIP KUMAR PATRA)
Chairman,
Institutional Ethics Committee,
Bodoland University,
Kokrajhar, Assam.

CHAIRMAN
Institutional Ethics Committee
Bodoland University
Kokrajhar, Assam

Appendix – II

Consent form

Proposed work on Glucose-6-Phosphate Dehydrogenase (G6PD) variants in sickle cell anaemic subjects among the tea tribes of malaria endemic Indo-Bhutan border districts of India.

Principal Investigator/ Guide: Dr. Jatin Sarmah
Department of Biotechnology
Bodoland University
Kokrajhar, Assam

Informed Consent for Genetic Analysis

By signing below, I hereby authorize Dr Jatin Sarmah to obtain

blood (*Nature*) sample from [redacted] (*Patient Name*)

of Udalguri, Assam, India. (*Address*)

for the genetic analysis of haemoglobinopathies and G6PD deficiency. (*Disease*)

It has been explained to me and I have understood that:

* DNA testing, which is done on a small sample of blood or other tissue, looks at one or more parts of the particular gene associated with above disease. Genes contain the information that guides proper fumctioning of the body. A change in genetic information can result in an abnormal gene that doesn't work properly.
* Most often DNA testing directly detects the most common disease-causing changes in a gene, the test result is highly accurate (~98%). In other cases, an indirect method called linkage analysis is used which may produce an (3-5%) uncertainty in predicting carrier status or diagnosis due to naturally occurring rearrangements in the DNA (recombination). Rare variations in individuals can also cause uncertainty in the results. In other words, the test is not 100% accurate.
* The linked markers may not be informative in some families and hence, this DNA test can not provide results for the family, or for some members of that family.
* Based on the results from initial tests, subsequent analysis may be performed on the sample for better understanding of the disease.
* If the DNA testing does not show a known genetic change, the probability that the person is a carrier or is affected is reduced. However, there is still a small chance to be a carrier or to be affected because the current testing cannot find all the possible changes within a gene.
* The accuracy of DNA analysis is entirely dependent on clinical diagnosis made elsewhere and Bodoland University cannot be responsible for erroneous clinical diagnosis or sample related problems made at other centres.
* Unknown genetic changes are different in different populations. Providing the laboratory with accurate information about family history and ethnic background will make the interpretation of the test results more accurate.
* The results of this testing will be disclosed ONLY to the patient/relative specified by the patient/doctor named above and to associated medical personnel.
* A part of this sample not used for diagnostic testing may be stored and used for medical research or education as long as any names and other identifying information have been removed. In some cases, it may be possible to reanalyse the leftover samples in the future using new and improved methods.
* The clinical information/video/photographic material resulting from the tests may be used for publication.

[redacted] [redacted]

Signature *Name* *Date*

Relationship to patient: self/parent/guardian

[redacted] [redacted]

Signature of witness *Name* *Date*

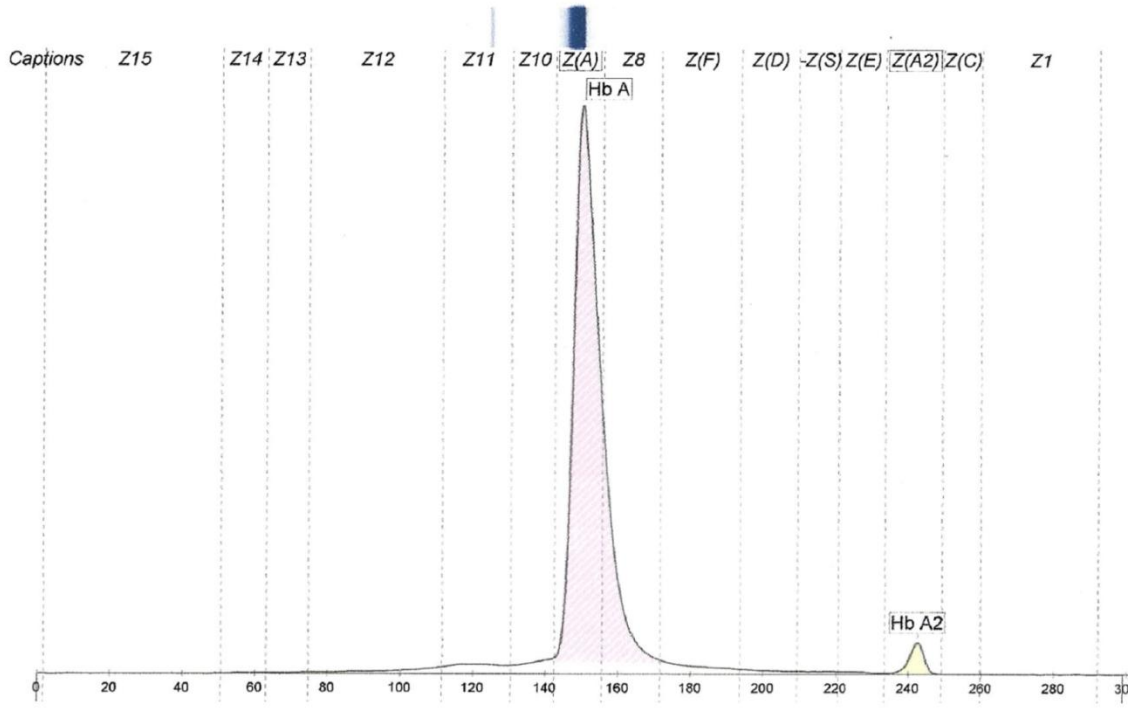
Appendix – III

CBC report

Investigation	Result	Unit	Bio. Ref. Interval
Haemoglobin (Hb)	: **10.5**	gm%	13 - 17
Total Leucocyte Count	: 8200	Cells/Cumm	4000 - 11000
DIFFERENTIAL COUNT			
Polymorphs	: 40	%	35 - 70
Lymphocytes	: **49**	%	20 - 40
Monocytes	: 08	%	02 - 08
Eosinophils	: 03	%	01 - 06
Basophils	: 00	%	00 - 02
Platelet Count	: 192	10^3uL	150 - 400
Total RBC Count	: 4.6	Million /Cumm	4.5 - 5.5
PCV	: **35**	%	45 - 54
MCV	: **74**	fl	76 - 98
MCH	: **22**	pg	27 - 32
MCHC	: **30**	gm/dl	32 - 36
RDW	: **15**	%	11 - 14

Appendix – IV

Hb-typing report showing normal Hb type



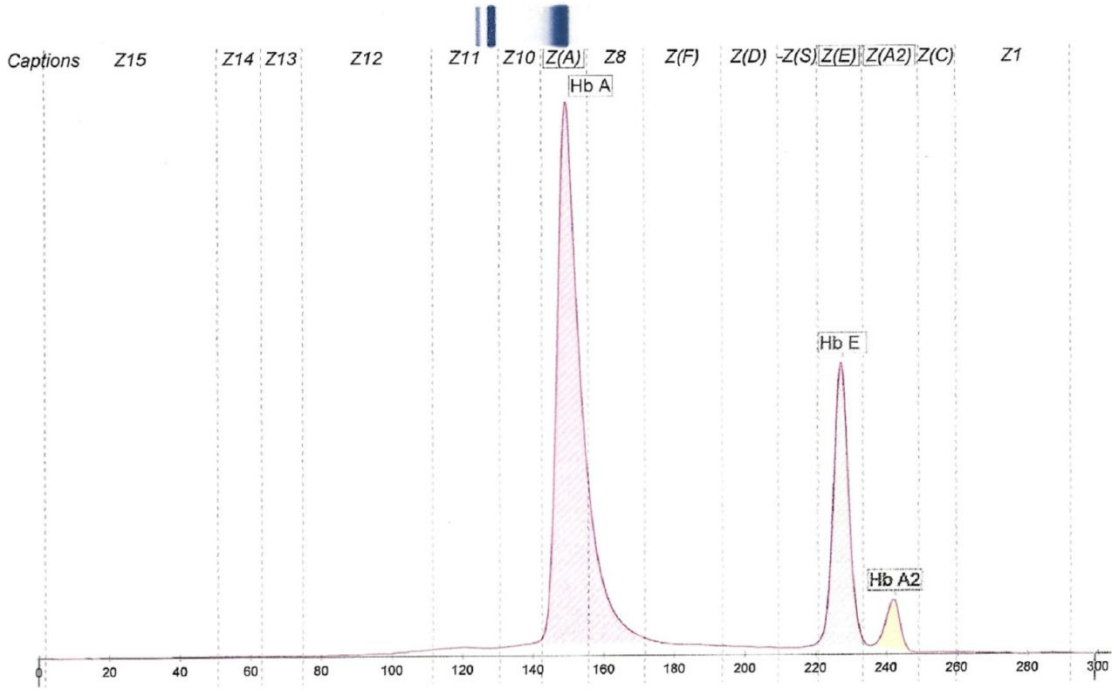
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb A	**97.2**	96.8 - 97.8
Hb A2	**2.8**	2.2 - 3.2

Comment:- Normal chromatogram.No hemoglobinpathy detected.

Appendix – V

Hb-typing report showing HbE trait



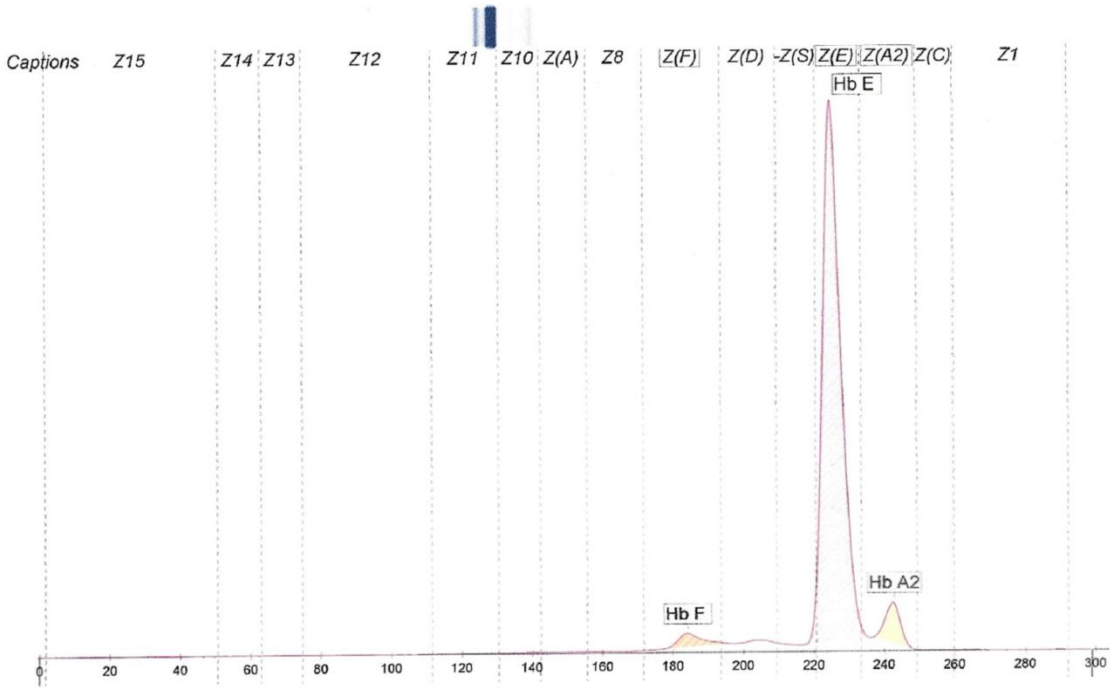
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb A	**72.4**	
Hb E	**23.8**	
Hb A2	**3.8**	

Comment:- Chromatogram is suggestive of Hb E heterozygous.(E Trait)

Appendix – VI

Hb-typing report showing HbE disease



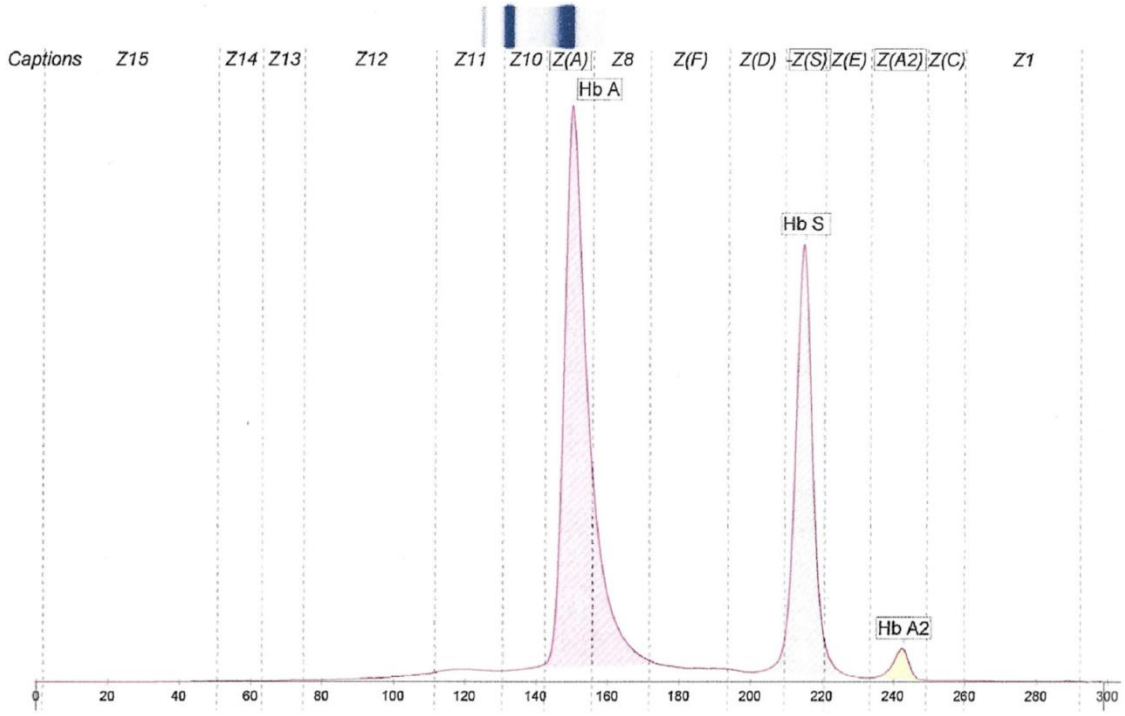
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb F	2.9	
Hb E	91.6	
Hb A2	5.5	

Comment:- Chromatogram is suggestive of Hb E homozygous.(E disease)

Appendix – VII

Hb-typing report showing HbS trait



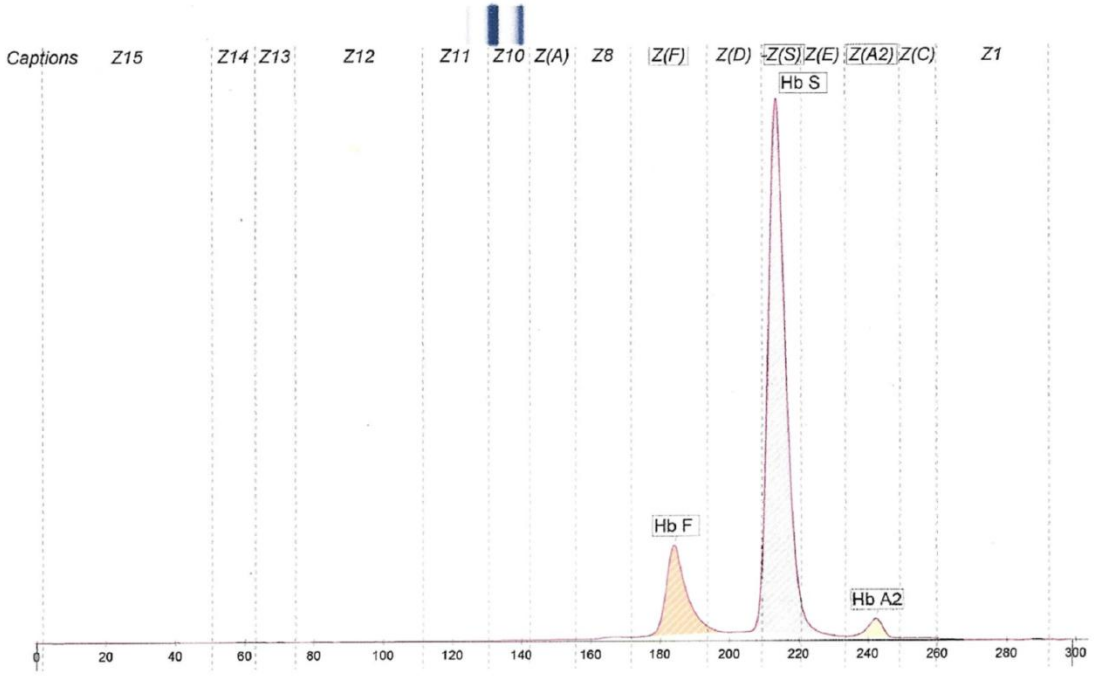
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb A	63.3	
Hb S	34.5	
Hb A2	2.2	

Comment:- Chromatogram is suggestive of Hb S heterozygous.(S Trait)

Appendix – VIII

Hb-typing report showing HbS disease



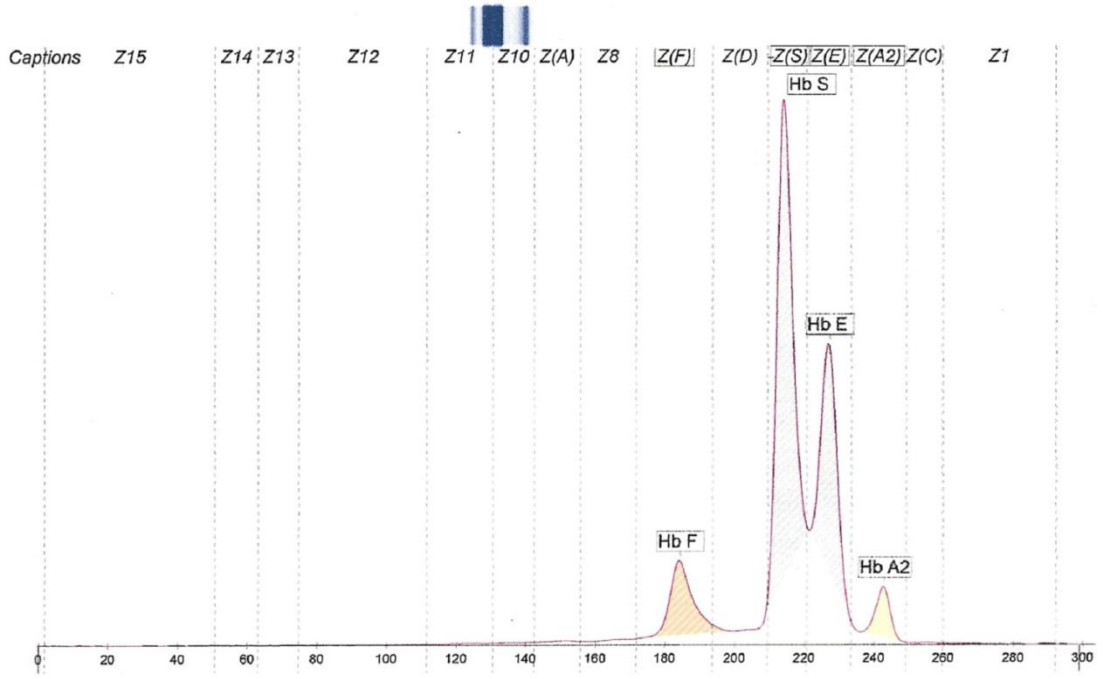
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb F	16.1	
Hb S	81.5	
Hb A2	2.4	

Comment:- Chromatogram is suggestive of Hb S homozygous.(S disease)

Appendix – IX

Hb-typing report showing compound heterozygous HbE and HbS trait



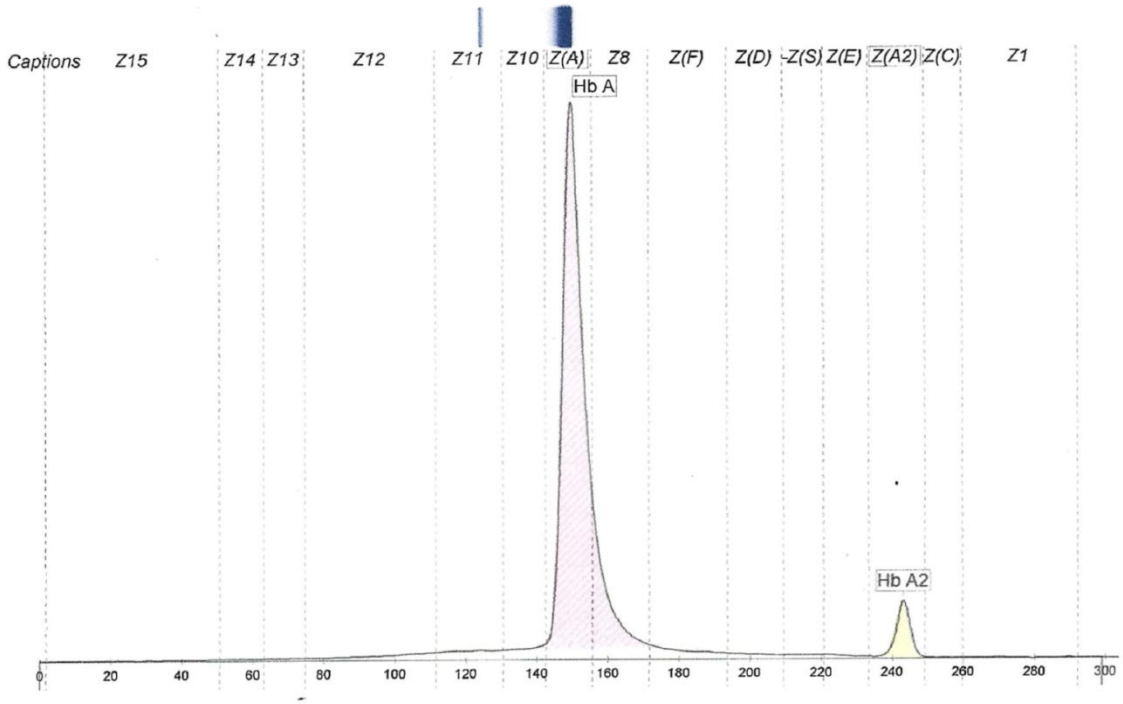
Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb F	**12.7**	
Hb S	**55.2**	
Hb E	**26.7**	
Hb A2	**5.4**	

Comment:- Chromatogram is suggestive of double haterozygous for Hb E and Hb S tra it.

Appendix – X

Hb-typing report showing beta-thalassaemia trait



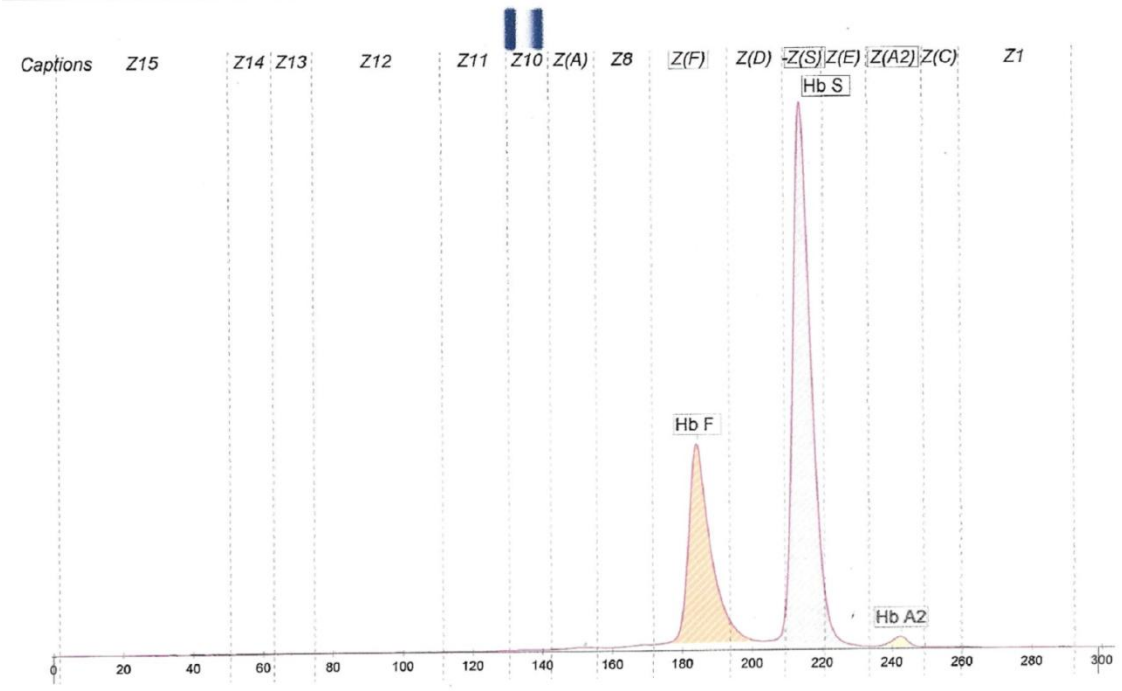
Hemoglobin Electrophoresis

Name	%		Normal Values %
Hb A	**94.3**	<	96.8 - 97.8
Hb A2	**5.7**	>	2.2 - 3.2

Comment:- Chromatogram is suggestive of beta thalassaemia trait.

Appendix – XI

Hb-typing report showing high HbF



Hemoglobin Electrophoresis

Name	%	Normal Values %
Hb F	**30.7**	
Hb S	**68.2**	
Hb A2	**1.1**	

Comment:- Chromatogram is suggestive of Hb S homozygous.(S disease)