ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 01 | January - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CASE REPORT ON RARE BETA THALASSAEMIA MUTATIONS -90 (C→ T) AND IVS 1-130 (G→ C) FOUND IN ASSAM, INDIA.

Hematology

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ABSTRACT

Beta thalassaemia is genetic haematological disease and caused due to mutations in the beta globin gene. There are more than 200 different beta thalassaemia mutations found worldwide and in Indian population beta thalassaemia mutations like IVS 1-5 G→C, IVS 1-1 G→A, IVS 1-1 G→T, Cd 8/9, 619bp and Cd 41/42 are commonly found. During a study on Hb variants in a tertiary care hospital, beta thalassaemia cases were identified by HPLC based Haemoglobin typing and mutation patterns were identified by ARMS-PCR. The cases where mutations were not identified, those samples were sent for DNA sequencing. On DNA sequencing, rare beta thalassaemia mutations -90 (C→ T) and IVS 1-130 (G→ C) were identified in a family.

KEYWORDS

Beta thalassaemia, rare mutation, Assam.

INTRODUCTION:

Haemoglobinopathies and thalassaemia are the genetic haematological diseases prevalent worldwide. The Northeast region of India including Assam has a wide prevalence of these Hb variants. The beta thalassaemia is of serious concern as the patients with beta thalassaemia major are transfusion dependent and shows clinical manifestations at an early age. There are more than 200 beta thalassaemia mutations identified worldwide. Earlier studies have shown that there are around six to seven common beta thalassaemia mutations in India (1-6). Beta thalassaemia mutations like IVS 1-5 G→C, IVS 1-1 G→A, IVS 1-1 G→T, Cd 8/9, Cd 41/42, 619bp, nonsense codon 15 are common in the Indian population (7). In Assam also mutations like IVS 1-5 G→C, Cd 41/42 are commonly encountered. During a study of Hb variants in a tertiary care hospital, two rare beta thalassaemia mutations -90 (C→ T) and IVS 1-130 (G→C) were identified in a family after doing DNA sequencing.

-90 (C→T) and IVS 1-130 (G→C) mutations were found in around 2% of the beta thalassaemia carrier subjects as per a study report of Bangladesh (8). These mutations -90 (C→T) and IVS 1-130 (G→C) are reported to be very less common (9). -90 (C→T) beta thalassaemia mutation was first reported and described in Portugese individual (10). A rare case of -90 (C→T) mutation was reported earlier from Maharashtra (11). Rare beta thalassaemia mutation -90 (C→T) was reported among the Meiti Brahmins of Manipur (12). A beta thalasasemia genotyping profiling showed variability and -90 (C→T) cases was reported in few cases with a frequency rate 1.43% (13). Low frequency of IVS 1-130 (G→C) was reported among Turkish children (14).

Case Report:

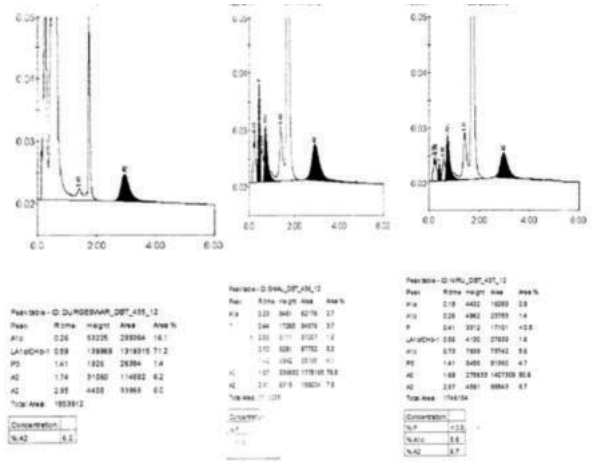
During a study on Haemoglobinopathies and thalassaemia in a tertiary care hospital of Northeast India, a family with beta thalassaemia was identified. The patient along with his parents were positive for beta thalassaemia. The patient was 9 years old who was anaemic, complained of fever, weakness, bodyaches, low appetite. After examining, the Proforma was filled to take the medical history and written Informed Consent was taken from the parents. The samples were collected in EDTA coated vacutainers for doing Complete Blood Count and Haemoglobin typing. The CBC was done in Cell Counter (SYSMEX, TRANSASIA) and patient had a very low haemoglobin level. The HPLC based Haemoglobin typing was done in D10 (BIORAD) and the patient was diagnosed as beta thalassaemia major. Blood samples from the parents of the boy were also collected after taking written informed consents. The father (36years old) who complained of weakness was diagnosed as beta thalassaemia trait and mother (30 years old) who complained of weakness and bodyache was also diagnosed to be beta thalassaemia trait. Haematological Indices are shown in Table 1. The HPLC based haemoglobin typing reports are shown in Figure 1.

For mutational pattern study, the samples were processed for doing molecular analysis. DNA extraction were done by using the Column based DNA extraction method and Amplification Refractory Mutation System- Polymerase Chain Reaction (ARMS- PCR) was done for analyzing the beta thalassaemia mutation pattern. The samples were not positive for the five common beta thalassaemia mutations IVS 1-5 G→C, IVS 1-1 G→A, IVS 1-1 G→T, Cd 8/9 and Cd 41/42. The samples were sent for DNA sequencing and it was found that the samples were positive for two rare beta thalassaemia mutations -90 (C→T) and IVS 1-130 (G→C).

The father was beta thalassemia heterozygous and showed -90 (C→T) mutations. The beta thalassaemia mutation of mother was identified to be IVS 1-130 (G→C), which is also rare in the Indian population. The patient carried both the -90 (C→ T) and IVS 1-130 (G→C) beta thalassaemia mutation.

Table 1: Haematological Indices of the patient, father and mother.

Haematological Indices	Patient	Father	Mother
RBCx106µL	1.6	5.6	5.37
HGB g/Dl	3.3	13.1	11.1
HCT %	11.5	40.8	33.9
MCV Fl	71.9	72.6	63.1
MCH pg	20.6	23.3	20.7
MCHC g/Dl	28.7	32.1	32.7



(a)Patient **(b)Father** **(c)Mother**

Figure1: Haemoglobin typing Chromatogram reports of Patient (a), Father (b) and Mother ©

DISCUSSION:

Identifying and reporting rare or new beta thalassaemia mutations are important for treating patients and also it help in diagnostics specially

in prenatal cases. Data on beta thalassaemia mutational pattern in any area or place can serve as a beneficial tool for population genetic studies as it highlights the various links and other migration history. The beta thalassaemia mutation characterization studies have revealed that these genetic mutations is now present in almost all groups of people in Indian population due to mixing up, intercaste marriages and migrations.

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