Case Report

A Rare Case of Homozygous δβ-Thalassemia in Childhood: Molecular Diagnosis and Comprehensive Family Analysis

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ABSTRACT

Delta- Beta (δβ)-Thalassemia is a rare autosomal recessive hemoglobinopathy caused by deletions in the δ- and β-globin genes, leading to prolonged fetal hemoglobin (HbF) production. δβ-Thalassemia can resemble β-thalassemia major due to anemia and increased HbF. A step-by-step method is required for accurate diagnosis, which includes initial Capillary electrophoresis screening, family hemoglobin studies, and molecular tests. A four-year-old female presented with anemia. Initial Capillary electrophoresis results showed HbF 99.2%, HbA 0.8%, and no HbA_2, indicating a rare hemoglobinopathy. Subsequent family Capillary electrophoresis tests revealed inheritance patterns, but conclusive carrier status was not identified until molecular testing. Molecular investigation verified a homozygous loss of HBB, HBD, and HBG1. Pedigree analysis indicated autosomal recessive inheritance in which both parents and siblings were identified as heterozygous carriers. The identification of unique laboratory and molecular features facilitates genetic counselling and family screening, thereby aiding in the prevention of misdiagnosis and the avoidance of unwarranted transfusions.

Keywords: Thalassemia, Hemoglobinopathies, Anemia.

Beta (β) thalassemia is an inherited blood disorder that reduces the production of hemoglobin (Hb). Mutations in the HBB gene cause β thalassemia. The HBB gene is responsible for the synthesis of a protein called β-globin, which is a component (subunit) of Hb. Mutations in this gene can result in decreased (β+) or no (β0) β-globin production, leading to autosomal recessive disorders like β-thalassemia and sickle cell anemia [1]. Approximately 20 mutations, including deletions, insertions, base substitutions, and alternate splice variants, are known to be responsible for abnormal β-globin production in South-East Asians. Delta-β (δβ) -thalassemia is a rare form of thalassemia caused by deletions of the δ- and β-globin genes on chromosome 11 [2]. δβ-thalassemia, also known as deletional δβ0-thalassemia, β-globin gene cluster deletion (HBD–HBB deletion), Fetal hemoglobin (HbF)-persistent thalassemia [3, 4].

It can be a thalassemia heterozygous or homozygous genotype. While thalassemia trait (heterozygous) is rare, the homozygous state is exceedingly uncommon. Heterozygotes for δβ-thalassemia exhibit clinical signs of thalassemia minor. On the other hand,homozygous δβ-thalassemia may present clinically as thalassemia intermedia with mild anemia. HbF is a globin protein with two alpha (α)- and two gamma (γ)-globin chains (α2 γ2) and normally decreases to less than 1 percent of total Hb within a few months after birth, but in some genetic conditions, high levels persist into adulthood. [5]. δβ-Thalassemia spans a wide molecular spectrum of deletions, such as the Sicilian (~13 kb), Spanish (~5.2 kb), and Indian (~100 kb) deletions that silence the δ- and β-globin genes completely, but do not affect γ-globin expression, resulting in HbF levels ranging from 10% to near 100% in the heterozygote or homozygote, respectively [6].

Because of the identical laboratory features, especially in the absence of family history and molecular confirmation, misdiagnosis is common. Mutation analysis is the confirmatory test for the diagnosis of this rare disorder [7]. It

Access this article online

Received – 27th February 2026
Initial Review – 07th March 2026
Accepted – 26th March 2026

DOI: 10.32677/ijch.v13i4.8142

Quick Response Code

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is used to diagnose other possibilities like β-thalassemia major and hereditary persistence of HbF (HPFH) to assist in clinical therapy and to identify carriers among relatives [5]. The objective is to evaluate the hematological profile, Capillary electrophoresis findings, and molecular test for thalassemia.

CASE PRESENTATION

A 4-year-old girl came with complaints of chronic tiredness. Hematological investigations showed mild anemia with microcytic hypochromic red cells. She had previously received iron and nutritional supplements. There was no history of jaundice, chronic infections, bone pain, structural dysfunction, or past blood transfusion. The infant was born to non-consanguineous parents, and her 13-year-old brother was in optimal health. There was no known family history of malnutrition or inherited anemia such as thalassemia.

Table 1. Capillary electrophoresis Findings of Patient

Hb Fraction	Result	Reference Range
HbA	0.8%	96.8–97.8%
HbA_2	0%	2.2–3.2%
HbF	99.2%	≤0.5%

The observation of markedly elevated HbF, with almost non-existent HbA and HbA_2, suggests a rare hemoglobinopathy characterized by persistent HbF. This Hb pattern is most indicative of homozygous δβ-thalassemia or deletional hereditary persistence of HPFH. Since both conditions can exhibit comparable Hb profiles on Capillary electrophoresis, additional investigation through family studies and confirmatory molecular genetic testing is necessary to diagnose and distinguish between these conditions accurately. Figure 1 shows the Capillary electrophoresis findings of the patient, and Table 1 shows the Capillary electrophoresis results of the family, which was done before the molecular confirmation.

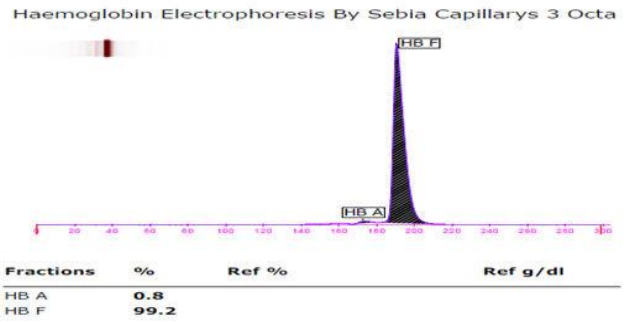


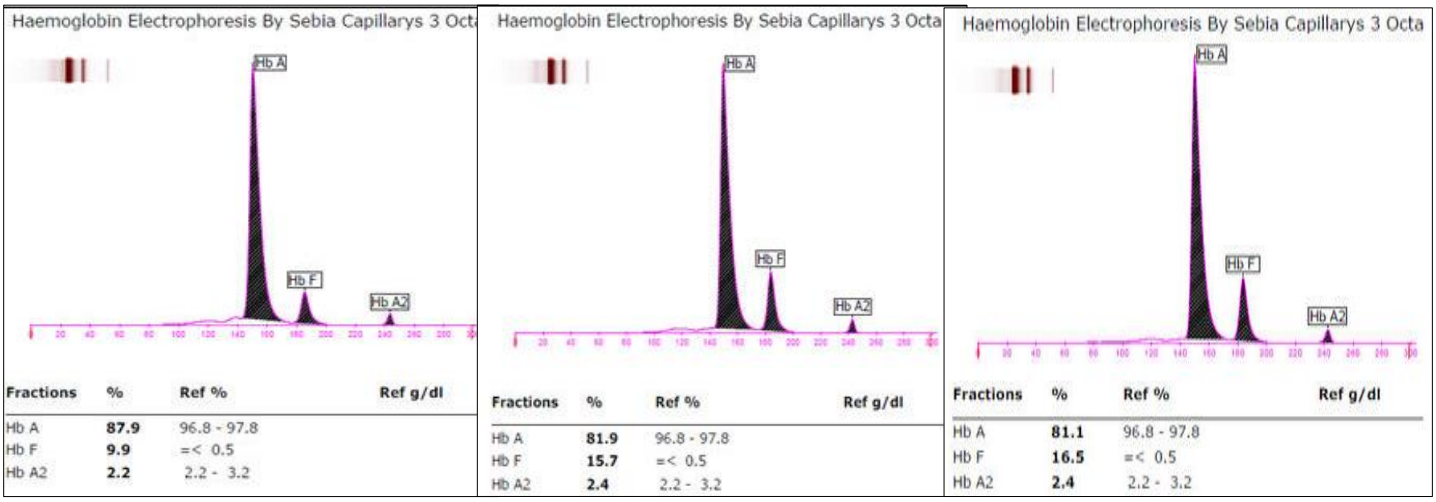
Figure1.Capillary electrophoresis Findings of Patient

Table 2. Family Capillary electrophoresis Results

Hb Fraction	Mother	Father	Sibling	Reference
HbA	87.9	81.9	81.1	96.8–97.8
HbA_2	2.2	2.4	2.4	2.2–3.2
HbF	9.9	15.7	16.5	≤0.5

HbA: Adult Hb

To investigate the inheritance pattern, Hb analysis using Capillary electrophoresis was performed for both parents and the elder sibling. Mildly elevated HbF levels observed in both parents and siblings indicated a potential carrier status of a hemoglobinopathy such as δβ-thalassemia. (Figure. 2)



(a) **(b)** **(c)**

Figure 2. Capillary electrophoresis Findings of Family (2a Mother, 2b.Father, 2c.Brother)

A homozygous deletion affecting several globin gene cluster regions was found in the patient, including the upstream region, exon 1, intron 1, and intron 2 of the HBB gene, exon 3 of the HBD gene, and exon 3 of the HBG1 gene. These molecular findings are shown in Figure 3.

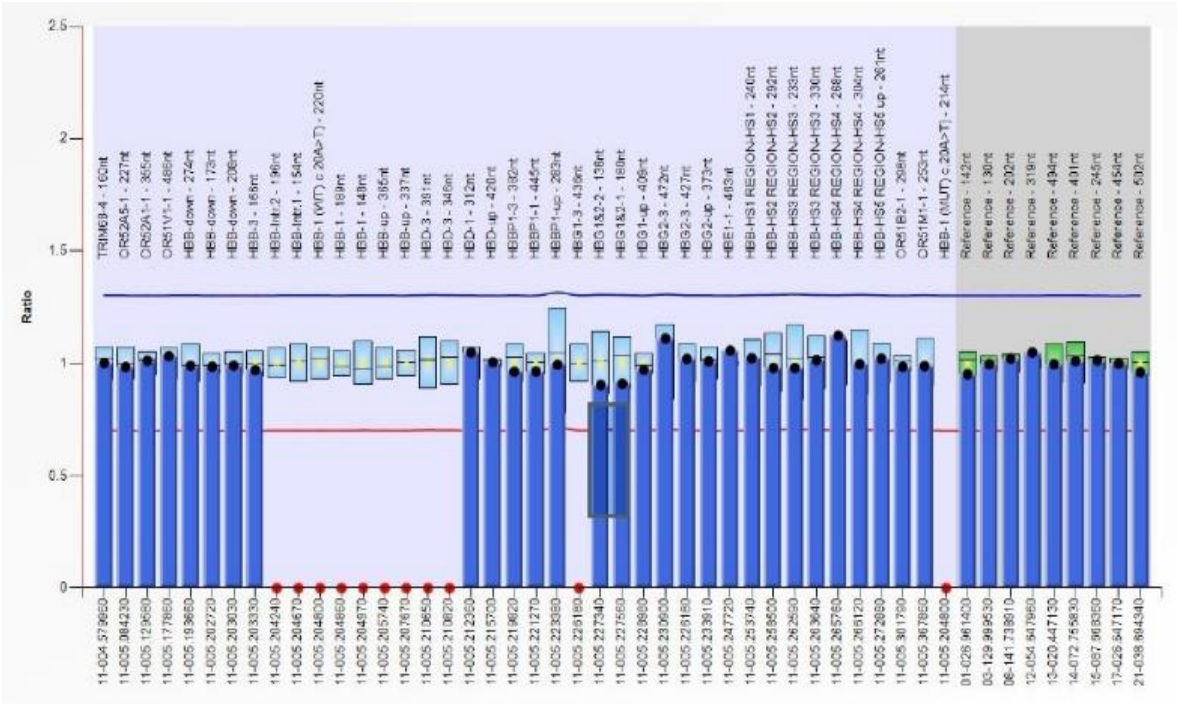
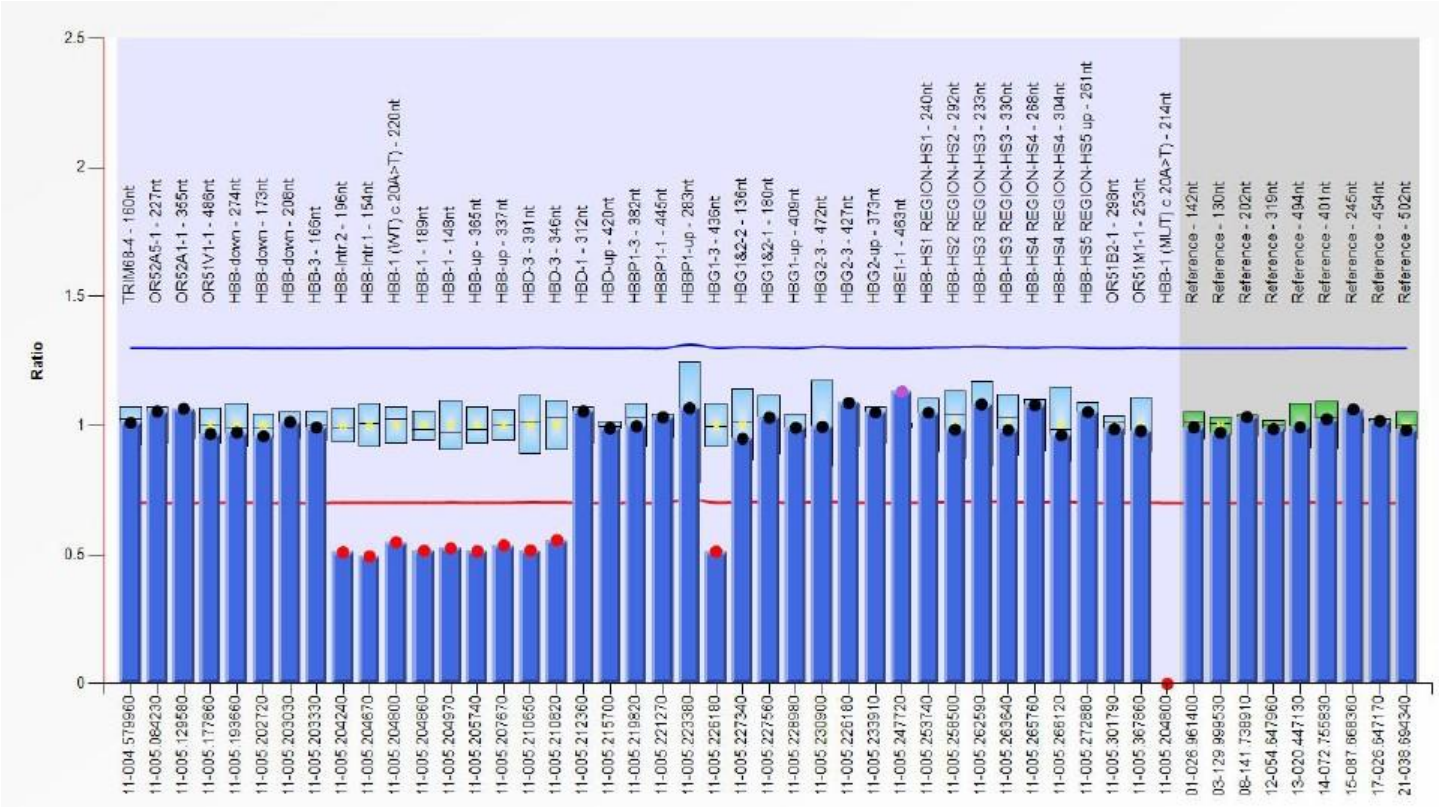
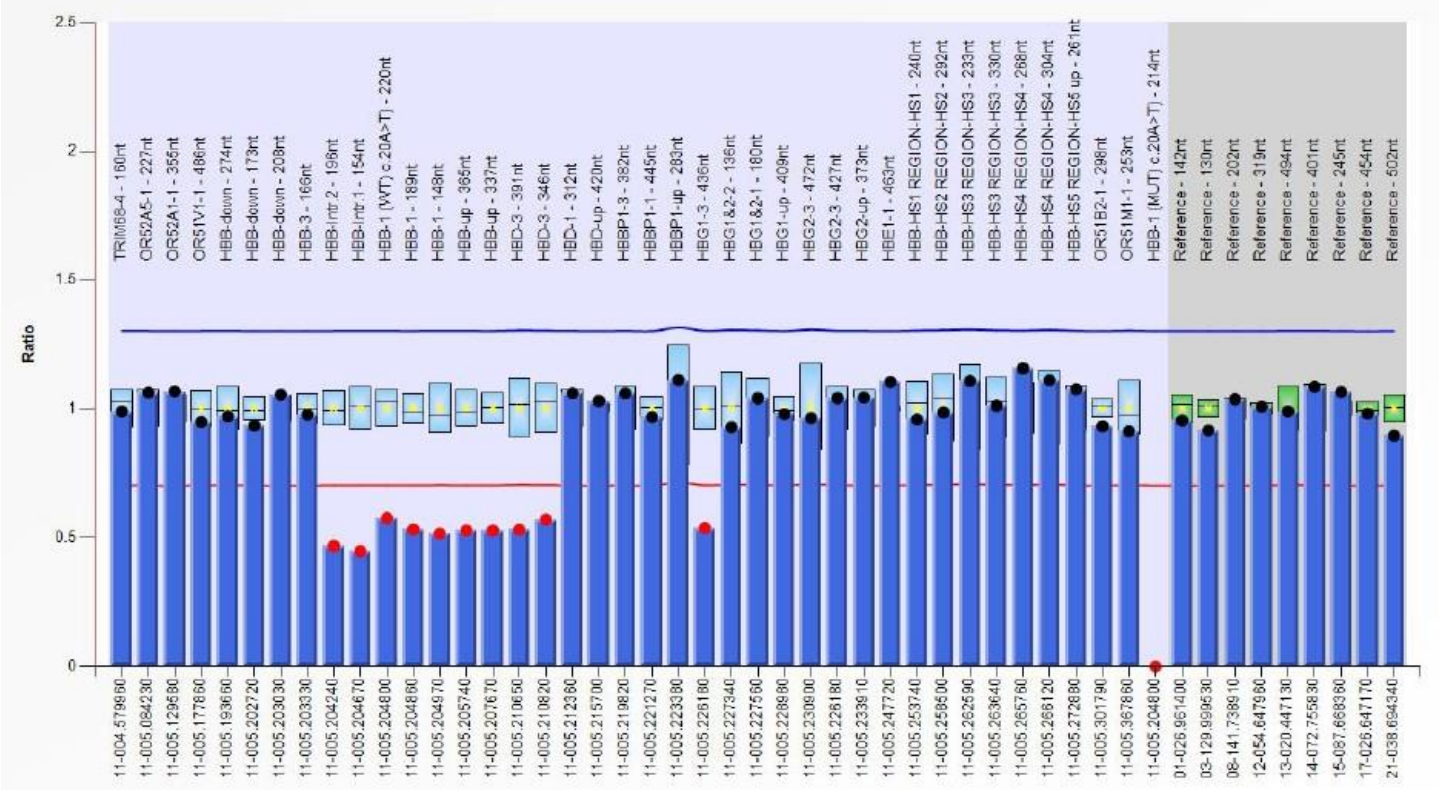


Figure 3. Molecular Findings of the Patient

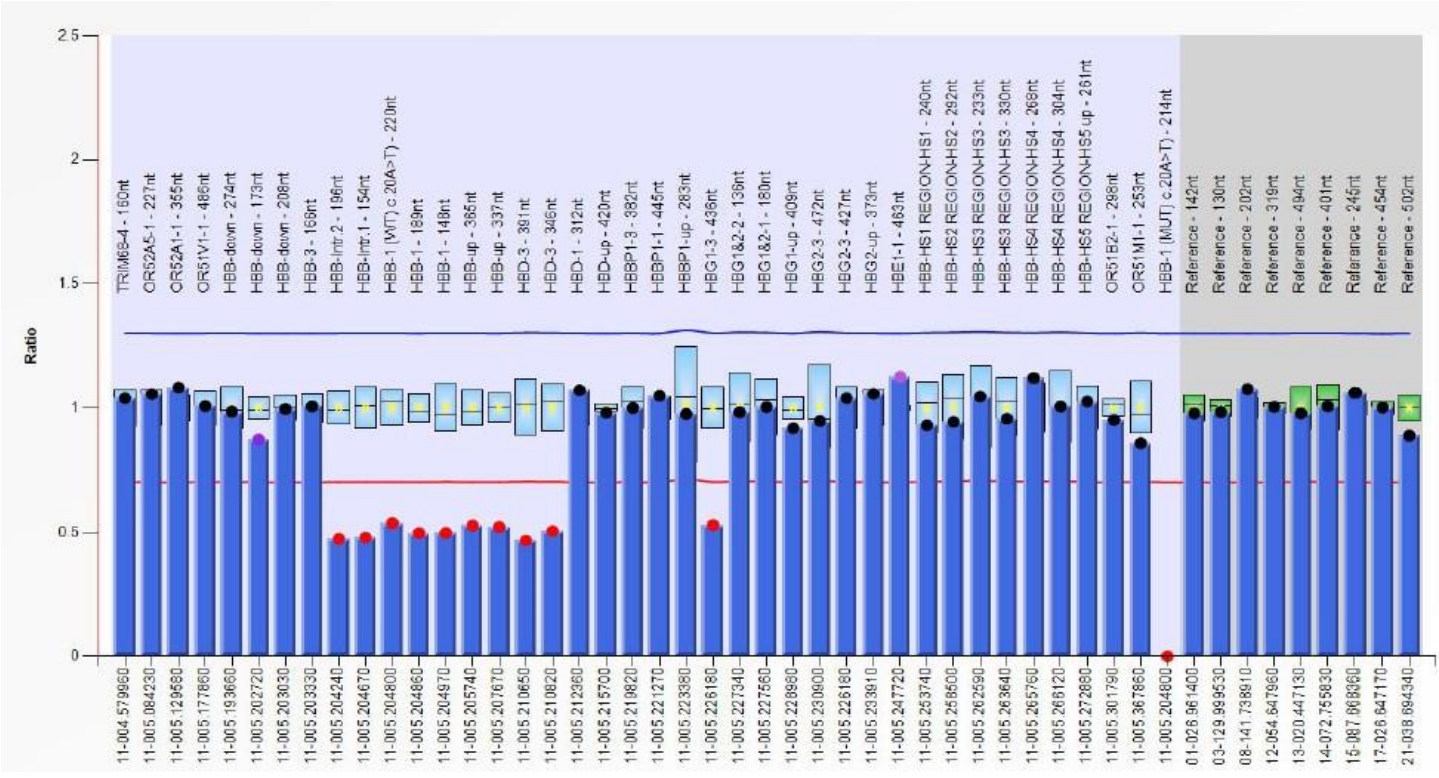
The patient's hematological profile, which includes near-total HbF at 99.2 percent, minimal HbA at 0.8 percent, and absent HbA_2, was explained by the diagnosis of homozygous δβ–-thalassemia. Mutation testing confirmed the heterozygous δβ-thalassemia in the parents and older siblings. Figure 4 shows the family's molecular findings.



(a)



(b)



(c)

Figure 4.Molecular Findings of Family (4a.Mother, 4b.Father, 4c.Brother)

Pedigree analysis using the molecular findings confirmed the inheritance pattern (Figure. 5), where the parents were found to be heterozygous carriers of δβ-thalassemia, and the sibling was found to be a heterozygous carrier, with the patient confirmed to be homozygous. Through molecular confirmation, accurate detection of carriers, appropriate risk assessment of future children, and a strong basis for genetic counselling for clinical management were obtained.

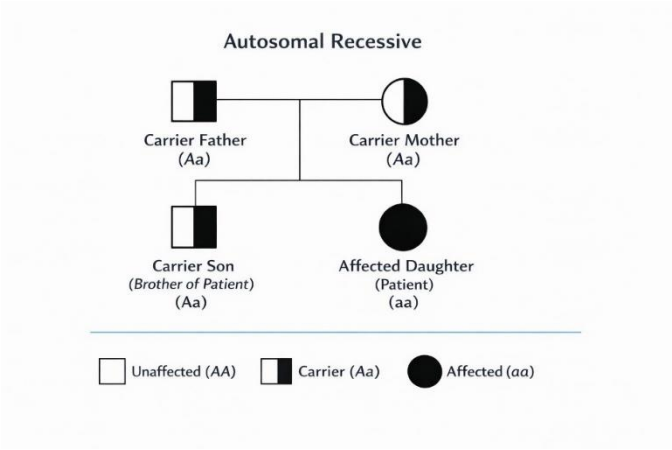


Figure 5. Pedigree Diagram

DISCUSSION

Homozygous δβ thalassemia is an uncommon form of thalassemia, occurring in less than 1% of cases in most screening studies, characterized by a lack of β and δ-globin chains. In this study, the female kid was homozygous for δβ-thalassemia, while her parents and older brother were heterozygous carriers. This inheritance pattern is compatible with the autosomal recessive transmission seen in hemoglobinopathies.

Verma et al. reported a similar discovery, describing a 4-year-old male child with an acute onset of jaundice lasting 7-8 days and a history of intermittent diarrhea for four months. Capillary electrophoresis analysis revealed that the infant was homozygous for δβ-thalassemia, while both parents were heterozygous carriers. The study emphasized the significance of family screening and Capillary electrophoresis analysis in confirming the diagnosis and finding carriers among affected families [7]. A PubMed search of the Indian literature revealed few studies on heterozygous δβ-thalassemia, whereas homozygous cases were rarely reported [7].

In a study of 1197 patients in northern India, Jain et al. found 6 heterozygous and two homozygous cases of δβ thalassemia [8]. In another study from West Bengal, despite screening over 1 lakh patients over 10 years, only 24 cases of δβ thalassemia were found, with none being homozygous [9]. In a population-based analysis of 2,905 individuals from seven villages in southern Sardinia, Antonio Cao et al. reported six cases of heterozygous δβ-thalassemia, confirming the low but detectable number of cases of hemoglobinopathy in the region [3].

Management of thalassemia requires a collaborative approach. These molecular approaches aid in the detection of quiet mutations and complex genetic variants that would otherwise go undetected by regular blood tests [10]. Accurate diagnosis, carrier identification, and genetic counseling could only be made by molecular testing, which prevents misdiagnosis, unnecessary transfusions, and ensures proper management.

CONCLUSION

Homozygous δβ-thalassemia is very rare, and although many cases are underreported in India. A stepwise diagnostic approach is necessary to confirm homozygous δβ-thalassemia and differentiate it from the other β-thalassemia categories.

REFERENCES

1. Thein SL. The molecular basis of β-thalassemia. Cold Spring Harbor perspectives in medicine. 2013;3(5):a011700.
2. Mansoori H, Asad S, Rashid A, Karim F. Delta beta thalassemia: a rare hemoglobin variant. Blood research. 2016;51(3):213-214
3. Cao A, Melis MA, Galanello R, Angius A, Furbetta M, Giordano P, Bernini LF. Delta beta (F)-thalassaemia in Sardinia. Journal of Medical Genetics. 1982;19(3):184-192.
4. Debbarma S, Bhamre N, Shetty P, Pawar RN. Homozygous delta beta-thalassemia: A rare case report. Journal of Hematology and Allied Sciences. 2023;3(2):61-63.
5. Carrocini GC, Ondei LS, Zamaro PJ, Bonini-Domingos CR. Evaluation of HPFH and δβ-thalassemia mutations in a Brazilian group with high Hb F levels.Genet Mol Res. 2011 Dec 21;10(4):3213-3219
6. Stamatoyannopoulos G. The molecular basis of hemoglobin disease. Annual review of genetics. 1972;6(1):47-70.
7. Verma S, Bhargava M, Mittal SK, Gupta R. Homozygous delta-beta thalassemia in a child: a rare cause of elevated fetal hemoglobin. Iranian journal of pediatric hematology and oncology. 2013;3(1):222.
8. Jain P, Marwah N, Dalal N, Pawar R, Gill M, Kumar S. Delta beta thalassemia, a rare hemoglobin variant: An experience from nodal centre in North Indian state. Journal of Applied Hematology. 2022;13(1):1-4.
9. Mondal SK, Mandal S. Prevalence of thalassemia and hemoglobinopathy in eastern India: A 10-year high-performance liquid chromatography study of 119,336 cases. Asian journal of transfusion science. 2016;10(1):105-110.
10. Sameen S, Aden D, Jairajpuri ZS, Jetley S. Delta-beta thalassemia trait–A case series. Journal of Medicine, Surgery, and Public Health. 20;1:100019.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: DavePG, ParikhPM, ShahBS, ShahSC, MurnalAG. A Rare Case of Homozygous δβ-Thalassemia in Childhood: Molecular Diagnosis and Comprehensive Family Analysis. Indian J Child Health. 2026; 13(4):48-52.