

CASE REPORTS

Recurrent Pallor in a 3-Year-Old Girl: A Rare Case of Co-Inherited Hemoglobin S and Hemoglobin D-Punjab

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Abstract

Haemoglobinopathies represent a major genetic health burden in South Asia, including Bangladesh, due to high carrier frequency and lack of systematic screening program. While Hb E and β -thalassemia are most prevalent in Bangladesh, rare variants such as haemoglobin D-Punjab are under-recognised. Hb D-Punjab trait is usually clinically silent, but co-inheritance with haemoglobin S can cause significant haemolysis. We report a 3-year-4-month-old girl from Bangladesh presenting with recurrent pallor since infancy, requiring multiple transfusions. Laboratory investigations revealed haemolytic anaemia, indirect hyperbilirubinaemia, high reticulocytosis, hepatosplenomegaly, and a positive sickling test. Hb electrophoresis confirmed Hb S/D-Punjab disease. Family screening revealed the mother is Hb S trait and father Hb D trait, while the sibling carried Hb S trait. She was managed with multiple transfusion, antibiotic, folate, zinc, and hydroxyurea. This case underscores the importance of considering compound haemoglobinopathies in children with recurrent haemolysis in Bangladesh and highlights the need for improved diagnostic and preventive strategies.

Keywords: Haemoglobinopathies, Hb D-Punjab, Hb S, Bangladesh, haemolytic anaemia.

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Introduction

Haemoglobinopathies are the most common monogenic disorder worldwide, with the highest burden in South Asia. In Bangladesh, around 10–12% of the population are carrier of a haemoglobin variant, mainly Hb E and β -thalassemia.^{1,2} Although Hb D is the fourth most common haemoglobin variant globally, it is rare in Bangladesh, and most cases remain underdiagnosed.³ Haemoglobin D-Punjab (also called Hb D-Los Angeles) results from a glutamic acid-to-glutamine substitution at codon 121 of the β -globin chain.⁴ In the heterozygous or homozygous state, Hb D-Punjab is usually asymptomatic or mildly anaemic.⁵ However, co-inheritance with Hb S or β -thalassemia can lead to significant morbidity due to haemolysis and vaso-occlusive complications.⁶

Reports of Hb S/D-Punjab disease are extremely rare in Bangladesh. Here we present a paediatric case, with emphasis on clinical features, diagnostic challenges, and implications for public health awareness in the Bangladesh context.

Case Report

A 3-year-4-month-old girl, the second child of a non-consanguineous couple, was admitted with fever, cough, and recurrent pallor. She had been experiencing pallor since 6 months of age, usually following respiratory tract infections, required multiple hospital admission and transfusion. She was treated symptomatically and remained well between episodes. However she was not evaluated properly earlier. Her current illness began with high-grade intermittent fever (up to 103°F), cough, respiratory distress, and progressive pallor for

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7 days. There was no history of bleeding, abdominal pain, jaundice-related pruritus, bone pain, neurological deficits, or travel to malaria-endemic region. On examination she appeared ill, febrile, tachypnoeic, and moderately pale, with mild icterus. There was chest indrawing, bilateral crepitations, hepatomegaly (3 cm), and splenomegaly (4 cm).

Laboratory investigations (Table 1) showed Hb: 7.0 g/dL, Hct: 22.7%, RBC: $2.83 \times 10^6 / \mu\text{L}$, WBC: $29,670 / \mu\text{L}$, Platelets: $472 \times 10^3 / \mu\text{L}$, Reticulocyte count: 15.05% and peripheral smear: anisopoikilocytosis, target cells, schistocytes, (suggestive of haemolytic anaemia), LDH: 599 U/L; Indirect hyperbilirubinaemia (Total 3.8 mg/dL, Indirect 3.23 mg/dL), Vitamin B12: 51

mcg (low), CRP: 68.8 mg/L, Coombs' tests: negative, Sickling test: positive. On haemoglobin electrophoresis (Table II) findings of the patient and family members showed patient had Hb S/D-Punjab disease (Figure-1), her mother had Hb S trait (Figure-2), her father had Hb D trait (Figure-3) and sibling had Hb S trait (Figure-4).

She was treated with intravenous antibiotic for pneumonia, received 2 unit packed cell transfusion, and hydroxyurea, folic acid, and zinc supplementation. Parents were counselled, genetic counselling was provided and the child was discharged on day 13 with advice for regular follow-up in paediatric haematology clinic.

Table I
Hematological profile of the patient

Parameter	Result	Reference range (3–5 years)	Interpretation
Haemoglobin (Hb)	7.0 g/dL	11–13 g/dL	Low (anaemia)
Hematocrit (Hct)	22.7%	33–39%	Low
RBC count	$2.83 \times 10^6 / \mu\text{L}$	$4.0\text{--}5.2 \times 10^6 / \mu\text{L}$	Low
WBC count	$29,670 / \mu\text{L}$	$6,000\text{--}15,000 / \mu\text{L}$	High (leukocytosis)
Platelet count	$472 \times 10^3 / \mu\text{L}$	$150\text{--}400 \times 10^3 / \mu\text{L}$	High (thrombocytosis)
Reticulocyte count	15.05%	0.5–1.5%	Markedly elevated
Peripheral smear	Anisopoikilocytosis, target cells, schistocytes	—	Suggestive of haemolysis
LDH	599 U/L	140–280 U/L	High (haemolysis)
Total bilirubin	3.8 mg/dL	0.2–1.2 mg/dL	Elevated
Indirect bilirubin	3.23 mg/dL	<1.0 mg/dL	Elevated
Vitamin B12	51 mcg	200–900 mcg	Low
CRP	68.8 mg/L	<10 mg/L	Elevated (infection)

Table II
Haemoglobin electrophoresis findings of the patient and family members

Individual	Hb Variant(s) Detected	Diagnosis
Patient (Index)	Hb S + Hb D-Punjab	Hb S/D-Punjab disease
Mother	Hb S trait	Sickle trait
Father	Hb D trait	Hb D trait
Sibling	Hb S trait	Sickle trait

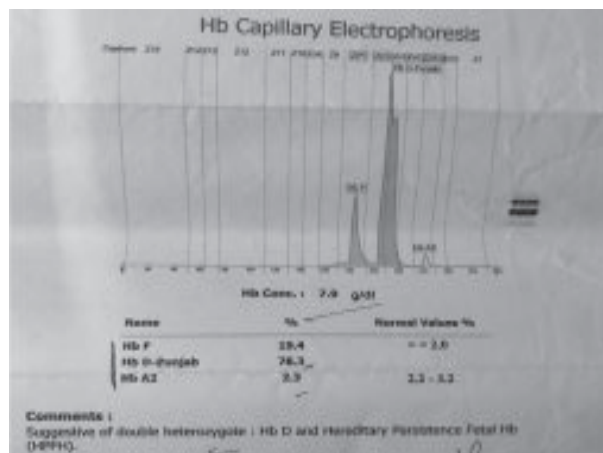


Figure 1. Haemoglobin electrophoresis of the patient showing compound heterozygosity for Hb S and Hb D-Punjab.

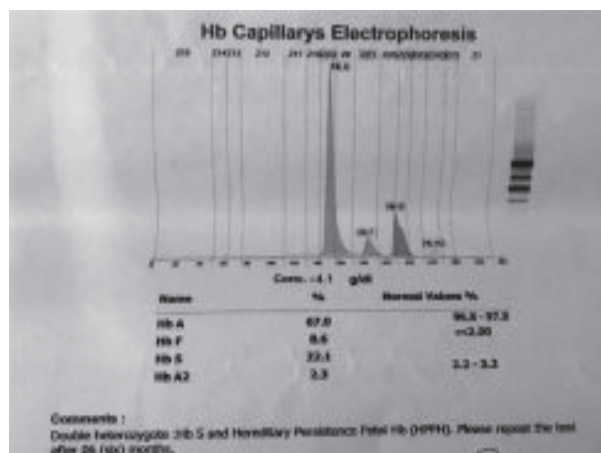


Figure 4. Haemoglobin electrophoresis of the sister showing Hb S trait (at 6 month age)

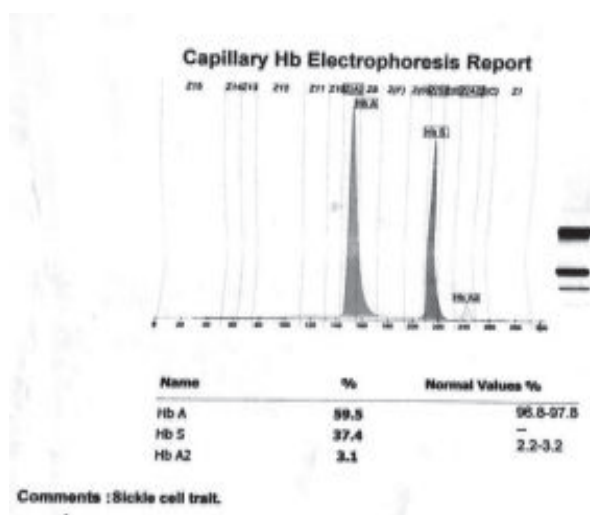


Figure 2. Haemoglobin electrophoresis of the mother showing Hb S trait.

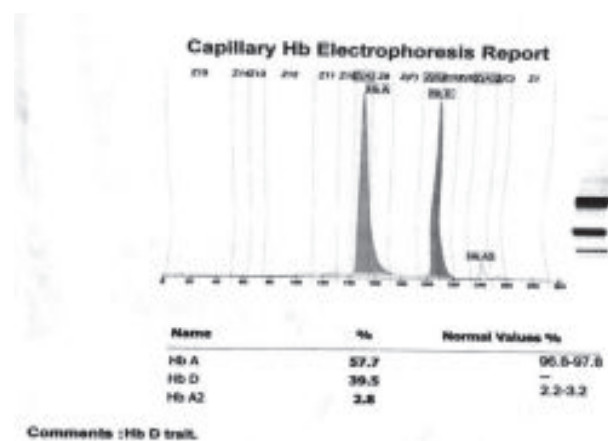


Figure 3. Haemoglobin electrophoresis of the father showing Hb D trait.

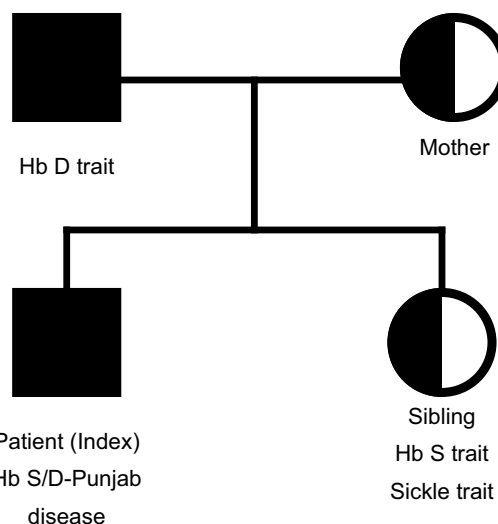


Figure 5. Pedigree diagram showing inheritance of Hb S/D-Punjab in the family.

Discussion

Hb D-Punjab is most frequently reported in Punjab (India and Pakistan), with carrier frequencies up to 2% in some Sikh communities.⁷ Although largely benign in the trait or homozygous state, its interaction with Hb S can mimic sickle cell disease.⁸ Patients often present with recurrent anaemia, haemolysis, splenomegaly, and vaso-occlusive episodes.

Our patient presented with recurrent haemolysis following infections, with high reticulocytosis, indirect hyperbilirubinaemia, and needs transfusion. This clinical picture is

consistent with Hb S/D-Punjab, which behaves similarly to sickle cell anaemia.

In Bangladesh, most haemoglobinopathy research has focused on Hb E and β -thalassemia.^{1,9} Rare variants like Hb D-Punjab are seldom diagnosed due to limited availability of HPLC (High-Performance Liquid Chromatography) and genetic testing. Around 10–12% of Bangladeshis carry a haemoglobinopathy, though Hb E and β -thalassemia predominate.^{1,2} Rare variants like Hb D-Punjab remain under-reported. Many cases may be misdiagnosed as thalassemia or sickle cell disease, leading to inappropriate management.

Most district-level hospitals lack HPLC or molecular facilities, leading to under-diagnosis of mixed haemoglobinopathies. Bangladesh lacks a national haemoglobinopathy control program, unlike Iran or Cyprus, where premarital/antenatal screening reduced disease incidence.¹⁰

This case illustrates the importance of family screening and genetic counselling, which revealed both parents as carriers of different haemoglobinopathies, placing future offspring at risk.

Hydroxyurea has been shown to reduce haemolysis and vaso-occlusive crises in Hb S/D-Punjab, though data is limited.¹¹ Supportive measures such as folate supplementation, vaccination, infection control, and transfusion remain cornerstones of management. Stem cell transplantation, the only curative option, is not widely available in Bangladesh.

Establishing a national screening strategy, strengthening diagnostic laboratories, and introducing genetic counselling services could reduce haemoglobinopathy-related morbidity in Bangladesh.

Conclusion

This case highlights Hb S/D-Punjab as a rare but clinically significant haemoglobinopathy in Bangladesh. Children with recurrent haemolysis should be evaluated with Hb

electrophoresis, and family members should undergo screening. Public health measures including premarital/antenatal screening and genetic counselling are urgently needed in Bangladesh to address the growing burden of haemoglobinopathies.

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