

Case Report

# Case Report of a Child with Beta Thalassemia Major in a Tribal Region of India

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## Abstract

**Introduction:** Thalassemia is an inherited blood disorder of haemoglobin (Hb) synthesis, which affects different regions around the world. India has the largest number of children with beta-thalassemia major in the world, particularly in the tribal population. Heterozygous conditions are milder and even go unreported than the condition of homozygous where regular blood transfusion is required.

**Case report:** This report focuses on a case of major beta-thalassemia in a child, whose parents are beta thalassemia minor to intermediate conditions, and who was treated by blood transfusion once a month. However, Thalassemia may be cured by allogeneic hematopoietic stem cell transplantation, although not everyone is a good candidate. Genetic counselling, prenatal diagnosis, and selective termination of affected fetuses are effective ways to control thalassemia.

**Discussion and conclusion:** The paper reports a unique case of Thalassemia in rural India. The blood disorder while commonly presented in a juvenile whose parents were Thalassemia positive resulted in the termination of a fetus diagnosed with it. It archives the story of the parents who are now in the process of planning future offspring while mitigating disease risk. The case leads the way for effective management and containment of hereditary genetic disorders through carrier detection while planning alliances and offspring.

## Introduction

Thalassemia refers to blood-related, hereditary genetic disorders classified as alpha and beta thalassemia according to the hemoglobin alpha and beta chain mutation respectively. Abnormal beta chain genes in pairs lead to major beta-thalassemia morbidity. Further single mutated gene of the beta chain causes Intermediate and Minor beta thalassemia conditions with confers to its severity [1]. Major thalassemia manifestation appears as early as 6-24 months in children with growth retardation, severe hemolytic anemia, fever abdomen pain, delayed development, and bone abnormalities and may lead to mortality in grim cases [2]. Complete blood count (CBC) includes HGB (hemoglobin), MCV (mean corpuscular volume), MCH (mean corpuscular hemoglobin), high-performance liquid chromatography

(HPLC) includes HbA (hemoglobin adult  $\alpha_2\beta_2$ ), HbA2 (hemoglobin subtype  $\alpha_2\delta_2$ ), HbF (hemoglobin fetal  $\alpha_2\gamma_2$ ) deviated ranges indicate the severity of the disorder ranging from minor, intermediate and major. According to Thalassemia International Federation transfusion must be done every 2-3 weeks for maintenance of hemoglobin (Hb) normal range (8 gm/dl) for proper growth and development of children up to 10-12 years [3]. The life expectancy of a patient can be increased further through bone marrow and hematopoietic stem cell transplantation. Novel techniques Erythropoiesis modification strategies, gene therapy, and gene editing technologies: using the editing tools like zinc-finger nucleases (ZFN), transcription activator-like effector nucleases (TALENs), and clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated-nuclease 9 (CRISPR-Cas9) are under experimentation [4,5].

## More Information

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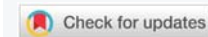
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**Keywords:** Beta-thalassemia; Blood transfusion; Genetic disorder; Hemoglobin

**Abbreviations:** Hb/HGB: Haemoglobin; CBC: Complete Blood Count; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; HPLC: High-Performance Liquid Chromatography; HbA: Hemoglobin Adult  $\alpha_2\beta_2$ ; HbA2: Hemoglobin Subtype  $\alpha_2\delta_2$ ; HbF: Hemoglobin Fetal  $\alpha_2\gamma_2$ ; PCR: Polymerase Chain Reaction



The physical, physiological, and financial burden of these treatments poses inaccessibility, especially in developing nations. The preventive medicines discussed in our case include genetic counseling, disorder carrier detection, and prenatal gene sequencing are approachable and effective tools for effective management of such genetic disorders.

## Case report

This case study is a classic example of family inheritance of beta thalassemia from the village of Shahdol, Madhya Pradesh, India. Our finding reports the case of a couple with beta thalassaemic minor, intermediate (HbA2) trait. Born to them major thalassaemic girl (present age 5.5 years) and a fetus diagnosed with beta thalassemia major at 13 weeks were terminated. Further planning a normal child for transplantation and family planning.

## Clinical findings

In the 7<sup>th</sup> month, the child was hospitalized with whitish tinge & paleness of the skin (hand and feet), growth retardation, and low Hb level (5gm/dl) symptoms (Table 1). Treated with blood transfusion 1<sup>st</sup> time and recovered well.

At the 9<sup>th</sup> month, she was admitted to the hospital with fever, weight loss, retarded growth, shortness of breath, and severe anemia. Based on the CBC report and physical examination concludes blood-related genetic disorder. Elevated HbA2 and HbF were observed. Recommended HPLC at the age of 1 year and showed minor thalassemia trait in child and mother.

At the 11<sup>th</sup> month of age, rehospitalization was done due to chronic anemia (sudden drop in hemoglobin level). Treated with blood transfusion and iron chelating therapy with DFO and Deferasirox. Suggested for family CBC and HPLC/Hb electrophoresis tests for a clear diagnosis of beta thalassemia trait (Table 2).

At the 13<sup>th</sup> month, Hb electrophoresis test (Table 3) concluded beta thalassemia minor traits in father (HbA2:

**Table 1:** CBC parameters, MCV: mean corpuscular volume, MCH: Mean corpuscular haemoglobin.

CBC parameter	7 months old	11 months old	Mother	Father	Reference range
Hemoglobin (g/dl)	5.50	3.6	11.1	15.3	13 - 17
MCV (fl)	78.40	66.7	61.8	83.5	80 - 99
MCH (pg)	18.90	19.4	18.5	27.7	26 - 32
RBC count (ml/mm <sup>3</sup> )	2.91	1.86	-	5.53	3.90 - 5.10
Neutrophil %	17	45	-	-	50 - 70
Lymphocyte %	74	49	-	-	20 - 40

**Table 2:** HPLC Analysis, A: Adult, F: fetal, A2: hemoglobin subtype A.

HPLC parameters	7 months old	Mother	Father	Reference Range
HbA	36.60%	94.1	95.6	94.3% - 98.5%
HbF	50.20%	0.8	1.4	0.2% - 2.0%
HbA2	4.30%	5.1	3.0	2.0% - 3.4%
RBC Appearance	Microlytic, hypochromic	Microcytic, hypochromic	Normocytic, normochromic	Normocytic, normochromic

**Table 3:** Electrophoresis Pattern of the case and her family.

Hb electrophoresis pattern	13 months old	Mother	Father	Reference range
HbA2 (%)	4.1*	5.5	3.8	2.0 - 3.4

\*Either due to repeated blood transfusion or sample collected just after blood transfusion, test may be masked the suspected beta thalassemia major

3.8%, higher), intermediate thalassaemic mother (anemic with HbA2: 5.5%, higher) and child with beta-thalassemia major (HbF: 6.2%). Confirmation of beta thalassemia major was done by molecular testing of the patient. Other biochemical tests like liver function tests, urine tests, and ferritin levels, thyroid tests performed were observed to be normal. With these findings, regular blood transfusion and iron chelating therapy are advised for up to 10-12 years of age for proper growth and development. Further bone marrow or hematopoietic stem cell transplantation is suggested to avoid secondary symptoms associated. Currently, she is on regular follow-ups and doing well.

The couple planned the birth of another child for bone marrow transplantation or hematopoietic stem cell transplantation by prenatal diagnosis early termination of the fetus (13 weeks old) was done due to abnormality.

## Discussion

India has the largest number of children population suffering from Thalassemia major in the world, particularly in tribal population prevalence rate (0.36% - 13.20%) is higher compared to non-tribals [6,7]. Particularly in central and northern India presence of disease is exorbitant. In Madhya Pradesh population 76% of the population suffers from anemia associated with hemoglobinopathies but reporting is difficult due to unawareness [7,8]. Primary symptoms are microcytic and hypochromic anemia (mean corpuscular volume < 70fL). The normal level of Ferritin level (24 ng/mL to 336 ng/mL for adult males) in serum [9] helps in the control of secondary symptoms with regular blood transfusion i.e. heart (dilated cardiomyopathy and pericarditis), liver (chronic hepatitis, fibrosis, and cirrhosis), endocrine gland (diabetes mellitus, hypoparathyroidism, hypothyroidism, hypopituitarism, and low adrenal secretion).

Bone marrow or hematopoietic stem cell allogeneic transplantation [10] after 10-12 years in a child increases the life expectancy.

The case described here underscores several critical aspects of thalassemia management. The patient's initial presentation with severe anemia, hepatosplenomegaly, and growth retardation is typical of  $\beta$ -thalassemia major, the most severe form of the disease. Early diagnosis is paramount, a first confirmative test was done by complete blood count, abnormal hemoglobin count, and unresponsiveness of iron supplements. The severity of the case was detected through HPLC (high-performance liquid chromatography) or capillary electrophoresis by measuring fractions of



hemoglobin subtypes haemoglobin F (major thalassemia), haemoglobin a<sub>2</sub> (intermediate and minor), confirming the homozygous  $\beta^0/\beta^0$  genotype. The patient's third line of conformation prenatal diagnosis can be done by Gap-PCR and DNA sequencing [11,12].

Since infancy, the patient has been receiving regular blood transfusions, which have significantly improved their quality of life and prevented complications associated with severe anemia. However, iron overload remains a major concern in thalassemia patients undergoing chronic transfusion therapy [13]. Effective iron chelation therapy, as demonstrated in this case, is essential to prevent iron-induced organ damage, particularly in the heart and liver. Regular monitoring of serum ferritin levels and cardiac function is crucial to adjust chelation therapy appropriately [14,15].

In our case, the proactive role of parents and health workers helped in the early screening of beta-thalassemia major to greatly improve the child's condition, additionally preparing them for future endeavors of family planning.

## Conclusion

In conclusion, this case highlights the clinical challenges and complexities associated with the management of  $\beta$ -thalassemia major. Through early diagnosis, comprehensive care, and vigilant monitoring, individuals with thalassemia can lead fulfilling lives despite the burdens of their condition. Moreover, ongoing research into curative therapies to overcome iron overload in case of transfusion and advanced diagnosis techniques offers hope for a brighter future for thalassemia patients worldwide.

Awareness and early diagnosis of disorder assist couples in planned parenthood even with the hereditary disease. Our case study assists the health care provider and young couples in thalassemia cases in early diagnosis and timely action plan. To reduce the burden of this malady effective management of carries by genotyping in prevalent areas and literacy among the masses about various hereditary disorders is a preventive cure.

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