

The Masked Thalassemia: A Rare Case of a Patient with Normal HbA2 Levels, β -Thalassemia Pathogenic Variant (CD39 C>T), and a Novel δ -Globin Gene Deletion

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Abstract: Thalassemia is a group of inherited blood disorders caused by defects in hemoglobin production, the protein that transports oxygen in red blood cells. These diseases are characterized by either diminished or missing production of one of the globin chains, which are often the alpha or beta chains that comprise hemoglobin. Diagnosis is based on a combination of laboratory tests, including hemoglobin electrophoresis, globin chain chromatography, and genetic analysis. However, diagnosis can become challenging when typical hematological features of thalassemia are not matched by expected biochemical findings. One such situation occurs when HbA2 levels appear normal despite a suspected β -thalassemia trait. This can happen when a β -globin gene variant is present alongside a δ -globin gene pathogenic variant, producing an atypical profile that may mask the true diagnosis. In this case report, we describe a patient carrying a heterozygous β -globin pathogenic variant (*HBB* c.118C>T; p.Gln40Ter, also known as codon 39) coexisting with a large novel 1.6 kb deletion in the delta-globin gene (*HBD*) that removes the first two exons. We discuss the diagnostic challenges and clinical implications associated with this rare genetic combination, emphasizing the critical role of comprehensive molecular testing in accurately identifying complex thalassemia cases. This report contributes to the literature by documenting a novel δ -globin deletion in combination with a β -thalassemia variant, providing valuable insights for clinicians and geneticists in the interpretation and management of atypical thalassemia profiles.

Keywords: β -thalassemia, novel δ -globin deletion, normal HbA2, masked thalassemia, molecular diagnosis, next-generation sequencing

Introduction

Thalassemia is a form of hemolytic anemia caused by variants or deletions in the globin gene, leading to impaired synthesis of globin chains. It is a hereditary condition that poses serious public health consequences. The disease is prevalent mainly in the Mediterranean region, the Middle East, Southeast Asia, Africa, and the Indian subcontinent, with marked ethnic and geographic variations. In Italy, thalassemia is especially widespread in southern regions such as Sicily, Sardinia, Calabria, and Apulia.¹

The clinical diagnosis of thalassemia primarily relies on hematological screening and genetic testing. Hematological investigations typically include a complete blood count (CBC) to assess red blood cell indices and detect microcytosis or anemia, hemoglobin electrophoresis for the identification and quantification of abnormal hemoglobin variants, and, less commonly, red blood cell osmotic fragility testing. Although this test is now used less frequently due to advances in molecular diagnostics, it remains useful in certain cases, such as distinguishing specific forms of thalassemia from other microcytic anemias, by evaluating the susceptibility of erythrocytes to hemolysis under hypotonic conditions. Genetic

analysis is essential to identify the major variants or deletions associated with thalassemia, particularly within the Italian context.²

One of the most common β -thalassemia variants in Italy is the codon 39 (*HBB* c.118C>T) nonsense variant, which accounts for approximately 30–40% of β -thalassemia variants in the Italian population. This pathogenic variant introduces a premature stop codon, leading to the absence of β -globin chain production and a β^0 -thalassemia phenotype.³

In Campania, the codon 39 variant is among the most frequent, as evidenced by its presence in the genotypes of transfusion-dependent thalassemia (TDT) or non-transfusion-dependent thalassemia (NTDT) patients followed at the hemoglobinopathy center of Cardarelli Hospital in Naples.^{4,5}

A study conducted in the province of Trapani, Sicily, identified 12 distinct β -globin pathogenic variants, with *HBB* c.118C>T accounting for 38% of cases. Other frequently observed variants included IVS1.6 T>C and IVS1.110 G>A, indicating their significant role in the regional β -thalassemia spectrum.⁶ Similarly, a broader study across various Sicilian provinces confirmed codon 39 as the most prevalent variant, representing 31.85% of the β -globin gene variants identified.^{7,8}

In northern Italy, particularly in the Po Delta area, *HBB* c.118C>T remains a significant pathogenic variant. It is often found in compound heterozygosity with the IVS1.110 (G>A) variant, contributing to the β^+ -thalassemia phenotypes in that region. The widespread distribution of the *HBB* c.118C>T variant across different Italian regions underscores its relevance in molecular diagnostics and genetic counseling for β -thalassemia.⁹

Another notable genetic alteration is the deletion of the δ -globin gene. In Italy, particularly in southern regions such as Sicily, Campania, and Basilicata, deletions and pathogenic variants of the δ -globin gene (*HBD*) are relatively common and can complicate the diagnosis of β -thalassemia.¹⁰

A study conducted in Sicily screened 7153 individuals for β -thalassemia and identified δ -globin gene variants in 183 cases (about 2.5%). The researchers found 12 distinct pathogenic variants, five of which were previously unreported, reflecting the region's notable genetic diversity.¹¹ In Basilicata, the screening of nearly 10,000 students revealed 53 carriers of δ -globin gene variants from 43 unrelated families. Similarly, in Campania, cases were identified during routine thalassemia counseling, uncovering 12 different alleles, including four novel variants and two novel variants in noncoding regions.¹²

These δ -globin gene alterations can result in normal or decreased HbA2 levels, potentially masking the presence of β -thalassemia when relying solely on standard hematological parameters. Therefore, comprehensive molecular analysis is essential for an accurate diagnosis and effective genetic counseling in these populations. This scenario illustrates the critical importance of genetic testing in detecting atypical β -thalassemia carriers, where concurrent δ -globin gene deletions may lead to misleading hematological profiles.¹³

Methods

Sample Collection and DNA Extraction

The patient provided written informed consent for the publication of the case details. The study was carried out in strict accordance with the institutional regulations of the Ethics Committee of Cardarelli Hospital, Naples, Italy, and with national regulatory guidelines. In line with these regulations, no additional institutional approval was required for the publication of this case report. The advanced genetic testing was performed as part of a diagnostic development protocol and did not incur additional costs for the patient. Genomic DNA was extracted from whole blood samples using the MagCore® Automated Nucleic Acid Extraction System (RBC Bioscience). For each sample, 200 μ L of whole blood was processed with the MagCore® Genomic DNA Whole Blood Kit, following the manufacturer's standard protocol. DNA concentration and purity were assessed using a NanoDrop™ spectrophotometer (Thermo Fisher Scientific).

Library Preparation

For the genetic diagnosis of thalassemia, DNA libraries were prepared using the Devyser Thalassemia v2 library preparation kit, a state-of-the-art solution that integrates multiple detection strategies into a single next-generation sequencing (NGS)-based workflow. This approach significantly streamlines the diagnostic process, reduces hands-on time, and enhances overall efficiency. Genomic DNA was processed in accordance with standardized procedures to ensure high-quality and intact DNA suitable for downstream NGS applications.

The kit includes reagents for library preparation, such as unique sample-specific indices for multiplexing and components for post-amplification purification. The library preparation protocol follows a simplified, contamination-minimizing workflow, ensuring reproducibility and high performance.

Target Enrichment

Devyser Thalassemia v2 enables target specific library generation for NGS analysis of genetic variants (SNVs, indels, and CNVs) in the *HBA1*, *HBA2*, *HBD*, *HBG1*, *HBG2*, and *HBB* genes.

Common deletions in alpha and beta thalassemia are detected with a direct detection (DD) method using primers aligned to both ends of the deletion (GAP-PCR). For the direct detection of the $\alpha 3.7$ and $\alpha 4.2$ deletions, Long Range-PCR is used to target the regions flanking the deletion. Other regions within the alpha- and beta-globin gene clusters are included for detection of CNVs by relative sequence coverage analysis. Beta thalassemia modifiers, including critical regulatory elements such as *KLF1*, *HBSIL-MYB*, and *BCL11A*, are also part of the design, with complete sequencing of all *KLF1* exons, due to their role in modulating HbF expression. Several other deletions in alpha- and beta-globin can be detected by relative sequence coverage analysis CNV.

Sequencing

Sequencing was performed on a compatible NGS platform, specifically the Illumina MiSeq system, using a paired-end mode with 150 bp read length. Standard Illumina protocols were followed to ensure high-quality data output, with deep coverage across all target regions to facilitate precise variant detection. This configuration supports the reliable identification of both single-nucleotide variants (SNVs) and structural changes across all relevant genes (Figure 1).

Bioinformatics Analysis

Post-sequencing data analysis was conducted using Amplicon Suite (SmartSeq), which offers efficient and intuitive interpretation of genetic variants. The software is specifically optimized for thalassemia diagnostics and includes advanced tools for the evaluation of genetic modifiers that may influence the clinical manifestation of beta-thalassemia. The pipeline integrates variant annotation, pathogenicity classification, and CNV analysis, providing a comprehensive molecular profile for each patient (Figure 2).

Case Report

A 51-year-old Caucasian male was referred to the Rare Red Blood Cell Disorders Clinic at Cardarelli Hospital (Naples) for further evaluation of a chronic microcytic anemia. The patient was referred for evaluation due to persistent microcytosis and hypochromia despite normal iron studies, combined with a family history of microcytic anemia, raising clinical suspicion for a thalassemia trait. The absence of prior testing is unknown, but this is not uncommon in asymptomatic adults.

Despite a relatively preserved hemoglobin level of 12.1 g/dL, laboratory findings were indicative of microcytosis (MCV: 62.2 fL) and hypochromia (MCH: 20.0 pg), accompanied by an elevated red blood cell count ($6.06 \times 10^6/\mu\text{L}$), which is a typical feature suggestive of a thalassemic phenotype. However, high-performance liquid chromatography (HPLC) revealed HbA₂ at 2.7% and HbF at 1.2%, values that do not align with the classical hematologic profile of β -thalassemia trait, which is usually characterized by elevated HbA₂ levels (>3.5%). Iron studies were within normal limits (serum iron: 100 $\mu\text{g/dL}$; ferritin: 228 ng/mL), effectively ruling out iron deficiency anemia as a cause of the microcytosis. The discordance between the hematologic indices and HbA₂ levels raises the possibility of an atypical β -thalassemia variant with normal HbA₂, a diagnostic challenge that may be explained by the presence of a δ -globin gene mutation co-inherited with β -thalassemia.¹⁴

Given the persistent clinical suspicion, molecular testing via NGS was performed. This revealed a heterozygous *HBB* c.118C>T (codon 39) variant, commonly associated with β^0 -thalassemia, and a 1.6 kb deletion identified in the delta-globin gene (*HBD*, NM_000519), located on chromosome 11 between positions 5,254,354 and 5,255,926. The deletion spans a continuous genomic region covered by multiple overlapping amplicons (HBD_9 through HBD_1), indicating loss of the entire segment from amplicon HBD_9 (chr11:5,254,354–5,254,514) through HBD_1

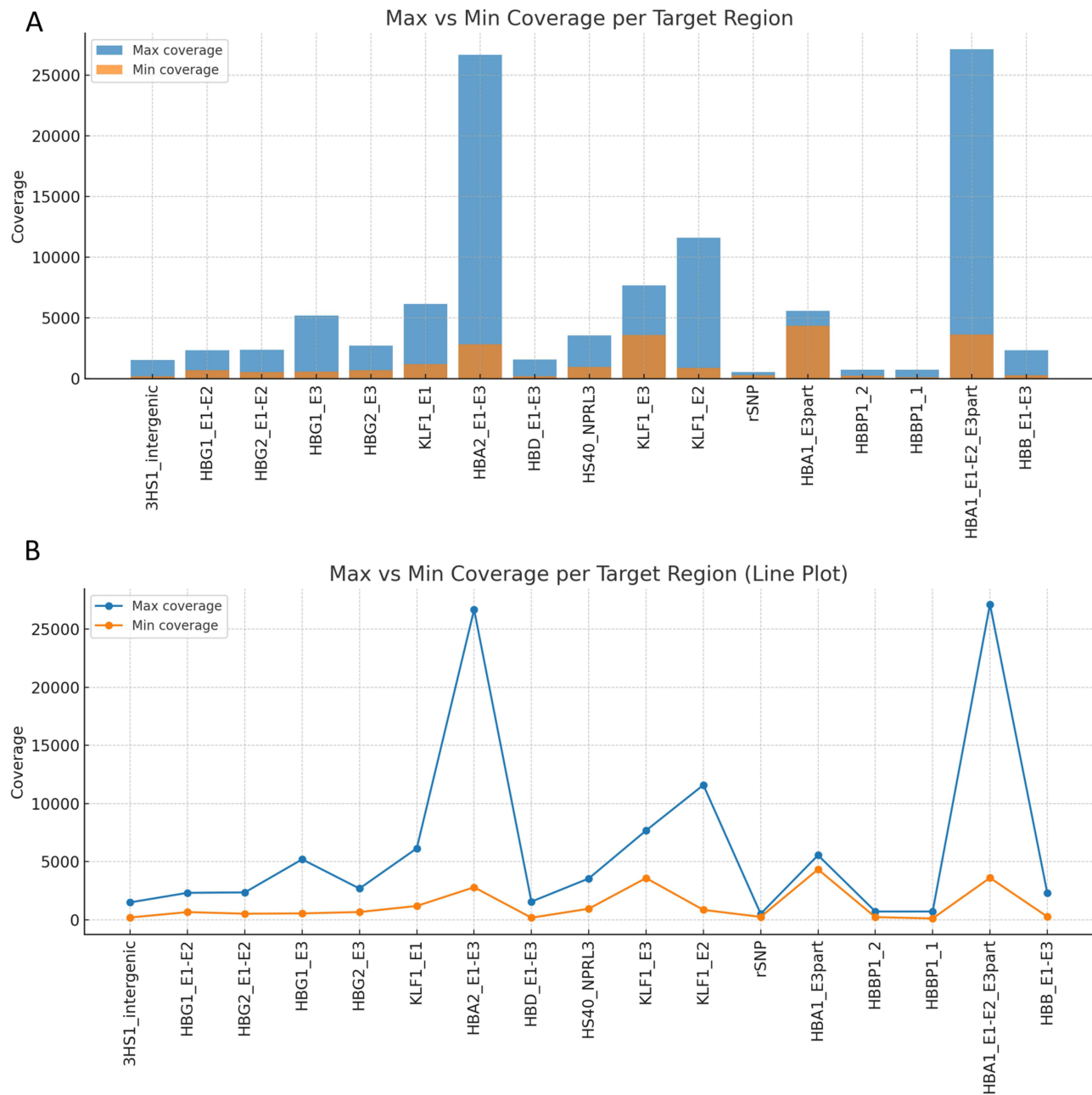


Figure 1 Coverage distribution across target regions. ((A) bar chart) displays the maximum (blue) and minimum (Orange) coverage values for each target region, allowing direct comparison of absolute read depth levels. Regions such as HBA2_E1-E3 and HBA1_E1-E2_E3 part exhibit the highest maximum coverage (>25,000), while others such as HBBP1_1 and rSNP show much lower values (<1000). The bar chart highlights the wide variability in sequencing depth across different loci, with consistently high coverage (>200×). ((B) line chart) presents the same data in a trend format, emphasizing the relative differences between maximum and minimum coverage across regions. The parallel shape of the two lines indicates that although coverage levels vary greatly between targets, the relationship between maximum and minimum coverage remains broadly consistent. All target regions achieved 100% coverage >200×, indicating high-quality and reliable sequencing performance across all analyzed loci.

(chr11:5,255,698–5,255,926). A comprehensive search of IthaGenes, HbVar, ClinVar and public structural-variation resources did not reveal an identical record; therefore, we consider this deletion novel. This extensive deletion affects both exonic and intronic sequences, and given its size and position, it is expected to disrupt normal transcription of *HBD*, most likely leading to the absence or severe reduction of delta-globin chain production. Codon 39 introduces a premature stop codon, leading to either truncated protein production or mRNA degradation via nonsense-mediated decay (NMD), thereby abolishing β -globin synthesis.¹⁵

A

Position	Class	VCC	Report	Type	Transcript	c.HGVS	p.HGVS	# Samples (Closed)	# Samples (All)	dbSNP ID	VAF%	Gene	Amplicon
chr11:g.5248004G>A	5	H		s_SPG	NM_000518.5	c.118C>T	p.Gln40Ter	0	8	rs11549407	53.1	HBB	HBB_4
chr11:g.5246356T>A	3	H		s_3OG	-	-	-	0	34	rs10837631	42.04	HBB	HBB_13
chr19:g.12996740A>G	1	H		s_MV	NM_006563.5	c.304T>C	p.Ser102Pro	0	8	rs2072597	98.45	KLF1	KLF1_E02_2
chr16:g.223735A>G	1	H		s_3OG	-	-	-	0	65	rs2685121	98.5	HBA2	HBA2_7
chr16:g.223706A>G	1	H		s_3UTR	NM_000517.6	c.*107A>G	-	0	70	rs2541640	98.46	HBA2	HBA2_7
chr11:g.5270539C>A	1	H		s_INT	NM_000559.3	c.315+59G>T	-	0	15	rs33988501	53.57	HBB	HBB_14
chr11:g.5269799A>C	1	H		s_INT	NM_000559.3	c.316-82T>G	-	0	16	rs28440105	53.39	HBB	HBB_17
chr11:g.5269583_5269586delinsAGAG	1	H		s_3UTR	NM_000559.3	c.*3_6delinsCTCT	-	0	16	rs386750130	42.46	HBB	HBB_1_8
chr11:g.5248243A>G	1	H		s_SYV	NM_000518.5	c.9T>C	p.His3=	0	71	rs713040	98.06	HBB	HBB_2
chr11:g.5247791C>G	1	H		s_INT	NM_000518.5	c.315+16G>C	-	0	71	rs10768683	99.58	HBB	HBB_5
chr11:g.5247733A>C	1	H		s_INT	NM_000518.5	c.315+74T>G	-	0	55	rs7480526	51.44	HBB	HBB_5
chr11:g.5247141G>A	1	H		s_INT	NM_000518.5	c.316-185C>T	-	0	71	rs1609812	98.61	HBB	HBB_9
chr11:g.5246512T>G	1	H		s_3OG	-	-	-	0	71	rs7110263	99.08	HBB	HBB_12
chr16:g.163667G>A	0	H		s_INT	NM_001077350.3	c.394-893C>T	-	0	49	rs11865131	54.02	NPR3	HS40_2
chr16:g.163598G>A	0	H		s_INT	NM_001077350.3	c.394-824C>T	-	0	49	rs11248850	51.99	NPR3	HS40_1
chr11:g.5275802G>A	0	H		s_INT	NM_000184.3	c.93-58C>T	-	0	14	rs1894398	45.83	HBB	HBB_2_3
chr11:g.5275407T>C	0	H		s_INT	NM_000184.3	c.315+115A>G	-	0	14	rs2070973	52.07	HBB	HBB_2_5
chr11:g.5275343C>T	0	H		s_INT	NM_000184.3	c.315+179G>A	-	0	14	rs11036476	52.06	HBB	HBB_2_5
chr11:g.5275240G>A	0	H		s_INT	NM_000184.3	c.315+282C>T	-	0	14	rs11036475	52.79	HBB	HBB_2_6
chr11:g.5274717A>C	0	H		s_INT	NM_000184.3	c.316-82T>G	-	0	15	rs2070972	52.32	HBB	HBB_2_7
chr11:g.5274267C>T	0	H		s_3OG	-	-	-	0	14	rs2236794	49.11	HBB	HBB_2_9
chr11:g.5270878G>A	0	H		s_INT	NM_000559.3	c.93-58C>T	-	0	14	rs202216517	48.02	HBB	HBB_1_3
chr11:g.5270418A>G	0	H		s_INT	NM_000559.3	c.315+180T>C	-	0	14	rs11036455	51.13	HBB	HBB_1_5

B

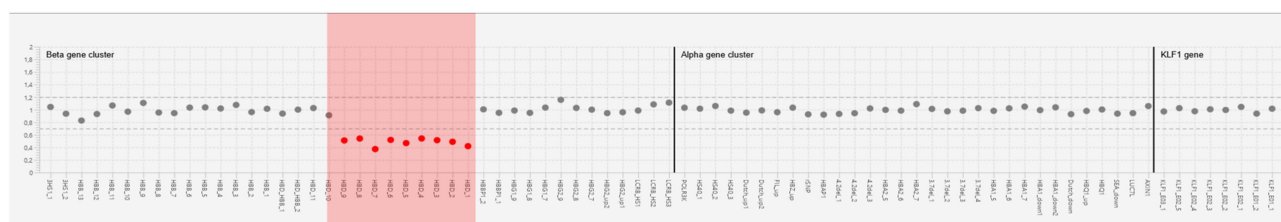


Figure 2 The image is divided into two main sections. ((A) upper part) is a screenshot from analysis software displaying a list of sequence variants. The table contains multiple columns, each representing different attributes of the detected variants: The first row is highlighted in red, corresponding to a pathogenic nonsense variant in the *HBB* gene (chr11:g.5248004G>A, c.118C>T, p.Gln40Ter), with a VAF of 53.1%. Other rows represent different synonymous, intronic, or non-coding variants with various allele frequencies. ((B) lower part) shows a scatter plot used to detect copy number variations (CNVs). The x-axis represents different amplicons spanning across genomic regions (beta gene cluster; alpha gene cluster; KLF1 gene). The y-axis shows relative copy number values (normalized ratio). Each dot corresponds to an amplicon, with gray dots indicating normal copy number and red dots highlighting abnormal regions. A cluster of red dots is clearly visible in the delta gene region, suggesting a copy number loss in this genomic area.

Heterozygous carriers of β -thalassemia variants typically show elevated HbA₂ levels (3.5–7%), reflecting compensatory overproduction of the δ -globin chain encoded by *HBD*, since HbA₂ ($\alpha_2\delta_2$) normally accounts for only 2–3% of total hemoglobin.¹⁶ When a β -thalassemia variant coexists with a δ -globin gene deletion, this compensatory response is abolished due to impaired δ -globin synthesis, leading to normal or even reduced HbA₂ levels. Rare cases of such combined defects have been reported, producing atypical diagnostic profiles in which β -thalassemia carriers do not exhibit the expected HbA₂ increase, thereby complicating diagnosis. A δ -globin deletion alone reduces δ -globin synthesis and maintains HbA₂ levels below the normal range (2–3.5%).^{17,18} In certain case, especially when the deletion encompasses both the δ - and β -globin gene clusters, as in $\delta\beta$ -thalassemia, there is a substantial upregulation of fetal hemoglobin (HbF), which often reflects the persistent expression of γ -globin genes into adulthood. This phenomenon arises because the deletion of both δ - and β -globin genes abolishes the production of adult forms of hemoglobin (HbA₂ and HbA), leading to compensatory de-repression of γ -globin expression. The resulting increase in HbF helps mitigate the α/β -chain imbalance characteristic of thalassemia, thereby improving erythropoietic efficiency and ameliorating anemia.^{19,20}

The genetic modifiers of β -thalassemia that can be thoroughly investigated with NGS include the Genome Risk Score (GRS) and the Thalassemia Severity Score (TSS), which are primarily designed to predict the severity of the disease in homozygous or compound heterozygous patients.²¹ These scoring systems integrate the contribution of single nucleotide

polymorphisms (SNPs) at loci such as BCL11A, HBS1L-MYB, and the HBG2/HBBP1 region, which are recognized quantitative trait loci (QTLs) involved in the regulation of HbF.^{22–25} In the present case, however, which represents an asymptomatic carrier state without increased HbF, these indices provide limited additional value, as their predictive utility is mainly relevant in patients with overt β -thalassemia. Developed by Danjou et al in 2015, the Thalassemia Severity Score (TSS) represents a significant refinement in the correlation of genotype to phenotype for β -thalassemia major and intermedia. This scoring system achieves a more nuanced prognostic picture by integrating a patient’s genetic information with pivotal clinical surrogates, most notably the age at first transfusion. The TSS was derived from the distribution of a linear predictor score, resulting in a continuous scale from 0 to 10 designed to quantify increasing disease severity. This scale is categorized into tiers of clinical impact: a low severity classification corresponds to a TSS of less than 3, mild severity is indicated by a score greater than or equal to 3 but less than 5, high severity encompasses scores from 5 to below 7, and a very high severity designation is reserved for scores of 7 and above.²¹

While this score is highly informative for distinguishing transfusion-dependent from non-transfusion-dependent forms, and for guiding therapeutic strategies and genetic counseling,²⁶ its application is of marginal relevance in a clinically silent carrier. Nevertheless, although GRS and TSS are not directly applicable in this context, the comprehensive genomic data obtained through NGS remain valuable for clarifying carrier status and preventing diagnostic misclassification (Figure 3).



Figure 3 Genetic modifiers of β -thalassemia analyzed using NGS, including the Genome Risk Score (GRS) and the Thalassemia Severity Score (TSS), which are primarily designed to predict disease severity in homozygous or compound heterozygous patients. ((A) top) summarizes the genotypes of key SNPs affecting fetal hemoglobin (HbF) levels and their contributions to the GRS, which totals 5 in this case. ((B) bottom left) shows the parameters used to calculate the TSS, integrating both genotype and phenotype data. ((C) bottom right) illustrates the predicted TSS of 3.2, indicating mild clinical severity, as reflected by the violet transfusion-free survival curve. TSS was derived from the linear predictor score distribution to obtain a scale of increasing severity ranging from 0 to 10 (low severity TSS ≤ 3 , mild severity TSS ≤ 5 , high severity TSS ≤ 7 , very high severity TSS ≥ 7).

Discussion

Thalassemia, in its multifaceted genetic expression, is not only a hematological disorder but also a mirror of human history, evolution, and displacement. Its persistence across centuries testifies to the selective advantage conferred in malaria-endemic regions, while its present-day distribution reflects the accelerated mobility of populations driven by migration and globalization. What was once a geographically circumscribed condition now emerges in diverse populations and new clinical contexts, raising novel challenges for diagnosis, prevention, and management. Thalassemia thus embodies a convergence of medical science, human migration, and social responsibility. The burden of this disorder extends far beyond its biological basis. Healthcare systems are compelled to adapt by integrating molecular diagnostics, genetic counseling, and culturally sensitive strategies for care delivery. The introduction of NGS has revolutionized our approach, providing unprecedented accuracy in identifying both classical mutations and rare or novel variants, such as large deletions in the δ -globin gene. These molecular tools not only refine diagnostic precision but also expand our capacity to predict complex interactions between variants, a crucial advance in an era when compound heterozygosity is increasingly observed in migrant populations.²⁷ Indeed, the intensification of migratory flows has dramatically altered the genetic landscape of thalassemia. Individuals now present with composite genotypes that were previously rare or geographically isolated. δ -globin deletions, for example, may coexist with β -thalassemia variants, producing hematological profiles that defy traditional interpretative frameworks. In such cases, the expected hallmark of β -thalassemia carriers (elevated HbA₂) may be absent, leading to underdiagnosis or misclassification. Several examples of carriers with normal HbA₂ due to δ -globin deletions or isolated δ -globin gene losses in individuals with β -thalassemia variants that result in falsely normal HbA₂ levels have been reported in the literature.^{28,29} Similarly, Kocak et al illustrated the diagnostic ambiguity of an HBB C.118C>T heterozygote with borderline HbA₂ and microcytosis, where molecular testing uncovered a concurrent δ -globin deletion.³⁰ These cases underscore how traditional biochemical screening, once considered definitive, is insufficient in the face of evolving mutational spectra shaped by migration.

The clinical ramifications are extensive, and misinterpreting a thalassemic profile may lead to improper treatment, including superfluous iron supplementation for suspected iron deficiency anemia. More critically, undetected carriers may unknowingly transmit severe genotypes to their offspring if their partner is also a carrier, leading to β -thalassemia major in children.³¹ Genetic counseling thus becomes crucial, requiring family-wide analysis to uncover hidden risks and prevent reproductive consequences. The detection of atypical variants highlights the importance of comprehensive molecular testing in all suspected cases, regardless of biochemical outcomes. These situations, increasingly observed in multiethnic populations, require clinicians to reconcile inconsistent laboratory findings with detailed molecular data. They also emphasize the need for more advanced approaches to genetic counseling, particularly in culturally diverse settings where health literacy and access to genomic medicine can differ significantly.³²

Thalassemia ultimately illustrates the complex intersection of biology, society, and ethics. It is both a medical condition and a reflection of human migration, carrying the imprint of past selective pressures while posing new challenges in a globalized world. Its management requires more than scientific innovation; it demands a collective commitment to equity, autonomy, and the preservation of human dignity. As technological capacity advances alongside demographic change, the future of thalassemia care will depend not only on identifying rare and compound genetic variants but also on ensuring fair access to treatment and supporting resilience in affected individuals and their families. Addressing it with foresight and compassion will define our ability, as both scientists and as a global community, to meet this evolving burden.³³

Conclusions

This case demonstrates that normal HbA₂ levels on globin fraction chromatography do not exclude a thalassemia diagnosis. Given the heterogeneity of the disorder, reliance on a single test is insufficient; accurate diagnosis requires integration of clinical evaluation, hemoglobin studies, and molecular analysis. Advances in sequencing technologies now allow precise identification of rare and complex variants that conventional methods may overlook. The adoption of NGS-based approaches represents a major step forward in the molecular diagnosis of thalassemia, offering rapid, reliable, and comprehensive genetic profiling while improving the detection of clinically relevant variants.

Informed Consent Statement

All research activities were carried out in full compliance with institutional guidelines and national regulations governing the ethical conduct of research involving human subjects. The study protocol adhered to the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments. The patient gave their written informed consent, which permitted the use of their medical data for scholarly publications, even if those data were anonymized. After being fully informed of the study's purpose, the patient consented to the publication of the anonymized data.

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Disclosure

The authors report no conflicts of interest in this work.

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