e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 1450-1456

Original Research Article

Sickle Cell Anemia and Thalassemia: A Comparative Study of Clinical Profile, Hematological Parameters and Pulmonary Hypertension

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Received: 01-03-2026 / Revised: 15-04-2026 / Accepted: 21-05-2026

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Conflict of interest: Nil

Abstract

Background: Hemoglobinopathies are among the most common inherited monogenic disorders worldwide and represent a significant public health burden, particularly in developing countries. Sickle cell anemia (SCA) and thalassemia are the most prevalent hemoglobinopathies and are associated with chronic anemia, recurrent hospitalizations, organ dysfunction, and premature mortality. Advances in transfusion therapy, iron chelation, hydroxyurea treatment, and supportive care have substantially improved survival, resulting in increasing recognition of chronic cardiovascular complications.

Aim: To compare the clinical profile, hematological parameters, and prevalence of pulmonary hypertension among patients with sickle cell anemia and thalassemia.

Materials and Methods: A prospective cross-sectional observational study was conducted among 50 patients with confirmed hemoglobinopathies attending a tertiary care teaching hospital between December 2017 and October 2019.

Results: Among the 50 patients studied, sickle cell anemia constituted 40% of cases, beta-thalassemia major 12%, beta-thalassemia intermedia 8%, beta-thalassemia trait 14%, sickle cell trait 12%, and compound hemoglobinopathies 14%. Severe anemia (Hb <7 g/dL) was observed in 48% of patients. Pulmonary hypertension was identified in 58% of patients, with mild pulmonary hypertension accounting for 52% of cases. Among sickle cell anemia patients, 70% demonstrated mild pulmonary hypertension. In beta-thalassemia major patients, pulmonary hypertension was present in 83.3%, including moderate and severe forms. Beta-thalassemia major showed a statistically significant association with pulmonary hypertension (p=0.011).

Conclusion: Pulmonary hypertension is a common cardiovascular complication in both sickle cell anemia and thalassemia. Thalassemia major appears to be associated with more severe pulmonary vascular involvement than sickle cell anemia. Routine echocardiographic screening should be integrated into the long-term management of hemoglobinopathy patients for early diagnosis and timely intervention.

Keywords: Sickle cell anemia, Thalassemia, Pulmonary hypertension, Hemoglobinopathy, Echocardiography, Chronic hemolytic anemia, Beta-thalassemia major, Sickle cell disease.

DOI: 10.25258/ijcpr.18.6.234

Introduction

Hemoglobinopathies constitute a diverse group of inherited disorders affecting the structure, function, or synthesis of hemoglobin. These disorders are among the most common monogenic diseases worldwide and pose a major public health challenge, especially in low- and middle-income countries.

According to the World Health Organization, approximately 5% of the global population carries genes responsible for clinically significant hemoglobin disorders, resulting in millions of affected births annually. [1] Among inherited hemoglobinopathies, sickle cell anemia and thalassemia represent the most prevalent and clinically significant disorders. Both conditions are inherited in an autosomal recessive manner and are characterized by chronic anemia, recurrent complications, reduced quality of life, and increased mortality. [2]

Sickle cell anemia results from a single point mutation in the β-globin gene, leading to substitution of valine for glutamic acid at the sixth position of the β-globin chain. This mutation produces hemoglobin S (HbS), which polymerizes

under deoxygenated conditions. The resultant erythrocyte sickling causes vaso-occlusion, chronic hemolysis, endothelial dysfunction, inflammation, and progressive organ damage. [3,4] Thalassemia comprises a heterogeneous group of inherited disorders characterized by reduced or absent synthesis of globin chains. Depending upon the affected globin chain, thalassemias are classified as α-thalassemia and β-thalassemia. Beta-thalassemia major is the most severe form and requires lifelong transfusion support. Ineffective erythropoiesis, chronic anemia, iron overload, and transfusion-related complications contribute significantly to morbidity. [5,6]

India is considered one of the global epicenters of hemoglobinopathies. Sickle cell disease is highly prevalent among tribal populations of Maharashtra, Gujarat, Madhya Pradesh, Chhattisgarh, Odisha, and Jharkhand. Carrier frequencies vary from 10% to 35% in several tribal communities. [7] Similarly, β-thalassemia is distributed widely throughout India, with carrier frequencies ranging from 3% to 17% in different ethnic groups. [8]

Historically, mortality among hemoglobinopathy patients was primarily related to severe anemia, infections, and acute crises. However, advances in supportive care, blood transfusion services, iron chelation therapy, vaccination programs, hydroxyurea treatment, and stem cell transplantation have significantly improved survival. Consequently, chronic complications involving the cardiovascular, pulmonary, renal, endocrine, hepatic, and nervous systems have become increasingly important determinants of long-term outcomes. [9,10]

Cardiovascular complications represent a major cause of morbidity and mortality among patients with hemoglobinopathies. Chronic anemia produces a hyperdynamic circulatory state characterized by increased cardiac output and ventricular remodeling. Additional factors such as chronic hemolysis, endothelial dysfunction, iron overload, oxidative stress, inflammation, and hypercoagulability contribute to progressive cardiovascular injury. [11]Pulmonary hypertension has emerged as one of the most serious cardiovascular complications in patients with chronic hemolytic disorders. It is characterized by elevated pulmonary artery pressure and increased pulmonary vascular resistance, eventually leading to right ventricular dysfunction and heart failure. [12]

In sickle cell disease, chronic intravascular hemolysis results in release of cell-free hemoglobin and arginase into the circulation. Cell-free hemoglobin rapidly scavenges nitric oxide, while arginase reduces arginine availability, resulting in endothelial dysfunction, vasoconstriction, platelet activation, and pulmonary vascular remodeling. [13,14] In thalassemia, pulmonary hypertension is multifactorial in origin. Chronic transfusion therapy, iron overload, splenectomy, hypercoagulability, endothelial injury, oxidative stress, and chronic hemolysis all contribute to pulmonary vascular disease. [15,16] Several studies have demonstrated a strong association between pulmonary hypertension and mortality among patients with sickle cell disease and thalassemia.

Gladwin et al. reported pulmonary hypertension as an independent predictor of mortality in sickle cell disease, while Aessopos et al. and Derchi et al. highlighted its significance in thalassemia. [17-19]

Echocardiography remains the most widely used non-invasive screening tool for pulmonary hypertension. Doppler assessment of tricuspid regurgitation velocity allows estimation of pulmonary artery pressure and facilitates early identification of high-risk patients. [20,21]

Despite increasing recognition of pulmonary hypertension in hemoglobinopathies, comparative data evaluating sickle cell anemia and thalassemia remain limited in India. Most available studies focus on individual disorders rather than direct comparisons.

Understanding differences in clinical profile, hematological parameters, and pulmonary vascular involvement may facilitate disease-specific screening and management strategies. Therefore, the present study was undertaken to compare the clinical profile, hematological characteristics, and occurrence of pulmonary hypertension among patients with sickle cell anemia and thalassemia attending a tertiary care teaching hospital.

Aim: To compare the clinical profile, hematological parameters, and prevalence of pulmonary hypertension among patients with sickle cell anemia and thalassemia.

Objectives:

1. To study the demographic profile of patients with sickle cell anemia and thalassemia.
2. To compare hematological parameters among different hemoglobinopathies.

Materials and Methods:

Study Design: Prospective cross-sectional observational study.

Study Setting: The study was conducted in the Department of General Medicine of a tertiary care teaching hospital attached to a Government Medical College in Maharashtra, India.

Study Duration: December 2017 to October 2019.

Study Population: All diagnosed patients with hemoglobinopathies admitted to the Department of

Medicine or attending outpatient services during the study period were considered eligible.

Sample Size: A total of 50 patients were included in the study.

Inclusion Criteria:

1. Patients aged more than 12 years.
2. Confirmed diagnosis of hemoglobinopathy by HPLC.
3. Patients willing to provide informed consent.

Exclusion Criteria:

1. Ischemic heart disease.
2. Congenital heart disease.
3. Rheumatic heart disease.
4. Structural cardiac abnormalities unrelated to hemoglobinopathy.
5. Chronic pulmonary diseases.
6. Patients unwilling to participate.

Data Collection:

A detailed clinical history was obtained including age, gender, family history, transfusion history, presenting symptoms, previous hospitalization, and comorbid conditions. Comprehensive physical examination was performed.

Laboratory Investigations: Complete blood count, Hemoglobin estimation, Peripheral blood smear, Sickling test, Reticulocyte count, Liver function tests, Renal function tests, High-performance liquid chromatography (HPLC).

Echocardiographic Assessment: All patients underwent two-dimensional echocardiography.

Pulmonary artery systolic pressure (PASP) was calculated using:

$PASP = 4(TRV^2) + RAP$**

Pulmonary hypertension was classified as:

- Normal: <25 mmHg
- Mild: 25–40 mmHg
- Moderate: 41–55 mmHg
- Severe: >55 mmHg

Additional parameters assessed included left ventricular dimensions, right ventricular function, ventricular hypertrophy, systolic function, and diastolic function.

Statistical Analysis:

Data were entered into Microsoft Excel and analyzed using SPSS version 20. Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequencies and percentages. Chi-square test was used for comparison. A p-value less than 0.05 was considered statistically significant.

Observations and ResultsA total of 50 patients with confirmed hemoglobinopathies were enrolled in the study. All patients underwent detailed clinical evaluation, hematological investigations, and two-dimensional echocardiographic assessment.

Demographic Characteristics: The age of patients ranged from 12 to 60 years. The mean age was 25 ± 10.35 years. The majority of patients belonged to the age group of 21–30 years (52%), followed by 12–20 years (30%). Among the study population, 32 patients (64%) were females and 18 (36%) were males, yielding a female-to-male ratio of 1.77:1.

Table 1: Distribution of Hemoglobinopathies

Hemoglobinopathy	Number	Percentage
Sickle Cell Anemia	20	40%
Sickle Cell Trait	6	12%
Beta-Thalassemia Major	6	12%
Beta-Thalassemia Intermedia	4	8%
Beta-Thalassemia Trait	7	14%
Sickle Cell Anemia + Beta-Thalassemia Major	6	12%
Beta-Thalassemia Major + HbE Homozygous	1	2%

Sickle cell anemia was the most common hemoglobinopathy encountered, accounting for 40% of all cases. The high frequency of sickle cell anemia reflects the endemic nature of the disorder in Maharashtra.

Hematological Findings: The mean hemoglobin level for the entire study population was 7.2 ± 2.1 g/dL. Out of 50 patients 24 (48%) had severe ane mia (Hb <7 g/dL), 16 (32%) had moderate anemia (Hb 7–10 g/dL) and 10 (20%) had Hb >10 g/dL.

Table 2: Hemoglobin Level in Sickle Cell Anemia and Thalassemia

Disease	Hb <7	Hb 7–10	Hb >10
Sickle Cell Anemia	45%	45%	10%
Beta-Thalassemia Major	83.3%	16.7%	0%
Beta-Thalassemia Intermedia	100%	0%	0%
Beta-Thalassemia Trait	28.6%	28.6%	42.8%

Among sickle cell anemia patients: 45% had Hb <7 g/dL, 45% had Hb 7–10 g/dL and 10% had Hb >10 g/dL. Among beta-thalassemia major patients, 83.3% had Hb <7 g/dL and 16.7% had Hb 7–10 g/dL

All beta-thalassemia intermedia patients had severe anemia. Severe anemia was significantly more prevalent among thalassemia patients.

Clinical Profile

Common Clinical Manifestations: The most common presenting complaints were Generalized weakness – 88% followed by Pallor – 84%, Easy fatigability – 72%, Dyspnea on exertion – 54%, Recurrent painful crises – 40% (limited to sickle cell disease), Splenomegaly – 48%, Hepatomegaly – 34% and Jaundice – 28% Painful vaso-occlusive episodes were characteristic of sickle cell anemia, whereas growth retardation and transfusion dependence were more common among thalassemia patients.

Echocardiographic Findings: Pulmonary hypertension was the most important cardiovascular abnormality identified.

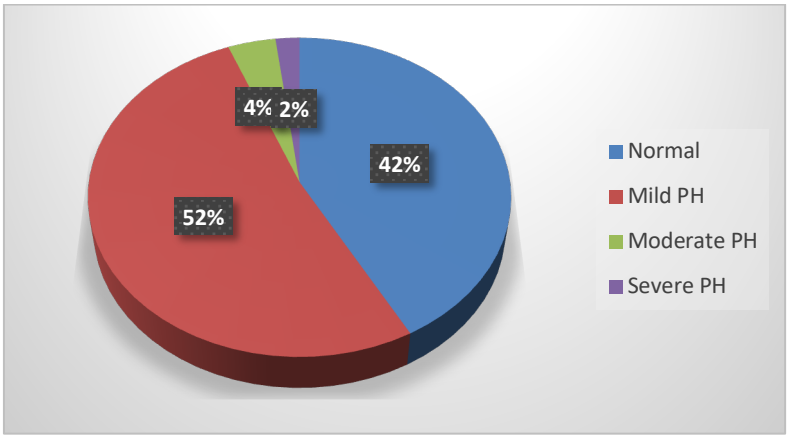

Figure 1: Pulmonary Hypertension

Thus, pulmonary hypertension of varying severity was observed in 58% of patients. Mean systolic pulmonary artery pressure (SPAP) was 25.8 ± 9.06 mmHg.

Table 3: Pulmonary Hypertension in Sickle Cell Anemia

	Sickle Cell Anemia		Beta-Thalassemia Major	
Category	**Number**	**Percentage**	**Number**	**Percentage**
Normal	6	30%	1	16.7%
Mild PH	14	70%	3	50%
Moderate PH	0	0%	1	16.7%
Severe PH	0	0%	1	16.7%

Among the 20 patients with sickle cell anemia. Mild pulmonary hypertension predominated. Moderate and severe pulmonary hypertension occurred only in beta-thalassemia major. The association between beta-thalassemia major and pulmonary hypertension was statistically significant (p=0.011).

Table 4: Other Echocardiographic Findings

Finding	Number
Diastolic Dysfunction	3
Concentric LVH	1
Systolic Dysfunction	0
Dilated Left Ventricle	0

Diastolic dysfunction represented the most common non-pulmonary hypertension cardiac abnormality.

Discussion

The present study was undertaken to compare the clinical profile, hematological characteristics, and prevalence of pulmonary hypertension among patients with sickle cell anemia and thalassemia. Hemoglobinopathies represent a major healthcare burden in developing countries, particularly in India where both disorders are highly prevalent. Improved survival resulting from advances in supportive care has shifted attention toward chronic cardiovascular complications. The mean age of study participants was 25 ± 10.35 years. Most patients belonged to the 21–30 years age group. Similar findings have been reported by Pathak et al. [16] and Aessopos et al. [21] who observed that cardiovascular complications in

hemoglobinopathies are increasingly recognized during adolescence and young adulthood. Improved survival owing to advances in blood transfusion services, iron chelation, and hydroxyurea therapy likely contributes to this age distribution.

Female predominance was observed in the present study. Although hemoglobinopathies are inherited equally among males and females, referral patterns and healthcare-seeking behavior may influence gender representation. Humbert et al. [13] similarly reported a female predominance among patients with pulmonary hypertension.

Sickle cell anemia constituted the most common hemoglobinopathy observed (40%). This finding is consistent with epidemiological studies from Maharashtra where sickle cell disease is highly prevalent among tribal populations. Kate and Lingojwar[15] reported carrier frequencies ranging from 10% to 35% in several tribal communities of Maharashtra.

A major observation was the higher severity of anemia among thalassemia patients. Beta-thalassemia major patients demonstrated the highest prevalence of severe anemia. This can be explained by ineffective erythropoiesis resulting from reduced beta-globin synthesis and intramedullary destruction of erythroid precursors. Weatherall and Clegg [17] and Taher et al. [8] have similarly described severe anemia as a characteristic feature of beta-thalassemia major.

In contrast, anemia in sickle cell disease primarily results from chronic hemolysis and shortened erythrocyte survival. Although severe anemia occurred in 45% of sickle cell patients, hemoglobin levels were generally higher than those observed in beta-thalassemia major.

Pulmonary hypertension emerged as the most important cardiovascular complication identified in the present study. Overall prevalence was 58%, with mild pulmonary hypertension accounting for the majority of cases. Pulmonary hypertension has increasingly been recognized as a major determinant of prognosis in hemoglobinopathies. [5,6] The pathogenesis of pulmonary hypertension in sickle cell disease is multifactorial. Chronic intravascular hemolysis leads to release of cell-free hemoglobin, which scavenges nitric oxide and promotes endothelial dysfunction. [5,6,11] Reduced nitric oxide bioavailability results in vasoconstriction, platelet activation, inflammation, and pulmonary vascular remodeling. These processes contribute to progressive increases in pulmonary vascular resistance. Among sickle cell anemia patients, 70% demonstrated mild pulmonary hypertension. Similar observations have been reported by Gladwin et al. [5] and Parent et al. who demonstrated a strong relationship between elevated pulmonary artery pressure and mortality in sickle cell disease.

A particularly important finding of the present study was the greater severity of pulmonary hypertension among beta-thalassemia major patients. Moderate and severe pulmonary hypertension occurred only among beta-thalassemia major patients. The association between beta-thalassemia major and pulmonary hypertension was statistically significant (p=0.011).

Several mechanisms may explain this observation. Chronic transfusion therapy results in iron overload, which contributes to myocardial injury and endothelial dysfunction. Hypercoagulability and splenectomy further increase pulmonary vascular risk. Chronic hemolysis, oxidative stress, and endothelial injury collectively contribute to pulmonary vascular remodeling. [7,9,12]

Our findings are supported by Aessopos and Farmakis [7], Derchi et al. [9], Morris et al. [10], Hagar et al. [11], and Fraidenburg and Machado [12] who reported a high prevalence of pulmonary hypertension among thalassemia patients.

No significant relationship was observed between age and pulmonary hypertension. Similar findings were reported by Taher et al. [22] and Morris et al. [25], suggesting that disease-specific factors are more important determinants than age alone.

Likewise, no significant association was observed between gender and pulmonary hypertension. Similar observations have been reported in most hemoglobinopathy studies. [13,16] Diastolic dysfunction was the most common additional cardiac abnormality identified. Chronic anemia produces a hyperdynamic circulation characterized by increased cardiac output and ventricular volume overload. Over time, these changes contribute to ventricular remodeling and impaired relaxation. [18,19]

The absence of systolic dysfunction in the majority of patients indicates preservation of ventricular contractility despite chronic disease burden. However, progressive myocardial damage may occur with advancing age and cumulative transfusion exposure.

The findings of the present study emphasize the importance of regular cardiovascular surveillance in patients with hemoglobinopathies. Echocardiography remains a practical and non-invasive screening tool for early detection of pulmonary hypertension. Early identification permits timely intervention, optimization of transfusion protocols, iron chelation therapy, hydroxyurea use, and management of cardiovascular risk factors.

Conclusion

The present study demonstrates that pulmonary hypertension is a common cardiovascular complication in hemoglobinopathies. Sickle cell anemia was the most prevalent hemoglobinopathy, whereas beta-thalassemia major was associated with more severe anemia and more advanced pulmonary vascular involvement.

Pulmonary hypertension was detected in 58% of patients. Mild pulmonary hypertension predominated among sickle cell anemia patients, whereas moderate and severe pulmonary hypertension occurred mainly among beta-thalassemia major patients. Routine echocardiographic screening should be incorporated into the long-term management of hemoglobinopathy patients to facilitate early diagnosis and treatment.

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