



RESEARCH ARTICLE

Evaluation of Inflammatory Biomarkers and Oxidative Stress Parameters Before and After Low-Dose Thalidomide Therapy in Patients with β -Thalassemia

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ABSTRACT

Background: β -Thalassemia is a hereditary hemoglobinopathy characterized by ineffective erythropoiesis, chronic hemolytic anemia, iron overload, oxidative stress, and persistent inflammation. Increased production of reactive oxygen species and elevated inflammatory cytokines contribute significantly to disease progression and multiple organ complications. Low-dose thalidomide has emerged as a promising therapeutic option due to its ability to induce fetal hemoglobin production, improve erythropoiesis, reduce transfusion requirements, and exert anti-inflammatory effects. However, limited data are available regarding its influence on inflammatory biomarkers and oxidative stress parameters in patients with β -thalassemia.

Objective: To evaluate changes in inflammatory biomarkers and oxidative stress parameters before and after low-dose thalidomide therapy in patients with β -thalassemia.

Materials and Methods: A retrospective observational study was conducted in the Department of Clinical Hematology, S.C.B. Medical College and Hospital, Cuttack, Odisha, India, from September 2025 to June 2026. Medical records of patients with β -thalassemia receiving low-dose thalidomide therapy were reviewed. Demographic characteristics, clinical features, hematological parameters, inflammatory biomarkers including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and oxidative stress markers including malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and total antioxidant capacity (TAC) were collected before initiation of therapy and after six months of treatment. Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation and compared using paired Student's t-test. A p-value <0.05 was considered statistically significant.

Results: Following six months of low-dose thalidomide therapy, significant reductions were observed in serum CRP, IL-6, TNF- α , and MDA levels (all $p < 0.001$). Antioxidant parameters including SOD, GPx, and TAC showed significant improvement after treatment ($p < 0.001$). Mean hemoglobin concentration increased significantly, while annual transfusion requirements decreased. No serious adverse events requiring permanent discontinuation of therapy were observed.

Conclusion: Low-dose thalidomide significantly reduced systemic inflammation and oxidative stress while improving antioxidant defense and hematological parameters in patients with β -thalassemia. These findings support its potential role as an effective adjunctive therapy in the management of transfusion-dependent β -thalassemia.

Keywords: β -Thalassemia; Thalidomide; Oxidative stress; Inflammatory biomarkers; C-reactive protein; Interleukin-6.

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INTRODUCTION

β -Thalassemia is one of the most common inherited monogenic disorders worldwide and represents a major public health challenge, particularly in South Asia, the Mediterranean region, and the Middle East. The disease results from mutations in the β -globin gene, leading to reduced or absent synthesis of β -globin chains. The imbalance between α - and β -globin chains causes ineffective erythropoiesis, chronic hemolytic anemia, compensatory bone marrow expansion, and progressive iron overload. Patients with transfusion-dependent β -thalassemia (TDT)

require lifelong regular blood transfusions and iron chelation therapy to maintain adequate hemoglobin levels and prevent complications [1].

In addition to chronic anemia and iron overload, increasing evidence suggests that persistent inflammation and oxidative stress play a crucial role in the pathogenesis of β -thalassemia. Excess free iron catalyzes the formation of reactive oxygen species (ROS) through the Fenton reaction, resulting in lipid peroxidation, protein oxidation, DNA damage, and apoptosis of erythroid precursor cells. Oxidative stress contributes to ineffective erythropoiesis,

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endothelial dysfunction, immune dysregulation, and progressive organ damage involving the heart, liver, endocrine glands, and kidneys [2].

Patients with β -thalassemia exhibit elevated circulating inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and C-reactive protein (CRP), reflecting chronic immune activation. Persistent inflammation further aggravates oxidative injury and promotes tissue fibrosis, vascular complications, and impaired erythropoiesis. Consequently, assessment of inflammatory and oxidative stress biomarkers has gained increasing importance for monitoring disease activity and evaluating therapeutic response [3].

Recent advances in disease-modifying therapies have shifted attention beyond supportive transfusion therapy toward agents capable of improving erythropoiesis and reducing transfusion dependence. Thalidomide, originally developed as a sedative, possesses potent immunomodulatory, anti-inflammatory, anti-angiogenic, and fetal hemoglobin-inducing properties. Low-dose thalidomide has demonstrated encouraging results in patients with transfusion-dependent β -thalassemia by increasing hemoglobin concentration, reducing transfusion frequency, and improving quality of life. The drug enhances γ -globin gene expression, thereby increasing fetal hemoglobin (HbF) production and reducing ineffective erythropoiesis. Furthermore, its inhibitory effects on TNF- α and other pro-inflammatory cytokines may reduce chronic inflammation and oxidative damage [4].

Although several studies have reported improvements

in hemoglobin levels following thalidomide therapy, evidence regarding its impact on inflammatory biomarkers and oxidative stress parameters remains limited, particularly in the Indian population. Understanding these biochemical changes may provide important insights into the broader therapeutic benefits of thalidomide beyond erythropoiesis and transfusion reduction (5).

Therefore, the present retrospective observational study was undertaken to evaluate inflammatory biomarkers and oxidative stress parameters before and after low-dose thalidomide therapy in patients with β -thalassemia attending the Department of Clinical Hematology, S.C.B. Medical College and Hospital, Cuttack. The study also aimed to assess associated hematological changes and explore the potential role of thalidomide in reducing inflammation and oxidative stress in this patient population (6).

MATERIALS AND METHODS

Study Design

This retrospective observational study was conducted by reviewing hospital records of patients with β -thalassemia receiving low-dose thalidomide therapy.

Study Setting

The study was carried out in the Department of Clinical Hematology, S.C.B. Medical College and Hospital, Cuttack, Odisha, India.

Study Duration

September 2025 to June 2026.

Study Population

Patients diagnosed with transfusion-dependent β -thalassemia who received low-dose thalidomide therapy during the study period.

Sample Size

A total of 60 patients fulfilling the eligibility criteria were included in the analysis.

Inclusion Criteria

- Confirmed diagnosis of transfusion-dependent β -thalassemia by hemoglobin electrophoresis or HPLC.
- Age ≥ 5 years.
- Patients receiving low-dose thalidomide (approximately 2–5 mg/kg/day or equivalent low-dose regimen) for at least six months.
- Availability of complete laboratory records before initiation and after completion of therapy.

Exclusion Criteria

- Patients with acute infection or inflammatory disorders.
- Patients with autoimmune diseases or malignancy.
- Chronic liver or renal failure unrelated to β -thalassemia.
- Incomplete clinical or laboratory records.
- Patients receiving investigational drugs during the study period.

Data Collection

The following information was extracted from medical records

- Age
- Sex
- Duration of disease
- Age at first transfusion
- Transfusion frequency
- Splenectomy status
- Serum ferritin
- Hemoglobin concentration
- Complete blood count
- Inflammatory Biomarkers
- C-reactive protein (CRP)
- Interleukin-6 (IL-6)
- Tumor necrosis factor-alpha (TNF- α)
- Oxidative Stress Parameters
- Malondialdehyde (MDA)
- Superoxide dismutase (SOD)
- Glutathione peroxidase (GPx)
- Total antioxidant capacity (TAC)

Laboratory values recorded immediately before initiation of thalidomide therapy and after six months of treatment were included for comparison.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Comparisons between baseline and post-treatment values were performed using the paired Student's *t*-test for normally distributed variables or the Wilcoxon signed-rank test for non-normally distributed variables. Pearson's correlation analysis was performed to evaluate associations between inflammatory biomarkers, oxidative stress parameters, and hemoglobin levels. A *p*-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional

Ethics Committee of S.C.B. Medical College and Hospital, Cuttack. As this was a retrospective record-based study, patient confidentiality was maintained by anonymizing all data before analysis. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and institutional guidelines for biomedical research.

RESULTS

A total of 60 patients with transfusion-dependent β -thalassemia who received low-dose thalidomide therapy for at least six months were included in the study. The mean age of the patients was 15.8 ± 6.4 years (range: 6–32 years). Males constituted 36 (60.0%) of the study population, while females accounted for 24 (40.0%). Significant improvements were observed in hematological parameters, inflammatory biomarkers, and oxidative stress markers following treatment.

Low-dose thalidomide therapy resulted in significant improvements in hemoglobin concentration, antioxidant status, and transfusion requirements while substantially reducing inflammatory biomarkers and oxidative stress parameters. Correlation analysis further demonstrated that reductions in inflammation and oxidative stress were closely associated with improved hematological outcomes.

Interpretation

The study population predominantly consisted of adolescent patients with long-standing transfusion-dependent β -thalassemia. The majority had substantial iron overload, reflected by elevated serum ferritin levels, and required frequent blood transfusions before initiation of thalidomide therapy.

Interpretation

Following six months of therapy, mean hemoglobin concentration increased significantly by 1.7 g/dL. Red blood cell count also improved significantly, while reticulocyte

Table 1: Baseline demographic and clinical characteristics (n=60)

Variable	Value
Age (years), Mean $\pm$ SD	15.8 ± 6.4
Male	36 (60.0%)
Female	24 (40.0%)
Disease duration (years)	12.3 ± 5.1
Age at first transfusion (months)	10.2 ± 4.8
Splenectomized patients	18 (30.0%)
Mean serum ferritin (ng/mL)	2865 ± 810
Annual transfusions before therapy	17.6 ± 3.5

Table 2: Hematological parameters before and after low-dose thalidomide therapy

Parameter	Before Therapy	After Therapy	p-value
Hemoglobin (g/dL)	7.2 ± 0.9	8.9 ± 1.1	<0.001
RBC count (×10 ¹² /L)	2.89 ± 0.42	3.45 ± 0.46	<0.001
Reticulocyte count (%)	6.8 ± 1.9	5.1 ± 1.6	0.002
Serum ferritin (ng/mL)	2865 ± 810	2540 ± 760	0.014

Table 3: Changes in inflammatory biomarkers

Biomarker	Before Therapy	After Therapy	p-value
CRP (mg/L)	14.8 ± 4.5	7.6 ± 2.9	<0.001
IL-6 (pg/mL)	19.4 ± 5.6	10.2 ± 3.8	<0.001
TNF-α (pg/mL)	26.7 ± 7.8	15.3 ± 5.1	<0.001

Table 4: Oxidative stress parameters before and after therapy

Parameter	Before Therapy	After Therapy	p-value
MDA (nmol/mL)	6.82 ± 1.31	4.48 ± 1.02	<0.001
SOD (U/mL)	1.92 ± 0.46	2.83 ± 0.55	<0.001
GPx (U/L)	36.5 ± 8.4	49.8 ± 9.2	<0.001
TAC (mmol/L)	0.89 ± 0.22	1.28 ± 0.31	<0.001

Table 5: Transfusion requirement before and after therapy

Variable	Before Therapy	After Therapy	p-value
Annual transfusions	17.6 ± 3.5	11.2 ± 3.1	<0.001
Mean transfusion interval (days)	19.4 ± 4.2	30.6 ± 6.5	<0.001

Table 6: Pearson correlation between inflammatory biomarkers and hemoglobin after therapy

Variable	Correlation coefficient (r)	p-value
CRP vs Hemoglobin	-0.56	<0.001
IL-6 vs Hemoglobin	-0.61	<0.001
TNF-α vs Hemoglobin	-0.58	<0.001

Table 7: Correlation between oxidative stress markers and inflammatory biomarkers

Variables	Correlation (r)	p-value
MDA vs CRP	0.63	<0.001
MDA vs IL-6	0.59	<0.001
SOD vs Hemoglobin	0.52	0.001
GPx vs Hemoglobin	0.49	0.002

Table 8: Adverse events during low-dose thalidomide therapy

Adverse event	Number (%)
Constipation	8 (13.3)
Mild drowsiness	6 (10.0)
Peripheral neuropathy	2 (3.3)
Skin rash	2 (3.3)
No adverse events	42 (70.0)

count and serum ferritin demonstrated significant reductions, suggesting improved erythropoiesis and reduced ineffective hemolysis.

Interpretation

Significant reductions were observed in all inflammatory biomarkers following low-dose thalidomide therapy. CRP, IL-6, and TNF-α levels decreased by approximately 49%, 47%, and 43%, respectively, indicating a marked reduction in systemic inflammation.

Interpretation

Thalidomide therapy significantly reduced lipid peroxidation, as reflected by lower MDA levels, while antioxidant defense mechanisms improved significantly with increased SOD, GPx, and total antioxidant capacity.

Interpretation

Patients demonstrated a significant reduction in annual transfusion requirements and a corresponding prolongation of transfusion intervals following treatment, indicating improved hematological stability.

Interpretation

A significant negative correlation was observed between inflammatory biomarkers and hemoglobin concentration, indicating that lower inflammatory activity was associated with improved hematological response following therapy.

Interpretation

Oxidative stress was positively associated with systemic inflammation, whereas improved antioxidant enzyme

activity correlated positively with hemoglobin concentration, suggesting interconnected improvements in oxidative balance and erythropoiesis.

Interpretation

Low-dose thalidomide was generally well tolerated. Mild constipation and drowsiness were the most frequently reported adverse effects, while peripheral neuropathy occurred in only two patients. No patient required permanent discontinuation of therapy because of adverse events.

DISCUSSION

This retrospective study assessed how low-dose thalidomide therapy affected oxidative stress parameters and inflammatory biomarkers in individuals with transfusion-dependent β -thalassemia. After six months of treatment, the results showed notable improvements in haematological parameters, decreases in inflammatory cytokines, attenuation of oxidative stress, and a reduction in the need for transfusions. These findings corroborate the mounting evidence that thalidomide modulates inflammatory and oxidative processes implicated in the pathophysiology of β -thalassemia to provide therapeutic advantages beyond foetal haemoglobin induction (7).

The substantial rise in haemoglobin concentration combined with a decrease in the yearly need for transfusions was one of the study's most notable findings. These results are in line with earlier clinical research showing that thalidomide increases the expression of the γ -globin gene, which improves erythropoiesis and increases foetal haemoglobin synthesis. By prolonging erythrocyte longevity and reducing inefficient erythropoiesis, enhanced erythroid maturation lessens the need for frequent blood transfusions. The haematological effectiveness of low-dose thalidomide is further supported by the observed extension of transfusion intervals (8).

It is becoming more well acknowledged that chronic inflammation plays a major role in the development of β -thalassemia. Erythroid apoptosis, endothelial dysfunction, and tissue damage are all facilitated by persistently high levels of inflammatory mediators, including IL-6, TNF- α , and CRP. All of the inflammatory biomarkers in this research significantly decreased following therapy. These results are biologically realistic because thalidomide suppresses many pro-inflammatory signalling pathways and decreases TNF- α production by speeding up the breakdown of TNF- α messenger RNA. Improved erythropoiesis and

fewer consequences from the disease may result from a decrease in systemic inflammation (9, 10).

Another characteristic of β -thalassemia is oxidative stress, which is brought on by recurrent blood transfusions, iron excess, and chronic hemolysis. Reactive oxygen species overproduction results in membrane damage, lipid peroxidation, and erythroid precursor death. Following treatment, antioxidant enzymes like SOD, GPx, and total antioxidant capacity significantly enhanced whereas malondialdehyde (MDA), a measure of lipid peroxidation, was significantly decreased. These results imply that low-dose thalidomide reduces oxidative cellular damage by suppressing inflammatory pathways and restoring antioxidant defence mechanisms. Red blood cell survival may be further improved by improving antioxidant status, which may also reduce organ damage brought on by long-term oxidative stress (11, 12).

Significant negative correlations between haemoglobin concentration and inflammatory biomarkers were found by correlation analysis, suggesting that individuals with higher decreases in inflammation had superior haematological responses. In a similar vein, favourable correlations between haemoglobin and antioxidant enzymes highlight the intimate connection between reduced oxidative stress and enhanced erythropoiesis. These findings provide credence to the idea that oxidative stress and inflammation are linked pathological processes in β -thalassemia and that concurrently modifying both pathways may enhance clinical outcomes (13).

This study's safety profile was positive. Constipation and temporary sleepiness were the most frequent side effects, which were often moderate and self-limiting. Rarely did peripheral neuropathy arise, and no patient needed to stop treatment permanently. These results are consistent with other studies showing that, when given under close clinical supervision, low-dose thalidomide is typically well tolerated (14).

The examination of oxidative stress and inflammatory biomarkers along with haematological results in the same patient group is one of the study's many strong points. However, the results' generalizability is limited by its retrospective methodology, small sample size, single-center location, and lack of a control group. Furthermore, there was no way to evaluate foetal haemoglobin levels or long-term clinical effects. To validate these findings and clarify the function of low-dose thalidomide as a disease-modifying treatment for β -thalassemia, prospective multicenter randomised studies with bigger populations and longer follow-up are needed. Overall, the current

research indicates that in individuals with transfusion-dependent β -thalassemia, low-dose thalidomide may offer clinically significant advantages by concurrently enhancing erythropoiesis, lowering oxidative stress, and regulating inflammation (15).

CONCLUSION

Patients with transfusion-dependent β -thalassemia showed notable clinical and biochemical advantages from low-dose thalidomide therapy. Patients demonstrated significant improvements in haemoglobin concentration, longer transfusion intervals, and lower yearly transfusion requirements after six months of treatment, suggesting improved erythropoiesis and decreased transfusion reliance. Significant decreases in inflammatory biomarkers, such as CRP, IL-6, and TNF- α , along with lower levels of malondialdehyde and increased activity of antioxidant enzymes, such as SOD, GPx, and total antioxidant capacity, indicate that thalidomide effectively reduces oxidative stress and chronic inflammation, two major mechanisms that contribute to organ damage and disease progression in β -thalassemia. Only minor and controllable side effects were noted, and the medication was typically well tolerated. These results suggest that by modifying oxidative and inflammatory pathways, low-dose thalidomide has therapeutic advantages beyond foetal haemoglobin induction. Including biomarkers for oxidative stress and inflammation in routine monitoring could aid in a more thorough evaluation of therapy response. To confirm these results, assess long-term safety, and determine the function of thalidomide as a disease-modifying treatment in β -thalassemia, larger prospective multicenter studies with longer follow-up are necessary. The effectiveness and acceptable safety profile of thalidomide in lowering transfusion burden and raising haemoglobin levels in β -thalassemia are also supported by recent systematic studies.

REFERENCES

1. Yang WJ, Kang QP, Zhou Q, Lin T, Gong XM, Huang CJ, et al. Clinical efficacy of thalidomide for various genotypes of beta thalassemia. *BMC Med Genomics*. 2024; 17:191.
2. Yang K, Liu X, Peng W, Hua F, Li L, Chen K, et al. Effects of thalidomide on erythropoiesis and iron homeostasis in transfusion-dependent β -thalassemia. *Mediterr J Hematol Infect Dis*. 2024;16: e2024001.
3. Ju W, Din G, Huang J, Zheng M, Wang X, Liu L, et al. Efficacy and safety of thalidomide in patients with β -thalassemia intermedia and major. *Medicine (Baltimore)*. 2024;103: e40328.
4. Atta T, Subhan Z, Nabi M, Ain NU, Ali W. Long-term thalidomide therapy's efficacy and safety in transfusion-dependent beta-thalassemia major patients: a systematic review. *Khyber Med Univ J*. 2024;16(3):198-206.
5. Lin S, Zheng Y, Chen M, Xu L, Huang H. The interactions between ineffective erythropoiesis and ferroptosis in β -thalassemia. *Front Physiol*. 2024; 15:1346173.
6. Mohamed SOO, Mohamed AEA, Salih MSK, Abdelrahman ASEE, Ahmed MGA. Serum lipid profile abnormalities among beta-thalassemia patients: a systematic review and meta-analysis. *Lipids Health Dis*. 2024; 23:388.
7. Chen JM, Zhu WJ, Liu J, et al. Safety and efficacy of thalidomide in patients with transfusion-dependent β -thalassemia: a randomized clinical trial. *Signal Transduct Target Ther*. 2021; 6:405.
8. Tuo Y, Li X, et al. Global, regional, and national burden of thalassemia, 1990–2021: findings from the Global Burden of Disease Study 2021. *eClinicalMedicine*. 2024; 75:102619.
9. Rao E, Kumar Chandraker S, Singh M, Kumar R. Global distribution of β -thalassemia mutations: an update. *Gene*. 2024; 896:148022.
10. Thein SL. Molecular basis of β -thalassemia and potential therapeutic targets. *Blood Cells Mol Dis*. 2020; 80:102370.
11. Cappellini MD, Farmakis D, Porter J, Taher A. Guidelines for the Management of Transfusion-Dependent β -Thalassaemia. 5th ed. Nicosia: Thalassaemia International Federation; 2025.
12. Taher AT, Musallam KM, Cappellini MD. β -Thalassemias. *N Engl J Med*. 2021; 384:727–743.
13. Viprakasit V, Kattamis A, Porter J, et al. Advances in the treatment of transfusion-dependent β -thalassemia. *Lancet Haematol*. 2022;9: e660-e672.
14. Sharma P, Sharma S, Aggarwal R, et al. Oxidative stress and antioxidant status in transfusion-dependent β -thalassemia: current evidence and therapeutic implications. *Ann Hematol*. 2023; 102:1547–1558.
15. Alhuneafat L, Al-Khabori M, Daar S. Emerging disease-modifying therapies for β -thalassemia: current evidence and future perspectives. *Hematology*. 2023;28(1):2205674.