

Impact of Thalidomide Addition on Health-Related Quality of Life in Transfusion-Dependent Thalassemia Patients: A Prospective Study

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Abstract

Objective:

To evaluate the impact of adding thalidomide on health-related quality of life in patients with transfusion-dependent thalassemia receiving blood transfusion for at least two years, using SF-36 questionnaire.

Study Design:

Prospective cohort study with before-after design.

Place and Duration of Study:

Department of Hematology, Peshawar Institute of Medical Sciences, from April-2025 to March-2026.

Methodology:

A total of 80 patients aged ≥ 10 years with β -thalassemia major and receiving regular blood transfusions since at least past two years were included in this study and thalidomide was added to standard therapy at a dose of 2–5 mg/kg/day. Health-related quality of life was assessed for each patient using the validated SF-36 questionnaire before initiation of therapy and after 6 months of initiating the therapy. The primary outcome of the study was improvement in health-related quality of life after 6 months of thalidomide treatment. Hemoglobin level, transfusion interval, and monthly transfusion requirement were also compared before and after treatment as secondary outcomes.

Results:

Mean age of patients was 19.28 ± 5.26 years, with a predominance of male population (57.5%). Significant improvement was observed after 6 months of thalidomide therapy in all eight domains of SF-36 ($p < 0.001$ for all) reflecting significant improvement in health-related quality of life of these patients. A significant increase was also observed in hemoglobin level and transfusion intervals, while a decrease in monthly transfusion requirements after the initiation of thalidomide therapy ($p < 0.001$ for all).

Conclusion:

Thalidomide treatment was associated with improvement in health-related quality of life and reduced transfusion burden in transfusion-dependent thalassemia patients

Clinical Trial Number: Not Applicable

INTRODUCTION

Thalassemia is one of the most common hereditary hemoglobinopathies in the world, which is caused by defects in globin chain, resulting in chronic hemolytic anemia and multi-organ complications.¹ Approximately 1.5% of the world's population carries thalassemia traits, with the highest prevalence in the Mediterranean region, Middle East, South Asia (SA) and Southeast Asia.² Patients with transfusion-dependent thalassemia (TDT), such as the β -thalassemia major, have to receive lifelong regular transfusion of red blood cells every 2–4 weeks. This is essential to keep their hemoglobin level above 9–

10 g/dL and to inhibit ineffective erythropoiesis. This lifesaving transfusion therapy invariably leads to iron overload, necessitating concurrent chelation therapy to avert cardiac, hepatic, and endocrine complications.³

The TDT patients often suffer from chronic fatigue, growth retardation, endocrine disorders, cardiac complications and psychosocial stress. Evidence from multiple studies indicates that patients with thalassemia have a compromised health-related quality of life (HRQoL) than healthy people.⁴ Measuring HRQoL is therefore a crucial part of evaluating the treatment outcomes in thalassemia. The status of HRQoL reflects the impact of disease and treatment on the physical, emotional, social, and mental health of thalassemia patients. Impaired HRQoL is correlated with factors such as transfusion frequency, disease complications, socioeconomic status, iron overload and disease severity. Thus, therapeutic measures that decrease transfusion requirements and enhance functional capacity can have positive effects on patients' quality of life (QoL).⁵

Thalidomide is an immunomodulatory, anti-angiogenic, and anti-inflammatory agent that has recently received attention in the treatment of TDT. The drug upregulates the gamma-globin gene (HbG), stimulates the production of fetal hemoglobin (HbF) and erythroid proliferation, thereby decreasing ineffective erythropoiesis and transfusion needs.⁶ Several studies have reported encouraging hematological responses with thalidomide therapy in TDT patients, including increased hemoglobin levels and prolonged intervals between transfusions. In addition to its hematological benefits, reduction in transfusion dependence may improve physical activity, emotional well-being, and overall QoL.⁷ Most of the studies have primarily concentrated on hematological parameters rather than patient-centered outcomes, however, HRQoL assessment is important because improvement in laboratory parameters may not adequately reflect the overall well-being of these patients.⁸

The SF-36 questionnaire is a validated and widely used instrument that offers a comprehensive assessment of HRQoL across all the eight domains. The tool has been successfully applied in various research studies across different chronic hematological conditions.⁹

Pakistan is situated within the thalassemia belt and is considered among the heavily affected nations in terms of thalassemia prevalence. The carrier rate of thalassemia in Pakistan ranges from 5–8%. Consequently, thousands of children are affected annually, with an estimated 5,000–9,000 new patients with thalassemia major born every year in the country, posing a substantial social, economic, and psychological burden not only on the patients but also on their families.¹⁰

Despite this increasing popularity of thalidomide treatment, there is a dearth of local data regarding the impact of thalidomide on the HRQoL of TDT patients in Pakistan. This study was conducted to evaluate the impact of adding thalidomide on HRQoL using the widely used SF-36 questionnaire in TDT patients after 6 months of treatment. The findings of this study may help clinicians to better understand the potential of thalidomide therapy in improving QoL of TDT patients and to support evidence-based decision-making in this regard.

METHODOLOGY

This prospective cohort study with a before-after design was conducted at the Department of Hematology, Peshawar Institute of Medical Sciences, Peshawar, Pakistan, from April-2025 to March-2026. The approval of conducting the study was taken from the Ethical Review Committee of Pak International Medical College Hayatabad Peshawar (Ref No: PIMC/DMR/2025/03). Written informed consent was obtained from patients or parents/guardians (in case of minor participants) before their enrollment in the study.

Sample size was calculated using the single population mean formula. Based on mean general health (GH) score of 48.19 ± 16.94 on the SF-36 among TDT patients after the treatment with thalidomide, 95% confidence level and precision of ± 4 points, the minimum required sample size was calculated as 69 patients. However, to account for non-responsive patients and incomplete questionnaires, the final target sample size was set as 80 patients.¹¹

A total of 80 patients aged ≥ 10 years with a confirmed diagnosis of β -thalassemia major and receiving ≥ 8 transfusions/year for at least past 2 years were included in this study through consecutive sampling.¹² This age limit was set to ensure reliable assessment of HRQoL using the SF-36 questionnaire.

Patients with severe hepatic or renal impairment, uncontrolled infections, malignancy, peripheral neuropathy, with known hypersensitivity to thalidomide, and those already receiving thalidomide therapy were excluded from the study. Moreover, pregnant women or those with potential for pregnancy without contraception were also excluded.

All relevant demographic details and clinical information such as age, gender, duration of disease, frequency of blood transfusion, splenectomy status, family income status and presence of comorbid conditions were collected on a predesigned proforma. Medical records were used to obtain hemoglobin level and transfusion history.

Thalidomide was initiated in all patients in addition to the standard treatment regimens including regular blood transfusions and iron chelation therapy. Thalidomide was given orally, at a dose of 2–5 mg/kg per day, adjusted based on patient tolerance and hematological response.¹³ Patients were monitored regularly at the outpatient department for treatment response and adverse effects throughout the study period.

The validated SF-36 questionnaire was used to measure HRQoL which included eight domains: physical functioning (PF), role limitation due to physical health (RPH), bodily pain (BP), general health perception (GHP), vitality (VT), social functioning (SF), role limitations due to emotional problems (REP), and emotional well-being (EW). The range of the scores in each domain was from 0 to 100, with a higher score indicating a higher QoL.⁹

The SF-36 questionnaire was completed for each patient prior to the start of study treatment, by interviewing them in Urdu or Pashto, based on patient preference, to ensure proper understanding of the questionnaire. Patients who were unable to complete the questionnaire independently were assisted by trained research staff. This interview using the SF-36 questionnaire was repeated after 6 months of thalidomide therapy to compare the pre- and post-treatment scores.

The primary outcome of the study was the improvement in HRQoL after 6 months of thalidomide treatment, assessed by improved SF-36 scores. The secondary outcomes were changes in hemoglobin level, transfusion interval, and monthly transfusion requirement before and after treatment.

Data were analyzed with the help of SPSS version 26. The quantitative variables such as age, duration of disease, hemoglobin level, transfusion interval and SF-36 scores were expressed as mean $\pm$ standard deviation. Qualitative variables including gender, splenectomy status, and comorbidities were presented as frequencies and percentages. The paired sample t-test was used (after checking the normality of continuous variables using the Shapiro-Wilk test) to compare pre and post treatment mean HRQoL scores, hemoglobin levels and transfusion intervals, where statistically significant p value was defined as ≤ 0.05 .

RESULTS

Mean age of patients in this study was 19.28 ± 5.26 years (ranged from 10 to 29 years). Male patients were 57.5% while females were 42.5% of total study population. The details of demographics and baseline clinical characteristics are shown in Table-I.

Table-I: Demographics and baseline clinical characteristics

n = 80

Demographics and baseline clinical characteristics		
Age (Mean $\pm$ SD) years		19.28 $\pm$ 5.26
Gender	Male n (%)	46 (57.5)
	Female n (%)	34 (42.5)
Duration of disease (Mean $\pm$ SD) years		11.87 $\pm$ 4.37
Splenectomy performed	Yes n (%)	26 (32.5)
	No n (%)	54 (67.5)
Family income status	Low n (%)	42 (52.5)
	Medium n (%)	29 (36.25)
	High n (%)	9 (11.25)
Comorbidities	Yes n (%)	22 (27.5)
	No n (%)	58 (72.5)
Hemoglobin (Mean $\pm$ SD) g/dL		7.33 $\pm$ 1.09
Transfusion interval (Mean $\pm$ SD) days		18.32 $\pm$ 4.01
Monthly transfusion requirement (Mean $\pm$ SD)		2.89 $\pm$ 0.71

The primary outcomes of the study showed significant improvement in HRQoL scores after initiation of thalidomide therapy, as significant improvement was noted in all major SF-36 domains including PF, RPH, BP, GHP, SF, VT, REP and EW ($p < 0.001$ for all). The details of comparison between the scores of all 8 domains at initiation of therapy and at completion of 6 months are shown in Table-II.

Table-II: SF-36 domain scores before and after 6 months thalidomide therapy

n = 80

SF-36 Domains	Score at initiation of therapy (Mean ± SD)	Score after 6 months of therapy (Mean ± SD)	p-value*
Physical functioning	55.26 ± 11.60	68.80 ± 12.08	< 0.001
Role limitation due to physical health	54.77 ± 12.96	67.51 ± 13.09	< 0.001
Bodily pain	61.54 ± 10.73	71.51 ± 10.89	< 0.001
General health perception	48.61 ± 10.29	63.75 ± 10.12	< 0.001
Social functioning	55.52 ± 12.23	70.84 ± 12.39	< 0.001
Vitality	49.54 ± 10.31	64.51 ± 10.88	< 0.001
Role limitation due to emotional problems	51.63 ± 14.26	67.45 ± 14.09	< 0.001
Emotional well-being	52.48 ± 12.88	67.46 ± 13.25	< 0.001
Paired sample t-test*			

The secondary outcomes of this study showed a significant improvement in transfusion interval following six months of thalidomide therapy (from 18.32 ± 4.01 days before treatment to 31.5 ± 6.2 days after treatment, $p < 0.001$). There was also significant improvement in Hb level (g/dL) and monthly transfusion requirement before and after treatment ($p < 0.001$ for both), as shown in Table-III.

Table-III: Transfusion parameters and Hemoglobin levels before and after Thalidomide therapy

n = 80

Secondary outcome parameters	Baseline values (Mean ± SD)	Values after 6 months of therapy (Mean ± SD)	p-value*
Hemoglobin level (g/dL)	7.33 ± 1.09	9.14 ± 1.15	< 0.001
Transfusion interval (days)	18.32 ± 4.01	31.50 ± 5.13	< 0.001
Monthly transfusion requirement (units)	2.89 ± 0.71	1.75 ± 0.76	< 0.001
Paired sample t-test*			

The study also monitored the adverse effects of thalidomide during 6 months treatment which were found to be generally mild to moderate in severity. The most common adverse effects were constipation (17.5%), drowsiness/sedation (13.75%), mild peripheral neuropathy (12.5%), and dizziness (9.0%). No

cases of deep vein thrombosis (DVT), or severe neuropathy (grade ≥ 3), or discontinuation due to adverse effects were recorded. The details are shown in Table-IV.

Table-IV: Adverse effects during thalidomide therapy

n = 80

Adverse effects	n (%)	Management steps taken
Constipation	14 (17.50)	Dietary advice / laxatives
Drowsiness / sedation	11 (13.75)	Dose timing adjusted
Peripheral neuropathy (mild)	10 (12.50)	Dose reduction / monitoring
Dizziness	7 (8.75)	Observation was suggested.

DISCUSSION

The present study evaluated the impact of thalidomide therapy on HRQoL in TDT patients using the SF-36 questionnaire. Significant improvement was observed in all eight domains of SF-36 after six months of adding thalidomide to standard treatment ($p < 0.001$ for all). This addition improved hemoglobin level from 7.33 ± 1.09 g/dL to 9.14 ± 1.15 g/dL, while transfusion interval increased from 18.32 ± 4.01 days to 31.50 ± 5.13 days. The initiation of thalidomide also led to a decreased monthly transfusion requirement. This adjuvant therapy was generally well tolerated as the adverse effects observed during the study were mostly mild to moderate and were manageable with regular observation, small dietary changes or dose adjustments.

The current study findings are largely supported by recent regional and international studies demonstrating thalidomide as a useful therapeutic agent in improving hematological parameters, reducing transfusion burden, and enhancing HRQoL among TDT patients. A review by Shah and Badawy on HRQoL in thalassemia patients showed that disease-modifying therapies and adjunctive therapies demonstrated improvement in multiple HRQoL domains, particularly physical, emotional, and mental health components.¹⁴ This comprehensive review supports the rationale for evaluating thalidomide as a useful therapeutic option particularly for improvement in QoL of in TDT patients.

The validity and utility of SF-36 questionnaire for evaluating the HRQoL among thalassemia patients was demonstrated in a study conducted by Hossain MJ et al. in Bangladesh. The mean total SF score in TDT patients was 61.24 ± 16.68 . The lowest scores were noted in SF (44.24 ± 23.33), GH (48.19 ± 16.94), and RPH (51.05 ± 37.72). The study also mentioned a gender-based difference in BP ($p < 0.01$) and PHC ($P = 0.046$). The impaired HRQoL was found to be particularly associated with disease severity, transfusion dependence, comorbidities, and the low socioeconomic status.¹¹

A recently published study by Mishra V. et al. evaluated the impact of thalidomide therapy on HRQoL in TDT patients using the SF-36 questionnaire. This study conducted in SA (Indian) population, also demonstrated significant improvement in both physical health component (PHC) and mental health component (MHC) scores when compared to standard therapy. This significant improvement was reported in multiple domains of SF-36, including VT, EW, REP, and SF. Subgroup analysis showed that better PHC scores were observed in patients aged ≤ 20 years ($P = 0.03$), and without splenectomy ($P < 0.001$), while improved MHC scores were noted in patients aged > 20 years ($P < 0.01$) and those with intact spleen ($P < 0.001$). Moreover, the study reported that thalidomide rendered 64% patients' transfusion-free, while the other 30% showed prolonged transfusion intervals from 20 to 35 days.¹⁵ These findings of Mishra study are closely parallel to the HRQoL hematological and improvements observed in our study.

A systemic review conducted by Atta T et al. assessed the efficacy of thalidomide therapy in TDT patients, in SA countries, especially in India and Pakistan. The review including 780 subjects, showed that thalidomide treatment resulted in significant improvements in hemoglobin level, fetal hemoglobin (HbF), serum ferritin, spleen size, transfusion requirement, and QoL. It is important that about 69.6% of the patients became transfusion independent. The majority of side effects were mild and easy to manage. The results indicated that thalidomide may be a useful and effective add-on treatment in improving clinical outcomes and HRQoL among transfusion-dependent β -thalassemia patients.¹⁶

These findings are further strengthened by the evidence provided by another study conducted in SA demographics, supporting thalidomide as a beneficial adjunctive therapy in TDT. Bhattacharjee S et al. studied the effectiveness and safety of combination of a low dose thalidomide and hydroxyurea therapy in a prospective study in Indian patients with TDT. The results showed that treatment responders had significant improvements in HRQoL, higher Hb levels and lower transfusion needs and ferritin levels. The overall response rate was 63.4%, and importantly 46.3% patients became transfusion independent. Therapy was well tolerated, and there were no significant adverse effects. The study therefore validated the results of above studies that thalidomide therapy can serve as a beneficial adjunctive treatment to enhance clinical outcomes and HRQoL in patients with TDT.¹⁷

A recent systematic review published in 2026 including 1731 patients, strongly endorsed the secondary outcomes of our study as thalidomide was found to have a strong effect on transfusion independence in TDT, with many patients becoming transfusion independent over the long term. The study also showed that thalidomide treatment has satisfactory tolerability, favoring the use of thalidomide as a promising add-on treatment over the long term for the management of β -thalassemia.¹⁸

In conclusion, the results of our study largely support the evidence provided by other recent studies which support the significant impact of thalidomide therapy on HRQoL outcomes and hematological parameters of TDT patients. This decrease in transfusion dependence and the enhanced physical, emotional and psychosocial function demonstrates the potential long-term clinical utility of thalidomide as an adjunctive therapy in the treatment of TDT.

Limitations of this study include its single-center design with a relatively small sample size, which may limit the generalizability of these findings. Moreover, the follow-up duration was limited to six months, which may not be sufficient to fully assess the long-term efficacy, safety and QoL related benefits of thalidomide therapy.

CONCLUSION

This study demonstrated significant benefits of adding thalidomide to standard therapy in terms of improved HRQoL in TDT patients. These advantages were observed across physical, emotional, and social domains of the SF-36 questionnaire, along with a reduced transfusion burden and improved hemoglobin levels. This study therefore suggests the potential role of thalidomide as an adjunctive therapeutic option to positively influence the functional capacity and overall well-being of these patients. Future studies with larger sample size and longer follow-up duration are suggested to evaluate long-term efficacy, safety profile and sustainability of improved QoL in TDT patients.

Declarations

Ethical Approval:

The ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent revisions, or similar guidelines, were followed in the conduct of this study. The Pak International Medical College Hayatabad Peshawar, Institutional Research and Ethical Review Board (IREB) granted ethical approval (Ref No: PIMC/DMR/2025/03).

Consent

Informed consent

was obtained from the parents of patients in a language that they comprehend.

Competing Interests:

The authors declare that they have no competing interests.

MU

Collection of data and interpretation

NUH

Collection of data and interpretation, Manuscript writing

AZ

Literature search, Critical Review

AK

Collection of data and interpretation

FS

Study Concept, Planning, Manuscript writing, Data interpretation

AR

Critical Review, Data Interpretation

MI

Literature search, study design

AJ

Critical Review. Final checking of manuscript

Consent to Publish:

All authors involved in this manuscript have followed the guidelines set by the International Committee of Medical Journal Editors (ICMJE) in terms of authorship criteria. All the authors agree upon final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Author Contribution

TH: Study Concept, Planning, Manuscript writing, Data interpretation
MU: Collection of data and interpretation
NUH: Collection of data and interpretation, Manuscript writing
AZ: Literature search, Critical Review
AK: Collection of data and interpretation
FS: Study Concept, Planning, Manuscript writing, Data interpretation
AR: Critical Review, Data Interpretation
MI: Literature search, study design
AJ: Critical Review. Final checking of manuscript

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Data Availability:

The data for this study is available; however, it cannot be shared publicly due to privacy and confidentiality concerns. The data is, however, available from the authors upon reasonable request.

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