

ORIGINAL ARTICLE

Efficacy of immunomodulator drug thalidomide in multi-transfused thalassemia patients: A single center experience from South Punjab, Pakistan.

Muhammad Tariq Aziz¹, Sajjad Hussain², Sara Rubab³, Muhammad Aslam Shiekh⁴

ABSTRACT... **Objective:** To determine the efficacy of thalidomide in multi transfused Thalassemic Children. **Study Design:** Quasi-experimental study. **Setting:** Thalassemia Center, The Children's Hospital and Institute of Child Health, Multan, Pakistan. **Period:** August 2023 to December 2024. **Methods:** A total of 121 transfusion dependent thalassemia (TDT) children of either gender, aged between 2 to 15 years, were analyzed. Non-probability, consecutive sampling technique was adopted. Children were given thalidomide at a dose of 1.5mg/kg/day. CBC evaluation and clinical examination were done at 3-months interval for a duration of 6 months. At each visit, side effects, subjective complaints and rise /fall of Hemoglobin was noted. Statistical analysis was conducted using IBM-SPSS version 26.0. **Results:** In a total of 121 children, the median age was 8.00 years (IQR, 5.00-11.00), while 77 (63.6%) children were males. At baseline, the median hemoglobin level was 8.00 g/dL (IQR, 6.75-8.75), increasing to 8.90 g/dL (IQR, 7.65-9.80) at 3 months, and 9.90 g/dL (IQR, 8.70-11.00) at 6 months ($p < 0.001$). By the end of 6-months period, excellent, partial, and no response were noted among 59 (48.8%), 41 (33.9%), and 21 (17.4%) children, respectively. The most common treatment related side effects were constipation ($n=9$, 7.4%), neutropenia ($n=6$, 5.0%), and skin rash ($n=5$, 4.1%). No reported cases of severe adverse effects leading to discontinuation. **Conclusion:** In children with TDT, thalidomide significantly increased hemoglobin levels and reduced transfusion needs over six months.

Key words: Constipation, Hemoglobin, Neutropenia, Thalassemia, Thalidomide.

Article Citation: Aziz MT, Hussain S, Rubab S, Shiekh MA. Efficacy of immunomodulator drug thalidomide in multi-transfused thalassemia patients: A single center experience from South Punjab, Pakistan. Professional Med J 2026; 33(10):1916-1920. <https://doi.org/10.29309/TPMJ/2026.33.10.10517>

INTRODUCTION

Thalassemia is one of the most prevalent inherited hemoglobinopathies worldwide, particularly in regions with high consanguinity rates, such as South Asia.¹ In Pakistan, approximately 5-7% of the population carries the β -thalassemia gene, with an estimated 5,000 to 9,000 children born annually with transfusion-dependent β -thalassemia.^{2,3} These children require regular blood transfusions to maintain adequate hemoglobin levels, but this lifelong dependence leads to iron overload and related complications, necessitating iron chelation therapy.⁴

Conventional treatment strategies focus on transfusion support, iron chelation, and in some cases, hematopoietic stem cell transplantation, which is often inaccessible due to cost and donor availability.⁵ Emerging therapies, such as fetal

hemoglobin (HbF) inducers, have shown promise in reducing transfusion requirements.⁶ Thalidomide, an immunomodulatory and anti-angiogenic drug, has gained interest in recent years due to its potential role in stimulating γ -globin gene expression, thereby increasing fetal hemoglobin levels.^{7,8} Data on safety and efficacy of thalidomide in multi-transfused thalassemic children remain limited, particularly in low-resource settings like Pakistan. Thalidomide's role in β -thalassemia has been explored in small-scale studies, demonstrating a significant rise in hemoglobin levels and a reduction in transfusion dependence.^{8,9} Thalidomide's mechanism of action involves upregulating erythropoiesis and increasing fetal hemoglobin levels, which may compensate for defective β -globin synthesis.⁷

Given the significant burden of transfusion dependency, an effective inducer could improve

1. MBBS, FCPS, Associate Professor Pediatric Medicine, The Children's Hospital and Institute of Child Health, Multan, Pakistan.

2. MBBS, FCPS, Associate Professor Pediatric Medicine, The Children's Hospital and Institute of Child Health, Multan, Pakistan.

3. MBBS, FCPS, Assistant Professor Pediatric Medicine, The Children's Hospital and Institute of Child Health, Multan, Pakistan.

4. MBBS, FCPS, Associate Professor Pediatric Gastroenterology and Hepatology, The Children's Hospital and Institute of Child Health, Multan, Pakistan.

Correspondence Address:

Dr. Muhammad Aslam Shiekh

Department of Pediatric Gastroenterology and Hepatology, The Children's Hospital and Institute of Child Health, Multan, Pakistan.

aslamsh68@gmail.com

Article received on:

11/02/2026

Accepted for publication:

22/04/2026



quality of life and reduce the healthcare costs associated with frequent transfusions and iron chelation therapy. Due to historical association of thalidomide with teratogenicity, there is a need for rigorous evaluation of its safety, particularly in pediatric populations.^{10,11} This study was designed to determine the efficacy of thalidomide in multi-transfused thalassemic children by evaluating hemoglobin response, transfusion needs, and treatment-related adverse effects over a six-month period.

METHODS

This quasi-experimental study was conducted at the Thalassemia Center, The Children's Hospital and Institute of Child Health, Multan, Pakistan, from August 2023 to December 2024. Considering the response rate of thalidomide as 94.7% after 6 months of treatment⁷, with 95% confidence level, and 4% margin of error, the sample size was calculated to be 121. The study enrolled children aged 2-15 years, with transfusion-dependent thalassemia (TDT), and parents/guardians showing willingness to adhere to follow-up visits. Children with uncontrolled infections, significant hepatic or renal dysfunction, malignancy, or known contraindications to thalidomide were excluded. Non-probability, consecutive sampling technique was adopted. Ethical approval was obtained from the Institutional Ethical Committee (Ref. No. 1214, dated: 12-08-2023), and informed as well as written consents were sought from the parents/guardians. This clinical trial was registered as NCT06888232 (<https://clinicaltrials.gov>).

At baseline, a comprehensive clinical examination was performed, and relevant laboratory investigations, including complete blood count (CBC), serum ferritin, along with liver and renal function tests, were evaluated. Thalidomide was administered at a dose of 1.5 mg/kg/day, and all patients continued standard iron chelation therapy and other supportive treatments as per institutional protocols. Clinical and laboratory assessments were performed at three-month intervals for a total duration of six months. At each follow-up visit, hemoglobin levels, transfusion need, adverse events, and subjective symptoms were documented. Treatment response was categorized as excellent

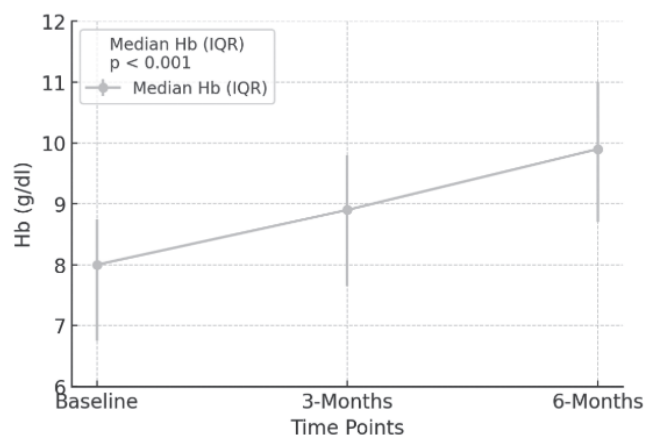
response showing an increase in hemoglobin by 1–2 g/dL or freedom from blood transfusions, partial response as an increase in hemoglobin <1 g/dL or a decrease in transfusion frequency, or no response if there was no increase in hemoglobin or an increase in transfusion requirement within three months. Adverse events were documented based on clinical symptoms, physical examinations, and laboratory findings. A special format was created to record study data.

Statistical analysis was conducted using IBM-SPSS version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD), or median and interquartile range (IQR) depending upon the normality distribution. Normality distribution of the data were checked applying Shapiro-Wilk test. Qualitative data were shown as frequencies and percentages. Chi-square test was applied to compare categorical data. Independent sample t-test or Mann-Whitney U test, or analysis of variance or Kruskal Wallis test were performed for the comparison of continuous data. P-value <0.05 was considered statistically significant.

RESULTS

In a total of 121 children, the median age was 8.00 years (IQR, 5.00-11.00), and the median weight was 26.90 kg (IQR, 16.60-34.90). The cohort comprised of 77 (63.6%) males, and 44 (36.4%) females. There were 71 (61.2%) children who were residing in rural areas. There were 63 (52.1%) households with a monthly income of $\leq$ 30,000. No significant differences were observed for baseline hemoglobin levels with respect to any of the socio-demographic characteristics. Table-I is showing descriptive details about the quantitative demographic and laboratory data.

At baseline, the median hemoglobin level was 8.00 g/dL (IQR, 6.75-8.75), increasing to 8.90 g/dL (IQR, 7.65-9.80) at 3 months, and 9.90 g/dL (IQR, 8.70-11.00) at 6 months ($p < 0.001$), and the details are shown in Figure-1.

FIGURE-1**Changes in hemoglobin during study period**

By the end of 3-months period, excellent, partial, and no response were noted among 55 (45.5%), 37 (30.6%), and 29 (23.9%) children, respectively. By the end of 6-months period, excellent, partial, and no response were noted among 59 (48.8%), 41 (33.9%), and 21 (17.4%) children, respectively. Baseline hemoglobin did not correlate significantly with leukocyte count ($r = -0.091$, $p = 0.320$), platelet count ($r = -0.107$, $p = 0.245$), alanine transaminase ($r = 0.005$, $p = 0.958$), or creatinine (r

$= 0.035$, $p = 0.702$). Hemoglobin at 3 months was negatively correlated with platelet count, and this was statistically significant ($r = -0.212$, $p = 0.019$). No significant correlations were found between hemoglobin at 6 months and laboratory parameters (Table-II). Treatment was generally well tolerated, with no reported cases of severe adverse effects leading to discontinuation. The most common treatment related side effects were constipation ($n=9$, 7.4%), neutropenia ($n=6$, 5.0%), and skin rash ($n=5$, 4.1%).

DISCUSSION

In this study, the median Hb increased from 8.00 g/dL (IQR, 6.75-8.75) at baseline to 8.90 g/dL (IQR, 7.65-9.80) at three months and 9.90 g/dL (IQR, 8.70-11.00) at six months ($p < 0.001$). The overall response rate at six months was 82.6%, with 48.8% achieving an excellent response and 33.9% demonstrating a partial response. Ju et al., reported a 94.7% response rate at six months in β -thalassemia patients, with Hb predominantly increasing due to elevated fetal hemoglobin (HbF) levels.⁷

TABLE-I**Descriptive statistics of quantitative data (n=121)**

Parameters	Median	IQR	Minimum	Maximum
Age (years)	8.00	5.00-11.00	2.00	14.00
Weight (kg)	26.90	16.60-34.90	8.30	44.50
Baseline hemoglobin (g/dl)	8.00	6.75-8.75	5.50	9.80
Leukocyte count ($10^9/L$)	7.80	6.10-9.35	4.60	10.50
Platelets ($10^9/L$)	289.00	211.50-375.00	152.00	444.000
Alanine aminotransferase (U/L)	29.00	21.00-37.50	15.00	44.00
Serum creatinine (mg/dl)	0.81	0.54-1.01	0.30	1.20

TABLE-II**Correlation of hemoglobin with laboratory parameters (n=121)**

Parameters		Leukocytes count ($10^9/L$)	Platelets ($10^9/L$)	Alanine Transaminase (U/L)	Creatinine (mg/dl)
Baseline Hemoglobin (g/dl)	Pearson Correlation	-0.091	-0.107	.0005	0.035
	P-value	0.320	0.245	0.958	0.702
Hemoglobin after 3-months (g/dl)	Pearson Correlation	-0.043	-0.212*	0.032	-0.016
	Sig. (2-tailed)	0.638	0.019	0.724	0.864
Hemoglobin after 6-months (mg/dl)	Pearson Correlation	0.006	0.047	0.024	-0.002
	Sig. (2-tailed)	0.944	0.609	0.793	0.987

Chen et al., found that thalidomide led to a median Hb rise of 14 g/L and significantly reduced transfusion requirements ($p < 0.001$).¹² In a meta-analysis by Ali et al., thalidomide induced transfusion independence in 54% of TDT patients, with an overall response rate of 85% (95% CI, 80–90%).¹³ The differences in the response to thalidomide in some studies may be attributed to variations in patient demographics, genetic factors, and study duration. Chen et al., included only patients ≥ 14 years, while this study comprised relatively younger children (median age, 8.00 years), potentially affecting drug metabolism and treatment response.¹² Differences in HbF upregulation, which was not assessed in this study, may have contributed to variation in response rates.¹⁴

This study found no significant association between treatment response and socio-demographic factors. This aligns with other researchers indicating that thalidomide response is primarily determined by intrinsic erythropoietic and genetic factors rather than socio-economic status.¹⁵ Yang et al., and Lu et al., suggested that β -globin gene mutations and specific polymorphisms influenced response, emphasizing the need for genetic stratification in future research.^{16,17}

A notable finding in this study was the significant negative correlation between Hb levels at three months and platelet count ($r = -0.212$, $p = 0.019$), suggesting a possible link between erythroid expansion and reduced megakaryopoiesis. This is in agreement with findings by Zahid et al., who reported a decline in platelet counts following thalidomide therapy, potentially due to its anti-angiogenic effects.¹⁸ The safety profile in this study was favorable, with no severe adverse effects necessitating treatment discontinuation. The most common side effects included constipation (7.4%), neutropenia (5.0%), and skin rash (4.1%). These adverse effects were mild. Chen et al., reported drowsiness, dizziness, and fatigue, likely due to differences in patient populations and drug dosages.¹² Zahid et al., documented rare but serious complications, including cerebrovascular accidents and portal vein thrombosis, reinforcing the need for close monitoring, especially in high-risk patients.¹⁸

The clinical implications of the present findings suggest that thalidomide is a promising therapeutic option for TDT, particularly in resource-limited settings, where access to curative therapies such as hematopoietic stem cell transplantation is restricted.^{19,20} The significant Hb increase observed in this study suggests that thalidomide can effectively reduce transfusion dependence, thereby mitigating iron overload and its associated complications.^{21,22} The long-term effects on iron metabolism and end-organ function remain unclear and warrant further investigation.

This study has several limitations. The absence of a control group limits causal inference regarding thalidomide's efficacy. HbF levels were not measured, preventing direct comparison with studies that have identified HbF induction as the primary mechanism of action. The short follow-up period precludes assessment of long-term sustainability and potential late-onset adverse effects. Genetic factors influencing thalidomide response were not evaluated, which may have provided insights into inter-individual variability.

CONCLUSION

In children with TDT, thalidomide significantly increased hemoglobin levels and reduced transfusion needs over six months. The findings support the potential role of thalidomide as a cost-effective alternative for TDT management, particularly in settings where transfusion support is limited.

ACKNOWLEDGEMENTS

The authors are thankful to M. Aamir Latif (RESnTEC) for his assistance in trial registration of this research.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Copyright© 22 April, 2026.

REFERENCES

- Anwar R, Arzoo K, Riaz A, Ali R, Saghir S, Habib B. **Types of inherited hemoglobin disorders among the patients attending a tertiary care hospital: Types of inherited hemoglobin disorders among the patients.** Pakistan Journal of Health Sciences. 2024 Dec 1:24-9.
- Khaliq S. **Thalassemia in Pakistan.** Hemoglobin. 2022; 46(1):12-14.
- Ansari SH, Shamsi TS, Ashraf M, Bohray M, Farzana T, Khan MT, et al. **Molecular epidemiology of β -thalassemia in Pakistan: Far reaching implications.** Int J Mol Epidemiol Genet. 2011; 2(4):403-8.
- Forni GL, Kattamis A, Kuo KHM, Maggio A, Sheth S, Taher AT, et al. **Iron chelation therapy for children with transfusion-dependent β -thalassemia: How young is too young?** Pediatr Blood Cancer. 2024; 71(8):e31035.
- Caocci G, Orofino MG, Vacca A, Piroddi A, Piras E, Addari MC, et al. **Long-term survival of beta thalassemia major patients treated with hematopoietic stem cell transplantation compared with survival with conventional treatment.** Am J Hematol. 2017; 92(12):1303-10.
- 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(1):e2024001.
- 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(43):e40328.
- Li Y, Ren Q, Zhou Y, Li P, Lin W, Yin X. **Thalidomide has a significant effect in patients with thalassemia intermedia.** Hematology. 2018; 23(1):50-54.
- Jain M, Chakrabarti P, Dolai TK, Ghosh P, Mandal PK, Baul SN, et al. **Comparison of efficacy and safety of thalidomide vs hydroxyurea in patients with Hb E- β thalassemia - a pilot study from a tertiary care Centre of India.** Blood Cells Mol Dis. 2021; 88:102544.
- Ito T, Ando H, Handa H. **Teratogenic effects of thalidomide: Molecular mechanisms.** Cell Mol Life Sci. 2011; 68(9):1569-79.
- Asatsuma-Okumura T, Ito T, Handa H. **Molecular mechanisms of the teratogenic effects of thalidomide.** Pharmaceuticals (Basel). 2020; 13(95):1-16.
- Chen JM, Zhu WJ, Liu J, Wang GZ, Chen XQ, Tan Y, et al. **Safety and efficacy of thalidomide in patients with transfusion-dependent β -thalassemia: A randomized clinical trial.** Signal Transduct Target Ther. 2021; 6(1):405.
- Ali Z, Ismail M, Khan MTM, Rehman IU. **Safety and efficacy of Thalidomide in transfusion-dependent β -Thalassemia: A Systematic Review and meta-analysis.** Khyber Med Uni J. 2022; 14(3):201-06.
- Gambari R, Waziri AD, Goonasekera H, Peprah E. **Pharmacogenomics of drugs used in β -Thalassemia and sickle-cell disease: From basic research to clinical applications.** Int J Mol Sci. 2024; 25(8):4263.
- Rehman W, Arfons LM, Lazarus HM. **The rise, fall and subsequent triumph of thalidomide: Lessons learned in drug development.** Ther Adv Hematol. 2011; 2(5):291-308.
- 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(1):e2024001.
- 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(1):191.
- Zahid A, Ismail M, Rehman IU, Rani GF, Ali M, Khan MTM. **Long-term clinical efficacy and safety of thalidomide in patients with transfusion-dependent β -thalassemia: Results from Thal-Thalido study.** Sci Rep. 2023; 13(1):13592.
- Khan SM, Sultana N, Siddiqui S, Nizammuddin M. **Comparison of efficacy and safety of thalidomide vs hydroxyurea in thalassemia patients: A single-centre pilot study.** Nat J Health Sci. 2024; 9:149-155.
- Idrees M, Khan MTM, Bawazir W, Hazzazi MS, Kabrah SM, Altayar MA, et al. **Safety and efficacy of low-dose thalidomide in patients with transfusion dependent thalassemia: a clinico-hematological assessment.** JPTPC. 2023; 30(17):1344-53.
- Nag A, Radhakrishnan VS, Kumar J, Bhawe S, Mishra DK, Nair R, et al. **Thalidomide in patients with transfusion-dependent E-Beta Thalassemia refractory to hydroxyurea: A single-center experience.** Indian J Hematol Blood Transfus. 2020; 36(2):399-402.
- Che J, Luo T, Huang L, Lu Q, Yan D, Meng Y, et al. **Magnetic resonance imaging quantification of the liver iron burden and volume changes following treatment with thalidomide in patients with transfusion-dependent β -Thalassemia.** Front Pharmacol. 2022; 13:810668.

AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Muhammad Tariq Aziz: Data collection, data analysis.
2	Sajjad Hussain: Critical revisions, proof reading.
3	Sara Rubab: Methodology, data analysis.
4	Muhammad Aslam Shiekh: Literature review, proof reading.