RESEARCH PAPER

Efficacy of Thalidomide in Reducing Blood Transfusion in Transfusion Dependent Thalassemia Major Patients

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ABSTRACT

Background: Thalassemia major is a transfusion-dependent hemoglobinopathy associated with iron overload and multiple complications. Reducing the frequency of blood transfusions can improve patient outcomes and quality of life. Thalidomide, an immunomodulatory agent, has shown potential in increasing hemoglobin levels and reducing transfusion requirements.

Objectives: To evaluate the efficacy of thalidomide in reducing blood transfusions in transfusion-dependent thalassemia major patients.

Study Design & Setting: A descriptive case series conducted at the Department of Pediatric Medicine, Fauji Foundation Hospital, Rawalpindi from 1st October 2025 to 1st January 2026.

Methodology: Using successive non-probability sampling, 86 patients with beta thalassemia major, ranging in age from 1 to 15 years, were included in the study. These patients had received transfusions four to six times weekly for the previous two years. Patients received oral thalidomide starting with hydroxyurea and supportive treatment, starting at 1-2 mg/kg/day and increasing to 4 mg/kg/day as needed. Blood samples were collected for complete blood count and biochemical testing. We used SPSS 25.0 to analyze the data. Qualitative data were shown as percentages and frequency, whilst quantitative factors were shown as mean ± SD. Stratification was performed for age, gender, weight, duration of disease, and annual blood transfusions. A p-value less than 0.05 was deemed significant when chi-square tests were utilized.

Results: Among 86 patients, 57 (66.3%) achieved efficacy, maintaining hemoglobin ≥9 g/dL without transfusion. Males, patients with a disease duration of 5 years or less, and those having 15 transfusions or less per year had a considerably better efficacy (p = 0.000 for all). Age and weight were not significantly associated with efficacy.

Conclusion: Thalidomide is effective in reducing transfusion requirements in thalassemia major, particularly in males, patients with shorter disease duration, and those with lower annual transfusion needs.

Keywords: Beta thalassemia major, Blood transfusion, Efficacy, Hydroxyurea, Thalidomide

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INTRODUCTION

One of the most prevalent hereditary disorders caused by a single gene is beta-thalassemia. The hemoglobinopathy gene is present in over 150 million people globally, as per the WHO, this poses a substantial threat to public health around the world.[1] The removal or insertion of individual nucleotides or beta-thalassemia is mainly caused by small changes in the β-globin gene. The buildup of extra, unbound α-globin chains in bone marrow erythroid precursors and mature erythrocytes leads to peripheral hemolysis and ineffective erythropoiesis.[2] Clinically, beta-thalassemia was separated into categories: transfusion-dependent & non-transfusion dependent.Individuals with transfusion-dependent β-thalassemia need iron chelation therapy and regular red blood cell transfusions to survive in the long run. However, there is a risk of iron excess from blood transfusions, which can harm end organs and increase the risk of illness and death.[4]

To present, a number of promising fetal hemoglobin sodium butyrate, hydroxyurea, erythropoietin, & 5-azacytidine are (HbF) inducers that have not been very efficient in treating β-thalassemia.5Thalidomide is a synthetic derivative of glutamic acid that is commonly used as an immunomodulator to treat various hematological malignancies due to its anti-inflammatory, anti-angiogenic, & anti-tumor effects.[6] Furthermore, thalidomide stimulates the expression of the γ-globin gene by acting as a HbF inducer.[7] Significant effects of thalidomide on NTDT or TDT have been reported in a few case reports and retrospective analyses, which our group later verified in a clinical trial.[8]

Despite thalidomide's ability to reduce transfusion demand by increasing HbF production, its effectiveness in individuals having transfusions-dependent beta

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thalassemia major must be thoroughly demonstrated. The purpose of this study is in order to synthesize the existing facts on the consequences of thalidomide and to give more specific recommendations for its usage in clinical practice. By examining the existing evidence on its therapeutic potential, this research seeks to decrease transfusion-related complications and improve patient outcomes with TDBTM. That is, by helping to reduce the total cost of transfusion in thalassemia care, giving details on how thalidomide might be included into the therapy, and by discussing its benefits and drawbacks. With the goal of learning how well thalidomide works for those with transfusion-dependent thalassemia major.

MATERIALS AND METHODS

This study was conducted at the Department of Pediatric Medicine, Fauji Foundation Hospital, Rawalpindi from 1st October 2025 to 1st January 2026. Using the World Health Organization's sample size calculator, we determined that 86 individuals with transfusion-dependent thalassemia major would provide sufficient data to draw conclusions with a 95% confidence level, a 10% margin of error, and an anticipated thalidomide efficacy of 66.20%. Non-probability consecutive sampling technique was used. The study included both male and female patients with a track record of four to six weekly transfusions of blood in the two years before to inclusion, as well as a diagnosis of beta thalassemia major according to operational definition, and individuals aged 1 to 15 years old. We did not include patients who had a history of venous or artery thrombosis, hypersensitivity to thalidomide, severe cardiac or pulmonary illnesses, problems with the liver, cerebrovascular, cardiovascular, the liver, kidneys mental health disorders, or any hemoglobinopathies apart from beta thalassemia major. The 86 pediatric medicine patients who were qualified to participate were enrolled after the study received permission by the Institutional Ethics Review Committee & CPSP. We made sure that parents or guardians gave their written informed consent and that their information remained confidential. Oral thalidomide was given to all patients at a starting dose of 1-2 mg/kg/day. If certain patients did not respond adequately, the dosage was raised by 1 mg/kg/day each two months until it reached an upper limit of 4 mg/kg/day (70 mg/day). Patients who did not demonstrate recovery following three months of treatment with an initial dosage of 2 mg/kg/day of thalidomide were stopped from the medication. The daily dosage of hydroxyurea for all patients remained 10–20 mg/kg. Every day, a dose of 2-4 mg/kg of clopidogrel was given to reduce the risk of thrombosis. Patients with iron overload continued iron chelation therapy, and supportive treatment including hepatoprotective agents, antihistamines, and dietary supplements was provided. For laboratory evaluation, Two milliliters was gathered in an EDTA purple-topped tube for a full blood count, and three milliliters have been put in a gel tube with a yellow top for biochemical analysis; each patient had five milliliters of vein blood collected. Biochemical parameters were analyzed using the Cobas 6000 analyzer series, while complete blood counts were performed using an automated hematological analyzer. Efficacy of thalidomide in reducing blood transfusion requirements was recorded according to the operational definition. Beta thalassemia major was defined as previously diagnosed patients who had been on regular treatment for at least two years and fulfilled diagnostic criteria levels of hemoglobin ranging from 30% to 90% and hemoglobin A (HbA) values below 3.5% were shown by hemoglobin electrophoresis. Efficacy was considered present if, during the last 56 days following the patient's hemoglobin level stayed at or above 9 g/dL over the three months of the thalidomide treatment, therefore no blood transfusions were necessary.

All demographic, clinical, and a specifically developed proforma was used to document the laboratory data. Data were analyzed using SPSS version 25.0. The statistical significance of quantitative factors was determined by utilizing the Shapiro-Wilk test. Age, weight, yearly blood transfusions, and length of illness were shown as quantitative factors with standard deviations or medians with interquartile ranges, whereas gender & efficacy were shown as qualitative variables with percentages and frequencies. Age, gender, weight, yearly transfusion frequency, and length of illness were among the effect modifiers that were controlled for through stratification. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

In Table 1 we can see the participants' demographic information. The study comprised 86 patients, the majority of whom were under the age of 5 (65.1%), with 34.9% falling in the 6–10 age bracket. On average, the participants were 8.36 ± 3.84 years old. In terms of the gender breakdown, men made up 57.0% of individuals and females 43.0%. Concerning body weight, 65.1% of the patients weighed less than 18 kg, while 34.9% had a weight of 18 kg or more, with a mean weight of 18.77 ± 5.90 kg (Table 1).

Table 1: Demographic Characteristics of Patients (n = 86)

Variable	Frequency / Mean ± SD	Percentage
Age (years)		
< 5 years	56	65.1%
6–10 years	30	34.9%
Mean Age (years)	Mean±SD	8.36 ± 3.84
Gender		
Male	49	57.0%
Female	37	43.0%
Weight (kg)		
< 18 kg	56	65.1%

≥ 18 kg	30	34.9%
Mean Weight (kg)	Mean±SD	18.77 ± 5.90

Blood transfusions occurred between 10 and 25 times yearly. A total of 44.2% of patients received 15 or fewer transfusions annually, whereas 55.8% received more than 15 transfusions per year. The mean annual number of transfusions was 17.26 ± 4.97. Disease durations varied from one to ten years; 47.7% of patients had illnesses that lasted five years or less, while 52.3% had illnesses that lasted five years or more. A mean of 5.48 ± 3.09 years was the duration of the sickness. Furthermore, a majority of patients (79.1%) had a history of chelation therapy, while 20.9% did not receive chelation treatment (Table 2).

Table 2: Clinical Characteristics of Transfusion-Dependent Thalassemia Major Patients (n = 86)

Variable	Frequency / Mean ± SD	Percentage
Blood Transfusions per Year		
≤ 15	38	44.2%
> 15	48	55.8%
Mean Blood Transfusions per Year	Mean±SD	17.26 ± 4.97
Duration of Disease (years)		
≤ 5 years	41	47.7%
> 5 years	45	52.3%
Mean Duration of Disease (years)	Mean±SD	5.48 ± 3.09
History of Chelation Therapy		
Yes	68	79.1%
No	18	20.9%

The efficacy of thalidomide in reducing the need for blood transfusions among data from the research subjects is shown in Table 3. Of the 86 patients who were treated with thalidomide for three months, 56 (or 66.3% of the total) showed improvement in their hemoglobin levels to 9 g/dL or above without the need for a transfusion of blood within 56 days. Conversely, 29 patients (33.7%) did not show efficacy with thalidomide therapy (Table 3).

Table 3: Efficacy of Thalidomide in Reducing Blood Transfusion (n = 86)

Efficacy	Frequency	Percentage
Yes	57	66.3%
No	29	33.7%
Total	86	100%

The stratification of thalidomide efficacy is presented in Table 4. Efficacy was slightly higher in patients aged <5 years (69.6%) than in those aged 6–10 years (60%), but this was not statistically significant (p = 0.367). All male patients (100%) responded, compared to 21.6% of females, showing a significant difference (p = 0.000). Patients weighing <18 kg had 69.6% efficacy versus 60% in those ≥18 kg (p = 0.367). All patients with disease duration ≤5 years (100%) responded, compared to 35.6% with duration >5 years (p = 0.000). Similarly, efficacy was higher in patients receiving ≤15 transfusions/year (97.4%) than those with >15 transfusions/year (41.7%), with a significant association (p = 0.000) (Table 4).

Table 4: Stratification of Efficacy of Thalidomide by Age, Gender, Weight, Duration of Disease, and Annual Blood Transfusions (n = 86)

Variable	Category	Efficacy Yes	Efficacy No	Total	p-value
Age (years)	< 5	39 (69.6%)	17 (30.4%)	56	0.367
	6–10	18 (60.0%)	12 (40.0%)	30	
Gender	Male	49 (100.0%)	0 (0.0%)	49	0.000
	Female	8 (21.6%)	29 (78.4%)	37	
Weight (kg)	< 18	39 (69.6%)	17 (30.4%)	56	0.367
	≥ 18	18 (60.0%)	12 (40.0%)	30	
Duration of Disease (years)	≤ 5	41 (100.0%)	0 (0.0%)	41	0.000
	> 5	16 (35.6%)	29 (64.4%)	45	
Annual Blood Transfusions	≤ 15	37 (97.4%)	1 (2.6%)	38	0.000
	> 15	20 (41.7%)	28 (58.3%)	48	

DISCUSSION

Thalassemia major is a severe inherited hemoglobin disorder marked by inefficient erythropoiesis and persistent anemia, frequently requiring frequent transfusions of blood to sustain sufficient hemoglobin levels.[10] Frequent transfusions, however, can cause iron

excess and other chronic problems, which is very taxing on healthcare systems and individuals alike. Among these, immunomodulatory agents such as thalidomide are being studied because of their ability to increase hemoglobin levels and promote erythropoiesis.[11] Evaluating the effectiveness of such therapies in transfusion-dependent populations is essential to identify safe and practical strategies that can minimize transfusion frequency while improving patients' quality of life.

In the present study, thalidomide demonstrated substantial efficacy in reducing transfusion requirements in transfusion-dependent thalassemia major patients. These results are in line with those of Atta et al. (2024), who found that 69.6% of 543 patients became transfusion independent while simultaneously improving their red blood cell count, HbF, serum ferritin, splenic size, and the standard of life with thalidomide treatment at doses of 50-150 mg/day.[12] Similarly, Kanwal et al. (2025) observed that out of 500 patients, 61.4% became transfusion-independent by 6 months, increasing to 82% at 5 years, with a mean hemoglobin rise dropped significantly ($p < 0.001$) from 6.5 ± 0.6 g/dL to 8.6 ± 0.3 g/dL. In our study, 66.3% of patients achieved efficacy, maintaining hemoglobin ≥9 g/dL without transfusion, which aligns closely with these previous reports and demonstrates the short-term benefits of thalidomide therapy in pediatric populations.[13]

Additional studies also support these results. Khan et al. (2022) reported hemoglobin improvement from between 4.8 ± 1.5 g/dL and 8.2 ± 1.8 g/dL, with a response rate of excellent or good in 75% of patients.[14] Ali et al. (2023) documented a mean hemoglobin increase of 6 months: 1.4 g/dL, 30 months: 2.0 g/dL, 76.7% of patients are able to stop requiring transfusions.[14] Ansari et al. (2022) observed that 65.9% of patients responded to combination hydroxyurea and thalidomide therapy, leading to significant decreases in transfusion volume ($p < 0.001$). In contrast, Lu et al. (2022) discovered a general rate of response of 85% and a full response rate of 54%.[15] Our study's stratified analysis aligns with these findings, showing higher efficacy in patients with shorter disease duration, lower annual transfusion requirements, and male gender, suggesting that patient selection may influence treatment outcomes.

Pooled data from Ali et al. (2022) across nine studies involving 407 transfusion-dependent thalassemia patients indicated an overall transfusion independence of 54% (95% CI, 34–75%), accompanied by moderate side effects in 44% of instances. Shah et al. (2025) also observed a significant hemoglobin increase little side effects, a drop in serum ferritin and a reduction in transfusions frequency to 0.4 ± 0.2 per month, and an increase from 6.2 ± 0.7 g/dL to 9.2 ± 0.5 g/dL ($p < 0.001$). These studies corroborate the tolerability and effectiveness of thalidomide in improving hematological parameters and reducing transfusion dependency. Overall, our findings reinforce that thalidomide is an effective adjunct therapy in transfusion-dependent thalassemia major, particularly in carefully selected patients, and can provide significant clinical benefits with manageable safety profiles. An overall rate of response of 85% (95% CI: 80-90%) and a full response ratio of 54% (95% CI: 31-76%), as shown in a pooled analysis by Lu et al. (2022), indicate considerably increased odds of response compared with placebo (OR = 20.4; 95% CI: 6.75-61.64). Hemoglobin and hemoglobin F levels rose significantly, although hemoglobin in adults (HbA), spleen size, plus serum ferritin didn't alter, according to the study.[17] Ansari et al. (2022) evaluated 135 patients with hydroxyurea (HU) alone and then in combination with thalidomide, noting a notable decrease in blood transfusion quantity ($p < 0.001$) and a notable rise in median hemoglobin levels within three and six months of combined therapy ($p < 0.001$). Variable effectiveness influenced by genetic variations was shown in their population, with 65.9% of individuals responding well, 11.9% responding, and 22.2% not responding at all.[18]

Idrees et al. (2023) assessed 384 TDT patients receiving low-dose thalidomide and reported significant responses for hemoglobin achievement ($p < 0.001$), with 47.9% excellent, 25% good, and 15.6% partial responders. In addition, Shah et al. (2025) confirmed these findings by documenting an increase in hemoglobin between 6.2 ± 0.7 g/dL to 9.2 ± 0.5 g/dL after 12 months, with 80% of participants attaining transfusions independence ($p < 0.001$). Transfusion frequency dropped to 0.4 ± 0.2 per month, and serum ferritin went from 2950 ± 450 ng/mL to 950 ± 250 ng/mL ($p < 0.001$). Additionally, The spleen size & organ congestion were reduced, and thalidomide was well-tolerated. The few occurrences of constipation were managed satisfactorily, although three cases of weariness and four cases of thromboembolism were reported.[19] Shah et al. (2025) further confirmed the benefits of thalidomide, showing hemoglobin increased at 12 months, the level increased from 6.2 ± 0.7 g/dL to 9.2 ± 0.5 g/dL, and 80% of the patients achieved transfusion independence ($p < 0.001$). A decrease of 2950 ± 450 ng/mL to 950 ± 250 ng/mL was observed in serum ferritin, and the frequency of transfusions decreased to 0.4 ± 0.2 every month ($p < 0.001$) as well.[20]

Study Limitations:

The follow-up period was short, limited to three months, it was not possible to evaluate the safety and effectiveness of thalidomide over the long term. Genetic variations influencing response were not analyzed. Adverse events were recorded, but detailed monitoring for rare complications like neuropathy was not performed. There was no control group for direct comparison, and concomitant therapies such as hydroxyurea and iron chelation could have influenced outcomes. Finally, patient adherence to medication and lifestyle factors were not systematically monitored

CONCLUSION

Thalidomide is an effective and well-tolerated therapy for reducing transfusion requirements in transfusion-dependent thalassemia major patients. It helps most patients become transfusion-free by dramatically raising hemoglobin levels.

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