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Incidence of Peripheral Neuropathy and Cardiovascular Adverse Effects in β-Thalassemia Patients Following Off-Label Thalidomide Therapy

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Abstract

Background: Thalidomide, used off-label as an HbF inducer, is associated with significant neurological and cardiovascular toxicity. This study examines the incidence of peripheral neuropathy and cardiovascular adverse effects among β-thalassemia patients using externally sourced thalidomide.

Methods: A retrospective review was conducted at JSF (jan 2024 to oct 2025) including patients who reported independent thalidomide use. Clinical data were analyzed to identify neurological and cardiovascular complications.

Results: Peripheral neuropathy and generalized body aches were the most prevalent neurological complications, while arrhythmias represented the most significant cardiovascular toxicity.

Conclusion: Off-label thalidomide poses substantial risks when used without clinical supervision. Improved regulation and patient education are required to prevent avoidable morbidity. However it has beneficial effect in thalassemic patient having allo antibodies.

Keywords: β-Thalassemia, Thalidomide, Periphral neuropathy, Cardiovascular toxicity, Arrythmias, Adverse drug reactions, Off label drug use

Introduction

β-thalassemia is a hereditary hemoglobin synthesis disorder requiring lifelong transfusion therapy. Thalidomide has gained renewed interest as a low-cost fetal hemoglobin inducer in resource-limited settings without being approved by authorities for thalasemic patient. Despite reported hematological benefits, its safety profile remains concerning.

Recent observations at JSF identified a pattern of neurological and cardiovascular toxicities among patients who obtained thalidomide from off label external sources. Given the known risks of thalidomide-induced peripheral neuropathy (TIPN), coagulopathy etc and its effects on cardiac conduction, evaluating these adverse reactions is crucial. This study aims to quantify and describe the incidence of these complications in our patient population.

Methods

A retrospective review was conducted at JSF. Inclusion criteria:

- Confirmed β-thalassemia major/intermedia
- Patient-reported thalidomide use not prescribed by JSF
- New neurological or cardiovascular symptoms plus other generalized and non specific symptoms

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Data parameters included duration of thalidomide intake, onset of symptoms, neurological evaluation, ECG findings, and associated systemic complaints.

Results

A total of 72 out of 90 symptomatic patients were confirmed to be using thalidomide obtained externally. Neurological complications were most frequently observed, followed by cardiovascular symptoms including palpitations and documented arrhythmias. Below is the distribution of adverse effects:

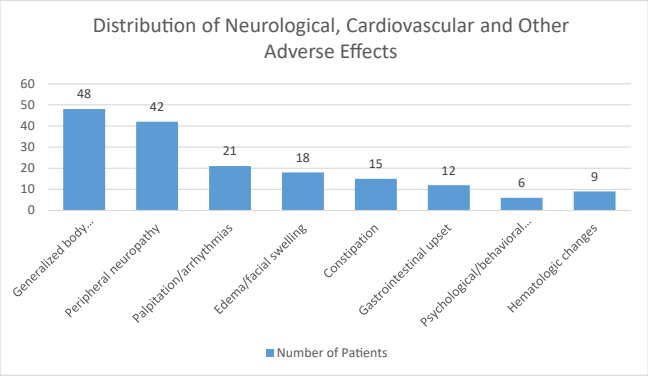

Figure 1: Distribution of adverse effects in β-Thalassemia patient using thalidomide

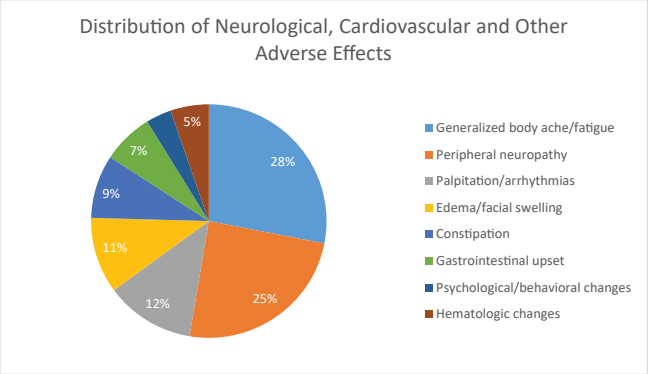

Figure 2: Distribution of multisystem complications observed in patients following Thalidomide use

Table 1: Systemic adverse effects associated with thalidomide therapy

Adverse Effect	Number of Patients
Generalized body ache/fatigue	48
Peripheral neuropathy	42
Palpitation/arrhythmias	21
Edema/facial swelling	18
Constipation	15
Gastrointestinal upset	12
Psychological/behavioral changes	6
Hematologic changes	9

This table shows the number of patients developed differet side effects after taking off-label thalidomide

Discussion

Peripheral neuropathy is a well-established adverse effect of thalidomide therapy, often dose-dependent and irreversible. Our findings align with global data showing high incidence of TIPN among unmonitored users. Cardiovascular toxicity, although less recognized, poses serious risks particularly arrhythmias in thalassemia patients already predisposed to iron-overload cardiomyopathy. Lack of baseline cardiac assessment and ECG monitoring increases vulnerability. These findings highlight the consequences of unregulated thalidomide distribution in Pakistan.

Conclusion

Off-label use of thalidomide for thalassemia, especially when based on limited early studies, carries significant risks, including peripheral neuropathy, thromboembolic events, and other systemic toxicities. These dangers are heightened by inconsistent dosing and lack of clinical monitoring. Despite this, clinical evidence shows that thalidomide can offer meaningful benefits in selected patients particularly those with transfusion-dependent thalassemia complicated by alloantibodies and individuals with thalassemia intermedia by improving hemoglobin levels and reducing transfusion needs. Thus, while therapeutically promising, thalidomide requires strict medical supervision and regulatory oversight to ensure safe use.

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