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Original Article

Dermatological Manifestations of Chemotherapy in Pediatric Cancer Patients: A Prospective Cohort Study from a Tertiary Center in Pakistan

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Abstract

Objective: Dermatological manifestations are common but under-recognized complications of chemotherapy in children, particularly in low- and middle-income countries (LMICs) such as Pakistan where supportive care systems are limited. This study prospectively assessed the spectrum and onset of dermatological toxicities in pediatric cancer patients at a tertiary care center in Pakistan.

Methodology: A prospective cohort study was conducted from March to December 2023 at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS) Islamabad, Pakistan. Sixty-eight children (aged 1–13 years) with cancer receiving chemotherapy were enrolled and systematically examined for dermatological manifestations at each cycle by a dermatologist. Dermatological toxicities such as skin, hair, and nail changes were recorded using standardized clinical definitions, and infections were confirmed by microbiological or histopathological testing when indicated. Associations with demographic and treatment characteristics were analyzed using chi-square tests.

Results: Overall, 86.7% of patients developed at least one dermatological toxicity. Nail changes were most frequent (69.1%), followed by skin (57.4%) and hair changes (42.6%). Common findings included Beau's lines (30.9%), maculopapular rash (16.1%), and complete alopecia (25.0%). Most dermatological toxicities appeared within 30 days of treatment initiation and only 7.3% of dermatological toxicities led to temporary treatment delay. Younger children (1–5 years) and those on continuous chemotherapy regimens experienced significantly higher rates of dermatological toxicities (p-value < 0.05). Secondary infections occurred in 29.4% of patients, with viral etiologies predominating.

Conclusion: Dermatological manifestations are highly prevalent and often occur early in pediatric cancer patients receiving chemotherapy, particularly among younger children and those on continuous regimens. Routine dermatological surveillance and timely management should be integrated into pediatric oncology supportive care in Low- and middle-income countries to minimize morbidity and treatment disruption.

Keywords: Chemotherapy, Dermatological toxicities, Low- and middle-income countries, Pediatric cancer, Supportive care

Introduction

Childhood cancer is a growing global health challenge, with approximately 400,000 new cases annually among individuals aged 0–19 years.[1] The burden is disproportionately concentrated in low- and middle-income countries where nearly 90% of childhood cancer deaths occur.[2] Contributing factors include delayed diagnosis, limited treatment access, therapy abandonment, and underdeveloped supportive care systems. In Pakistan, between 8,000 and 12,000 pediatric cancer cases are reported each year; however, underreporting and the absence of comprehensive national registries likely lead to substantial underestimation of the true incidence.[3] Over the past few decades, chemotherapy has transformed outcomes in pediatric malignancies such as acute lymphoblastic leukemia (ALL), lymphomas, and sarcomas, converting previously fatal conditions into treatable diseases.[4] Despite these advances, chemotherapy induces profound immunosuppression and multisystem toxicities, including dermatological adverse effects that are frequently underrecognized in children.[5,6] These cutaneous toxicities manifesting as maculopapular eruptions, alopecia, nail dystrophies, pigmentary alterations, and opportunistic infections are rarely life-threatening but can cause pain, discomfort, psychosocial distress, and, in severe cases, treatment interruption.[7] To date, no pediatric oncology center in Pakistan routinely uses the Common Terminology Criteria for Adverse Events (CTCAE) to grade dermatological toxicities, limiting comparability with global literature.

The pathophysiology of chemotherapy-induced dermatological toxicity is multifactorial, involving direct cytotoxic damage to rapidly dividing epidermal cells, disruption of keratinocyte turnover, drug-related inflammatory responses, and increased susceptibility to infections due to neutropenia and compromised barrier integrity.[8] Agents such as methotrexate, vincristine, doxorubicin, and cytarabine are among the most frequently implicated drugs.[9]

High-income countries (HICs) have established standardized dermatologic surveillance and supportive care protocols, which enable timely recognition and management of chemotherapy-related toxicities.[10] In contrast, Low- and middle-income countries such as Pakistan face critical gaps in detection, documentation, and management of these complications.[11] Key barriers include a shortage of dermatology expertise, limited diagnostic resources for confirmatory testing (e.g., microbiological cultures, skin biopsies), and fragmented follow-up systems. Psychosocial challenges compound these issues, as visible dermatological changes can lead to stigma and significantly impair quality of life in children.

Although previous South Asian studies have examined general chemotherapy adverse effects, few have systematically evaluated dermatological manifestations using predefined criteria, onset timelines, and infection confirmation. Reports from Karachi, Peshawar, and Lahore describe mucocutaneous toxicities as a major source of morbidity but often lack detailed classification of clinical spectrum, temporal onset, and differentiation between infectious and non-infectious etiologies.[12, 13]

This study therefore aimed to comprehensively characterize the onset, duration, clinical patterns, and etiologies (infectious versus non-infectious) of dermatological manifestations in immuno-compromised pediatric patients receiving chemotherapy at a tertiary oncology center in Pakistan. By delineating the frequency and nature of skin, hair, and nail changes, we aim to inform early diagnostic protocols, optimize supportive care, and ultimately improve treatment adherence and quality of life among children with cancer.

Methodology

This prospective observational cohort study was conducted through interdisciplinary collaboration between the Departments of Pediatric Oncology and Dermatology at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from March to December 2023. Ethical approval was obtained from the Institutional Ethical Review Board of Shaheed Zulfiqar Ali Bhutto Medical University (Approval No. F.1-1/2015/ERB/SZABMU/1087, dated 1 March 2023).

Children aged 1–13 years with a confirmed cancer diagnosis who were scheduled to receive chemotherapy were eligible. Patients with pre-existing chronic dermatological disorders unrelated to chemotherapy (e.g., eczema, psoriasis, genetic skin conditions) were excluded. The sample size of 68 children was determined based on the number of newly diagnosed pediatric oncology patients receiving chemotherapy during the study period, allowing comprehensive evaluation of dermatological manifestations across multiple chemotherapy cycles. Written informed consent was obtained from parents or legal guardians, and assent was obtained from children aged ≥ 7 years using age-appropriate forms in both English and Urdu.

Baseline demographic and clinical data, including age, sex, cancer type, chemotherapy regimen, and cycle number, were recorded using a structured proforma developed in consultation with pediatric oncologists, dermatologists, and infectious disease specialists. Chemotherapy regimens were classified as either continuous, with repeated administration of cytotoxic agents without planned breaks, or cyclic, administered in defined cycles with planned recovery periods. Full-body dermatological examinations were performed at baseline and during each chemotherapy cycle by a board-certified dermatologist, with documentation of skin, hair, and nail changes. Laboratory or histopathological investigations, including skin scrapings, nail clippings, bacterial or fungal cultures, and biopsies, were conducted where clinically indicated to differentiate infectious from non-infectious etiologies. Although internationally recognized Common Terminology Criteria for Adverse Events (CTCAE) grading was not used due to resource constraints, detailed qualitative and quantitative documentation of severity was performed.

Dermatological manifestations were categorized into three domains: (i) cutaneous changes (macular, maculopapular, pustular, papular, vesicular, vesiculobullous, maceration, and purpuric lesions); (ii) nail changes (Beau's lines, nail fragility, onycholysis); and (iii) hair changes (partial alopecia, complete alopecia, and hair thinning). Secondary dermatological diagnoses including bacterial, viral, fungal, and parasitic infections, as well as benign drug reactions, were also documented. Figure 1 shows representative clinical features of patients following chemotherapy: (A) cutaneous changes, (B) hair changes, and (C) nail changes. Data were analyzed using IBM SPSS Statistics version 21.0. Descriptive statistics were presented as frequencies and percentages for categorical variables, and as mean ± standard deviation (SD) for continuous variables. Comparative analyses were performed using chi-square test to assess associations between demographic or clinical characteristics (age, sex, diagnosis, and chemotherapy regimen) and dermatological manifestations. To account for cohort size effects, proportion-adjusted comparisons were conducted to ensure that higher toxicity rates in the 1–5 year age group reflected true risk rather than sample distribution. P-values < 0.05 were considered statistically significant.

Results

A total of 68 pediatric cancer patients were enrolled, with a median age of 7 years (IQR: 4–11) and a mean age of 6.2 ± 3.3 years. Males comprised 55.9% (n = 38) and females 44.1% (n = 30). Acute lymphoblastic leukemia (ALL) was the most common malignancy (47.1%), followed by Hodgkin's lymphoma (22.1%) and nephroblastoma (11.8%), while non-Hodgkin's lymphoma, acute myeloid leukemia, and other solid tumors accounted for smaller proportions (Table 1). More than half of the cohort (61.8%) received continuous chemotherapy regimens, and 38.2% received cyclic regimens.

A wide range of chemotherapeutic agents were administered, including vincristine, cytarabine, methotrexate, dexamethasone, etoposide, cyclophosphamide, ifosfamide, doxorubicin, asparaginase, carboplatin, procarbazine, daunorubicin, actinomycin-D, cisplatin, vinblastine, idarubicin, bleomycin, 6-mercaptopurine, cyclosporine, and temozolomide.

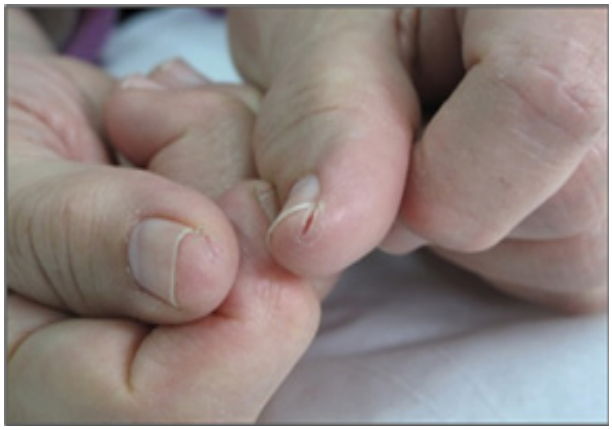
Dermatological manifestations were frequent, with hair changes observed in 42.6% (n = 29), nail changes in 69.1% (n = 47), and skin changes in 57.4% (n = 39) (Figure 2). Among cutaneous toxicities, maculopapular rash was most common (16.1%), followed by purpuric lesions (11.8%),

pustular eruptions (10.3%), vesicular rashes (7.3%), macular lesions (5.9%), papular eruptions (2.9%), and vesiculobullous rashes (2.9%). Hair changes included complete alopecia (25.0%), partial alopecia (13.2%), and hair thinning (4.4%). Nail toxicities were dominated by Beau's lines (30.9%) and nail fragility (25.0%), with onycholysis affecting 13.2% of patients. Most manifestations appeared within the first 30 days of treatment initiation ($p < 0.05$) (Table 2).

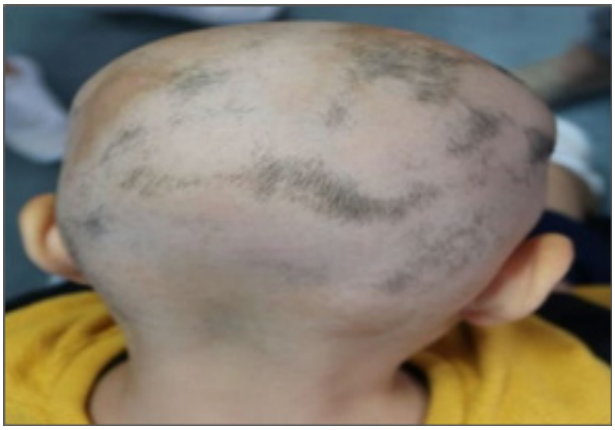
Table 1: Demographic and clinical information of pediatric patients on chemotherapy.

Variable	Categories	N	%
Age (in years)	1-5	34	50
	6-10	22	32.4
	11-13	12	17.6
Sex	Male	38	55.9
	Female	30	44.1
Type of malignancy	Acute Lymphoblastic Leukemia (ALL)	32	47.1
	Non-Hodgkin's Lymphoma (NHL)	6	8.8
	Nephroblastoma (Wilm's Tumor)	8	11.8
	Hodgkin's Lymphoma	15	22.1
	Acute Myeloid Leukemia (AML)	2	2.9
	Others	5	7.3
Chemotherapy regimen	Cyclic	26	38.2
	Continuous	42	61.8

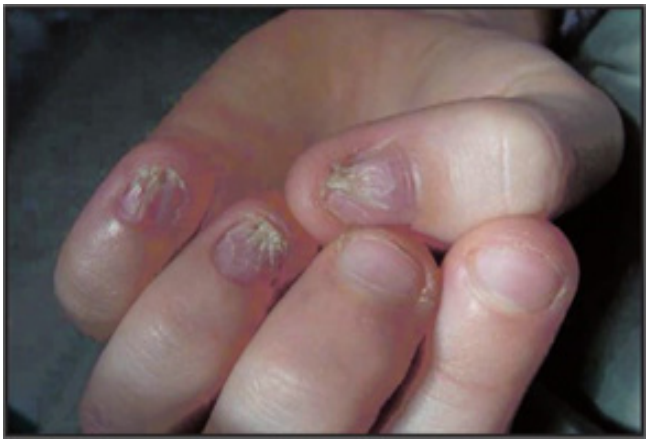
Mean age=6.2 years, SD=3.3



A. Cutaneous changes including erythematous rash.



B. Hair changes demonstrating alopecia



C. Nail changes showing ridging

Figure 1: Dermatological manifestations among pediatric cancer patients

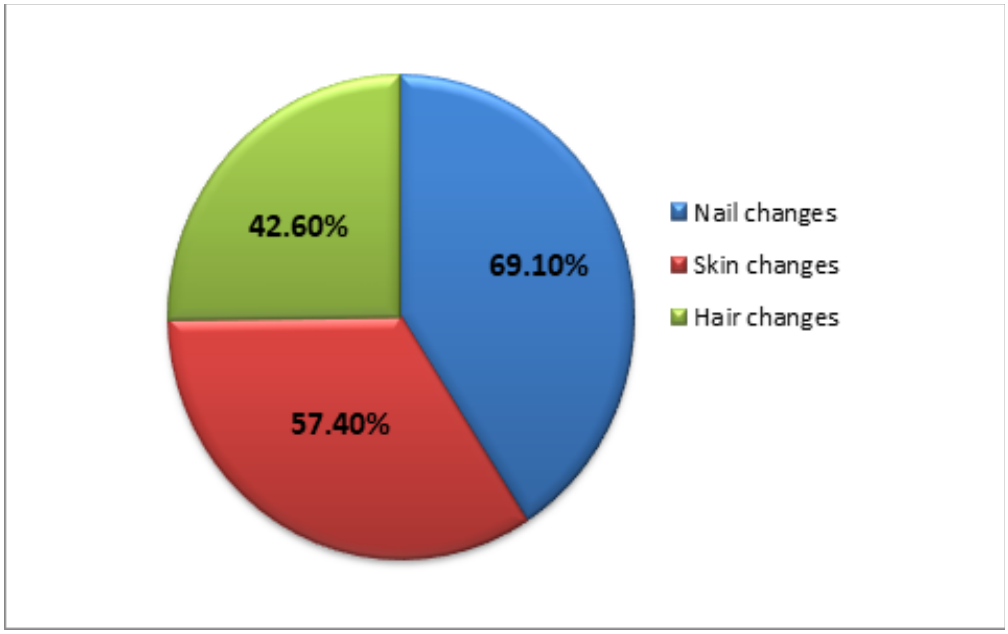


Figure 2: Dermatological manifestations among pediatric cancer patients

Table 2: Frequency and onset of dermatological manifestations among pediatric patients receiving chemotherapy.

Dermatological manifestation		Patients	Time of onset		
			0-30 days	30-90 days	After 90 days
		n (%)	n (%)	n (%)	n (%)
Cutaneous changes	Macular	4 (5.9)	2 (50.0)	1 (25.0)	1 (25.0)
	Maculo-papular	11 (16.1)	7 (63.6)	3 (27.3)	1 (9.1)
	Pustular	7 (10.3)	5 (71.4)	2 (28.6)	0 (0.0)
	Papular	2 (2.9)	1 (50.0)	1 (50.0)	0 (0.0)
	Vesicular	5 (7.3)	3 (60.0)	2 (40.0)	0 (0.0)
	Vesiculobullous	2 (2.9)	2 (100.0)	0 (0.0)	0 (0.0)
	Purpuric	8 (11.8)	5 (62.5)	2 (25.0)	1 (12.5)
Hair changes	Partial hair loss	9 (13.2)	2 (22.2)	4 (44.4)	3 (33.3)
	Complete hair loss	17 (25.0)	3 (17.6)	10 (58.8)	4 (23.6)
	Thinning	3 (4.4)	2 (66.7)	1 (33.3)	0 (0.0)
Nail changes	Beau's lines	21 (30.9)	13 (61.9)	6 (28.6)	2 (9.5)
	Nail fragility	17 (25.0)	11 (64.7)	6 (35.3)	0 (0.0)
	Onycholysis	9 (13.2)	0 (0.0)	6 (66.7)	3 (33.3)

p-value < 0.05

Secondary infections were also observed: viral infections in 19.1%, bacterial infections in 10.3%, fungal infections in 7.3%, and parasitic infestations in 4.4% of patients. Each percentage was calculated using the total study population (n = 68) as the denominator (100%), and categories were not mutually exclusive. Benign drug reactions occurred in 16.2% (Figure 3).

Statistical analysis indicated significant associations between several demographic variables and dermatological toxicities. Age showed a significant association with dermatological manifestations (p-value = 0.04), with the highest frequencies of hair (38.5%), nail (44.7%), and skin changes (37.9%) occurring in children aged 1–5 years. No significant sex-based differences were found (p-value = 0.218), although females showed slightly higher rates of nail and skin toxicities. Trends by malignancy type particularly among children with acute lymphoblastic leukemia and Hodgkin's lymphoma did not reach statistical significance (p-value = 0.062). Chemotherapy regimen demonstrated a significant association, with continuous therapy showing higher rates of dermatological manifestations compared with cyclic therapy (p-value = 0.04) (Table 3)

Table 3: Association of demographic and clinical characteristics with dermatological manifestations among pediatric cancer patients receiving chemotherapy

Variable	Categories	Skin changes	Nail changes	Hair changes	*p*-value
		n(%)	n(%)	n(%)	
Age (years)	1–5	15 (38.5)	21 (44.7)	11 (37.9)	0.04
	6–10	13 (33.3)	16 (34.0)	10 (34.5)	
	11–13	11 (28.2)	10 (21.3)	8 (27.6)	
Sex	Male	21 (53.8)	24 (51.1)	16 (55.2)	0.218
	Female	18 (46.2)	23 (48.9)	13 (44.8)	
Type of malignancy	ALL	17 (43.6)	20 (42.6)	13 (44.8)	0.062
	NHL	3 (7.7)	5 (10.6)	3 (10.3)	
	Nephroblastoma	5 (12.8)	6 (12.8)	4 (13.8)	
	Hodgkin's Lymphoma	8 (20.5)	11 (23.4)	6 (20.7)	
	AML	2 (5.1)	2 (4.3)	1 (3.4)	
	Others	4 (10.3)	3 (6.4)	2 (6.9)	
Chemotherapy regimen	Cyclic	14 (35.9)	17 (36.2)	11 (37.9)	0.04
	Continuous	25 (64.1)	30 (63.8)	18 (62.1)	

Discussion

Chemotherapy frequently causes dermatological adverse effects involving the skin, hair, and nails, since anti-cancer drugs target rapidly proliferating cells. These complications increase morbidity and impair quality of life, and early recognition and management are crucial for maintaining uninterrupted treatment.[13,14] This study characterized the spectrum of dermatological manifestations in pediatric cancer patients on chemotherapy and explored associations with demographic and clinical factors. The findings demonstrated that nail, skin, and hair toxicities were common, often appearing within the first 30 days of treatment. Younger children (1–5 years) and those receiving continuous chemotherapy regimens were significantly more affected, underscoring the need for targeted monitoring and supportive care. Although internationally recognized grading systems such as the Common Terminology Criteria for Adverse Events were not utilized, we employed a structured, dermatologist-validated assessment tool for pediatric patients, ensuring consistent and clinically meaningful classification of toxicities.

We observed that the most frequent malignancies were acute lymphoblastic leukemia (47.1%) and Hodgkin's Lymphoma (22.1%), consistent with Sous et al. (2023), who reported acute lymphoblastic leukemia (42.2%) and Hodgkin's lymphoma (12.0%) as predominant pediatric cancers.[15] In our study, nail changes (69.1%) were the most common adverse effect, followed by skin (57.4%) and hair changes (42.6%), aligning with Deutsch et al. (2020) who reported nail changes in 62.2% of patients.[16] This highlights the importance of identifying and managing dermatological toxicities in pediatric oncology. of pustular rash, often linked to neutropenia, reflects chemotherapy-induced immunosuppression and increased susceptibility to infection.[18] A small proportion of dermatological toxicities (7.3%) led to temporary interruption or delay of chemotherapy, primarily due to severe bacterial or fungal infections requiring stabilization prior to treatment continuation. The early onset of most cutaneous changes supports the need for vigilant monitoring during initial chemotherapy cycles.[19]

Beau's lines were most common (31.0%), consistent with Saraswat et al. (2020), who attributed these to temporary nail matrix arrest during systemic stress.[20] Nail fragility (25.0%) aligned with Günaydın & Çetingül (2015), highlighting impaired keratinization.[21] Onycholysis (13.2%) developed later (30–90 days), consistent with Chen et al. (2007), which described this as a delayed cumulative effect of chemotherapy.[22] These findings suggest different temporal patterns of nail toxicities, reinforcing the importance of ongoing nail examination throughout treatment.

Hair loss was another distressing side effect, with complete alopecia in 25.0% and partial loss in 13.2%. The drugs most often implicated were vincristine, cyclophosphamide, and doxorubicin. Similar patterns were reported by Sanmartín et al. (2019) (alopecia in 50.0%)[23] and Rajashekar et al. (2016) (68.3%).[24] Most hair changes occurred between 30–90 days, consistent with follicular cycle disruption by chemotherapy.[25] Given its psychological impact, hair loss requires pre-treatment counseling and supportive interventions.

Viral skin infections were most common (19.1%), followed by bacterial (10.3%), fungal (7.3%), and parasitic (4.4%). This distribution contrasts with Shedeed et al. (2019), who reported predominantly bacterial infections,[26] but is consistent with Gandhi et al. (2014), who found viral infections to be most frequent.[27] Benign drug reactions were seen in 16.2% of patients, higher than the 9.8% reported by Rajashekar et al. (2016).[24] These variations may reflect differences in chemotherapy regimens, immune status, and regional epidemiology.

Children aged 1–5 years had the highest rates of dermatological toxicities, with age reaching statistical significance. This supports Akbayrak et al. (2021), who linked younger age with higher susceptibility due to rapid cell turnover and immature immune defenses.[28] In contrast, Alkathiri et al. (2025) found no significant age-related effect, likely reflecting variability in regimens and dosing.[29] To ensure that the higher toxicity burden in younger children was not solely due to a larger cohort size, proportional statistical analyses and adjusted chi-square tests were performed, which confirmed a true association beyond group size differences. Our findings reinforce the need for age-tailored supportive care. Dermatological changes were most frequent in ALL and HL, consistent with Pramanik et al. (2025), while continuous chemotherapy regimens were significantly associated with more toxicities.[30] This supports Yan et al. (2024), who reported prolonged exposure as a risk factor,[31] though Tola et al. (2023) did not observe regimen differences. Variability likely reflects drug-specific toxicities and dose intensity.[32]

Limitations

This study was limited by its small sample size, single-center design, and relatively short follow-up (6 months), which restricted assessment of late-onset dermatological complications. The absence of a standardized dermatological toxicity grading system such as CTCAE represents a significant limitation; however, the structured dermatologist-guided assessment ensured consistency in evaluation. Quality-of-life outcomes, which are an important aspect of dermatologic morbidity, were not assessed and should be included in future research. Additionally, treatment delays were recorded, but the sample size limited deeper analysis of their predictors. Larger multicenter studies with extended follow-up, standardized grading scales, and QoL assessment tools are needed.

Conclusion

Dermatological manifestations are frequent, often early, and significantly influenced by age and chemotherapy regimen in pediatric cancer patients. Nail, skin, and hair changes substantially affect quality of life and may disrupt treatment adherence. Although only a minority of cases resulted in temporary chemotherapy delay, these findings highlight the importance of timely diagnosis and appropriate management of severe toxicities. Routine dermatological screening, early intervention, and infection control should be integrated into pediatric oncology protocols to minimize morbidity and ensure treatment continuity. Implementing standardized assessment frameworks and enhancing healthcare provider training, particularly in resource-limited settings, will further improve supportive care and optimize outcomes.

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Data Availability Statement: The data that support the findings of this study, apart from the data already presented in the results section, are available from the corresponding author upon reasonable request.

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