Article

Oral Mucositis in Pediatric Cancer Patients undergoing Chemotherapy in a Tertiary Care Hospital of Pakistan: Incidence, Severity and Key Risk Determinants

Authors: Hijab Shaheen . Ruqayya Manzoor . Ana Farooq . Nazia Rafique

Corresponding Author: Hijab Shaheen

Correspondence: drhijabshaheen@yahoo.com

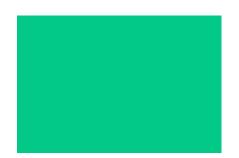
Association: Department of Pediatric Oncology, Children Hospital, PIMS, Islamabad,
Pakistan

Published: October 23, 2025



DOI: 10.69690/ODMJ-001-1023-4563

Article



Oral Mucositis in Pediatric Cancer Patients undergoing Chemotherapy in a Tertiary Care Hospital of Pakistan: Incidence, Severity and Key Risk Determinants

Authors: Hijab Shaheen . Ruqayya Manzoor . Ana Farooq . Nazia Rafique

Corresponding Author: Hijab Shaheeb

Correspondence: drhijabshaheen@yahoo.com

Association: Department of Pediatric Oncology, Children Hospital, PIMS,

Islamabad, Pakistan

Published: October 23, 2025

ABSTRACT

Introduction: Oral mucositis is a frequent and debilitating side effect of chemotherapy in pediatric cancer patients. It can cause severe pain, difficulty in eating, treatment delays, and an increased risk of infections. This study aimed to determine the frequency, severity, and risk factors associated with oral mucositis in children undergoing chemotherapy.

Methodology: A prospective observational study was conducted from February 2024 to March 2025 at the Pediatric Oncology Department, The Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad. Children aged 1–13 years with confirmed malignancies receiving chemotherapy were enrolled. Baseline demographic, clinical, and hematological parameters were recorded. Patients were followed weekly for 12 consecutive weeks after the initiation of chemotherapy, with weekly oral examinations. The World Health Organization (WHO) Oral Mucositis Grading Scale was used to assess severity. Chi-square tests and Spearman's correlation were applied (p < 0.05 considered significant). reducing the toll of this preventable and treatable disease.

Results: Of the 81 patients, 34 (42%) developed at least one episode of oral mucositis. Among them, 20 (58.8%)

experienced mild mucositis (Grade I–II), while 14 (41.2%) had severe mucositis (Grade III–IV). Mucositis was significantly more common in children aged 6–10 years (n = 11, 45.8%; p < 0.001), those with poor oral hygiene (n = 19, 73.1%; p = 0.002), and those diagnosed with acute lymphoblastic leukemia (n = 18, 72.0%; p = 0.003). Methotrexate use was observed in 23 children (50%) who developed mucositis (p < 0.001). Children with low hemoglobin levels (n = 15, 71.4%; p = 0.002) and neutropenia (n = 24, 80.0%; p = 0.01) were also at significantly higher risk. Cyclic chemotherapy regimens were significantly associated with the occurrence of mucositis (p = 0.005).

Conclusion: Oral mucositis is a common complication among pediatric patients receiving chemotherapy, particularly in younger children, those with leukemia, poor oral hygiene, and hematological abnormalities. Intensive chemotherapy regimens and the use of methotrexate further increase the risk. Preventive strategies, including regular oral assessments and improved oral hygiene, should be integrated into pediatric oncology care.

INTRODUCTION

Chemotherapy remains the cornerstone of pediatric cancer treatment, contributing significantly to improved survival outcomes worldwide, particularly over the last two decades¹. Despite its therapeutic benefits, the non-specific cytotoxicity of chemotherapy damages healthy, rapidly dividing cells, leading to a wide spectrum of adverse effects. Among these, oral mucositis (OM) is one of the most frequent, debilitating, and treatment-limiting complications². High-dose chemotherapy regimens including methotrexate, cytarabine, and doxorubicin are particularly associated with mucosal injury, often requiring treatment delays or dose reductions in up to 20% of cases, ultimately compromising treatment efficacy^{3,4}.

OM is a painful, inflammatory, and ulcerative condition of the oral mucosa resulting from direct cytotoxic injury to basal epithelial cells, typically induced by chemotherapy or radiotherapy⁵. Clinical manifestations include erythema, edema, ulceration, and severe oral pain, which negatively impact nutrition, speech, oral hygiene, and quality of life. Severecasescanleadtocomplications suchas dehydration, systemic infections, and prolonged hospital stays, and a reported increase of up to 40% in overall healthcare costs⁶.

Globally, the incidence of OM in pediatric oncology patients receiving chemotherapy ranges from 52% to 81%, with even higher rates observed in patients undergoing hematopoietic stem cell transplantation (HSCT). In low- and middle-income countries (LMICs) such as Pakistan, India, and Bangladesh, the burden of OM is compounded by malnutrition, poor oral hygiene, limited access to prophylactic care, and inconsistent clinical practices. By contrast, although high-income countries (HICs) also report OM as a common adverse event, it is more effectively addressed through established prevention and management protocols.

The World Health Organization (WHO) grading scale is the most widely used classification system to assess OM severity, ranging from Grade 0 to Grade IV. Grade 0 indicates no symptoms; Grade I includes mild erythema and soreness; Grade II involves ulcers with the ability to eat solids; Grade III includes severe ulceration with limited oral intake requiring a liquid diet; and Grade IV is the most severe, necessitating parenteral or enteral nutrition due to complete inability to eat or drink. Grades III and IV are typically associated with intense pain, heightened infection risk, opioid analgesic use, and the increased need for nutritional support¹⁰.

Multiple factors influence the development and severity of OM, including the chemotherapeutic regimen, dosage intensity, patient'sage, oralhygienestatus, nutritional status, immune competence, and the underlying malignancy¹¹. Children under 10 years are particularly vulnerable due to their higher mucosal cell turnover and relatively immature immune systems. Additional risk factors include malnutrition, poor oral care practices, and pre-existing oral infections including issues that are especially prevalent in under-resourced healthcare systems of LMICs¹².

Despite the clinical relevance and high frequency of OM, it remains underreported and understudied in resource-limited countries. In Pakistan, a lower-middle-

income country with constrained healthcare resources management of OM in pediatric oncology settings is particularly hampered by a lack of standardized protocols, limited caregiver education, and insufficient supportive infrastructure. For example, a study at a tertiary pediatric oncology center in Karachi found that only around 57% of patients maintained adequate oral care, and mucositis occurred in approximately 42.5% of children highlighting gaps in oral care protocol implementation and education¹³, while another study linked the high incidence of OM to neglect in oral hygiene and lack of caregiver education¹⁴.

In tertiary public-sector hospitals like the Pakistan Institute of Medical Sciences (PIMS), Islamabad where a large volume of pediatric oncology patients is managed, evidence on OM remains scarce. This lack of data hinders the development of targeted, context-specific strategies for prevention, early detection, and intervention. Therefore, the objective of this study was to determine the frequency and severity of OM among pediatric cancer patients receiving chemotherapy at the Children's Hospital, PIMS Islamabad. Furthermore, the study aimed to identify demographic, clinical, and treatment-related factors associated with OM in this population. By generating local evidence, this study seeks to inform improved clinical decision-making, enhance supportive care, and ultimately contribute to the existing body of knowledge on pediatric cancer toxicities in LMICs such as Pakistan.

METHODOLOGY

Thisisaprospectiveobservational study aimedatmonitoring the occurrence, severity, and associated risk factors of mucositis in pediatric patients undergoing chemotherapy. The study was conducted at the Pediatric Oncology Department of the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, from February 2024 to March 2025. The study population included children aged 1 to 13 years who were diagnosed with any form of malignancy and were receiving chemotherapy. These patients were identified through weekly reviews of the admission register of the outpatient department (OPD) of the Pediatric Oncology Department. Children were excluded if they had pre-existing oral lesions, known immunodeficiencies, or prior head/neck radiotherapy.

A total of 105 patients were initially included in the study. However, during the follow-up period, 23 patients were lost to follow-up, including 18 deaths, and 5 either transferred to other hospitals or left against medical advice (LAMA). As a result, the final analysis was conducted on 81 patients who were consistently monitored throughout the study evaluation period.

Data collection was conducted weekly using structured forms, laboratory records including complete blood count (CBC) reports, and the WHO Oral Mucositis Grading Scale. Each patient was followed up for a total of 12 consecutive weeks following the initiation of chemotherapy to assess the development and progression of oral mucositis. Demographic, clinical, and hematological information

were collected at enrollment, including sex, age, oral hygiene status, type of malignancy, methotrexate use, chemotherapy regimen, and laboratory findings such as hemoglobin (Hb) level, absolute neutrophil count (ANC) level, and platelet counts. For clarity, chemotherapy regimens were operationally defined as "cyclic" (administered in scheduled intervals with breaks for recovery) or "continuous" (administered on a regular, ongoing basis without significant breaks).

Evaluation for the presence of oral mucositis was conducted exclusively in the OPD of Pediatric Oncology via direct clinical examination. The weekly examination included inspection of the lips, tongue, buccal mucosa, gingiva, and palate for signs of mucositis. Each session was conducted by a senior pediatric oncologist accompanied by a clinical research assistant. Inter-rater reliability was considered by standardizing grading procedures between the oncologist and assistant through initial joint assessments and periodic consistency checks.



Table 1. The WHO Oral Mucositis Grading Scale

Grade	Description
0 (none)	No symptoms or lesions
l (mild)	Soreness/erythema without ulcers
II (moderate)	Erythema and ulcers; solid diet tolerated
III (Severe)	Ulcers with liquid diet only
IV (life-threatening)	Alimentation not possible due to severity

The study employed the WHO Oral Mucositis Grading Scale (Grades 0-IV) to classify mucositis severity, supplemented by parental feedback on the oral discomfort or feeding issues of the child **(Table 1)**.

The study was approved by the Ethical Review Board (ERB) of Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU)/PIMS, Islamabad (Reference No. F.1-1/2015/ERB/SZABMU/1245), dated 26 February 2024. Written informed consent was obtained from the parents or guardians of all participants, along with assent from children when appropriate. Data confidentiality was strictly maintained through anonymization and secure storage.

The data collected were organized in a Microsoft Excel database and analyzed using SPSS (version 23.0). Descriptive statistics were computed for continuous variables (e.g., age, hematological parameters) and categorical variables (e.g., gender, diagnosis). The mean and standard deviation were calculated for continuous variables, while frequencies and percentages were used

for categorical variables. The chi-square test was used to evaluate associations between categorical variables (e.g., mucositis presence and demographic, clinical and hematological variables). Ap-value of <0.05 was considered statistically significant. Spearman's rank correlation coefficient was used to determine the relationship between the number of mucositis episodes and severity.

RESULTS

At the beginning of the study, 105 patients were enrolled; 23 were lost to follow-up (18 deaths, 5 transfers to other hospitals or LAMA). The final analysis included 81 patients. The median age of the cohort was 5 years, with an interquartile range (IQR) of 3–9 years and an overall range of 1–13 years.

Males constituted 54.3% of the study population. At baseline, good oral hygiene was observed in 67.9% of patients, while the remaining 32.1% had poor oral

hygiene. The most common cancer diagnosis was Acute Lymphoblastic Leukemia (ALL), accounting for 30.9% of cases, followed by Wilms Tumor (14.8%), Hodgkin's Lymphoma (12.3%), and other less frequent malignancies.

Methotrexate had been administered to 56.8% of patients. Regarding the chemotherapy protocols, 70.4% of patients received cyclic regimens defined as scheduled cycles of drug administration followed by rest periods while 29.6% were on continuous regimens, in which chemotherapy was delivered without scheduled breaks.

In terms of hematological profiles at baseline, moderate anemia (hemoglobin 8.0–10.9 g/dL) was found in 44.4% of patients, severe anemia (<8.0 g/dL) in 25.9%, and normal hemoglobin levels (>10 g/dL) in 23.5%. Absolute neutrophil count (ANC) was within normal range (\geq 1.5 × 10 9 /L) in 63.0% of participants, while 37.0% exhibited neutropenia.

Platelet counts were normal (>150 \times 10 9 /L) in 65.4% of the cohort. Thrombocytopenia was noted in the remaining patients, with varying severity. The baseline characteristics of the pediatric cancer patients are shown in **Table 2**.

During the course of the study, 42.0% (n = 34) of the patients developed at least one episode of oral mucositis. Among them, the most frequently reported severity was Grade II mucositis (35.3%), followed by Grade III (32.4%), Grade I (20.6%), and Grade IV (8.8%). The majority of affected children experienced 1–2 episodes (58.8%), while 17.6% had 3–4 episodes, and 20.6% had five or more. A statistically significant positive correlation was observed between the number of mucositis episodes and their severity (r = 0.52, p < 0.01), indicating that patients with a higher number of episodes tended to develop more severe mucositis **(Table 3)**.



Table 2. Baseline Characteristics of Pediatric Cancer Patients (N = 81)

Variable	Frequency (n)	Percentage (%)
Age (years)		
1-5	43	53.1
6-10	24	29.6
11-14	14	17.3
Gender		
Male	44	54.3
Female	37	45.7
Oral hygiene status		
Poor	26	32.1
Good	55	67.9
Acute Lymphoblastic Leukemia (ALL)	25	30.9
Acute Myeloid Leukemia (AML)	7	8.6
Chronic Myeloid Leukemia (CML)	1	1.2
Hodgkin's Lymphoma (HL)	10	12.3
Non-Hodgkin's Lymphoma (NHL)	4	4.9

Wilms Tumor (WT)	12	14.8
Ewing's Sarcoma	6	7.4
Neuroblastoma	2	2.5
Medulloblastoma	3	3.7
Low Grade Glioma	1	1.2
Germ Cell Tumor	6	7.4
Rhabdomyosarcoma	1	1.2
Hemophagocytic Lymph- Histiocytosis (HLH)	1	1.2
Osteosarcoma	1	1.2
Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS)	1	1.2
Methotrexate use		
Yes	46	56.8
No	35	43.2
Chemotherapy regimen		
Cyclic	57	70.4
Continuous	24	29.6
HB level (gm/dL)		
Severe Anemia (< 8.0)	21	25.9
Moderate Anemia (8.0–10.9)	36	44.4
Mild Anemia (11.0–11.4)	5	6.2
Normal (> 10)	19	23.5
ANC level (× 10°/L)		
Normal (≥ 1.5)	51	63
Neutropenia (< 1.5)	30	37
Platelet count (Thrombocytopenia)		
Severe Thrombocytopenia (< 50)	9	11.1
Moderate Thrombocytopenia (50-100)	10	12.3
Mild Thrombocytopenia (100– 150)	9	11.1
Normal (>150)	53	65.4

Analysis of risk factors revealed that mucositis was significantly more prevalent among children aged 6–10 years (45.8%, p = 0.001) and those with poor oral hygiene (73.1% vs. 27.3%, p = 0.001). No significant association was found between mucositis and gender or underlying cancer diagnosis.

However, patients on cyclic chemotherapy regimens had a significantly higher incidence of mucositis compared to those on continuous regimens (52.6% vs. 16.7%, p = 0.003). Similarly, methotrexate use was associated with increased mucositis risk (50.0% vs. 31.0%, p = 0.001).



Table 2. Baseline Characteristics of Pediatric Cancer Patients (N = 81)

Correlation: r = 0.52, p < 0.01

	Grade I		Grade II		Grade IV		Grade III		Total	
Variables	N	%	n	%	n	%	n	%	N	%
1–2 episodes	6	30	7	35	5	25	2	10	20	58.8
3-4 episodes	1	16.7	2	33.3	2	33.3	1	16.7	6	17.6
≥ 5 episodes	0	0	3	42.9	4	57.1	0	0	7	20.6
Total	7	20.6	13	38.2	11	32.4	3	8.8	34	100

Further, hematological abnormalities were significantly associated with mucositis occurrence. Severe anemia was strongly linked to mucositis (71.4%, p = 0.001), as was neutropenia (80.0%, p = 0.001). The incidence of mucositis also increased progressively with the severity of thrombocytopenia: it was present in 100% of patients with severe or moderate thrombocytopenia and in 88.9% of those with mild thrombocytopenia (p < 0.001). In contrast, only 13.2% of patients with normal platelet counts experienced mucositis. These findings highlight the clinical significance of chemotherapy regimen type, methotrexate exposure, oral hygiene status, and baseline hematological parameters in predicting the risk and severity of oral

mucositis among pediatric cancer patients (Table 4).

DISCUSSION

Pediatric patients receiving antineoplastic treatment frequently suffer from severe side effects, among which OM stands out as one of the most prevalent and debilitating inflammatory complications. The incidence of mucositis in pediatric cancer patients undergoing chemotherapy has been reported to range from 40% to 60%, with higher rates associated with intensive regimens, such as methotrexate and 5-fluorouracil¹⁵.



Table 4. Association between Patient Factors and the Occurrence of Oral Mucositis (N = 81)

	Mucositis present		Absent			
∕ariable	n	%	n	%	p-value	
Age (years)						
1-5	18	41.8	25	58.2		
6-10	11	45.8	13	54.2	0.001*	
11-14	5	35.7	9	64.3		
Gender						
Male	21	47.7	23	52.8	0.017	
Female	13	35.1	24	64.9	0.617	

Oral hygiene status					
Poor	19	73.1	7	26.9	0.001*
Good	15	27.3	40	72.7	0.001
Diagnosis					
Acute Lymphoblastic Leukemia (ALL)	18	72	7		
Acute Myeloid Leukemia (AML)	3	42.9	4	57.1	
Chronic Myeloid Leukemia (CML)	1	100	0	0	0.39
Hodgkin's Lymphoma (HL)	3	30	7	70	
Non-Hodgkin's Lymphoma (NHL)	1	25	3	75	
Wilms Tumor (WT)	1	8.3	11	91.7	
Ewing's Sarcoma	2	33.3	4	66.7	
Neuroblastoma	1	50	1	50	
Medulloblastoma	0	0	3	100	
Low Grade Glioma	0	0	1	100	
Germ Cell Tumor	2	33.3	4	66.7	
Rhabdomyosarcoma	1	100	0	0	
Hemophagocytic Lymph- Histiocytosis (HLH)	1	100	0	0	
Osteosarcoma	0	0	1	100	
Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS)	0	0	1	100	
Methotrexate use					
Yes	23	50	23	50	0.001*
No	11	31	24	68.8	0.001
Chemotherapy regimen					
Cyclic	30	52.6	27	47.4	0.001*
Continuous	4	16.7	20	83.3	0.001**
HB level (gm/dL)					
Severe Anemia (< 8.0)	15	71.4	28.6	6	0.003*
Moderate Anemia (8.0–10.9)	14	38.9	22	61.1	
Mild Anemia (11.0–11.4)	1	20	4	80	
Normal (> 10)	4	21.1	15	78.9	

ANC level (× 10°/L)						
Normal (≥ 1.5)	10	19.6	41	80.4	0.001*	
Neutropenia (< 1.5)	24	80	6	20	0.001**	
Platelet count (Thrombocytopenia)		·		·		
Severe Thrombocytopenia (< 50)	9	100	0	0		
Moderate Thrombocytopenia (50-100)	10	100	0	0		
Mild Thrombocytopenia (100– 150)	8	88.9	1	11.1	0.000*	
Normal (>150)	7	13.2	46	86.8		

This prospective observational study aimed to evaluate the incidence, severity, and clinical correlates of oral mucositis in pediatric oncology patients undergoing chemotherapy. A thorough understanding of the underlying biological mechanisms, including basal epithelial cell apoptosis, inflammatory cytokine cascades, and impaired mucosal regeneration, is critical for developing timely and effective supportive care interventions that can improve both treatment adherence and clinical outcomes¹⁶.

In this cohort, OM was reported in 42% of pediatric cancer patients, which aligns closely with the global prevalence estimates ranging from 40% to 60%¹⁷. This rate is consistent with findings reported by Muhammad et al. (2018), who found a prevalence of 42.5% among Pakistani children receiving chemotherapy13, and Gandhi et al. (2017), who reported a higher rate of 58.1% in pediatric oncology patients in India¹⁸.

Conversely, lower prevalence rates have been observed in settings such as Bangladesh (37.5%)¹⁹ and Saudi Arabia (approximately 41%)²⁰, likely reflecting differences in treatment protocols and availability of supportive care. In resource-rich countries, prevalence rates tend to be comparable but vary slightly; for instance, 42.5% in Australia4, 50% in Italy⁹, and 40.2% in Brazil²¹. Collectively, these findings highlight that while the pathophysiology of OM remains largely consistent across various populations, its clinical incidence and severity are modulated by factors including chemotherapy intensity, healthcare infrastructure, and preventive care practices.

Therefore, comprehensive, context-sensitive

management strategies are imperative to reduce OM-related morbidity and improve the quality of life for pediatric cancer patients worldwide.

Moderate to severe mucositis (Grades II and III) was observed in 38.2% and 32.4% of patients, respectively. A significant positive correlation between frequency and severity indicates that repeated mucosal insults from cyclical chemotherapy induce cumulative epithelial damage and impair mucosal healing. This finding is consistent with studies by Zecha et al. (2022) and Carreón-Burciaga et al. (2018), who reported high recurrence rates of Grade II-III mucositis in children receiving intensive chemotherapy^{22,23}. The pathogenesis involves progressive depletion of mucosal progenitor cells and sustained elevation of pro-inflammatory cytokines such as TNF- α and IL-1 β with each chemotherapy cycle²⁴.

Children aged 6–10 years exhibited a significantly higher incidence of OM (45.8%) compared to those aged 11–14 years (35.7%). This statistically significant difference likely reflects age-related vulnerability due to immature immune function, thinner oral mucosa, and challenges with maintaining oral hygiene in younger children. Cheng et al. (2011) reported an overall OM incidence of 41% in children aged 6–18 years, with neutropenia and prior mucosal injury as key predictors, emphasizing the interplay of age, immune competence, and mucosal integrity²⁵.

Similarly, Mubaraki et al. (2020) found that 73.1% of children with poor oral hygiene developed mucositis following hematopoietic stem cell transplantation, highlighting the role of microbial colonization as a significant cofactor²⁶.

These convergent findings reinforce the need for age-specific oral care protocols and active caregiver involvement to mitigate OM risk in younger pediatric patients.

The type of chemotherapy regimen strongly influences the risk and severity of oral mucositis. Patients receiving intensive, cyclic chemotherapy often experience higher rates of OM due to insufficient mucosal recovery time between treatment cycles, which impairs epithelial regeneration. Cheng et al. (2011) observed that pediatric and adolescent patients undergoing more aggressive or cyclic chemotherapy regimens had significantly increased OM incidence and severity, highlighting regimen intensity as a key risk factor²⁵. Additionally, Huang et al. (2022), in a comprehensive scoping review, reported that regimens involving high-dose methotrexate and anthracycline were consistently associated with more severe mucositis in pediatric patients²⁷. These findings underscore chemotherapy scheduling and intensity as critical modifiable factors to reduce mucosal toxicity and improve patient outcomes.

Methotrexate, a folate antagonist widely used in pediatric oncology, is well-recognized for its mucotoxicity owing to inhibition of DNA synthesis and epithelial turnover. Our study confirmed that patients receiving high-dose methotrexate exhibited greater mucositis severity, consistent with global observations by Pustelnik et al. (2023)²⁸.

Methotrexate impairs mucosal repair through dihydrofolate reductase inhibition, leading to epithelial atrophy, ulceration, and secondary microbial invasion. Given its synergistic mucosal toxicity when combined with other cytotoxics, aggressive prophylactic oral care and leucovorin rescue therapy remain essential strategies to mitigate this risk.

Hematological abnormalities were significantly associated with mucositis development. Severe anemia (Hb < 8.0 g/dL) was strongly linked to OM, affecting 71.4% of anemic patients. Yu et al. (2024) reported that a ≥5% reduction in hemoglobin during chemotherapy correlated with poorer disease-free survival in osteosarcoma patients, while Ruggiero et al. (2022) similarly associated low hemoglobin with adverse clinical outcomes ^{29,30}. These findings suggest anemia may exacerbate mucosal vulnerability and negatively impact overall prognosis.

Neutropenia (ANC < 1.5×10^9 /L) also correlated strongly with mucositis, with 80% of neutropenic patients affected. This observation aligns with pediatric oncology and hematology literature, wherein neutropenic episodes coincide with

increased OM risk¹⁰. Inpatient studies further confirm neutropenia as an independent predictor of OM alongside diagnosis and chemotherapy timing4. Supportive measures, including blood producttransfusion, optimized nutrition, meticulous oral care, and hematopoietic growth factor administration, have demonstrated efficacy in reducing OM incidence and severity³¹. Conversely, some recent studies report heterogeneity in oral lesion frequencies and no significant subgroup population reflecting differences, patient and chemotherapy regimens³². diversity

Furthermore, thrombocytopenia (platelets < 100 \times 10³/µL) was strongly correlated with mucositis severity, with most patients experiencing moderate -to - severe thrombocytopenia developing this complication. This supports prior findings that oral mucosal complications, including mucositis, are influenced by peripheral blood counts, particularly platelets, during chemotherapy³³ Thrombocytopeniamayexacerbateulcerations and delay tissue repair due to impaired hemostasis³⁴ These finding highlight the importance of routine hematologic monitoring white blood cell and platelet counts and timely supportive interventions to mitigate mucositis risk and facilitate uninterrupted chemotherapy.

Strenghts and Limitation

This prospective study employed a standardized grading scale (WHO Oral Mucositis Grading Scale), and weekly follow-up assessments that allowed for a comprehensive assessment of mucositis onset and progression. The clear operational definition of chemotherapy regimens and hematological monitoring strengthen internal validity. However, limitations include the single-center design and relatively small sample size (n = 81), which restrict the generalizability of results. Key potential confounders such as nutritional status, hydration, oral microbial flora, and concurrent infections were not evaluated and may influence mucositis development.

Additionally, reliance solely on clinical grading without adjunctive biomarkers could underestimate subclinical mucosal injury.

Future multicenter studies with larger cohorts incorporating these variables are essential to fully elucidate the spectrum and determinants of oral mucositis in pediatric oncology populations.

CONCLUSION

Oral mucositis remains a common and distressing complication among pediatric patients receiving

chemotherapy, with younger age, poor oral hygiene, methotrexate use, cyclic chemotherapy, and hematological abnormalities being key associated risk factors. We recommend that pediatric oncology units, particularly in resourcelimited settings, adopt standardized mucositis screening using the WHO Oral Mucositis Grading Scale (Grades 0-IV) to objectively assess severity and guide interventions. Routine oral assessments, patient and caregiver education on oral hygiene, and tailored supportive care based on hematologic status should be incorporated into standard clinical protocols. This study offers valuable local evidence that may inform risk-based preventive strategies and highlight the need for further multicenter interventional research to minimize the burden of mucositis in pediatric cancer care.

Acknowledgment

We would like to express our sincere gratitude to the nursing and medical staff at the Pediatric Oncology Department of the Children's Hospital, PIMS Islamabad, for their invaluable assistance during data collection.

Conflict of Interest

The authors declare that there are no conflicts of interest relevant to the content of this manuscript.

Data Sharing

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

ABBREVIATIONS

Abbreviation	Explanation			
ОМ	Oral Mucositis			
PIMS	Pakistan Institute of Medical Sciences			
OPD	Outpatient Department			
WHO	World Health Organization			
HSCT	Hematopoietic Stem Cell Transplantation			
CBC	Complete Blood Count			
Hb	Hemoglobin			
ANC	Absolute Neutrophil Count			
LAMA	Left Against Medical Advice			
SZABMU	Shaheed Zulfiqar Ali Bhutto Medical University			
ERB	Ethical Review Board			
SPSS	Statistical Package for the Social Sciences			
SD	Standard Deviation			

REFERENCES

- 1. Braguês R, Marvão MF, Correia P, Silva RM. Oral mucositis management in children under cancer treatment: a systematic review. Cancers (Basel). 2024;16(8):1548.
- 2. Andriakopoulou CS, Yapijakis C, Koutelekos I, Perdikaris P. Prevention and treatment of oral mucositis in pediatric patients: systematic review and meta-analysis of randomized controlled trials. In Vivo. 2024 May 1;38(3):1016-29.
- 3. Anand U, Dey A, Chandel AK, Sanyal R, Mishra A, Pandey DK, De Falco V, Upadhyay A, Kandimalla R, Chaudhary A, Dhanjal JK. Cancer chemotherapy and beyond: current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis. 2023;10(4):1367-401.
- **4.** Allen G, Logan R, Revesz T, et al. Prevalence and risk factors of oral mucositis in pediatric oncology inpatient population: a prospective study. J Pediatr Hematol Oncol. 2018;40(1):15-21.
- 5. Suhaimi N, Abdul Razak NA, Ramli R. Pain control in oral mucositis according to the severity scale: a narrative literature review. J Clin Med. 2025;14(13):4478.
- 6. Da-Cruz Campos MI, Neiva Campos C, Monteiro Aarestrup F, Vieira Aarestrup BJ. Oral mucositis in cancer treatment: natural history, prevention and treatment. Mol Clin Oncol. 2014;2(3):337-40.
- 7. Ali M, Kerio AA, Khattak TA, Hussain M, Khan MA, Abbas Y. Oral mucositis in patients undergoing hematopoietic stem cell transplantation. J Coll Physicians Surg Pak. 2023;33:804-8.
- 8. Zahra N, Asad SR, Khan M, Asad SA, Asad SA, Syed QU. Addressing challenges of dental problems in Pakistan: a comprehensive review. Int J Biomed Res. 2024;3(1).
- 9. Attinà G, Romano A, Maurizi P, D'Amuri S, Mastrangelo S, Capozza MA, Triarico S, Ruggiero A. Management of oral mucositis in children with malignant solid tumors. Front Oncol. 2021;11:599243.
- 10. World Health Organization. WHO oral mucositis grading scale. WHO handbook for reporting results of cancer treatment. Updated 2022.
- 11. Hu FL, Lou N, Wu GL. Recent advances in oral cryotherapy for the management of anticancer therapy-induced oral mucositis. Future Sci OA. 2025;11(1):2527500.
- 12. Babu KL, Mathew J, Doddamani GM, Narasimhaiah JK, Naik LR. Oral health of children with acute lymphoblastic leukemia: a review. J Orofac Sci. 2016;8(1):3-11. DOI: 10.4103/0975-8844.181915

- 13. Muhammad SA. Oral care practices and oral mucositis in the pediatric oncology patients receiving chemotherapy at a tertiary care hospital, Karachi, Pakistan [master's thesis]. Karachi: Aga Khan University; 2018.
- 14. Amin M, Khan FR, Allana A, et al. Oral health of chemotherapy patients before and after provision of oral hygiene instructions at a tertiary care hospital: pre–post design. BMC Oral Health. 2024;24:655
- 15. He X, Li S, Chen W, Zhang M, Zhao Q, Liu F, Wang R, Yang H, Xu J, Zhou L. Prevalence and risk factors of chemotherapy-induced oral mucositis in 470 children with acute lymphoblastic leukemia. Pediatr Blood Cancer. 2025;72(1)\:e31400.
- **16.** Docimo R, Anastasio MD, Bensi C. Chemotherapy-induced oral mucositis in children and adolescents: a systematic review. Eur Arch Paediatr Dent. 2022;23(4):501-11. DOI: 10.1007/s40368-022-00727-5
- 17. Bahari H, Ghanam A, Hajaj H, Elouali A, Babakhouya A, Rkain M. Chemotherapy-induced mucositis in pediatric oncology: experience from 145 cases at the Mohammed VI University Hospital, Oujda. Cureus. 2025;17(4):e82885. DOI: 10.7759/cureus.82885
- 18. Gandhi K, Datta G, Ahuja S, Saxena T, Datta AG. Prevalence of oral complications occurring in a population of pediatric cancer patients receiving chemotherapy. International journal of clinical pediatric dentistry. 2017 Jun 1; 10(2):166.
- 19. Islam R, Jamal CY, Nargis W, Chakma T, Islam F, Mou M, Islam M. The impact of oral hygiene practice on the severity of oral mucositis in children with acute lymphoblastic leukemia receiving induction chemotherapy. Cancer J Bangladesh. 2024;5(2):62-8.
- 20. Alhussain A, Alkhayal Z, Ayas M, Abed H. Prevalence and risk factors of oral mucositis in paediatric patients undergoing haematopoietic stem cell transplantation. Oral Dis. 2022;28(3):657-69. DOI: 10.1111/odi.13777
- 21. Guimarães JR, de Carvalho LG, Damascena LC, Sampaio ME, Ribeiro IL, de Sousa SA, Valença AM. The incidence of severe oral mucositis and its occurrence sites in pediatric oncologic patients. Med Oral Patol Oral Cir Bucal. 2020;26(3):e299. DOI: 10.4317/medoral.24185
- 22. Zecha JA, Raber-Durlacher JE, Laheij AM, Westermann AM, de Lange J, Smeele

- LE. The potential contribution of dental foci and oral mucositis to febrile neutropenia in patients treated with myelosuppressive chemotherapy for solid tumors and lymphoma. Front Oral Health. 2022;3:940044. DOI: 10.3389/froh.2022.940044
- 23. Carreón-Burciaga RG, Castañeda-Castaneira E, González-González R, Molina-Frechero N, Gaona E, Bologna-Molina R. Severity of oral mucositis in children following chemotherapy and radiotherapy and its implications at a single oncology center in Durango State, Mexico. Int J Pediatr. 2018;2018:3252765. DOI:10.1155/2018/3252765
- 24. Georgiou M, Patapatiou G, Domoxoudis Pistevou-Gompaki Papanikolaou S, Κ, understanding Α. mucositis: Oral the pathology management. and Jul;16(3):215-216. 2012 Hippokratia.
- 25. Cheng KK, Lee V, Li CH, Goggins W, Thompson DR, Yuen HL, Epstein JB. Incidence and risk factors of oral mucositis in paediatric and adolescent patients undergoing chemotherapy. Oral Oncol. 2011;47(3):153-62. DOI: 10.1016/j. oraloncology.2010.11.019
- 26. Mubaraki S, Pani SC, Alseraihy A, Abed H, Alkhayal Z. The efficacy of two different oral hygiene regimens on the incidence and severity of oral mucositis in pediatric patients receiving hematopoietic stem cell transplantation: a prospective interventional study. Spec Care Dentist. 2020;40(6):566-73. DOI: 10.1111/scd.12525
- 27. Huang J, Hwang AY, Jia Y, Kim B, Iskandar M, Mohammed AI, Cirillo N. Experimental chemotherapy-induced mucositis: a scoping review guiding the design of suitable preclinical models. Int J Mol Sci. 2022;23(23):15434. DOI: 10.3390/ijms232315434
- 28. PustelnikE, PikoraK, PawelecK. Methotrexate-associated oral mucositis in children with acute lymphoblastic leukemia. Nowotwory. 2023;8(5):362-70. DOI: 10.5603/njo.96144
- 29. Yu W, Sun M, Wang W, Shen Z, Wang Y,

- Li H. Neoadjuvant chemotherapy-induced hemoglobin decline as a prognostic factor in osteosarcoma around the knee joint: a single-center retrospective analysis of 242 patients. Support Care Cancer. 2024;32(7):415. DOI: 10.1007/s00520-024-08592-2
- 30. Ruggiero A, Riccardi R. Interventions for anemia in pediatric cancer patients. Med Pediatr Oncol. 2002;39(4):451-4. doi:10.1002/mpo.10184
- 31. Crawford J, Tomita DK, Mazanet R, Glaspy J, Ozer H. Reduction of oral mucositis by filgrastim (r-metHuG-CSF) in patients receiving chemotherapy. Cytokine Cell Mol Ther. 1999;5(4):187-93. PMID:10850381
- 32. Al-Beesh FA, Martini N, Suleiman S, Aljoujou A. Oral manifestations associated with neutropenia in Syrian patients diagnosed with hematological malignancies and undergoing chemotherapy: a cross-sectional study. Medicine (Baltimore). 2024;103(2):e36780. doi:10.1097/MD.0000000000036780
- 33. Lalla RV, Bowen J, Barasch A, Elting L, Epstein J, Keefe DM, McGuire DB, Migliorati C, Nicolatou-Galitis O, Peterson DE, Raber-Durlacher JE. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2014;120(10):1453-61.
- 34. Wei WI, Mok VW. The management of neck metastases in nasopharyngeal cancer. Curr Opin Otolaryngol Head Neck Surg. 2007;15(2):99-102. DOI: 10.1097/MOO.0b013e3280148a06

Licensed under CC BY 4.0 | creativecommons.org/licenses/by/4.0