

Risk Factors of Oral Mucositis among Patients with Acute Leukemia

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Abstract

Background Patients with leukemia cancer are at risk of developing mucositis that may cause impair quality of life and can not only cause strong pain, but also lead to problems with basic physiological needs as eating and swallowing. **Aim:** Identify risk factors of oral mucositis among patients with acute leukemia. **Design:** A descriptive research design was performed in present study. **Setting:** The study was conducted in the critical care unit, south Egypt cancer institute at Assiut University hospitals. **Sample:** All available patients with acute leukemia for six month **Tool:** Assessment personal and medical data of studied groups, mucositis risk factors and oral mucositis assessment scale (OMAS) were used to collect data in this **Results:** It was found that the most common risk factors in mucositic group were poor oral hygiene, lack of ability of self-oral care, malnutrition (87.9%,78.8%,78.8%) , respectively. While the most common risk factors in non mucositis group were high dose of chemotherapy, poor oral hygiene, lack of ability of self-oral care and Pre-existing dental diseases (70.4%,55.6%,51.9%), respectively. **Conclusion:** There was statistically significant difference between dehydration, malnutrition, poor oral hygiene and deficit in ability of self-oral care and mucositis occurrence. **Recommendations:** The nurse must be aware of risk factors that increase prevalence of oral mucositis, develop and implement of oral care guidelines by nurses for mucositic patient with acute leukemia and nurses in intensive care unit should receive training on assessing oral health and identify of risk factors of oral mucositis .

Keywords: Acute leukemia, Oral mucositis & Risk factor.

Introduction

Leukemia is a kind of hematological cancer that is caused by an overproduction of white blood cell (WBC)-forming tissues resulting in a marked increase in circulating immature or abnormal WBCs. (Lee, et al., 2020)

Chemotherapy involves the use of chemicals or drugs that destroy or prevent the reproduction of cancer cells in the leukemia patients. (Lee, et al., 2020)

Chemotherapy can be aggressive toward the mucosa due to its effects on poorly differentiated cells or on those with a high mitosis rate. The effect of chemotherapy is directly toxic and, in some cases, drugs are secreted by saliva, causing damage to the oral cavity. Furthermore, such drugs may affect other tissues, e.g., bone marrow, causing a reduction in immunity and leading to infections and/or oral bleeding. These occurrences can cause indirect stomatotoxicity, resulting in the onset of oral mucositis. (Damascena,et al., 2018)

Oral mucositis is a toxic side effect of non-surgical cancer treatments: chemotherapy and radiotherapy, which strongly impair quality of life and can not only cause strong pain, but also lead to problems with basic physiological needs as eating and swallowing.

Development of oral mucositis is associated with type, dosage, and schedule of radiation or chemotherapy and other factors related to patients.

(Kusiak, et al., 2020)

Factors that affect the onset of mucositis include the dosage, duration of treatment and tumor type, in addition to factors such as oral hygiene and conditions intrinsic to the patient. As oral mucositis is a multifactorial event, it is crucial to understand how different clinical and treatment variables can be related not only to its occurrence but also to its development and duration. (Damascena, et al., 2018)

Oral mucositis may manifest to varying degrees of severity: mild, moderate, and severe. Severe oral mucositis (SOM) is highly prevalent, painful, and poses an increased risk for systemic infection, thus reducing patient survival. (Guimarães, et al., 2021)

With this regard, not only the onset but also the severity of oral mucositis should be considered. At the early stages of the disease, the affected patient remains capable of eating solid foods. On the other hand, severe oral mucositis has a harmful effect on the whole organism, causing changes in the diet, and contributing to parenteral food intake, dependence and weight loss among other effects. In some cases, it

is necessary to interrupt the oncological treatment, which would directly influence the patient's prognosis and survival. (Damascena, et al., 2018)

In patients undergoing chemotherapy, oral hygiene may be difficult due to pain associated with mucositis and general weakness. It is extremely important to make patients aware of the importance of maintaining optimal oral hygiene during treatment. Low awareness of this issue can lead to deterioration of the oral hygiene in these patients, which contributes to serious overall complications. There are several potential complications of mucositis. A person may, for example, lose their appetite for food and drink during a Cycle of Chemotherapy. (Ptasiewicz, et al., 2022)

There are several factors to consider in determining an individual patient's risk for developing mucositis, including the specific chemotherapy agent or radiation modality used and the dose, frequency, and duration of treatment. Patient factors that may influence the risk of developing mucositis and its severity include smoking, poor oral hygiene, younger age, female sex, pretreatment nutritional status, and pretreatment neutrophil counts. In addition, genetic factors not yet fully elucidated are likely related to an individual's risk for developing mucositis. (Brown, 2020)

A multidisciplinary team and collaboration are required in the prevention and treatment of OM. In this context, nurses, who play a key role in such a team, can play a unique role in identifying and eliminating OM risk factors (such as poor oral health habits, smoking, and malnutrition). Patients expect that healthcare professionals understand their ideals, beliefs, and values and design a treatment plan in line with those perceptions, so radiotherapy nurses should inevitably provide regular counseling and screening along with evidence-based care. (Kara, 2022)

The nurses are now more confident in assessing the severity of mucositis and utilizing consistent interventions. The intervention categories included dental Hygiene, oral rinses, dentures, lip care, pain control, medicated oral rinses and managing secretions. (Siefker, et al, 2018)

Significance of the study

Predisposing factors of mucositis are not fully understood in patients undergoing malignant disease treatment. It has been suggested that several risk factors contribute to mucositis; treatment related, genetic associated and microorganisms related factors. (Gamal, et al, 2022).

Oral mucositis has a negative impact on oral health and significantly deteriorates the quality of life. Therefore, a multidisciplinary team, including nursing, should be involved in the treatment. The

overall oral mucositis incidence was 89.4% worldwide. (Pacheco, et al., 2021)

Mucositis is a common and feared complication of anticancer therapy that can affect up to 90% of certain populations of patients with cancer. Even seemingly uncomplicated mucositis, which is often self-limited, can result in intense patient discomfort and decline in quality of life. Severe mucositis can be complicated by uncontrolled pain, superinfection or systemic infection, bleeding, and dehydration, and severe mucositis can lead to interruptions or de-escalation in anticancer treatment, resulting in worse oncologic outcomes. (Brown, 2020)

The reported incidence of leukemia patient in south Egypt cancer institute at (2020/2021) is (300patients) so the study was done due to increase number of leukemia patient who risk for mucositis.

Aim of the study

This study aimed to assess risk factors of oral mucositis among acute leukemia patients.

Research question:

What percentage of mucositis among patient with acute leukemia during six month?

What are risk factors of oral mucositis among acute leukemia patients?

Patients and Method

Research design:

Descriptive research design was used in this study.

Study setting:

The study was carried out in oncology intensive care unit in south Egypt cancer institute.

Patients:

All patients admitted to above mentioned setting of both sexes for six month who were 60 patients.

Inclusion criteria:

- 1- Newly admitted patient with leukemia with mucositis or non .
- 2- Both sexes (male and female).
- 3- Age range between (18-65years).

Exclusion criteria:

1. Patients on mechanical ventilation.
2. Diabetic patient.
3. Uncooperative patient (deteriorated patients).

Study tools:

Three tools will be developed by the researcher based on the relevant.

Literature and used to collect data pertinent to the study.

First Tool:

Personal and medical data assessment tool:

Personal data include: age, gender, education and marital status.

Medical data as type leukemia, dose of chemotherapy and patient with chemo and radiotherapy

Second Tool: Mucositis risk factors assessment tool

This tool was developed by the researcher after reviewing relevant Literature to assess risk factors for patients with mucositis as:

1. Cancer of the head and neck.
2. High dose of chemotherapy.
3. Old age.
4. Concurrent chemotherapy and radiotherapy.
5. Dehydration.
6. Malnutrition.
7. Lack of ability of self-oral care related to disease.
8. Poor oral hygiene.
9. Pre-existing dental problems.
10. Personal oral care routine.
11. Smoking.

Third tool: Oral assessment tool

Oral Mucositis Assessment Scale (OMAS): This tool was adopted from **Eilers et al., 1999**. Which used by (**Ebrahem, 2022**) for the assessment of oral mucositis. this tool grade as;

Grade (0): A mouth with a healthy appearance and no mucositis.

Grade (1): Points, erythematous lesions observed in the oral cavity.

Grade (2): Red zones with increased mucosa, and lesions separated from each other.

Grade (3): Reddening of the entire oral mucosa with a large number of combined ulcers.

Grade (4): If ulcers, hemorrhage and necrosis were present in the mouth

Methods

After obtaining permission from the hospital's administrative authority, the study was carried out after clarifying the objective of the study. This study was conducted in medical intensive care Unit at south Egypt cancer institute

1- The study tools were formulated by researcher after extensive national and international literature review.

Content validity: The tools were tested for content the validity by jury of 5 Experts in the field of critical care nursing from faculty of nursing and critical care medicine from south Egypt cancer institute and the necessary modification were done.

The internal consistency of reliability was carried out using the Cronbach alpha coefficient test to the study tool (first, second) which were, .80, .90 which were acceptable

A pilot study: Was conducting on 10% of patient in a selected setting to evaluate the applicability and clarity of the developed tools.

Ethical consideration

- Research proposal will be approved from ethical committee in the faculty of nursing.
- There is no risk for study subject during application of the research.

- The study will be follow common ethical- principles in clinical research.
- Informed consent will be obtained from patients or guidance that is willing to participate in the study after explaining the nature and purpose of the study.
- Confidentiality and anonymity will be assured.
- Patients have the right to refuse to participate and or with draw from the study without any rational any time.
- Patient privacy will be considered during collection of data.

Implementation phase:

- 1- An official permission was obtained from the head of the medical oncology department at south Egypt cancer institute often explanation of aim and nature of the study.
- 2- The researcher introduces herself to all patients or relatives and explains purpose and importance of the study so the approval for participation will be secured from them
- 3- 60 patients who are willing to participate in the present study were divided into two equal groups: mucositic and non mucositic group by using third tool .

Each patient from studied group assessed by researcher for six month:

1. Personal data includes: age, gender, education and marital status and medical data.
2. Risk factor of mucositis assessment tool includes: Cancer of the head and neck, High dose of chemotherapy, Old age, Concurrent chemotherapy and radiotherapy, dehydration, malnutrition, Deficit in ability of self-oral care, Poor oral hygiene, Pre-existing dental problems, Personal oral care routine, Smoking and alcohol history

Oral assessment should be carried out routinely prior to SACT (systemic anticancer treatment) administration as part of the pre SACT toxicity grading assessment. Inpatients with, or at risk of oral health problems should have at least twice a day oral inspection .Oral assessment by using third tool Oral Mucositis Assessment Scale (OMAS)

Statistical analysis:

The data were tested for normality using the Anderson-Darling test and for homogeneity variances prior to further statistical analysis. Categorical variables were described by number and percent (N, %), where continuous variables described by the mean and standard deviation (mean \pm SD), Chi-square test, and fisher exact test were used to compare between categorical variables while comparison between continuous variables was done by t-test. All analysis was performed with the IBM SPSS 20.0 software, Test of significance of < 0.05 was considered significant.

Result

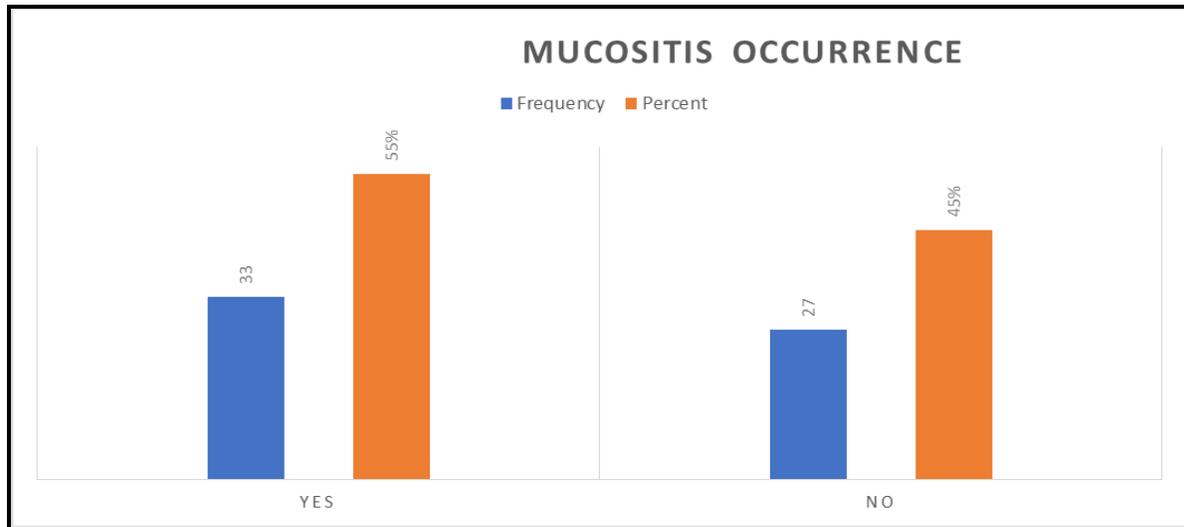


Figure (1): Percent distribution of mucositis occurrence among studied group

Table (1): Relation between mucositis occurrence and personal data

Personal data		Mucositis occurrence				P value
		Yes (33)		No (27)		
		No.	%	No	%	
Gender	Male	12	36.4	7	25.9	0.38
	Female	21	63.6	20	74.1	
Education	Education	0	0.0	2	7.4	0.42
	Eecondary	11	33.3	7	25.9	
	Basic	6	18.2	7	25.9	
	Read and write	5	15.2	2	7.4	
	Illiterate	11	33.3	9	33.3	
Marital	Single	7	21.2	4	14.8	0.51
	Married	25	75.8	23	85.2	
	Divorced	1	3.0	0	0.0	
Age	Mean ± Std. Deviation	42.2121±14.98282		41.3704±14.36917		0.8

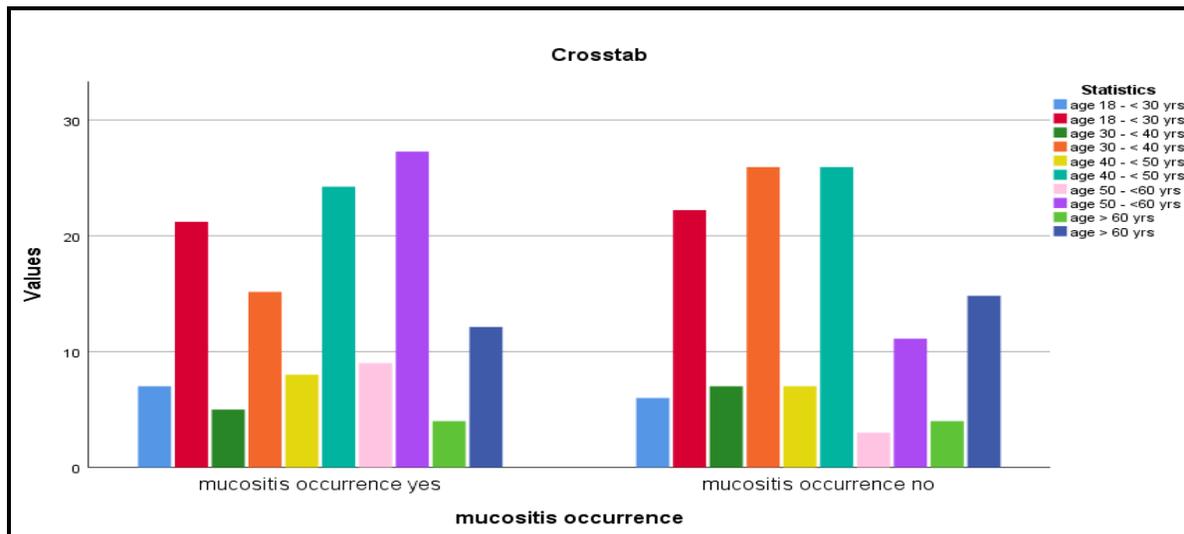


Figure (2): Relation between age and mucositis occurrence

Table (2): Correlation between mucositis occurrence and risk factors

Risk factor of mucositis	Mucositis occurrence				P value
	Yes (33)		No (27)		
	No.	%	No.	%	
Cancer of the head and neck	8	24.2	3	11.1	0.19
High dose of chemotherapy (with high side effect)	25	75.8	19	70.4	0.63
Elderly	21	63.6	11	40.7	0.07
Concurrent chemotherapy and radiotherapy	6	18.2	7	25.9	0.46
Dehydration	17	51.5	5	18.5	0.008*
Malnutrition	26	78.8	11	40.7	0.003*
Lack of ability to self-care (patient need help)	26	78.8	14	51.9	0.02*
poor oral hygiene	29	87.9	15	55.6	0.005*
Pre-existing dental problems	21	63.6	14	51.9	0.39
Smoking history	7	21.2	5	18.5	

Table (3): Relation between mucositis occurrence and Oral Mucositis Assessment Scale (OMAS) at admission.

Assessment Scale baseline		grade	Mucositis occurrence				P value
			Yes (33)		No(27)		
			No.	%	No.	%	
Oral Mucositis Assessment Scale (OMAS) baseline	A mouth with a healthy appearance and no mucositis	0	5	0.0	7	25.9	0.003*
	Points, erythematous lesions observed in the oral cavity. (Pain ,erythema)	1	14	42.4	15	55.6	
	Red zones with increased mucosa, and lesions separated from each other. (Ulcer,erythema)	2	5	15.2	2	7.4	
	Reddening of the entire oral mucosa with a large number of combined ulcers (Ulcer, increase erythema)	3	9	27.3	3	11.1	

Table (4): Relation between mucositis occurrence and Oral Mucositis Assessment Scale at discharge

Assessment Scale discharge		grade	Mucositis occurrence				P value
			Yes(33)		No(27)		
			No.	%	No.	%	
Oral Mucositis Assessment Scale discharge	A mouth with a healthy appearance and no mucositis	0	0	0.0	27	100.0	0.001*
	Points, erythematous lesions observed in the oral cavity. (Pain ,erythema)	1	9	27.3	0	0.0	
	Red zones with increased mucosa, and lesions separated from each other. (Ulcer,erythema)	2	14	42.4	0	0.0	
	Reddening of the entire oral mucosa with a large number of combined ulcers (Ulcer, increase erythema)	3	10	30.3	0	0.0	

Figure (1): Shows frequency and percent of mucositis among studied groups, this table summarizes that the percent of patient who had mucositis were (55%) from the studied patient and (45%) from the studied patient had non mucositis.

Table (1): Shows comparison between mucositis occurrence and personal data. This table show that no statistically significant difference between mucositis occurrence and personal data.

Figure (2): Shows distribution between age and mucositis, it illustrates that the most common

patients in mucositic group between age (50 –60yrs) and the most common patients in non mucositic group are between age (40-50yrs) and (30 -40yrs)

Table (2): Shows risk factors of mucositis among studied groups. It show that the most common risk factors in mucositic group were poor oral hygiene, lack of ability of self-oral care, malnutrition (87.9%,78.8%,78.8%) , respectively. While the most common risk factors in non mucositis group were high dose of chemotherapy, poor oral hygiene, deficit in ability of self-oral care and Pre-existing dental

problems (70.4%,55.6%,51.9%), respectively. With statistically significant difference between study.

Table (3): Show oral mucositis assessment Scale baseline among studied groups. It show that the most common assessment is Points, erythematous lesions observed in the oral cavity (Pain, erythema) in studied groups with (42.4%) in mucositic group and (55.6%) in non mucositic group. With statistically significant difference between studied groups.

Table (4): Show oral mucositis assessment scale at discharge among studied groups. It explain that the most common assessment at grade two in mucositic group. While the most common assessment at grade zero in non mucositic group, with statistically significant difference between studied groups.

Discussion:

Oral mucositis is a serious complication of chemotherapy. Severe mucositis can significantly interfere with malignant disease management and patient survival rates, as it often results in interruption of therapy, secondary infection, and sepsis. For acute lymphoblastic leukemia patients treated with standard and high dose chemotherapy, the incidence of chemotherapy induced mucositis ranges it begins 3 to 10 days after chemotherapy is initiated and can persist for 3 weeks (Pulito et al., 2020).

The present study shows that the majority of the studied patients with acute leukemia had mucositis.

More half of the patients had mucositis among leukemia patient this may be related to disease process, high dose of chemotherapy ,Old age ,Concurrent chemotherapy and radiotherapy ,dehydration ,malnutrition ,Deficit in ability of self-oral care ,Poor oral hygiene, Pre-existing dental problems and Smoking and alcohol history .This finding suggests that mucositis is a common complications in patients with acute leukemia and highlights the need for effective management strategies to alleviate its symptoms and improve patients' quality of life during treatment.

This study was agree with study by Wysocka-Slowik et al., (2021) investigated patients with acute leukemia and reported that more than half of them developed mucositis also it explored the correlation between mucositis severity and the duration of hospitalization, as well as the impact on nutritional status and the need for supportive care measures.

In this regards, a study conducted by Pulito et al., (2020) who found on utilization a standardized assessment tool to evaluate the severity of mucositis and its impact on patient outcomes, this study examined a cohort of 200 patients with acute leukemia and found that majority of them developed mucositis during their treatment.

Also, in a retrospective analysis by Wardill et al., (2020) about Prediction of mucositis risk secondary to cancer therapy. Brown & Gupta, (2020) investigated the association between mucositis and treatment-related complications, such as infections and treatment delays found a positive correlation between them and occurrence of mucositis.

However, Gamal et al., (2022) analyzed patients with acute leukemia and found that only two fifths of them had mucositis. However, this study had a limited sample size, which may have influenced the results and prevented generalization to a broader population.

The present study showed that there was no statistical significant difference of between the occurrence of the studied patients and their demographic data. This finding was agreeing with Marzooq et al., (2023) who reported that there were not any significant differences in the age, gender, and other demographic characteristics and occurrence of the mucositis among leukemia patients.

This agreed with Pulito et al., (2020) who mentioned that the average age of acute myeloid leukemia was 48.9 ± 18.3 years old. Lalla et al., (2019) monitored that AML is now cured in approximately 35%–40% of patients younger than age 60 years old.

This disagreed with Elad et al., (2022) who found that acute leukemia is most common in older people and affects males more than females.

This results match with a study by Wang et al., (2020) investigated the demographic characteristics of patients with acute leukemia and found a higher proportion of females in the studied group. Silva-Junior et al., (2019) also reported that married individuals constituted the majority of patients, aligning with the findings of the present study. While, In a study by Bhatnagar et al., (2021) which included a f acute leukemia patients, the mean age of patients was found to be consistent with the present study's findings.

In the other hand, an earlier study by Kakaje et al., (2020) focusing on acute leukemia patients did not find a significant difference in gender distribution within the studied group. A separate study by Wiernik et al., (2021) explored the marital status of patients with hematological malignancies but did not specifically focus on acute leukemia. As such, this study did not directly support or address the findings of the present study regarding the majority of patients being married.

In this line, Gupta et al., (2021) revealed that patients with acute leukemia are high risky for mucositis occurrence regardless their age, gender or marital status.

Also, Oganesyanyan et al., (2023) found that male patients with acute myeloid leukemia (AML) had a worse prognosis of mucositis. Another study of

Zhang et al., (2023) found that male patients with acute leukemia had a higher risk of relapse than female patients.

The present study revealed that majority of the acute leukemia and suffering with mucositis were female, Illiterate, married and their ages were 42.2121 ± 14.9 years old. The researcher point of view that it is possible that hormonal differences between males and females may play a role, as well as differences in genetics and immune function. These demographic characteristics provide insights into the affected population and potential risk factors associated with mucositis in acute leukemia patients.

A study by Lee et al., (2020) examined a large cohort of acute leukemia patients and found that a higher proportion of females half of developed mucositis compared to males. The study also reported that married individuals constituted the majority of patients experiencing mucositis.

In a retrospective analysis by Wysocka-Slowik et al., (2021) which included a diverse group of acute leukemia patients, it was observed that a significant portion of illiterate patients majority developed mucositis.

In the other hand, a study by Berger et al., (2020) investigated the demographic characteristics of acute leukemia patients with mucositis but did not find a significant gender difference. Another study by Sheshadri et al., (2022) focused on the age distribution of mucositis in acute leukemia patients but did not observe a consistent association between specific age groups and mucositis incidence.

The present study reported that the most common risk factors in mucositic group were poor oral hygiene, deficit in ability of self-oral care, malnutrition and dehydration. This attribute that nurse not aware how to identify risk factors and didn't receive any proper training on oral.

The researcher point of view suggest that Improving oral hygiene practices, enhancing self-oral care abilities, and addressing nutritional deficiencies could potentially help prevent or mitigate mucositis in individuals with these risk factors.

In the line of present study results, a study conducted by Marzog et al., (2023) investigated the relationship between oral hygiene and mucositis in cancer patients and found that poor oral hygiene was significantly associated with a higher incidence and severity of mucositis. Also, in another study by Çakmak & Nural, (2019) observed that patients with a deficit in the ability of self-oral care, such as those with physical limitations or cognitive impairments, had a higher risk of developing mucositis.

A systematic review by Bezerra et al., (2022) who identified that nutritional interventions were

suggested as a potential strategy to minimize mucositis in malnourished patients.

While, A study by Devi & Allenidekania, (2019) did not find a significant association between poor oral hygiene and mucositis development. A prospective cohort study by Chen et al., (2021) explored the role of self-oral care abilities in mucositis and reported conflicting findings and suggested that self-oral care deficits were not significantly associated with mucositis incidence.

Carra et al., (2020) concluded that the effectiveness of the oral hygiene intervention may depend on various factors, such as the specific intervention used, the population being targeted, and the duration and intensity of the intervention. Further research done by Wilson et al., (2019) who confirmed that the effectiveness of the practical oral care to determine the long-term impact on mucositis outcomes.

Regarding oral mucositis assessment Scale baseline among studied groups, it was found that the most common assessment is Points, erythematous lesions observed in the oral cavity (Pain, erythema) in studied groups. With statistically significant difference between studied groups.

This study agreed with a study by Ludovichetti et al., (2023) found that erythematous lesions and symptoms of pain and erythema were commonly assessed parameters and supported the use of this assessment method for evaluating oral mucositis severity. Gupta et al. (2021) found that many studies employed point-based scoring systems that included parameters related to erythematous lesions, pain, and erythema. Conversely, Elad et al., (2022) investigated the baseline assessment of oral mucositis in cancer patients but did not find a statistically significant difference in the prevalence of erythematous lesions, pain, or erythema between the studied groups. However, a study by Fardad et al., (2023) which assess the effectiveness of curcumin, mucosamin, and chlorhexidine in chemotherapy-induced oral mucositis and explored alternative assessment methods for oral mucositis, such as subjective patient-reported outcomes or imaging techniques, and did not specifically focus on erythematous lesions or symptoms of pain and erythema. While this study provided insights into alternative assessment approaches, it did not directly support the findings of the present study.

Regarding oral mucositis assessment Scale discharge among studied groups. The present study found that the most common assessment is Red zones with increased mucosa, and lesions separated from each other. (Ulcer, erythema) in mucositis group. While the most common assessment is A mouth with a healthy appearance and no mucositis in non mucositis group,

and there were a statistically significant difference between studied groups.

The researcher point of view suggest that there are distinct visual and symptomatic differences in oral mucositis between the two groups, highlighting the importance of assessing and monitoring these specific characteristics during patient discharge.

This supported by **Singh & Singh, (2020)** who found that red zones with increased mucosa and separate lesions, such as ulcers and erythema, were commonly observed in the mucositis group. **Shetty et al., (2022)** reported that the presence of red zones with increased mucosa, along with ulceration and erythema, was a significant factor in determining the severity and resolution of mucositis. This study supported the importance of assessing these specific features in the mucositis group.

On the other study by **Elad et al., (2022)** analyze oral health outcomes in cancer patients but did not specifically focus on the assessment of oral mucositis at discharge, this study did not directly support or address the findings of the present study.

A study by **McNamara & Kalmar, (2019)** did not specifically mention the presence of red zones, ulcers, or erythema among the majority of the studied patients with leukemia.

Conclusion

Based on the results of the study, it could be concluded that: More than half of patients with acute leukemia experienced mucositis and There were statistically significant difference between studied groups at dehydration, malnutrition, poor oral hygiene and deficit in ability of self-oral care.

Recommendations

Based on the current study findings, the following recommendations are suggested

The nurses at intensive care unit who gives care for leukemia patient should be trained on how to identify of risk factors of oral mucositis and aware of risk factors that increase prevalence of oral mucositis..They should develop and implement of oral care guidelines for mucositic patient with acute leukemia.

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