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FACTORS ASSOCIATED WITH ORAL MUCOSITIS INHEAD AND NECK CANCER PATIENTS RECEIVING CHEMO-RADIOTHERAPY- HOSPITAL BASED STUDY

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ABSTRACT :

Background: Oral mucositis is characterized by erythema, edema and ulcerations of oral mucosa, an adverse effect of chemotherapy and radiotherapy isa severely debilitating condition. Severe form of oral mucositis leads to worsening of patients' quality of life and limiting compliance with treatment leads to withdrawing. Aim of this study is to assess the factors related with oral mucositis (OM) in patients receiving chemotherapy and radiotherapy in head and neck cancer(HNC).

Methodology: Data on 30 patients with oral mucositis and head and neck cancer were gathered. The Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO), a research and educational organization published clinical practice guidelines for oral mucositis, served as the basis for the selection of factors.Verified collected data were then imported into SPSS. Bar charts were created in SPSS after each category's individual frequency distributions were evaluated. The Chi-square test and descriptive statistics were used.

Results: Factors associated with patient having oral mucositis were predominantly present in male patients18(60%) with Comorbidity like diabetes 21(70%), poor oral hygiene, decreased salivary secretion, reduced weight ,higher dosage treatment in shorter period 24(80%) respectively, low hematological parameters 27 (90%) , more than 5 cycles of chemotherapy 21 (70%) and majority of patients received cisplatin infusion 18(60%). Majority of male patients12 (40%) underwent radiotherapy twice per day. Chi square test value is 1.286 ; p value- 0.994 ($p>0.05$). Majority of male patients 15 (50%) underwent 5 and above cycles of chemotherapy and both genders were equally distributed among 6(20%) undergoing 1-4 cycles of chemotherapy. Chi square test value is 1.377 ; p value is 0.994 ($p>0.05$).

Conclusions:

In our study Oral mucositis (OM) onset and severity progressed as radiotherapy and chemotherapy fractions/ cycles increased. Confounding factors frequently bias oral mucositis prevention and treatment. To gain a better understanding of the significance of medical interventions, associative factors should be minimized or eliminated.

INTRODUCTION:

Standard treatment for HNC are chemotherapy, radiotherapy and surgery. Severe complications occur in both acute and late stage of radiotherapy and chemotherapy. Commonly occurring acute adverse events is OM. Erythema, edema, and ulcerations of the oral mucosa are the hallmarks of this extremely incapacitating illness. [1]. Acute severe OM leads to patients inability to eat, swallow, placement of feeding tubes and hospitalization[2].It lasts for 7–14 days and starts 5–10 days after chemotherapy is initiated. Oral mucositis lesions can be extremely painful, impair diet and oral hygiene, and increase the risk of both local and systemic infection. [3].

There are direct and indirect pathways involved in the pathophysiology of radiation-induced oral mucositis. The decrease in basal epithelium renewal is a direct consequence of radiation-induced DNA strand breakage and apoptosis. The oral mucosa is destroyed as a result of indirect effects like neutropenia, salivary gland secretion, and the release of inflammatory transmitters.

[4].The occurrence and progression of chemotherapy and radiation-induced oral mucositis (OM), is an evident reflection of cytotoxic therapy-induced epithelial damage that is understood to be a complex phenomenon affecting the connective tissue, are currently described by the five biological stages put forth by Sonis.This biological model comprises five overlapping stages of the chemo-radiotherapy-induced oral mucositis events: initiation, upregulation, message generation, ulceration, and healing. [5].All of these phases lead to pain, but in neutropenic patients in particular, bacteria can infiltrate the systemic blood circulation and cause bacteremia

and sepsis. [6].The World Health Organization (WHO) assigned a grade for oral mucositis, which ranges from 0 to 4. Painless ulcers, edema, or mild soreness is graded as 0, painful erythema, edema, or ulcers but able to eat is graded as 2, painful erythema, edema, or ulcers but unable to eat is graded as 3, and the patient is assessed as 4 if they require parenteral or enteral support[7]. Severe form of oral mucositis leads to worsening of patients quality of life and limiting compliance with treatment leading to withdrawing their chemo-radiation therapy.

Chemotherapy and radiation induced mucositis are associated with various factors [8].

While radiation therapy targets specific body part of cancer site, chemotherapy is given to patients on a systemic level. There are some differences in the mode of action of treatment, cycles, dosage, type of radiotherapy and dosage, fractions, drugs, form of chemotherapy which affect tissue causing oral mucositis[9].Therefore, the purpose of this study was to determine the associated factors for oral mucositis (OM) in patients receiving chemotherapy and radiation treatment for head and neck cancer.

MATERIALS AND METHODS:

Data were gathered from 30 head and neck cancer patients at Rai CBC, Saveetha Dental College who were experiencing oral mucositis receiving chemotherapy or radiation therapy. Institutional ethical committee number is **IHEC/SDC/UG-1899/23/OMED/269**. Demographic data like age, gender of the patients and oral hygiene, comorbidity, nutritional status, saliva secretion, hematological parameters, undergoing treatment includes dosage of radiotherapy, chemotherapy dosage, course of chemotherapy, name of the chemotherapy drugs were selected based on the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO) clinical practice guidelines for mucositis.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences, Chicago, USA) was used to import and verify the collected data. Bar charts were created in SPSS after each category's individual frequency distributions were evaluated. The results were compared using the Chi-square test and descriptive statistics.

RESULTS:

In this study the patients with oral mucositis were aged between 40-55 years old. Majority of them were from the age of 45-50 years(50%)[Fig.1]. Among them 18 (60%) were males and 12(40%) were females[Fig.2]. Among them 24(80%) of patients had poor oral hygiene and 6(20)% patients had fair oral hygiene[Fig.3]. 21(70)% of them were diabetic and 9(30)% had other Comorbidities like hypertension, heart disease, respiratory disorder [Fig.4]. According to BMI ,24(80)% of them were underweight and 6(20)% were normal weight[Fig.5]. Saliva secretion was reduced for the majority 24(80%) of them[Fig.6]. 27 (90)% of them showed reduced Hb and WBC count in hematological parameters[Fig.7].24 (80)% of them underwent higher dosage of radiotherapy in a shorter period of time[Fig.8]. 9(30)% of them underwent 1-4 cycles of chemotherapy and 21(70)% of them were above 5 cycles [Fig. 9]. Among the chemotherapeutic drugs used,majority of them had Cisplatin 18(60)%followed by capecitabine 9(30)%, cytarabine 3(10)% as infusion in chemoradiotherapy in Head and Neck cancer patients[Fig 10]

Majority of male patients 12 (40%) and female patients 9 (30%) underwent radiotherapy twice per day. Chi square test value is 1.286 ; p value is 0.994 ($p>0.05$). [Fig 11] Majority of male patients 15 (50%) underwent 5 and above cycles of chemotherapy and both genders were

equally distributed among 6 (20%) undergoing 1-4 cycles of chemotherapy. Chi square test value is 1.377 ; p value is 0.994 ($p>0.05$). [Fig 12]

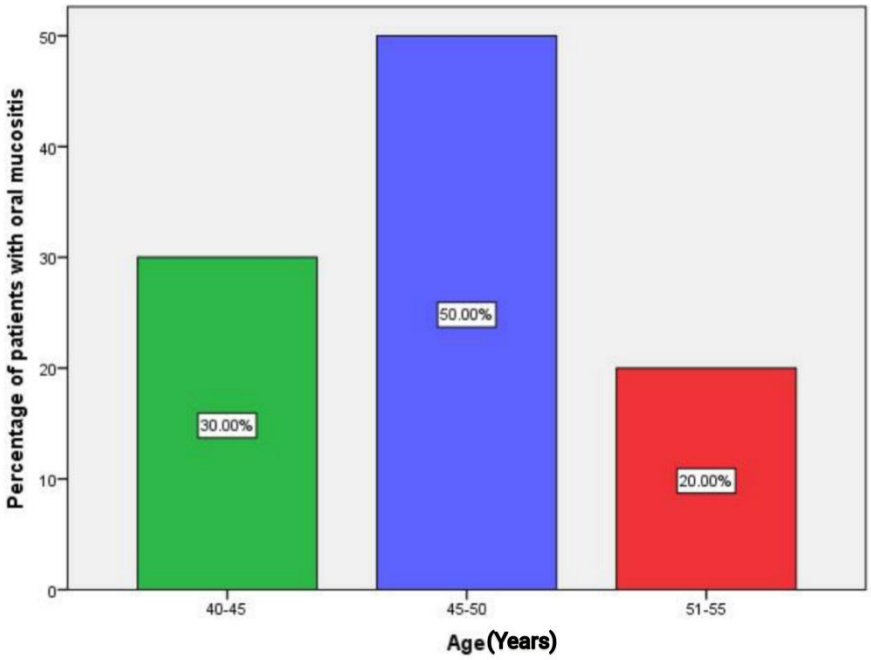

Figure 1: Age distribution of the patient with oral mucositis is displayed in a bar graph. Age is represented by x axis, and percentage of patients with oral mucositis is represented by the y axis. According to the graph 30% belonged to 40-45 years, 50% belonged to 45-50 years and 20% belonged to 51-55 years.

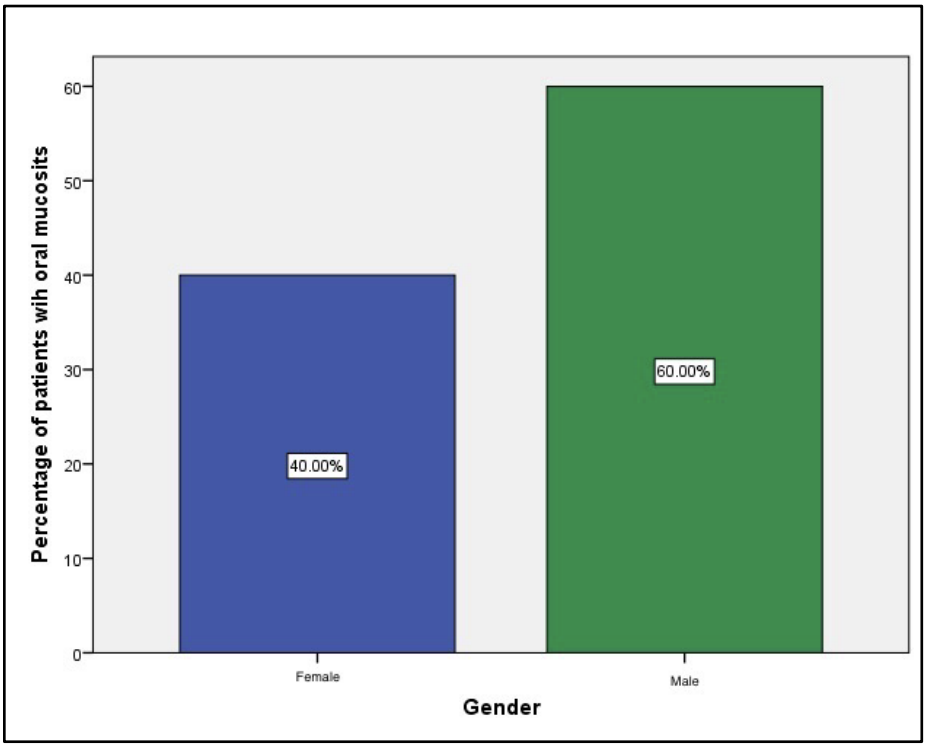

Figure 2: Bar graph shows the frequency distribution of the gender of the patient with oral mucositis. Percentage of patients with oral mucositis is represented by the Y axis, while X axis represents gender. According to the graph 40% were females, and 60% were male.

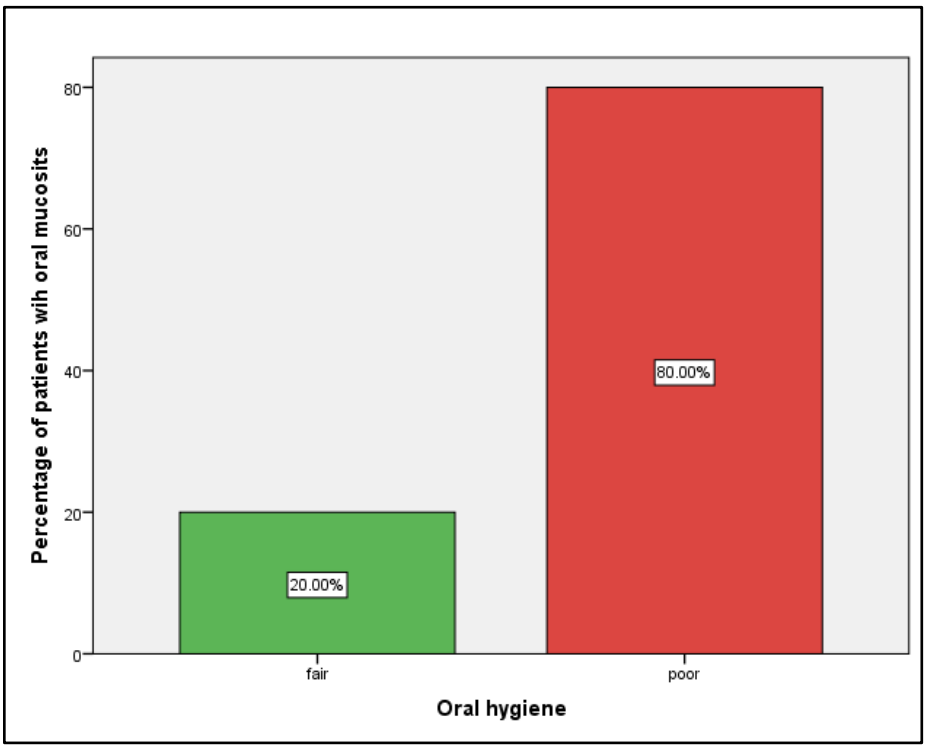

Figure 3: fequency distribution of the patient's oral hygiene for oral mucositis is displayed in a bar graph.Oral hygiene is represented by X axis, and the percentage of patients with oral mucositis is represented by the Y axis. According to the graph 20% had good oral hygiene , 80% had poor oral hygiene.

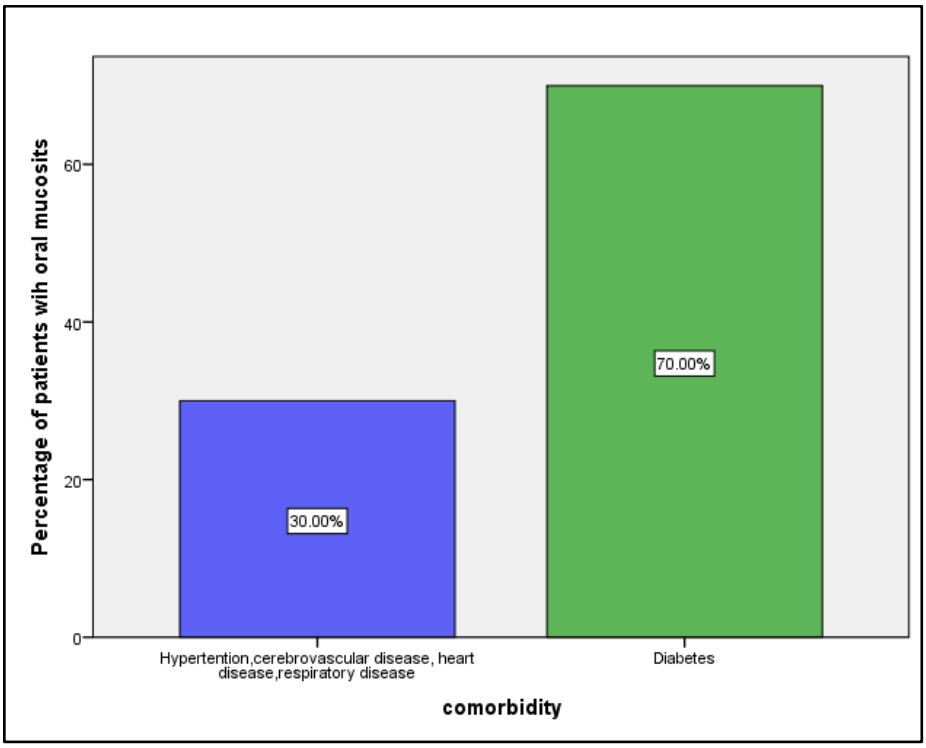

Figure 4: Bar graph shows the frequency distribution of the comorbidity of the patient with oral mucositis. Percentage of patients with oral mucositis is represented by the Y axis, while the X axis represents comorbidity. According to the graph 30% has hypertension, cerebrovascular disease, heart disease, respiratory disease and 70% has diabetes

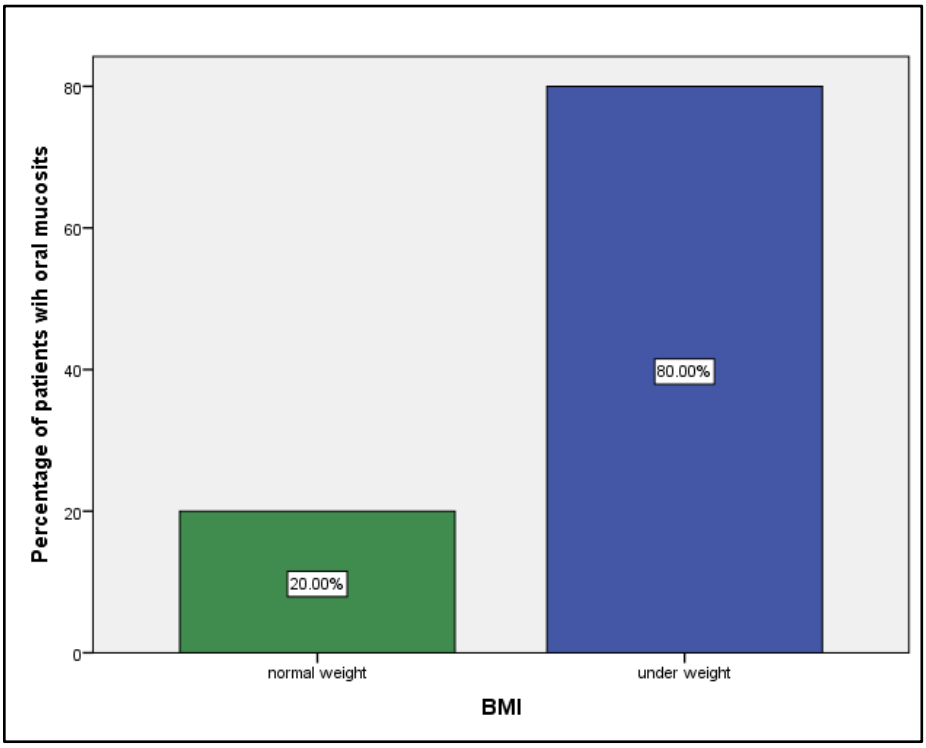

Figure 5: Bar graph shows the frequency distribution of the BMI of the patient with oral mucositis. BMI is represented by the X axis, and the percentage of patients with oral mucositis is represented by the Y axis. According to the graph 20% were categorized as normal weight and 80% were categorized as underweight

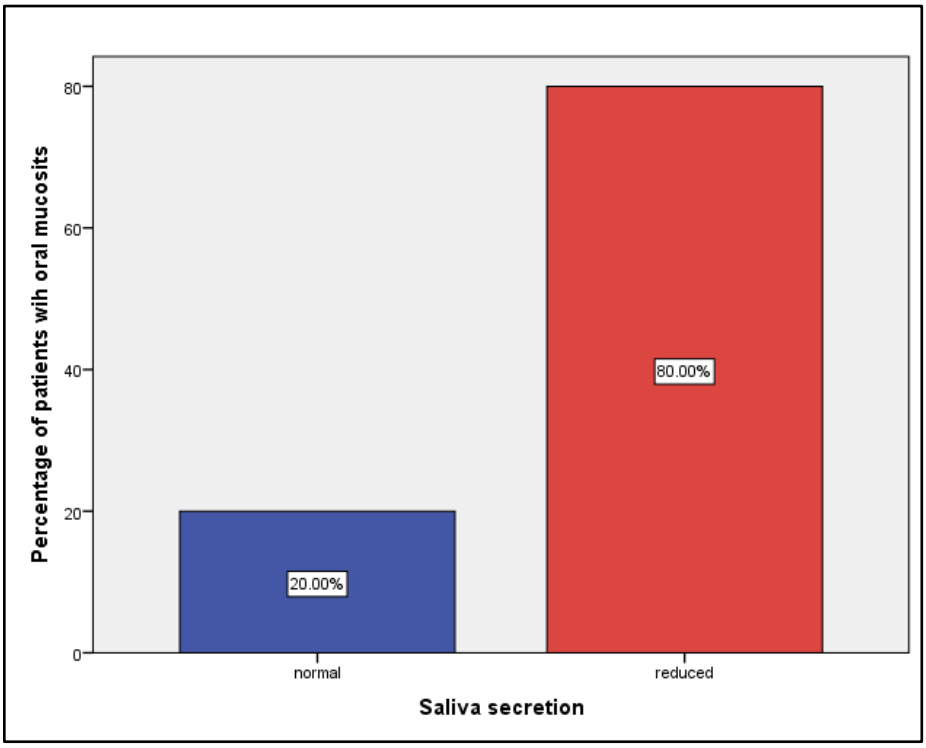

Figure 6: Bar graph shows the frequency distribution of the saliva secretion of the patient with oral mucositis. Saliva secretion is represented by the X axis, while the percentage of patients with oral mucositis is represented by the Y axis. According to the graph 20% were categorized under normal salivary secretion and 80% were categorized under reduced salivary secretion.

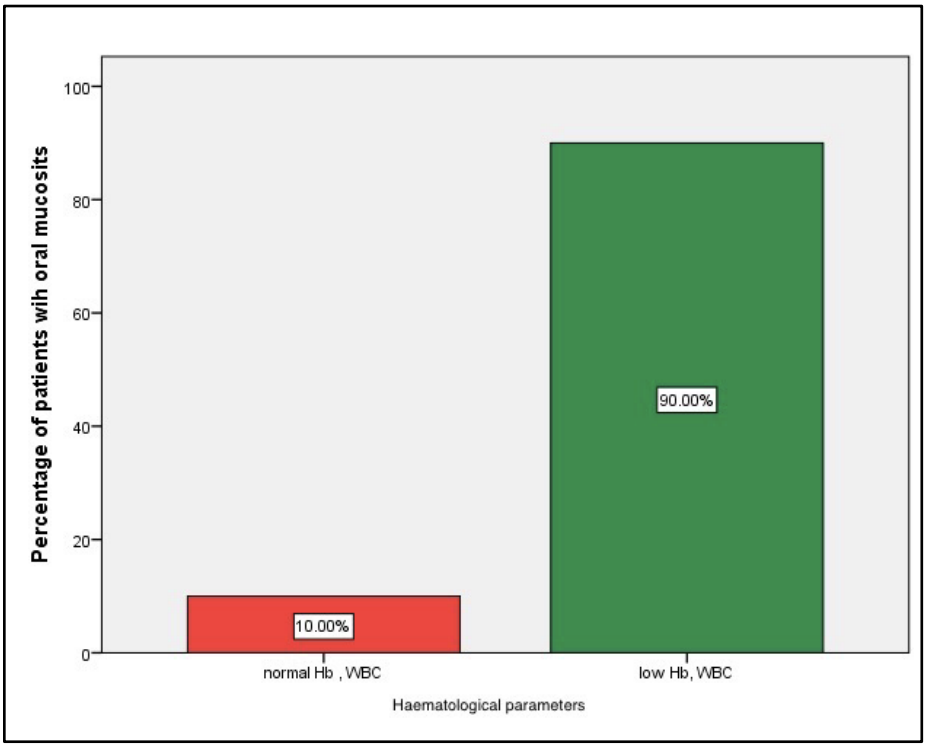

Figure 7: Bar graph shows the frequency distribution of the hematological parameters of the patient with oral mucositis. Percentage of patients with oral mucositis is represented by the Y axis, while the x axis represents hematological parameters.According to the graph 10% has normal Hb , WBC value and 90% has low Hb , WBC value.

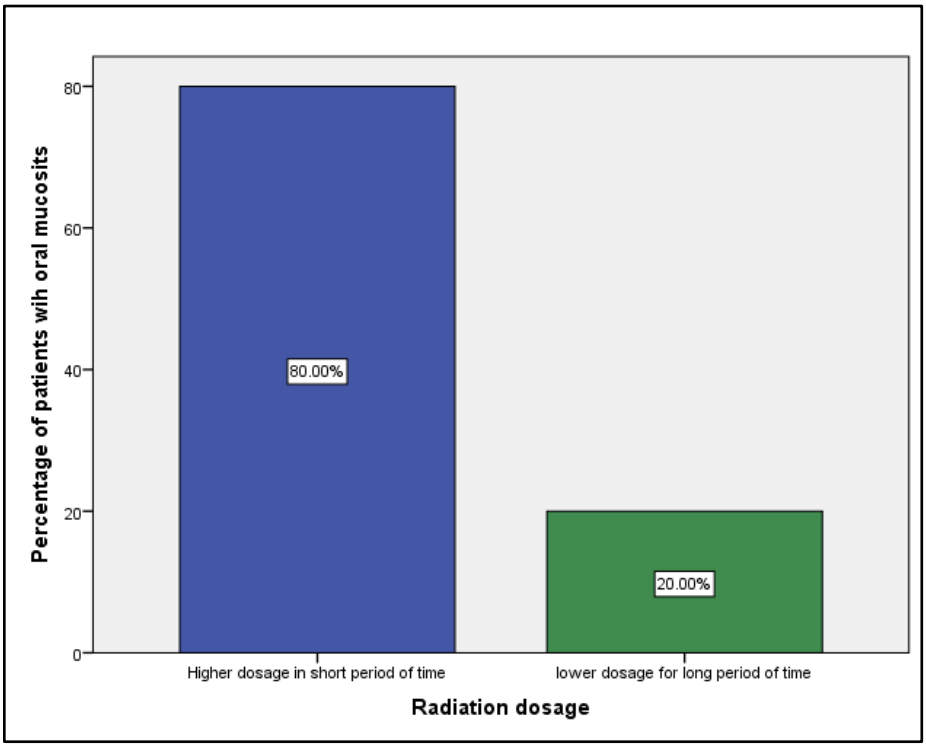

Figure 8: Bar graph shows the frequency distribution of the radiation dosage of the patient with oral mucositis. Percentage of patients with oral mucositis is represented by the Y axis, while the x axis represents the radiation dosage. According to the graph 80% underwent higher dosage in shorter period of time and 20% underwent lower dosage in a longer period of time as per their scheduled radiation therapy.

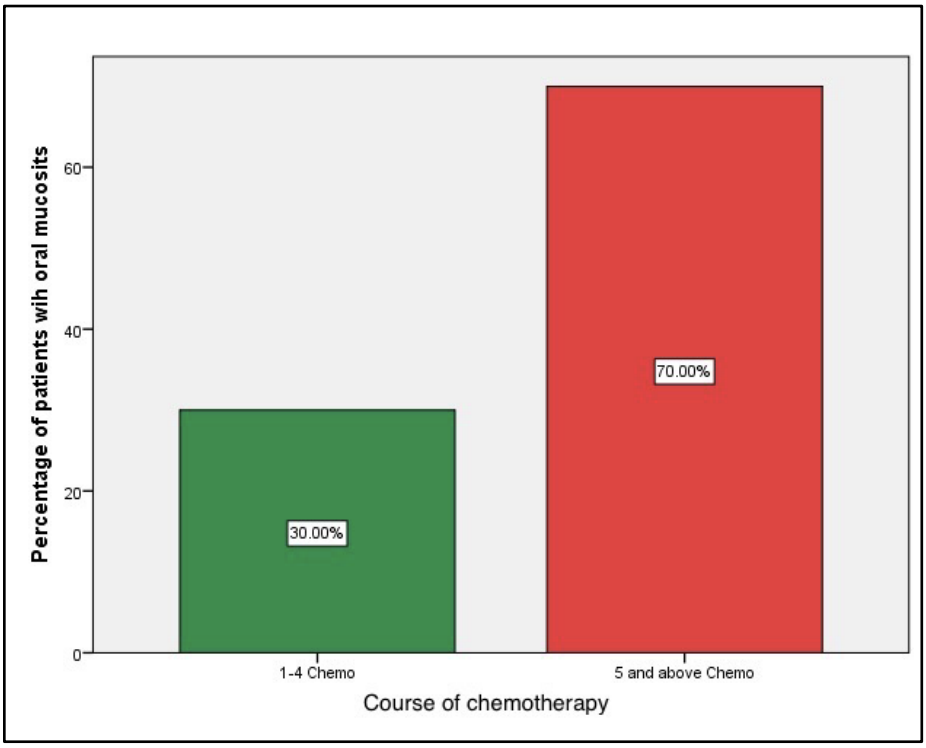

Figure 9: Frequency distribution of the patient's chemotherapy treatment for oral mucositis is displayed in a bar graph.Y axis represents the proportion of patients with oral mucositis, while the X axis represents the chemotherapy course. According to the graph 30% underwent 1-4 chemotherapy and 70% underwent 5 and above chemotherapy

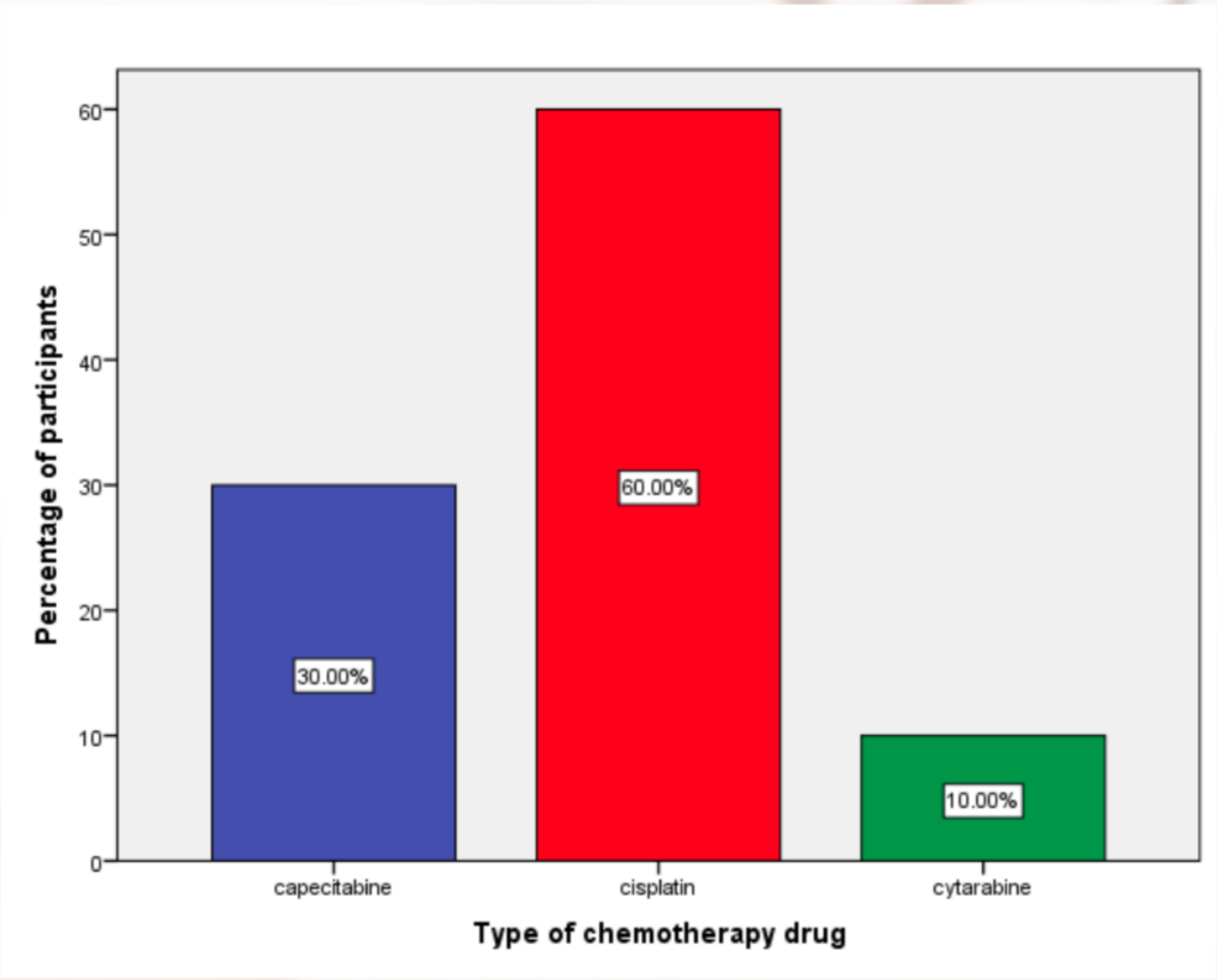

Figure 10: The chemotherapy drug type frequency distribution for patients with oral mucositis is displayed in a bar graph.X axis is representative of type of chemotherapy drug and the percentage of patients with oral mucositis is represented by the Y axis. Based on the graph, patients receiving chemoradiotherapy for head and neck cancer had an infusion of 60% cisplatin, 30% capecitabine, and 10% cytarabine.

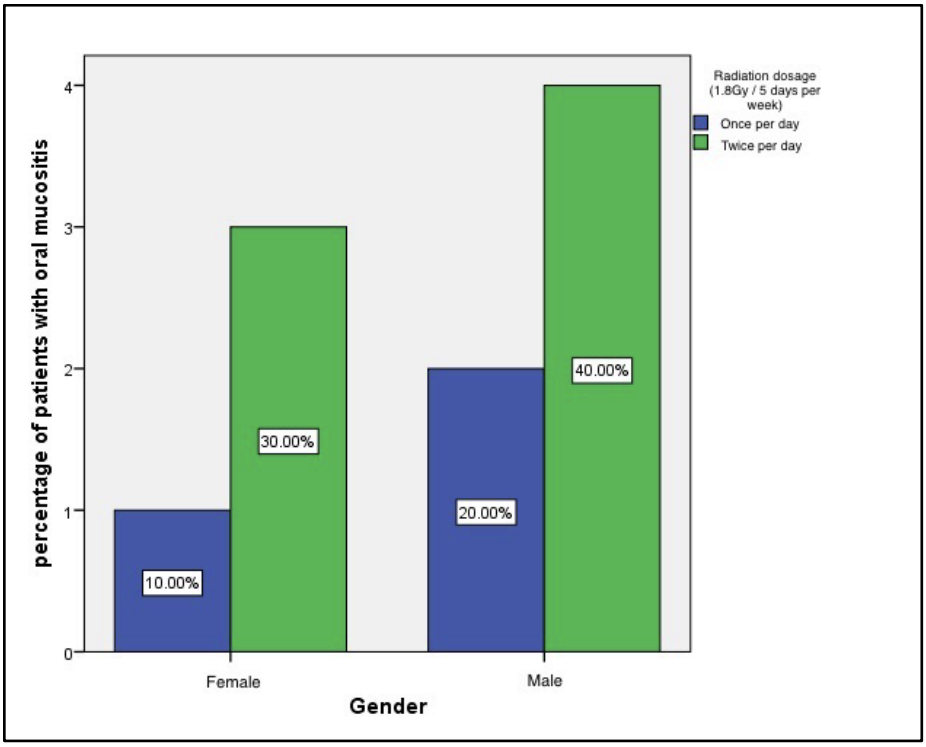

Figure 11: Association between radiation dosage and gender is displayed in a bar graph. (1.8Gy/5 days per week). X axis represents the gender of patients with oral mucositis and the percentage of radiotherapy dosage is represented by the Y axis. Blue represents patient with oral mucositis undergoing radiotherapy once per day and green represents a patient with oral mucositis undergoing radiotherapy twice per day. Majority of male patients(40%) and female patients (30%) underwent radiotherapy twice per day. Chi square test value is 1.286 ; p value is 0.994 ($p>0.05$). Statistically not significant.

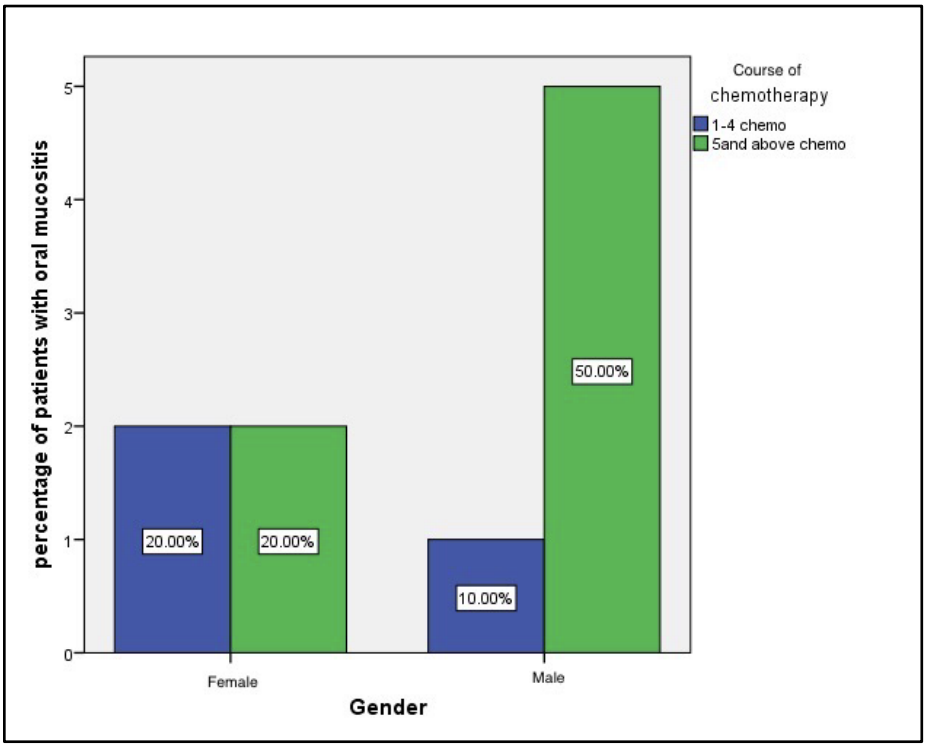

Figure 12: Bar graph illustrates the relationship between gender and course of chemotherapy. X axis represents the gender of patients with oral mucositis and Y axis depicts percentage of patientswho underwent different courses of chemotherapy . Blue color represents a patient with oral mucositis undergoing 1-4 chemo and green represents a patient with oral mucositis undergoing 5 and above chemo. Majority of male patients(50%) underwent 5 and above cycles of chemotherapy and both genders were equally were distributed among (20%) underwent 1-4 cycles of chemotherapy. Chi square test value is 1.377 ; p value is 0.994 ($p>0.05$). Statistically not significant.

DISCUSSION:

Oral mucositis is the most debilitating inevitable dose limiting toxicity of radiotherapy and chemotherapy inHNC,quality of life in these patients are hampered [10]. Various confounding factors influence development of oral mucositis. Aim of our research was to assess the factors for oral mucositis (OM) in patients receiving chemotherapy and radiation treatment for head and neck cancer. Higher risk of oral mucositis was reported in younger patients in previous studies. In a study by Morais-Faria et al, younger patients (< 45 years) displayed greater OM incidence and severity in HNC following CRT than older patients (> 58 years; $p < 0.01$), while clinical staging and treatment protocols were similar. Rapid epithelial mitosis and high cell renewal rate are the factors associated with high risk of oral mucositis in these group of patients[11]. Similarly, in our study, 15(50%) comprise from the age group of 45-50 years,9(30%) from 40-45 years, 6(20%) in the age group of 51-55 years.Among gender, females were more commonly affected, hormonal influence enhance the risk of oral mucositis[12].In contrast, majority of males (60%)have oral mucositis compared to females in our study.In our study,80% of patients had poor oral hygiene which was similar to a study done by Wuketic et al, 82 HNC patients who underwent CRT had severe OM due to higher levels of gram negative microbial colonisation[13].Due to changes in the composition of the oral microbiota, abnormalities in polymorphonuclear function, and abnormal collagen metabolism, a high prevalence of diabetes was identified as a risk factor. [14] Similarly in our study,70% were diabetes , most common comorbidity seen in oral mucositis patient.80% in our study the patients were underweight,Due to alterations in the host immune response, patients with oral cancer and a BMI >22 were more likely to develop OM during radiation therapy.

[15].In our study,80% of patient with oral mucositis experienced reduced salivary secretion, similarly 63 patients with a different kind of oral cancer receiving 5FU as chemotherapy, low salivary flow rate was found to be a risk factor for oral mucositis [16].

In our study,90% of patients receiving chemo radiotherapy had reduced hematological parameters such as low Hemoglobin,WBC. Similar to a study done by Wersalet al,erythrocytes, hemoglobin, platelets, and leucocytes significantly decrease while lymphocytes increase over the course of the patient's chemotherapy and radiation treatment. [17].

Onset of OM is due to fractionation, dosimetric parameters and radiotherapy techniques. Radiation dosage,altered fractionation has higher OM incidence.A conventional 66 Gy in 33 fractions with five fractions per week was compared to 54 Gy in 36 fractions in 12 days during the CHART trial.In our study,80%showed higher dosage in shorter period of time in patients with oral mucositis[18].

Elting et al. reported that regardless of the cancer site or treatment modality, the severity of OM peaked during week 5 of therapy and usually persisted through Week 7 for patients receiving chemotherapy., similarly in our study patients who underwent 5 and above cycles of chemotherapy(70%) developed severe OM [14]

Limitations of our current study includedprospective analysis in smaller samples. Future studies should be conducted as randomized clinical trials to understand the in depth knowledge of various confounding factors that influence oral mucositis and to find creative management strategies for them.Patient-Reported Outcome data can be included to enhance clinical management and elevate the standard of clinical trials.

CONCLUSION:

Factors associated with patient having oral mucositis were predominantly present in male patientswith Comorbidity like diabetes, decreased salivary secretion , and higher dosage drugs, higher dosage treatment in shorter period, with more than 2 cycles of radiotherapy,more than 5 cycles of chemotherapy,among chemotherapeutics used majority of them had Cisplatin infusion. Confounding factors give rise to bias in the treatment and prevention of oral mucositis.

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