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ASSESSMENT OF SOCIODEMOGRAPHIC CHARACTERISTICS AND COMPARATIVE ANALYSIS OF ADVERSE DRUG REACTIONS AMONG OROPHARYNGEAL CANCER PATIENTS RECEIVING DIFFERENT CHEMOTHERAPEUTIC REGIMENS IN KARACHI, SINDH, PAKISTAN

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ABSTRACT

Background and objective: Cancer remains one of the leading causes of mortality worldwide and poses a substantial socioeconomic burden on human life. Various chemotherapeutic regimens are employed in its management; nevertheless, differences in toxicity profiles may have important implications for patient management. There is a paucity of local evidence for comparative assessment of prescribing patterns and associated toxicities.

Methodology: A retrospective observational study was conducted to evaluate the adverse drug reactions (ADRs) associated with five chemotherapeutic regimens prescribed for the management of oropharyngeal cancer: Regimen 1 (Cisplatin + 5-Fluorouracil), Regimen 2 (Cisplatin + Methotrexate), Regimen 3 (Carboplatin + 5-Fluorouracil), Regimen 4 (Cisplatin + Paclitaxel) and Regimen 5 (Cetuximab). The study was undertaken at the Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) and Memon Medical Institute (MMI), Karachi, Sindh, Pakistan over a period of six months. The medical records of 320 oropharyngeal cancer patients were reviewed for demographic information, habitual risk factors, clinical characteristics, and treatment-related toxicities.

Results: The findings revealed that the highest incidence of nausea/vomiting was associated with Regimen 2, whereas patients receiving Regimen 4 exhibited the highest incidence of alopecia and mucositis. Patients treated with Regimen 3 experienced the highest incidence of myelosuppression, while Regimen 4 demonstrated an increased phenomenon of constitutional symptoms. The study population treated with Regimen 5 exhibited dermatological toxicities.

Conclusion: The findings of this study showed significant variations in ADR profiles among the commonly used chemotherapeutic regimens and may contribute to the selection of appropriate treatment strategies and enhance patient management in oropharyngeal cancer.

KEYWORDS: Oropharyngeal cancer; Chemotherapeutic regimen; Adverse drug reactions; Retrospective study

1. INTRODUCTION

Globally, cancer is recognized as a leading cause of mortality, and ultimately it enhances the socioeconomic burden on human life (Bray et al., 2021). Over the past decades, cancer remains a significant public health challenge and a foremost cause of mortality, with an increasing impact on young adult populations (Rana et al., 2021). According to recent estimates reported by the American Cancer Society (ACS), around 55,000 new cases of oropharyngeal cancer were diagnosed, accounting for nearly 12,000 deaths (Consalvo et al., 2024). High-throughput screening studies have characterized the pharmacological responses of approximately 148 anticancer agents across a diverse panel of more than 1,000 cancer cell lines, contributing to the understanding of factors influencing differential responses to anticancer agents (Bashi et al., 2024; Akhtari et al., 2021). Commonly prescribed chemotherapeutic drugs for the management of oral cavity and/or oropharyngeal cancers, which may be administered alone or in conjunction with radiotherapy, include Cisplatin, Carboplatin, 5-Fluorouracil (5-FU), Paclitaxel, Docetaxel, and Hydroxyurea, while Methotrexate and Capecitabine are used less frequently (Silva et al., 2023). Chemotherapeutic regimens may be employed as monotherapy or together with other anticancer medications depending on the treatment objectives. The use of multidrug regimens often results in greater tumor

reduction, although this benefit is often offset by an increased risk of treatment-related toxicity (Bagdasaryan et al., 2022; Basak et al., 2021).
A commonly used combination is Carboplatin and 5-FU. This combination works better than either drug alone in shrinking cancers of the oral cavity (Silva et al., 2023). Another combination often used is Cisplatin, 5-FU, and Docetaxel. In certain cases, chemotherapy might be given along with a targeted drug or immunotherapy (Xing et al., 2021). Generally, the contributing factors toward ADRs include unjustified concomitant use of other drugs with anticancer therapy, insufficient drug prescribing, poor adherence to treatment plans, and frequent dosing (Bellanca et al., 2023). Recently, many studies disclosed that ADRs are very complicated to report, but if reported appropriately, can play a very important role in optimizing the strategy of the treatment plan, which has been concluded as the biggest challenge for the proper treatment of patients with various types of tumors (Li et al., 2022; Tadge et al., 2023).

2. METHODOLOGY

2.1. Study design

A retrospective observational study was conducted on chemotherapy protocols of numerous anticancer drugs of oral cancer patients at two different cancer-treating hospitals, including KIRAN and MMI, Karachi, Sindh, Pakistan, over the period of six months. Medical records of oropharyngeal cancer patients were reviewed to evaluate the chemotherapeutic regimens and their attributed ADRs.

2.2. Study population

The study population consists of patients with histopathologically confirmed oropharyngeal cancer, who received at least one cycle of chemotherapy and whose medical records were available within the study period. Patients with incomplete medical records or insufficient documentation of treatment-related outcomes were excluded from the analysis. Thus, of the records screened, 320 patients fulfilled the inclusion criteria.

2.3. Data collection

Data were retrospectively extracted using a structured data collection form from the medical records of patients fulfilling inclusion criteria. Information collected included: demographic characteristics (age and gender), occupational status, habitual risk factors, and clinical features of chemotherapeutic regimens, including frequency of regimen and associated adverse drug reactions. Patient confidentiality and obscurity were maintained throughout the study.

2.4. Assessment of adverse drug reactions

The occurrence and severity of ADRs associated with chemotherapy were evaluated from documented clinical records. Adverse events were categorized as mild, moderate or severe according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) (Shah, 2022). The frequency and distribution of ADRs were assessed across different chemotherapeutic regimens.

2.5. Ethical declarations

Ethical approval was obtained from the Institutional Bioethics Committee (IBC), University of Sindh, Jamshoro (Approval No. ORIC/SU/165, dated September 17, 2025), and hospital consent was obtained from the Medical Superintendent of KIRAN and MMI Hospitals, respectively. Informed consent was secured, and its confidentiality was maintained.

2.6. Statistical Analysis

The Chi-square test was used to determine the associations between chemotherapeutic regimens and ADRs. A p-value of less than 0.05 was considered statistically significant. Moreover, descriptive statistics were used to summarize demographic and clinical characteristics. Categorical variables were presented as frequencies and percentages.

3. RESULTS

3.1. Baseline demographics and clinical characteristics of study population

Baseline demographics and clinical characteristics of the study population were obtained from the medical records of oropharyngeal cancer patients treated at two cancer care hospitals of Karachi. The total study population was 320, of which 224 were recruited from KIRAN Hospital, whereas the remaining 96 patients were from MMI Hospital, as tabulated in Table-01.

Table-01: Hospital-wise distribution of study population (N = 320)

HOSPITAL	**n, (%)**
KIRAN	224 (70)
MMI	96 (30)

N = Total study population, n = Number of patients, % = Percentage.

3.2. Gender wise distribution of study population

Among the study population of 320 patients, males constituted the majority, accounting for 172 patients from KIRAN Hospital and 52 from MMI Hospital, whereas female patients accounted for 52 and 44 cases of oropharyngeal cancer from KIRAN Hospital and MMI Hospital, respectively, as tabulated in Table-02.

Table-02: Gender wise distribution of study population (N = 320)

HOSPITAL	Male, n (%)	Female, n (%)
KIRAN	172 (76.79)	52 (54.20)
MMI	52 (23.21)	44 (45.80)
TOTAL	224 (70)	96 (30)

N = Total study population, n = Number of patients, % = Percentage.

3.3. Age-wise distribution of study population

The study population was age-wise categorized; it was observed that half of the entire population of oropharyngeal cancer patients belonged to the age group 45-64 years, whereas the age group 65-74 years accounted for 25% of the entire population, followed by age groups ≥ 75 years, 30-44 years, and <30 years. As tabulated in Table-03.

Table-03: Age-wise distribution of study population (N = 320)

Age limits	n (%)
<30 years	6 (2)
30-44 years	32 (10)
45-64 years	160 (50)
65-74 years	80 (25)
75 onwards	42 (13)

N = Total study population, n = Number of patients, % = Percentage.

3.4. Occupational status of study population

The study population was described in terms of occupational characteristics and tabulated in Table-04. Economically dependent individuals, including housewives and students, constituted the largest proportion (30%) of the entire pool; however, the participants belonging to government or private sectors also constituted a significant portion (25%), followed by unemployed (20%), labor (15%), and self-employed (10%).

Table-04: Occupational status-wise distribution of study population (N = 320)

Occupational status	n (%)
Employed (government/private job)	80 (25)
Unemployed	64 (20)
Business/Self employed	32 (10)
Labor	48 (15)
Economically dependent (housewives/students)	96 (30)

N = Total study population, n = Number of patients, % = Percentage.

3.5. Habitual risk factors among the study population

Table-05 represents the habitual risk factors, including smoking and chewing involving tobacco and non-tobacco items. It was observed that among the majority of oropharyngeal cancer patients, the common risk factor was cigarette smoking, reported as 42.5%; however, other habitual risk factors, including smokeless tobacco products such as gutka/pan, naswar and mainpuri/mawa were reported as 28.75, 15 and 5% respectively. Furthermore, the chewable non-tobacco product chalia constitutes about 8.75% of the total population of cancer patients; these findings reflect the high prevalence of habitual risk factors, including consumption of smoking and smokeless tobacco items among the oropharyngeal cancer patients, thus indicating their consumption as a predisposing risk factor for the disease.

Table-05: Habitual risk factor-wise distribution of study population (N = 320)

Habitual risk factors	n (%)
Cigarette smoking	136 (42.5)
Gutka/Pan (chewable tobacco preparation)	92 (28.75)
Naswar (smokeless tobacco preparation)	48 (15)
Mainpuri/Mawa (chewable tobacco preparation)	16 (5)

Chalia (chewable non-tobacco preparation)	28 (8.75)

N = Total study population, n = Number of patients, % = Percentage.

3.6. Pattern of ADRs among the study population

Table-06 demonstrates the comparison of chemotherapeutic regimens and their associated ADRs among the study population N = 320 by using the Chi-square test. It was observed that among the five chemotherapeutic regimens evaluated, Regimen 3 (Carboplatin + 5-FU) was most frequently prescribed accounting for n = 88 patients, whereas n = 84 patients received Regimen 2 (Cisplatin + Methotrexate), and n = 62 patients among the study population received Regimen 5 (Cetuximab), the frequency of prescription for Regimen 1 (Cisplatin + 5-FU) and 4 (Cisplatin + Paclitaxel) was n = 50 and n = 36 patients respectively. Assessment of ADRs revealed that Regimen 2 was highly associated with nausea/vomiting with an incidence of n = 70, 83.33%, whereas patients treated with Regimen 4 depicted the highest incidence of alopecia (hair loss) and mucositis (mucosal injury), accounting for n = 30, 83.33% and n = 16, 44.44% patients, respectively. n = 54, 61.36% patients were affected with myelosuppression (anemia/leukopenia) associated with Regimen 3, while constitutional symptoms (fever, chills, and fatigue) were most frequently observed among patients treated with Regimen 4, affecting n = 22, 61.11% patients. n = 46, 74.19% of the study population treated with Regimen 5 exhibited dermatological toxicities (papulopustular rash, dermatitis, acneiform eruption, and skin rash). A statistically significant association was observed between all the chemotherapeutic regimens and the evaluated ADRs, conversely for nausea/vomiting (X^2 = 110.1, p <0.0001), alopecia (X^2 = 18.79, p = 0.0003), mucositis (X^2 = 23.64, p <0.0001), constitutional symptoms (X^2 = 33.18, p <0.0001), dermatological toxicities (X^2 = 108.9, p <0.0001) and myelosuppression (X^2 = 19.37, p = 0.0002).

Table-06: Comparison of incidence of ADRs across chemotherapeutic regimens using the Chi-square test

ADR's	Regimen 1 (n=50)	Regimen 2 (n=84)	Regimen 3 (n=88)	Regimen 4 (n=36)	Regimen 5 (n=62)	X^2 (df)	p-value
Nausea and vomiting	44 (88%)	70 (83.33%)	40 (45.45%)	12 (33.33%)	06 (9.68%)	110.1 (4)	<0.0001
Alopecia	28 (56%)	34 (40.48%)	46 (52.27%)	30 (83.33%)	-	18.79 (3)	0.0003
Mucositis	20 (40%)	30 (35.71%)	26 (29.55%)	16 (44.44%)	04 (6.45%)	23.64 (4)	<0.0001
Constitutional symptoms	26 (52%)	20 (23.81%)	16 (18.18%)	22 (61.11%)	-	33.18 (3)	<0.0001
Dermatological toxicities	04 (8%)	10 (11.90%)	10 (11.36%)	06 (16.67%)	46 (74.19%)	108.9 (4)	<0.0001
Myelosuppression	18 (36%)	26 (30.95%)	54 (61.36%)	20 (55.56%)	-	19.37 (3)	0.0002

Regimen 1 = (Cisplatin + 5-FU), Regimen 2 = (Cisplatin + Methotrexate), Regimen 3 = (Carboplatin + 5-FU), Regimen 4 = (Cisplatin + Paclitaxel) and Regimen 5 = (Cetuximab), whereas a p-value of <0.05 is considered significant, X^2 indicates Chi-square, (df) indicates degrees of freedom.

4. DISCUSSION

The present study demonstrated significant variations in patient flow, socio-economic status, habitual risk factors, and treatment-related toxicities among oropharyngeal cancer patients receiving various chemotherapeutic regimens. Based on a retrospective evaluation of the medical records of N = 320 patients from two tertiary care hospitals, KIRAN and MMI, the findings revealed substantial heterogeneity in the treatment outcomes across the study population. Moreover, in the present study, the majority of patients (70%) were recruited from KIRAN Hospital, while the rest of the study population (30%) was from MMI Hospital. This variation in patient influx may be attributed to the availability of more advanced oncology facilities at KIRAN Hospital. The gender distribution revealed a predominant proportion of male patients (70%) compared with female patients (30%). A similar sort of male-dominated trend among the oropharyngeal cancer patients has been reported in previous studies (Park et al., 2022; Damgacioglu et al., 2022). This predominance of oropharyngeal cancer among male patients may be attributed to their greater exposure to established carcinogenic risk factors. Compared with females, males in this region are more likely to consume tobacco-related products and engage in other habitual risk factors, which may contribute to their susceptibility to the development of oral cancer (Noggle et al., 2024; Possenti et al., 2025). The highest prevalence of oropharyngeal cancer was seen in the patients aged 45-64 years (50%), followed by the age group, 65-74 years (25%).These findings are consistent with the fact reported in previous studies that middle-aged and older individuals are at greater risk of developing oropharyngeal cancer due to long-term exposure to the established carcinogenic risk factors (Roman and Aragones, 2021; Guo et al., 2022; Pilleron and Bastiaannet, 2024). The results of the present study also suggest that oropharyngeal cancer is more prevalent in individuals with a low socioeconomic status; this increased level of susceptibility may be linked

to their limited access and unaffordability of healthcare services, unhealthy dietary patterns, and their routine exposure to established risk factors including tobacco and related products (Afshar et al., 2021). Furthermore, the employment profile of the study population reflects the higher proportion of unemployed or economically dependent individuals; these findings highlight the potential influence of socioeconomic status on the risk of developing cancer. Habitual exposure to established risk factors, including smoking and smokeless tobacco products, was strongly associated with the disease burden observed in the study population. The most prevalent habitual risk factor was cigarette smoking (42.5%), followed by the consumption of smokeless tobacco items, i.e., gutka/pan (28.75%) and naswar (15%). These results are in agreement with previously reported literature, which recognizes smoking tobacco and smokeless tobacco consumption as a prominent risk factor for the development of oropharyngeal cancer (Kulothungan et al., 2024).The relatively high incidence of gutka/pan usage observed in the local population underscores the need for targeted public health interventions to mitigate the associated health risk of tobacco consumption. Although adverse drug reactions occurred with all treatment regimens, the highest frequency of nausea and vomiting was observed among patients receiving Cisplatin-based chemotherapy, consistent with previous reports that classify Cisplatin as a highly emetogenic chemotherapeutic agent (Kamiya et al., 2021; Celio, 2022). The frequency of alopecia (83.33%) was maximum in patients receiving the combination of Cisplatin and Paclitaxel, most likely due to the cytotoxic effect of taxanes on hair follicles (Perez et al., 2024; Chan et al., 2021). Whereas, Mucositis was significantly more frequent among the patients receiving Cisplatin-based regimens, possibly due to the susceptibility of rapidly proliferating oral mucosal cells to the cytotoxic action of platinum compounds (Alsholi et al., 2023; Huang et al., 2022). Thus, in contrast, a lower incidence of mucositis was observed in patients treated with Cetuximab. The chemotherapy combination Carboplatin + 5-FU was highly associated with myelosuppression (61.36%), likely due to the additive tendency of bone marrow toxicity of these agents (Gaumond et al., 2025). Moreover, dermatological toxicities were highly prevalent in patients treated with Cetuximab, consistent with its mechanism of targeting the epidermal growth factor receptor (EGFR). Blockade of EGFR signaling alters epidermal homeostasis and contributes to the development of skin toxicities (Li et al., 2026; De Luca et al., 2021). Conversely, Cetuximab was associated with a lower incidence of nausea/vomiting, likely due to its limited tendency to interfere with the vomiting center (Kumar et al., 2026). The Chi-square analysis revealed a statistically significant association among the different ADRs associated with treatment regimens ($p < 0.05$ for each major ADR). These findings highlight the importance of individual tailoring of treatment regimens depending on the patient's condition, characteristic risk factors, and treatment tolerability. Furthermore, early recognition and monitoring of ADRs may enhance treatment compliance, reduce the clinical complications associated with the treatment, and ultimately improve patients' quality of life.

5. CONCLUSION

The findings of the present study indicate that oropharyngeal cancer predominantly affected middle-aged to elderly males, with a higher prevalence observed among lower socioeconomic groups. Tobacco consumption was identified as the principal risk factor among the patients included in the study. Furthermore, cisplatin-containing regimens constituted the predominant treatment approach and were associated with increased incidence of ADRs, notably nausea/vomiting, mucositis, alopecia, and myelosuppression. A reduced frequency of gastrointestinal side effects and bone marrow suppression was observed among patients receiving Cetuximab; however, dermatological toxicities, particularly skin rash, were frequently observed. These findings underscore the importance of early risk-factor modification, particularly tobacco cessation, as well as the careful selection of chemotherapeutic regimens according to their adverse-effect profiles to enhance treatment effectiveness and patient outcomes.

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Author Contributions

All authors contributed to the conception, design, and preparation of the manuscript. Material preparation and data collection were performed by Waqar Ahmed. The study methodology was developed by Muhammad Ali Ghoto and Muhammad Akram. Rabia Parveen Mangi and Komal Zaman contributed to the conceptualization and validation of the study. The first draft of the manuscript was prepared by Mah'd Musa Eid Abu Dhair. Muhammad Aslam and Shah Bibi contributed to the review and editing of the manuscript. All authors commented on previous versions of the manuscript, read and approved the final version, and agreed to be accountable for all aspects of the work.

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Data availability statement
The data supporting the findings of this study are available from the corresponding author upon reasonable request. Access to the data is subject to approval by the relevant institutions and ethical requirements to protect patient confidentiality.

Ethical consideration
Ethical approval was obtained from the Institutional Bioethics Committee (IBC), University of Sindh, Jamshoro (Approval No. ORIC/SU/165, dated September 17, 2025), and hospital consent was obtained from the Medical Superintendent of KIRAN and MMI Hospitals, respectively; informed consent was secured, and its confidentiality was maintained.

Conflict of Interest
The authors declare that they have no conflict of interest regarding the publication of this manuscript

List of Abbreviations
5-FU – 5-Fluorouracil
ACS – American Cancer Society
ADR – Adverse Drug Reaction
EGFR – Epidermal Growth Factor Receptor
IBC – Institutional Bioethics Committee
KIRAN – Karachi Institute of Radiotherapy and Nuclear Medicine
MMI – Memon Medical Institute
NCI-CTCAE – National Cancer Institute Common Terminology Criteria for Adverse Events

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