

Clinical characteristics of head and neck cancers at a tertiary care hospital

Sajid Durrani¹, Saleh Al-Dhahari², Haneen Sebeih², Tariq Wani³, Khalid Al Qahatani⁴, Humariya Heena³

AFFILIATION

1 Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia

2 Department of Otolaryngology, Head and Neck Surgery, King Fahad Medical City, Riyadh, Saudi Arabia

3 King Fahad Medical City Research Center, Riyadh, Saudi Arabia

4 Department of Head and Neck Surgery, King Saud University, Riyadh, Saudi Arabia

CORRESPONDENCE TO

Sajid Durrani, Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia. E-mail: sdurrani@kfmc.med.sa

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ABSTRACT

INTRODUCTION Head and neck cancer (HNC) is common and accounts for thousands of deaths each year. In Saudi Arabia alone hundreds of cases and deaths due to head and neck cancers are reported owing to alarmingly high consumption of tobacco and infections such as Epstein-Barr virus (EBV) and human papillomavirus (HPV) that lead to metastatic or loco-regional or viral-associated HNC. Nasopharyngeal cancer (NPC) is most common among all HNCs in Saudi Arabia, with male predominance in having a poor survival rate. Comprehensive studies documenting extensive variables related to HNC are lacking in Saudi Arabia; hence, it is particularly important to document the clinical characteristics of this cancer, especially in the Saudi population. Therefore, the present study aimed to understand the clinical characteristics of patients with HNC treated at King Fahad Medical City (KFMC).

METHODS A hospital-based retrospective cohort study included patients diagnosed with HNC from 2009–2018 as per the electronic medical records and treated at KFMC. All patients with histopathologically confirmed cancer at sites

including oral cavity, nasopharynx, oropharynx, pharynx, larynx, sinonasal, and salivary glands were included. The endpoints were to assess tumour site of HNC, frequency of HNC based on histology, tumor-node-metastasis (TNM) staging, and etiological factors of HNC. The pattern of treatment failure was also recorded in reference to the site of tumour recurrence as local, general or distant.

RESULTS Out of 1349 patients screened, 652 were confirmed with HNC. The most common primary tumor site was the oral cavity (25.9%), followed by nasopharynx (23.8%), and larynx (17.5%). Squamous cell carcinoma was the most common HNC (78.1%). Based on TNM staging, the frequency of HNC varied from stage 0 to 4, with 64.6% of patients in stage 4. Infection with Epstein-Barr virus (EBV) was found in 8.5% of patients. Treatment failures were recorded in 24.3% of patients, and 62.5% of patients reported metastasis.

CONCLUSIONS High tobacco consumption in the region needs to be monitored and controlled by awareness and education campaigns. Effective management of HNC with early diagnosis and treatment is required by healthcare professionals to improve the overall quality of life of HNC patients.

INTRODUCTION

Head and neck cancer (HNC) is considered as the ninth most common cancer worldwide. According to the World Health Organization (WHO), more than 0.55 million annual cases of HNC occur worldwide, with around 0.30 million deaths each year¹. In Saudi Arabia also, the incidence of HNC is high. According to the cancer data factsheet of Saudi Arabia,

there were 769 cases registered in the HNC category in 2018, which resulted in 378 deaths.

Consumption of tobacco/smokeless tobacco/alcohol, infection with Epstein-Barr virus (EBV) and human papillomavirus (HPV) are considered the main etiological factors leading to HNC. These factors have recently been on the rise especially in the higher age group (40–55 years) in

the last few years around the world including Saudi Arabia²⁻⁴, leading to metastatic or locoregional or viral-associated HNC.

Different malignancies that develop in or around the throat, larynx, nasopharynx, nose, sinuses and mouth are categorized under HNC⁵. Out of various histological types in HNC, such as blastomas, lymphomas, sarcomas and neuroendocrine tumors, the majority is of epithelial origin (squamous cell carcinoma) and accounts for more than 90% of HNCs². Nasopharyngeal cancer (NPC) is one of the rare forms of HNC. It has been ranked first among all HNCs in Saudi Arabia, with male predominance (male: female=2:1)^{6,7}.

Cancer of head and neck is considered difficult to understand beyond a very early stage and shows a poor survival rate of five years⁸. Moreover, the published incidence of distant metastases (DM) in HNC treated for squamous cell carcinoma varies between 4% and 26%⁹. Nevertheless, the overall rate has been improved from 52.7% in the period 1982–1986 to 65.9% during 2002–2006, which might be due to the use of advanced treatment modalities in HNC¹⁰.

The HNCs are quite common in Saudi Arabia due to a very high incidence of smoking and other risk factors¹¹. It is extremely critical to document the pattern of treatment failure, especially on the Saudi population. However, in an extensive literature search, we found that comprehensive studies documenting extensive variables related to HNC to be lacking in Saudi Arabia. Therefore, the present study aimed to understand the clinical characteristics in patients with HNC treated at King Fahad medical city (KFMC).

METHODS

Study population

All histopathologically confirmed patients with cancer at sites including the oral cavity, nasopharynx, oropharynx (tongue, floor of the mouth, retromolar trigone, gingiva, tonsil, and lip), pharynx, larynx, sinonasal and salivary glands were included in the study. Patients with cancer at other sites or with incomplete data were excluded from the study.

Study design

A hospital-based retrospective closed cohort study design was employed to assess the clinical characteristics in patients with advanced HNC treated at KFMC, which is a tertiary care center. The medical records of all the patients who were diagnosed with HNC (in the period 2009–2018) and treated at KFMC were assessed from the tumor boards at the centre and reviewed.

Study endpoints

The endpoints of the study were to assess the clinical characteristics (tumor site of HNC, frequency of HNC based on histology, TNM staging and etiological factors) of HNC in Saudi Arabia.

Tumor-node-metastasis (TNM) staging was followed to categorize the different stages of the disease. The categorization of stages T0 to T4 is based on the presence of

a primary tumor and its size. A tumor is categorized as T0 if there is no evidence of primary tumor. The advanced stages (T1, T2, T3 and T4) are dependent on the size of the tumor and its extension. The TNM staging varies a little in the description as per the subtype of HNC, but the basic categorization is similar for all types of HNCs¹². The nodal status of the tumor is based on the involvement of lymph nodes. In N0 (nodal stage 0), no regional lymph node metastasis is involved, while in the next stages, there is metastasis at the lymph node and the size of tumor increases in more advanced stages¹². The failure rates were recorded in reference to whether the recurrence was local, general or distant.

Statistical analysis

Data were analyzed descriptively and presented as frequency (n) and percentage (%). The statistical package for social sciences (IBM SPSS statistics 22.Ink) was used for data analysis.

RESULTS

Study population

A total of 1349 patients were screened for HNC in KFMC in the period 2009–2018, of which 652 patients presented with HNC. Out of 652, 416 (63.8%) were males and 236 (36.2%) were females (Table 1). More than 80% (n=541; 82.9%) of the patients were of Saudi nationality while the rest (n=111; 17.1%) were non-Saudi patients (Table 1). The new cases of HNC registered at KFMC were 376 (57.6%) during the study, while 276 (42.4%) had been reported previously (Table 1).

Tumor site

The oral cavity was found to be the most common primary tumor site in 169 (25.9%) patients, closely followed by nasopharynx in 155 (23.8%) patients. A total of 114 (17.5%) patients were reported to have the larynx as their tumor site. The sinonasal, salivary glands, pharynx and oropharynx were also reported as tumor sites in 147 (22.6%) patients (Figure 1).

Table 1. Sociodemographic characteristics of the head and neck cancer patients involved in the study, Saudia Arabia (N=652)

Characteristics	n	%
Sex		
Male	416	63.8
Female	236	36.2
Residence		
Saudi Arabia	541	82.9
Other	111	17.1
Registered cases		
New	376	57.6
Previous	276	42.4

Frequency of HNC based on histology

In regard to histology, squamous cell carcinoma was the most abundantly found form of HNC in 509 (78.1%) patients, while 67 (10.2%) patients had salivary gland cancers (Figure 2).

Frequency of HNC based on TNM staging

Of the 652 HNC patients, 285 (43.8%) had stage T4 disease, while 117 (18.0%) patients were at stage T3. A total of 91 (13.9%), 111 (17.0%) and 48 (7.3%) patients were reported at stages T2, T1 and T0, respectively. In nodal categorization, 306 (47.0%) patients were in N0 stage and 203 (31.1%)

patients were in stage N2. In all, 9.9% of patients reported no distant metastasis (M0 stage), while 421 (64.6%) patients had stage-IV metastatic (M4) disease. Figure 3 represents the frequency of head and neck cancer based on TNM staging.

Frequency of HNC based on etiological factors

In the present study, EBV infection was positive in 8.5% of the study population.

Patterns of failure in the treatment of HNC patients

There were a total of 159 (24.3%) treatment failures among

Figure 1. Different sites of the tumor among head and neck cancer patients, Saudi Arabia (N=652)

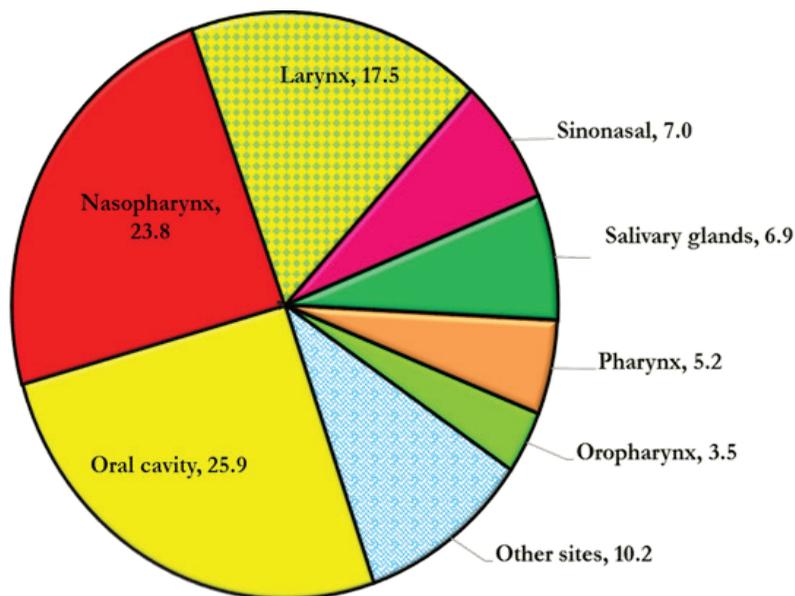


Figure 2. Histology of head and neck cancer among Saudi patients (N=652)

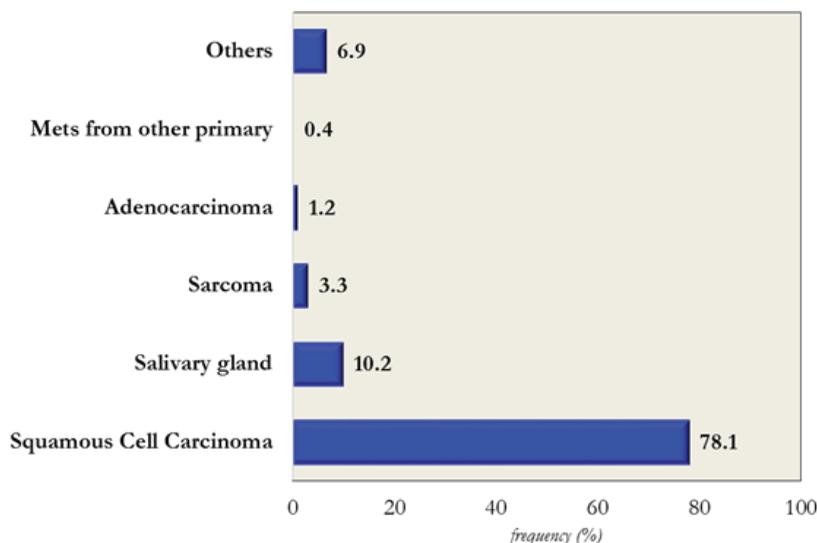
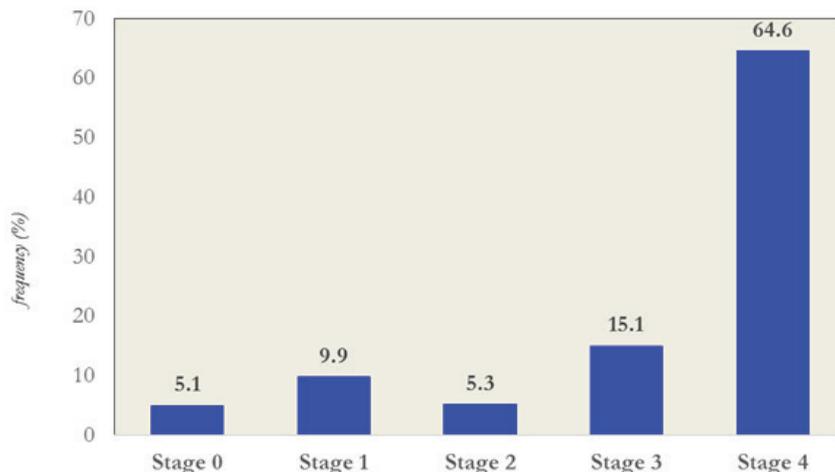


Figure 3. Frequency of head and neck cancer patients in Saudi Arabia, based on TNM staging (N=652)

which, the local failures were more in laryngeal, followed by nasopharyngeal and oral cavity cancers. However, nasopharyngeal and oral cavity cancers had the highest number of regional failures as well as distant failures. Notably, 407 (62.5%) patients were recorded for metastasis during their subsequent visits to the centre at KFMC.

DISCUSSION

Cancer of the head and neck is a heterogeneous disease with high incidence rates in the world. Only 3% of all malignant tumors are reported to be present in Europe and the United States^{5,8}. However, it is considered as one of the common malignancies in South-Central and South-East Asia¹³, clearly depicting the role of geographic factors in HNC incidence. Therefore, it is important to understand the clinical characteristics and prognostic risk factors of patients in Saudi Arabia.

Cancer of the head and neck are highly prevalent in Saudi Arabia. In an interview conducted in a sample of 124 adult patients in a major tertiary hospital in Saudi Arabia, HNC was the second most common cancer affecting 15.3% of the study population, after breast cancer (27.4%)¹⁴. In the present study as well, 48.33% had HNC, among which males were more commonly affected with HNC compared to females (416; 63.8% vs 236; 36.2%). Similar results were described in other studies where the number of male patients with HNC was comparatively more than females⁶.

Tobacco chewing is one of the major risk factors behind oral cancers in Saudi Arabia^{5,7}. According to a study conducted in Riyadh, Saudi Arabia, it was reported that a majority (58%) of HNC patients were tobacco users, further leading to high incidence of oral cancer¹⁵. Our study also reported oral cancer as the most frequent site of HNC, affecting 25.9% of patients that might be due to high tobacco consumption.

Histologically, head and neck squamous cell carcinoma

(HNSCC) is the most frequent subtype of HNC worldwide¹⁶. In concordance, the present study also showed nearly 78.1% of cases of HNSCC. In recent times, the incidence of nasopharyngeal squamous cell carcinoma (NPSCC) has increased in Arab countries, including Saudi Arabia. A total of 23.8% of cases of nasopharyngeal cancer were also reported in our study too, which was higher in comparison to other subtypes of HNC. This increase can be attributed to the increased exposure to related risk factors such as tobacco smoking, alcohol consumption, preserved food intake, exposure to different types of medicines, and family history of NPC and EBV infection¹⁷⁻²⁰.

Epstein-Barr virus (EBV) belongs to the family of the Herpes virus and has a ubiquitous presence with nearly 90% of the human adult population infected by the virus. Saliva is the main transmitter of the virus, causing HNC. EBV usually remains dormant without showing any symptoms, but sometimes, the virus can revert to its lytic state and transform the cells into malignant tumors¹⁷. Few studies are available regarding the relationship between EBV and HNC in Saudi Arabia. One study published in 1994 reported an examination of 25 Saudi patients with HNC (NPC) for the presence of EBV and revealed 92% of the tumor specimens positive for EBV DNA²¹. However, in the present study, EBV infection was positive in only 8.5% of the study population, which suggests a decrease in EBV infection in Saudi Arabia.

Apart from other risk factors, HPV is also one of the emerging causes of virus-related HNC incidence, particularly in HNSCC, worldwide^{22,23}. In comparison to EBV, HPV is considered more commonly responsible for causing HNSCC in western countries. This might be attributed to the changing sexual behaviours during recent decades²⁴. Various HNC malignancies have been associated with HPV such as cancer at the pharynxes, the base of the tongue, and tonsils (oropharynx area). According to a study by Kreimer et al.²⁵, about 35.6% of oropharyngeal, 23.5% of oral and 24% of

laryngeal cancers were associated with HPV. Due to cultural and religious boundaries in Saudi Arabia, the real impact of HPV on the HNCs has not been investigated to a full extent. Only a few reported studies are available that have reported a link between HNC and HPV².

The most important prognostic factor for HNC patients is the clinical staging of the tumor. Accurate mapping of the tumor is critical before commencing therapy. The tumor is categorised according to TNM staging, which assigns tumors as local (T), regional nodal (N) or distant (M). Tumors of the head and neck can further be classified from stage 0 to IV, based on the size of the tumor and extended presence from their site of initiation²⁶. In this study, the majority of HNC patients belonged to TNM stages III (15.1%) and IV (64.6%). A single modality treatment with a 5-year survival rate of 60–90% is required for early stages (I and II), while advanced stages (III and IV) require a combined modality and have a 5-year survival rate of <35%²⁷. According to a study, most (66.6%) of the cases of HNC are reported at an advanced stage (Stages III and IV) in Saudi Arabia⁵. In the present study as well, 79.7% of the patients had advanced stage HNC, which might be due to the poor awareness of the disease and limited hospital resources.

Various modalities such as recurrent/metastatic disease chemotherapy, biological treatment, radiation therapy, immunotherapy and extensive surgical resection of either primary tumor or lymph nodes are available as standard options in the treatment of HNC that can render a median survival of 6–12 months and a 20–40% rate of 1-year survival²⁸. However, the pattern of a major failure in the treatment of HNC is still represented by the local or regional recurrences. The problem is more challenging in patients with advanced stages. Maklad et al.²⁹ reported an overall failure of treatment in 21 out of 68 Saudi patients with nasopharyngeal cancer. Out of 21, seven were locoregional, 3 were regional with DM, and 11 had DM. Similarly, in another study by Al-Herabi, out of 44 HNC patients, 2 (5%) patients died perioperatively, and 2 (5%) patients had a locoregional recurrence³⁰. In our study, there were 24.3% treatment failures, and about 62.5% of patients were recorded with metastasis.

An improvement in the management of HNC can be expected with an early referral of the suspected individual to the specialty centres, which can enhance the survival outcome. The treatment of HNC varies according to the primary site, tumor stage, patient treatment preference, and practitioner's expertise³¹. The management of HNC requires a multifaceted approach that involves oncologists with expertise in medicine, radiology and surgery, dentists with expertise in HNC, radiologists, speech therapists, social volunteers (workers), psychologists, and plastic and/or reconstructive surgeons³².

In our study, the treatment failures were recorded as local as well as distant. The metastasis was also observed in patients during their subsequent visits. The nasopharyngeal

and oral cavity cancers had the highest number of regional failures as well as distant failures. Our study is in accordance with the study by Leeman et al.³³ that showed a majority of regional failures for oral cavity cancer.

The lack of knowledge about the disease in our patients is evident, which further hampers clinical understanding and delays timely diagnosis and treatment. Thus, the development of proper treatment strategies for this subgroup of patients as well as further research into more effective diagnosis and treatment are warranted.

Strengths and limitations

We consider our findings significant, as the results confirmed the pattern of HNC in the Saudi population in terms of its subtype, histological prevalence, and failures of treatment. The findings of this study are expected to guide the strategies to be adopted towards improvement in obtaining local and/or regional control or reducing the development of DM. However, the study has limitations in terms of being a single-centre retrospective study and having a relatively small sample size. Owing to this, complete information regarding etiological factors and N and M stages separately was not available.

CONCLUSIONS

The study highlights the increased use of tobacco in the region, which needs to be monitored by conducting epidemiological surveys and controlled by spreading awareness and educating people. There is a need to improve diagnosis and treatment modalities in the region. Moreover, regular training of healthcare professionals is also essential for early diagnosis. Patient factors, such as willingness to seek treatment, are also significant. These factors may have influenced the relatively low percentage of survival rate. However, a multicenter study with an extensive series of cases is required to confirm the present findings.

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CONFLICTS OF INTEREST

The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

PROVENANCE AND PEER REVIEW

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