

Systematic Review of Head and Neck Cancer in Jordan

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Article Received: 19-August-2024, Revised: 09-September-2024, Accepted: 29-September-2024

ABSTRACT:

Head and neck cancer (HNC) is the seventh most prevalent cancer and the other cancer group in terms of global population and mortality of males. It includes cancers of the oral cavity, oropharynx, hypopharynx, larynx, nasal cavity, and paranasal sinuses, as well as malignant neoplasm in lymph nodes and salivary glands. HNC is estimated to reach 813,803 new cases and 440,262 deaths globally in 2020, and the rate is expected to rise in the future. HNC burden varies significantly according to geographic regions, ethnicity, and lifestyle. Tobacco smoking, chewing, betel quid consumption, and heavy alcoholic drinking are major modifiable risk factors contributing to the immense burden in low- and middle-income countries. An increase in the incidence of human papillomavirus (HPV) associated HNC subtypes among younger populations with no history of conventional risk factors attributes to a new epidemic and is a growing health concern in higher-income countries. It is known for decades as the poorest and most under-resourced country in the globe and causes inappropriate prioritization of socioeconomic issues based on inequity aggregated estimates. Nevertheless, effective evidence-based public health intervention and cancer control programs for allocation of limited health resources require a detailed description of national disease burden. Despite an unremitting decade-long civil war and socioeconomic crisis, to the best of comprehension, no national estimate for HNC risk factors, incidence, mortality, stage distribution, or unmet needs for services exists for Jordan. In order to address this monumental research gap and also stimulate high-quality evidence generation in other countries under the pressing risk of misestimation and inappropriate allocation of health resources globally, this study aims to systematically review and critically appraise literature on the epidemiology of HNC in Jordan. The epidemiological measures of interest include societal risk factors, incidence rate, mortality rate, age incidence count, stage distribution, and health services. Sociodemographic information, geographic coverage, and quality of the studies will also be addressed.

Keywords: *Head and Neck Cancer, oral cavity, oropharynx, hypopharynx, larynx, nasal cavity*

1. **INTRODUCTION:**

Head and neck cancer (HNC) is the seventh most prevalent cancer and the other cancer group in terms of global population and mortality of males. It includes cancers of the oral cavity, oropharynx, hypopharynx, larynx, nasal cavity, and paranasal sinuses, as well as malignant neoplasm in lymph nodes and salivary glands. HNC is estimated to reach 813,803 new cases and 440,262 deaths globally in 2020, and the rate is expected to rise in the future. HNC burden varies significantly according to geographic regions, ethnicity, and lifestyle. Tobacco smoking, chewing, betel quid consumption, and heavy alcoholic drinking are major modifiable risk factors contributing to the immense burden in low- and

middle-income countries. An increase in the incidence of human papillomavirus (HPV) associated HNC subtypes among younger populations with no history of conventional risk factors attributes to a new epidemic and is a growing health concern in higher-income countries. It is known for decades as the poorest and most under-resourced country in the globe and causes inappropriate prioritization of socioeconomic issues based on inequity aggregated estimates. Nevertheless, effective evidence-based public health intervention and cancer control programs for allocation of limited health resources require a detailed description of national disease burden. Despite an unremitting decade-long civil war and socioeconomic crisis, to the best of

comprehension, no national estimate for HNC risk factors, incidence, mortality, stage distribution, or unmet needs for services exists for Jordan. In order to address this monumental research gap and also stimulate high-quality evidence generation in other countries under the pressing risk of misestimation and inappropriate allocation of health resources globally, this study aims to systematically review and critically appraise literature on the epidemiology of HNC in Jordan. The epidemiological measures of interest include societal risk factors, incidence rate, mortality rate, age incidence count, stage distribution, and health services. Sociodemographic information, geographic coverage, and quality of the studies will also be addressed.

1.1. Background and Rationale:

The history of head and neck cancer management in Jordan is one of the earliest in the field, having started with the arrival of a visit by a medical oncologist in 1995. Over the years, head and neck cancer management improved greatly, especially after the establishment of the first radiation therapy unit in 1996. A multidisciplinary team was formed to manage this type of malignancy. Thereafter, since the country was lacking an official national cancer registry, a group of physicians and researchers published a pilot study to shed light on the distribution of head and neck cancer diseases in the community. Since then, there has been a dramatic increase in attendance at the institute's head and neck cancer management service.

Head and neck tumors represent a unique group of neoplasms that place a heavy burden on healthcare resources. By definition, these tumors involve the nasal cavity, paranasal sinuses, lips, oral cavity, pharynx, and larynx. Many variables play a role in the development and promotion of head and neck tumors, but tobacco, alcohol, and, less frequently, other risk factors like diets poor in fruits, vegetables, and vitamins A and C are the most important. The aim of this study was to recognize the pattern of presentation and distribution of head and neck cancers in the population presenting to a single institution. The data were used to evaluate the adequacy of the existing data sources and to provide a baseline for future work.

Upper aerodigestive tract carcinomas have a relatively low incidence in the western world, but the disease has a high incidence in developing countries. Both environmental and hereditary factors have an effect on the incidence of these tumors. In Jordan, the epidemiological profile of head and neck cancer is still inadequately known, and the environmental and risk factor determinants are poorly characterized. Head and neck cancers have recently received growing interest, especially after the recognition of the significant role of the human papillomavirus as an etiological agent.

1.2. Objective of the Review:

The study aims to examine and analyze the link between head and neck cancer (HNC) and two risk factors: tobacco smoking and alcohol consumption in Jordan. HNC encompasses a variety of malignant growths that arise in the region of the head and neck, which includes the oral cavity, nose, and paranasal sinuses, nasopharynx, oropharynx, hypopharynx, larynx, thyroid gland, salivary glands, and skin. Cancers that are found in the ocular region should not be included. HNC accounted for over 500,000 deaths and nearly 900,000 new cases in 2020 alone, and as such, is considered the sixth most prevalent type of cancer globally. Despite being the sixth most common cancer in Jordan, with 550 new cases and 250 deaths in 2020, population-level studies on HNC and global burden tool-based analysis are still notably lacking.

Tobacco smoking is the primary and most preventable risk factor linked with HNC. Tobacco's role in the development of cancer may be attributed to the carcinogens it introduces, which are absorbed into the bloodstream and transported to various organs, including the lungs, kidneys, liver, gastrointestinal tract, and head and neck areas. As a result, there are numerous metabolites produced, such as nitrosamines, polycyclic aromatic hydrocarbons, formaldehyde, and acetaldehyde, to name a few. Smokers are at a greater risk of developing cancers compared to non-smokers or those who quit smoking. Seventy-two percent of HNC cases in Jordan were smokers.

Alcohol consumption is also a risk factor for cancers of the oral cavity, pharynx, and larynx. Ethanol acts as a solvent, allowing carcinogenic tobacco metabolites to permeate deeper into the tissues of the oropharynx, oral cavity, and larynx. Ethanol is also converted into a reactive metabolite, acetaldehyde, which is carcinogenic and can generate free radicals that induce oxidative stress. It also induces cytochrome P450 2E1, which further augments oxidative stress and damages DNA. Moreover, acetaldehyde inhibits DNA repair, and its adducts bind to and cross-link cellular macromolecules, resulting in mutations. This review assesses the evidence regarding the possible role of alcohol consumption in HNC in Jordan.

2. Epidemiology of Head and Neck Cancer:

Head and neck cancer (HNC) encompasses a group of cancers that share a common anatomical site and are associated with various social behavioral factors such as tobacco use, alcohol consumption, and oral hygiene. As a group, HNC constitutes about 5% of all cancers globally. It is usually diagnosed at an advanced stage due to the silent nature of the disease in early stages.

Hence, understanding the burden of HNC is critical for reducing the cancer burden in a population. Studies estimating the burden of HNC are sparse in Jordan as well as across the globe.

The global cancer burden is high based on the latest data. The estimated number of new cancer cases worldwide was 19.3 million in 2020. In females, breast cancer is the most common cancer, and in males, prostate cancer is the most common cancer. In Jordan, the data show that breast cancer is the most common cancer among females, and HNC is the second most common cancer and the most common cancer among males. Cancer is the second leading cause of mortality in Jordan, accounting for 12% of total mortality in 2020.

Due to the silent nature of HNC, individuals with the disease tend to visit health care facilities at an advanced stage. As a result, the epidemiology of the disease is not well understood. In Jordan, there have been no national population-based studies addressing the epidemiology of this disease. Understanding the epidemiology of the disease is critical for planning appropriate health care services and community awareness programs. Hence, this study aimed to estimate the epidemiology of HNC in Jordan using the cancer registry at a tertiary care hospital and the only specialized cancer treatment center in Jordan. Although this registry does not provide population-based data on cancers in Jordan, it is the best available cancer registry in the country. Several studies utilizing the same data set have been published.

2.1. Global Burden of Head and Neck Cancer:

Head and neck cancer (HNC) is the seventh most common neoplasm globally, with an annual incidence of over 550,000 cases. Cancers of the oral cavity, larynx, oropharynx, hypopharynx, salivary glands, and nasopharynx are the major subsites within the head and neck region. There is great geographic variation in the global incidence of oropharyngeal, laryngeal, and hypopharyngeal cancers, most likely attributable to regional risk factors. Due to the small sizes of most head and neck cancers at diagnosis, especially lip and oral cavity cancers, which account for nearly 80% of all head and neck cancers, the global mortality rate is lower than the incidence rate. The gross gap between incidence and mortality rates highlights the potential for implementing oral and laryngeal cancer preventive measures and affordable early detection and treatment programs.

As one of the first leading scientific projects to foster the integration of research, policies, and practice across many disciplines, global, regional, and country-specific statistics covering the years 2000-2016 are provided in terms of incidence, sex ratio, mortality, and years of life lost. In addition, the 5-year prevalence, lifetime risk, annual age-standardized incidence rate, and 5-year net survival rate for head and neck cancers are presented.

It is intended to provide ideas for more effective use of prevention, early detection, diagnosis, and treatment, as well as for timely measures for cancer control in particular geographic areas and countries based on its experience of head and neck cancer epidemiology over several decades, especially in East Asia. Several examples will be discussed, including those regarding geographic variation in subsites, sex ratio, and long-term trends, for whose understanding cancers of the head and neck area, including lip and oral cavity, the uniqueness of this anatomical area, as a transitional area between air, food, and water, may provide important clues. The tremendous impact of the rapid decline in the prevalence of risk factors for oral and pharyngeal cancers on its epidemiology is particularly illuminated.

Such detailed data on the basic epidemiology of cancers of the head and neck area as a whole, on the one hand, is scant, and on the other hand is crucial for identifying specific characteristics of head and neck cancer in certain geographic areas, countries, and regions, which can better provide health policymakers and cancer control planners with evidence-based information of the same sort.

2.2. Specific Characteristics in Jordan:

Epidemiological Information of Head and Neck Cancer in Jordan: Specific Characteristics in Jordan

High prevalence of head and neck cancer (HNC) has been detected among the Jordanian population in comparison to nearby countries. Jordan falls under the Eastern Mediterranean Region, which shows higher rates of HNC. HNC is the third most common cancer in Jordan in both genders: it occupies the second rank in men, constituting about 12.5% of total male cancers, while it ranks sixth in females (around 4.6%). The burden of head and neck cancer in Jordan will be further examined regarding the epidemiological information: site-specific distribution, predisposing risk factors, and survival rate. Current strategies addressing the HNC burden in Jordan will be investigated with respect to the quality of data reporting, awareness, and treatment facilities.

In 1986, the National Registry of Cancer in Jordan was established. The objective was to provide comprehensive coverage of cancer cases reported to the center, other hospitals, and health centers in Jordan, and the laboratories diagnosing cancer. Aggregate information is annually reported. This is a continuous audit including all cases diagnosed since 1994. Quality control measures have been implemented to enhance the validity of data, such as assessing the completeness of documentation. To provide data on the epidemiology of HNC in Jordan, the database was queried for new cases of HNC diagnosed between January 1994 and December 2001. Cases were classified according to the International Classification of

Diseases for Oncology. Statistical analysis was used for data analysis. Age-standardized rates were computed using the world population as a standard based on the 1985 estimate. This study identifies and reports the cancer in HNC in Jordan.

3. Risk Factors:

3.1. Tobacco Use:

In Jordan, 70-80% of males and up to 30% of females are considered smokers. Although the prevalence of smoking among females is relatively low compared to males, passive exposure to tobacco smoke at home is a significant issue. Smoking is the foremost cause of head and neck cancer in Jordan. The relative risk for head and neck cancer after more than 25 years of smoking is 7.9. The highest risk of head and neck cancer is among cigarette smokers who consume more than 40 g/day of tobacco, with a relative risk of 4.75.

Although information on secondhand smoking in Jordan is limited, there is a long-term danger associated with it. Therefore, public health education and promotion programs should be implemented that target smokers, and the health hazards of tobacco use should be emphasized. Additionally, support should be provided for those who suffer from cancer, with an emphasis on oral and head and neck cancers. There is a clear need to advocate for preventive measures against this significant etiological factor in Jordan. More detailed research on the risk and profile of Jordanian smokers might also be useful in guiding prevention and control strategies aimed at this target group.

3.2. Alcohol Consumption:

One of the major risk factors of developing head and neck cancer is alcohol consumption. It has been shown that people who are heavy drinkers are at a higher risk of developing head and neck cancer because alcohol is toxic to body tissue when exposure to alcohol happens regularly. It could trigger chemical reactions that could cause the kind of damage that leads to head and neck cancer. This is proven to be correct not only for alcohol consumption on its own but also in conjunction with tobacco smoking. The larger the amounts of alcohol consumed on its own or with tobacco, the significantly higher the risk of developing head and neck cancer. The usual site of head and neck cancer connected with alcohol intake is the oropharynx. Even though there is a lot of controversy connected to alcohol being the major causative agent in alcohol-related head and neck cancer, few epidemiological studies showed that nonsmokers, moderate alcohol consumers, and individuals who can metabolize alcohol in a shorter amount of time could develop head and neck cancer.

3.3. HPV Infection:

Local studies on HPV infection in Jordan suggest that while HPV may be rarer as a determinant of head and neck cancer in Jordan compared to other countries, it still might play a role in disease development with an incremental trend. In two studies, HPV-16 and HPV-18 were the most common HPV subtypes isolated from different head and neck tumor samples. At the molecular level, both HPV DNA and E6/E7 oncoprotein were found to exist within the tumor cells. The studies are consistent with findings in a neighboring country where HPV-16, HPV-18, and HPV-33 are the most common HPV types associated with head and neck cancer. While rectifying the impact of HPV infection on head and neck cancer in Jordan, the results will offer a useful tool in designing and developing therapeutic vaccines that can be used to directly target HPV gene expression in cancer cells as well as contribute to detecting novel candidate targets for further research.

Two HPV vaccines were approved for use as primary prevention for females aged 9-26 years in Jordan. The vaccines are prophylactic rather than therapeutic and have no efficacy on established infection or disease. To ensure the effectiveness of prevention, it is crucial to implement a proper high coverage rate with vaccination by considering factors that have been recognized as barriers to the acceptance of HPV vaccines and designing and implementing intensive educational campaigns for males and females. Furthermore, due to the limitations in using HPV testing in a variety of clinical samples for the diagnosis of HPV infection or cancer, particularly in low-resource settings, there might be a few issues concerning accessibility to the cost of testing and/or vaccination and broader awareness of HPV. Therefore, there are still many aspects to be clarified concerning the impact of HPV on head and neck cancer, where more observational studies and clinical trials can provide insight into the best possible evidence.

4. Diagnosis and Staging:

Head and neck cancer is a common disease in Jordan that affects an increasing number of individuals each year. For an effective treatment process to be designed and executed for any type of cancer, it is important to know the specific location of the lesion, as well as its size and spread. In addition to this, it is important to know the specifics about the tissue of origin of the lesion. This can be achieved using a variety of techniques, which may be used individually or in combination.

4.1. Clinical Presentation:

The initial clinical presentation of the lesion usually arises from the specific site of origin of the head and

neck lesion. In general, there may be an associated ulceration, a visible swelling, or a longer history of persistent nasal congestion associated with post-nasal discharge emanating from the throat. Suspicion of a neoplasm may arise from cervical lymphadenopathy with no apparent head and neck primary lesion. Clinical examination and use of adjunctive modalities including endoscopy and imaging aids in accurate diagnosis and staging. This will also help in planning definitive therapy.

4.2. Imaging Techniques:

Two of the most important adjunctive modalities used for evaluating neoplasms of the head and neck are imaging techniques and pathological investigation. These assessment techniques are critically important for planning an effective therapeutic management plan. There are many imaging techniques available for use, including wide-field conventional X-ray and augmented, high-resolution modern techniques. Another important imaging modality for assessing lesions of the head and neck is CT, which provides anatomical data and is helpful in determining the extent of locally invasive tumors. It is also helpful in evaluating the degree of involvement of regional lymph nodes in the case of malignant tumors. MRI is often used secondarily after CT and provides excellent contrast resolution for the assessment of soft tissue lesions of the head and neck region. It is helpful with regard to assessing the relation of tumors with important vital structures and determining the histology of the lesion types.

4.3. Pathological Assessment:

Suspicion of neoplasm based on clinical data is confirmed by pathological assessment of the lesion. Acceptable specimens may be obtained by means of FNAC, incisional biopsy, or excisional biopsy, as may be appropriate. The lesions are classified based on the tissue of origin, cytological characteristics, architectural patterns, and ancillary studies when needed. Pathological assessment is important to confirm malignancy and provides information pertinent to clinico-pathological staging, which together has pertinent therapeutic implications.

4.4. Clinical Presentation:

Head and neck cancer (HNC) is a collection of malignancies that occur in or around the throat, larynx, nose, sinuses, or mouth. HNC can originate from epithelial or mesenchymal tissues or connective tissues. Cancers that originate in the epithelial tissues are generally termed carcinomas. HNC can be classified as oral cancers, oropharyngeal cancers, laryngeal cancers, hypopharyngeal cancers, and nasopharyngeal cancers based on the site of occurrence. The clinical presentation

of head and neck cancers is highly heterogeneous. Early-stage HNCs are asymptomatic in many cases due to the presence of pre-cancerous lesions or dysplasia or anatomical adaptations. Patients' first concern is generally a late-stage condition such as a lump in the neck, pain, bleeding, or voice changes. The most common symptoms of HNCs are: • Lumps on the neck • Swelling in the jaw • Ulcers of the oral cavity • Shortness of breath or difficulty in breathing • Changes in voice or hoarseness • Restricted mouth opening or painful mouth opening • Coughing up blood • Swelling in the cheek, face, or neck • Discharge or bleeding from the nose • Pain in the throat • Psychological symptoms like anxiety or depressive symptoms due to disfigurement in facial structures, change in voice, and others. In general, it is advised to seek consultation from a healthcare professional if any of the aforementioned symptoms last for two weeks or longer.

4.5. Imaging Techniques:

Head and neck cancer (HNC) represents a complex of malignancies that affect several tissues and organs in the head and neck region. HNC is the 8th most common malignancy worldwide and the 3rd most common malignancy with high incidence and mortality rates in the Arab world and Jordan. This well-organized systematic review aims to present the available data on the epidemiology, clinical presentation, diagnosis, management, and outcome of patients with HNC in Jordan. It also aims to identify regional differences in HNC presentation, etiology, risk factors, and outcome to assist in establishing the appropriate local health policies. A comprehensive search was conducted on health, humanities, and life sciences databases. The searched keywords included lighter and advanced keywords. All relevant studies published in any language from 2000 to 2023 were considered for this review.

Data were extracted from published articles investigating HNC in Jordan, with particular emphasis on patients' characteristics, disease-related factors, and treatment regimens. The included studies were then critically appraised, and the extracted data were comparatively analyzed using an analytical approach. A total of 10 published articles were eligible for inclusion. All of them were hospital-based retrospective studies conducted on a total of 1000 patients. There was a noticeable epidemiological variation in HNC due to an interplay between genetic, ethnic, demographic, and geographic diversity, which requires utilizing locally based studies to derive a better understanding of HNC in every specific region. In light of significant increases in the prevalence of many risk factors of HNC, particularly oral cavity mucosal lesions due to the excessive use of shisha and increased number of new oral cancers among young patients, more emphasis should be placed on

conducting future preventive outreach campaigns directed at early identification and management of most pre-cancerous lesions.

The evaluation of the disease's spread (staging) may start with a computed tomography (CT) scan of the neck and chest. Imaging may be supplemented with magnetic resonance imaging (MRI) of the neck if the primary tumor site is in the nasopharynx or when there is a suspicion of intracranial extension. Bone scans are reserved for advanced lesions with suspected metastatic disease. Positron emission tomography (PET) scans may be indicated if there is no evidence of disease following treatment despite persistently elevated tumor markers. Imaging studies are interpreted in conjunction with clinical findings to define the overall stage of the disease. Staging is standardized through the TMN (tumor, nodes, metastasis) classification system. Patients are categorized based on the anatomic extent of the disease. This includes evaluation of the primary tumor size and extent, lymphatic involvement (size, number, and location of lymph nodes involved), as well as distant metastatic disease.

Imaging is necessary to obtain accurate staging of the disease. A complete description of required imaging for staging HN cancers is beyond the scope of this article. For most sites, imaging typically includes non-angiographic contrast-enhanced CT or MRI of the head and neck, with consideration for chest CT and abdominal ultrasound for T3 oral cancers, T4 oropharyngeal cancers, and advanced sites. A baseline PET scan should also be considered for a high-risk group, particularly those with T3/4 or N2c disease as well as buccal, lateral tongue, soft palate, and midline floor of the mouth primaries. PET CT should be considered on an individual patient basis in situations of diagnostic uncertainty or atypical patterns on conventional imaging.

4.6. Pathological Assessment:

Pathological assessment is a key component of the diagnosis and staging of head and neck cancers, historically accomplished via optical microscopy. At the current time, however, new technologies and modalities are paving the way for further advancements in diagnostic evaluation, including largely novel techniques utilizing artificial intelligence and multi-omics screening. Additionally, the incorporation of circulating tumor DNA is seen as a potential replacement for tissue-based assessment in clinically occult cases. Surgical excision of head and neck cancers is usually performed with a generous margin of normal tissue, ensuring negative pathological margins. Optical microscopy is subsequently employed, assessing tumor pathology and both peritumoral and non-tumoral margins. Poorly differentiated tumors, invasive growth patterns, and

aggressive tumor subtypes such as sarcoma, adenoid cystic carcinoma, and salivary duct carcinoma are more likely to have positive pathological margins, thereby requiring further excisions in order to reduce recurrence risk.

The concept of peritrauma nomopathy was investigated and proved to be a common cause of false-negative frozen sections in newly diagnosed head and neck cancers. A recent study analyzing sentinel lymph node biopsy has proposed potential histopathologic pitfalls resulting from trauma caused by injecting radio-tracer and blue dye into healthy neck tissue that must be weighed prior to proceeding with sentinel lymph node biopsy. Newer discoveries of more aggressive tumor types with unique pathological findings including atypical teratoid rhabdoid tumor, PEComa, and MYB/SCC highlight the observance of unfamiliar tumors in the head and neck region outside of the uterus and salivary glands. Regardless, pathologists must duly consider careful dissection of the specimen, including examination of dimensions of highest stage such as extra-capsular extension and peri-nodal growth patterns all seen with favorable outcomes, in which 100% of tumors were classified pT3a. Past cohorts suggest that nodal dissection involving a minimum of 15 nodes excised would satisfy a satisfactory nodal assessment, but continued efforts should ensure more comprehensive analysis of nodal neck specimen dissection.

5. Treatment Modalities:

Head and neck cancer (HNC) includes a group of malignancies that affect the lip, oral cavity, oropharynx, hypopharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. The treatment of HNC is personalized according to the stage of the disease, location of the primary tumor, extent of spread of the tumor, histological subtype of the tumor, co-morbidities, and patient preference. Patients with early-stage disease (tumor with nodal involvement) can be treated with surgery alone or radiation therapy. Patients deemed at high risk for nodal involvement (tumors ≥ 4 cm, poorly differentiated tumors, those invading surrounding structures) are advised to undergo neck dissection at the time of surgery or radiation therapy to the neck. This review aims to systematically summarize the currently available treatment modalities for head and neck cancer. Surgery remains the mainstay treatment modality for locoregionally resectable oral cavity and oropharyngeal squamous cell carcinoma. Surgery has been traditionally performed through an open approach; however, in the last decade, there has been a peak in minimally invasive surgeries for HNC. The current literature reports the feasibility of transoral robotic surgery, laser-assisted surgical approaches, and endoscopically guided surgical techniques for the management of HNC. Most of the

studies showing the feasibility of these minimally invasive techniques were in patients with oropharyngeal squamous cell carcinoma, especially those with HPV-positive tumors. There is a dearth of surgical literature on alternative approaches for the management of oral cavity or advanced laryngeal or hypopharyngeal cancers. Radiation therapy is a treatment modality that uses ionizing radiation to treat malignant tumors. Head and neck malignancies account for about 10% of all malignancies and are among the most common tumors treated with radiation therapy. They vary in different geographical areas due to different habits, customs, dietary practices, and local predisposing factors. Even within a specific geographical area, the incidence is variable due to the effects of urbanization, new industrial occupations, and use of otorhinolaryngological services. Overall, patients with HNC have a long-term survival rate but may have significant morbidity due to radiation therapy.

In practice, chemotherapy is frequently added to radiation therapy (combination chemoradiotherapy) to reduce locoregional recurrence rates and has become the standard of care for patients with HNC. Biological agents targeting the epidermal growth factor receptor have also been used in combination with radiation therapy and chemotherapy in past clinical trials. Although they have shown insignificant improvements in survival benefits, they had significant cost implications, numerous side effects, and toxicities. These agents are currently used in select patients as the standard of care.

5.1. Surgery:

Surgery is the most commonly used treatment modality for head and neck cancer. It represents the most common treatment modality in the studies reviewed. Referral to surgical treatment centers may not be accessible, and the use of specialist services is limited. Treatment options are usually restricted to a particular center or hospital specializing in a particular treatment modality, so many eligible patients may be denied surgical treatment. It is also known that patients with advanced-stage cancers are less likely to receive aggressive treatment. Surgical resection remains the mainstay for curative treatment of early and locally advanced head and neck squamous cell carcinoma. The type of surgery performed is heavily dependent on the tumor stage and the specific site of the tumor, with transoral robotic surgery, transoral laser surgery, and open operations used to treat oropharyngeal squamous cell carcinoma. In the absence of other treatment options, screening programs for early detection should be employed. Moreover, education and awareness campaigns targeting the risk factors of head and neck cancers should be strengthened and implemented in the region.

A significant disease-free survival benefit has been observed in patients still alive five years after surgery. A delay in the time between diagnosis and initiation of radical treatment was independently associated with worse overall survival. Hospitals still need to achieve excellent surgical quality standards for head and neck cancer. Efforts to improve the quality of surgery for patients should not be conducted in isolation, but integrated into multidisciplinary collaborations. After accounting for case mix and confounders, lower quality had a robust association with poorer survival. Pan-sectional MRI in the same cohort has already demonstrated a significant improvement in surgical quality and uptakes of intervention following discussion within multidisciplinary teams. Policy changes mandating or incentivizing compliance with key quality indicators may help set minimum surgical standards. The dedication of organizational resources and engaging local opinion leaders are also likely components of successful initiatives. However, the mortality burden in low- and middle-income countries after surgery for the commonest cancers has yet to be addressed.

One of the issues to consider when conducting a systematic review is the potential for under-reporting of surgical data. While surgical data has made up the preponderance of the articles analyzed over time, this trend should be kept in mind for future systematic reviews on this topic. Moreover, although smoking cessation and reduced alcohol intake were not well depicted in the papers, the impact of these confounders on the quality of evidence cannot be systematically evaluated, as the impact of risk factors on treatment outcome has still not been quantified. Despite the potential for under-use, surgical data for the treatment of head and neck cancer is better reported than that of many similar studies.

5.2. Radiation Therapy:

Radiation therapy (RT) is one of the principal modalities for managing head and neck cancer (HNC). It can be applied as an elective treatment modality on its own or in conjunction with surgery and chemotherapy. Also known as radiotherapy, external beam radiation (EBRT) utilizing megavoltage photons or machines of cobalt-60 has been in vogue since the late 1960s, following the introduction of 3-D planning RT. Conventional therapy typically employs X-rays with 6 MV energy, as this energy penetrates deeper tissue and minimizes burn and skin irritation.

IMRT, a major advance after 3-D planning, is now the treatment of choice in highly specialized centers with advanced equipment. Compared to EBRT, which has been associated with rash, odynophagia, xerostomia, fibrosis, and post-radiation budding, brachytherapy (BT) has its own advantages, especially for low-grade tumors.

Unlike EBRT, BT convincingly reduces this occurrence after treatment. Though RT can be used alone or in combination with surgery and chemotherapy for managing tumor grades, it has different advantages and disadvantages. For instance, RT is the modality of choice for completely resected T2 N+ laryngeal tumors. Radiation therapy planning involves treatment volume (TV), critical structure, and dose volume histogram (DVH). Expandable TV is divided into CTV (clinical target volume or target TV) and PTV (planning target volume). CTV includes the tumor itself with a margin to accommodate microscopic extension, while PTV is the CTV with a margin to accommodate setup uncertainties. Newer 3-D and IMRT techniques, doses, and fractionation schedules are reprioritized based on the tumor and clinical condition. Plans are devised and subjected to quality assurance before the commencement of treatment.

5.3. Chemotherapy:

Chemotherapy is a type of cancer treatment that uses drugs to destroy cancer cells. The drugs can be taken orally, injected into a vein, or applied topically, and the method of administration depends on the type and stage of cancer. These drugs work by targeting cells that are rapidly dividing; although most cancer cells are rapidly dividing, some normal cells such as those in hair, the lining of the mouth and throat, and the digestive system can also be affected. Chemotherapy can be administered in several ways. A single chemotherapy drug may be used to treat cancer, or a combination of different drugs may be offered. Chemotherapy is sometimes given before surgery to shrink tumors and make them easier to remove, and it is also sometimes offered after surgery to reduce the risk of cancer returning. Chemotherapy drugs are usually given in cycles, with each treatment followed by a recovery period. Chemotherapy drugs used in head and neck cancer can be classified as cytotoxic and targeted drugs. Some cytotoxic drugs used include methotrexate, perfolgan, premarin, and paracetamol. Other drugs like mustin and citotax are also used, but they can have side effects such as hair loss and should be used cautiously. The selection of drugs for chemotherapy depends on different factors, including the type of cancer, its stage, and the overall health of the patient. In recent years, targeted drugs have been developed to interfere specifically with cancer cell growth and metastasis, with less effect on normal cells. Targeted chemotherapy drugs for head and neck cancer include cetuximab and lapatinib. While chemotherapy can be effective in controlling cancer, it also affects normal cells that grow rapidly, which leads to side effects like mouth sores, fatigue, nausea, vomiting, and diarrhea. Other serious side effects can occur after several chemotherapy treatments, like low red blood cell

count, white blood cell count, and low platelets. Newer treatments are currently being developed to help minimize these side effects.

6. Conclusions and Future Directions:

A total of twenty-two studies were retrieved that met the inclusion criteria and were reviewed in this systematic search for peer-reviewed articles on HNC incidence, mortality, and risk factors in Jordan with data collected from January 1990 until December 2021. These studies varied in design, data collection methods, and geographical regions from which the data was derived, as well as HNC reporting mechanisms. One study provided data from the national cancer registry and covered both incidence and mortality rates, while twenty-one studies were community-based cross-sectional studies that reported only risk factors associated with HNC. Overall, the current body of literature regarding HNC in Jordan is limited. The majority of studies were performed in the northern region, perhaps due to greater convenience in accessing hospitals and other health facilities for researchers rather than due to a higher incidence of HNC. Regardless, the findings from these studies may not be generalizable to the entire Jordanian population, preventing a complete understanding of this disease. Future studies utilizing data from various regions using a uniform method for data collection are necessary to gain insight into the statewide incidence and mortality of HNC. Given the sensitivity of the data reporting mechanism, the Ministry of Health in Jordan should consider establishing a national registry for HNC. This system must be flexible enough to accept hospital data reporting using different methods. Another critical focus of future studies should be determining the level of awareness regarding HNC among the general population, as this represents a societal shift that may effectively reduce the occurrence of HNC. There is also a pressing need for studies that explore the risk factors associated with the recent increase in HNC incidence rates. The current literature is limited because studies were performed before 2010 and did not control for confounding variables, severely limiting their compatibility and comparability. Attention should be directed toward the inclusion of robust statistical methods in parallel studies as this disease continues to increase in incidence. The increasing incidence of HNC globally and in Jordan is concerning and warrants the attention of policymakers and public health officials.

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