EPIDEMIOLOGY OF NASOPHARYNGEAL CARCINOMA: UNDERSTANDING THE INTERPLAY OF GENETIC AND ENVIRONMENTAL FACTORS

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ABSTRACT

Background: Nasopharyngeal carcinoma (NPC) is a cancer that occurs in the nasopharyngeal area and has a unique epidemiology with varying incidence rates around the world. The epidemiological characteristics of NPC show the interaction of genetic and environmental factors. **Purpose:** The purpose of this study is to understand the epidemiology of NPC since it is crucial for understanding the causes and the prevention methods for NPC. Currently, the world faces health problems with an epidemiological transition from infectious diseases to non-communicable diseases, including cancer such as NPC. **Conclusion:** The risk factors for NPC are age, gender, race, education, socioeconomic status, genetic factors, Epstein-Barr virus infection, and exposure to carcinogens through food and smoking. The incidence of NPC is more commonly found in men and Asians. NPC patients found at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia are more commonly found in patients aged 41-50 years old, male, with a low level of education.

Keywords: *epidemiology, Nasopharyngeal carcinoma, risk factor*

Introduction

The World Health Organization (WHO) reports that cancer is a major global cause of death[1–4], and according to the Global Burden of Cancer (GLOBOCAN), in 2020 there were 19.2 million cases and 9.9 million deaths[5,6]. The International Agency for Research on Cancer (IARC) estimates that 20% of males and 20% of females worldwide will develop cancer in their lifetime[7].

Nasopharyngeal carcinoma (NPC) is a type of cancer that occurs in the nasopharynx, which is located above the tonsils and behind the nose. It is characterized by mild microscopic or ultrastructural squamous differentiation[5]. NPC is a disease with a unique distribution pattern that varies by region, race, and gender. The global incidence rate in 2018 was highest in Asia, particularly in East and Southeast Asia, with rates ranging from 2.1 to 0.4 per 100,000 in Asia and Europe, respectively.[6]

NPC has different characteristics depending on its geographical region. For example, the age distribution in areas with low incidence differs from endemic areas. In areas with low incidence, NPC incidence increases with age and has a bimodal peak: the first in adolescents and young adults and the second after the age of 65, while in endemic areas, incidence increases after the age of 30, peaking at 40-59 years and decreasing thereafter. The male-female incidence ratio is 2.75.[6,7]

Epidemiology is the field of study focused on understanding the spread of diseases and health conditions within populations and using this information to control health problems.[1,2] The world is facing a shift from infectious diseases to non-communicable diseases, creating a double burden for all countries. This includes ongoing efforts to control infectious diseases, as well as new efforts to address the increasing cases of non-communicable diseases such as cancer, which is a worldwide health burden characterized by uncontrolled cell growth and spread.[3]

The diversity of the epidemiological characteristics of NPC shows that NPC arises from the result of a multifactor interaction involving genetic and environmental factors. Understanding the epidemiology of NPC is important for studying the cause and effect of the disease, learning the natural course of the disease, outlining the health status of the population group, and evaluating health efforts to manage NPC, including prevention.

Discussion

1. Epidemiology

a. Geographical Distribution

The prevalence of nasopharyngeal carcinoma (NPC) is more frequently observed in Asian regions compared to non-Asian countries. Specifically, certain ethnic groups, predominantly residing in southern China, Hong Kong, and Southeast Asia, exhibit the highest incidence of NPC. When considering the overall landscape of cancer, NPC is relatively uncommon. In 2018, the International Agency for Research on Cancer (IARC) reported approximately 129,000 new cases of NPC, representing a mere 0.7% of all cancer diagnoses that year. According to the 2020 GLOBOCAN data, the estimated occurrence of NPC in Indonesia stands at 6.8 cases per 100,000 individuals. Globally, the incidence rate of NPC in 2020 was recorded as 1.5 cases per 100,000 population, with a corresponding mortality rate of 0.88 cases per 100,000.

It is noteworthy that NPC is more prevalent among men than women. The GLOBOCAN data for 2020 indicates an incidence rate of 2.2 cases per 100,000 in men, whereas the rate in women was 0.82 cases per 100,000. Additionally, even when individuals from southern China relocate to non-endemic areas, they continue to exhibit a high incidence of NPC, although the rate decreases in second-generation migrants.

Figure 1 illustrates the worldwide incidence of NPC across all age groups. Generally, the incidence of NPC remains below 1 case per 100,000 person-years. However, higher rates are observed among the southern Chinese population, while moderate rates are found in Southeast Asia, the Arctic, North Africa, and the Middle East. In 2018, it was estimated that approximately 129,079 cases of nasopharyngeal cancer were diagnosed globally, with 85% of these cases occurring in Asia. The estimated number of NPC-related deaths reached 72,987.[11]

Adham et al.'s study at Dr. Cipto Mangunkusumo Hospital involved medical records of 6000 head and neck cancer patients from 1995 to 2005. Nasopharyngeal carcinoma was found in 1121 patients, with 28.35% of patients coming from referral centers in remote areas.

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b. **Age Distribution**

Several studies have investigated the incidence of head and neck cancer in different populations and age groups. Chang et al. found that there is a difference in the incidence pattern in low-risk and high-risk populations. In the low-risk population, the first peak of head and neck cancer incidence occurs in young adulthood (15-24 years old), plateaus or decreases slightly until the age of 35-39 years old, and then increases towards a second, higher peak in the age group of 65-79 years old. In the high-risk population, only one peak was found, which was in the age group of 45-59 years old, followed by a plateau or slight decrease.[11]

Adham et al. studied the epidemiology, incidence, and presentation of signs and symptoms in Indonesia and found that the incidence in Indonesia was 5.66 per 100,000 population. The age distribution had a peak in the 40-49 year old group and over 80% of patients were diagnosed between the ages of 30 and 59 years old. Approximately 20% of patients were found to be under the age of 30 years old without a bimodal age distribution. The data distribution was found to increase steadily and peak in the fifth decade. The increase was found to occur every 5 to 12 years with age.

Nathania et al. studied the profile of head and neck cancer patients at Dr. Hasan Sadikin General Hospital and reported that the average age of patients found was 47.45 years old, with a range of 25-82 years old. The study subjects were grouped into the age group of less than 30 years old, followed by a division of age ranges every 5 years and a group of more than 80 years old. The incidence in the age range of 50-54 years old was found to be 371 patients or about 12.57% of patients.[12] Handayani et al. studied the prevalence of head and neck cancer at Dr. Hasan Sadikin General Hospital and reported that 34% of patients were in the age group of 41-50 years old.[13]

c. Gender

The incidence of head and neck cancer (HNC) is higher in men compared to women, with a ratio of two to three times more in most populations.[11] The incidence increases with age, peaking at 55-59 years old, and then slowly decreases. The predominance of men with HNC has been consistently found in Indonesia, with a ratio of 2.4:1 men to women. [14]

d. Race

In China, the risk of HNC is higher in the Southern Chinese population, specifically in the Tanka ethnic group. In Southeast Asia, the risk of HNC is correlated with the social and racial mixing of Southern Chinese and the Tanka ethnic group. In Singapore, the incidence is increasing among Chinese descendants and the lowest incidence is found among the Indian ethnic group. In the US, the incidence is highest among the Chinese population, followed by Filipinos, African Americans, Koreans, non-Hispanic whites, and Hispanic whites. In Indonesia, most HNC patients are of Javanese descent (35%), followed by Sundanese (25.8%) and Sumatran (23.9%) populations. The distribution of ethnic groups among HNC patients in Indonesia showed that the influence of Chinese genetics was not significant in determining the incidence of HNC, despite the risk of migration from China.

e. Education Level

A study by Handayani et al. on the prevalence of NPC at Dr. Hasan Sadikin General Hospital reported that most patients had a last education level of elementary school, which is 54.9%. Other education levels of patients are 24.8% in high school and 18.9% in junior high school.

f. Occupation

A study by Xie et al. on the risk factors of NPC in Hong Kong stated that the occupation associated with an increased likelihood of NPC is traders and manual workers with OR 2.09 (95% CI 1.09, 4.01) and 2.14 (95% CI, 1.04, 4.41). Jobs exposed to cotton dust, chemical smoke, and smelting smoke were found to have OR with 95% CI of 1.93 (1.13, 3.28), 13.11 (1.53, 112.17), and 9.18 (1.05, 80.35). [15]

According to Handayani et al., most NPC patients were housewives (28.1%). The jobs of NPC patients are very diverse, with manual workers (18.6%), unemployed (16.1%), entrepreneurs (10.3%), private sector employees (8.3%), farmers (6.9%), government employees (4.2%), students (3.5%), others (2.2%), and retirees (1.5%) also found among the patients.[13]

g. Classification and Stage of NPC

A study by Adham et al. reported that type III histopathology was most commonly found in the study, which was *undifferentiated carcinoma* (85%). Approximately 12.7% of patients in the study were type I histopathology (*keratinizing squamous cell carcinoma*) and were positive for EBV infection. Type II histopathology was only found in 2.3% of cases.

According to Nathania et al., the most common type of head and neck cancer among patients at Dr. Hasan Sadikin Hospital from 2013 to 2018 was NPC (31.2%). Most of the NPC found was stage IV (48.64%) with an *undifferentiated carcinoma* type (47.15%).[12] According to Handayani et al., the histopathological characteristics of NPC patients were mostly *undifferentiated carcinoma* (58.3%), followed by *keratinizing squamous cell carcinoma* (20%) and *non-keratinizing squamous cell carcinoma* (19.7%). These histopathological groups are endemic in Southeast Asia and closely related to Epstein-Barr virus infection.[13]

h. NPC Recurrence

A study by Prawiranata on the characteristics of recurrent NPC patients at Dr. Hasan Sadikin Hospital from 2017 to 2019 stated that 7.8% or 135 NPC patients experienced recurrence. Around 79% of the patients were found to have recurrence at the age of over 40 years. The last education of patients, their jobs, and the stage of the disease did not show any significant relationship with the recurrence of NPC.[16,17]

2. Risk Factor

The onset of nasopharyngeal carcinoma (NPC) results from the interaction of various factors that involve both genetic and environmental factors. A retrospective study by Hardianti et al. on the risk factors for NPC in Hasan Sadikin Hospital reported that the three most commonly found risk factors for NPC in patients at Hasan Sadikin Hospital in Bandung are consumption of salty fish (39.7%), use of mosquito-repelling incense (43.2%), and smoking (50.7%).[18]

Nasopharyngeal carcinoma (NPC) is influenced by several well-documented risk factors, including age, gender, and genetics. Let's delve deeper into each of these factors:

Age plays a significant role in the incidence of NPC, and the pattern varies depending on the geographical region. In areas with low NPC incidence rates, such as non-endemic regions, the occurrence of NPC tends to increase with age, exhibiting a bimodal distribution. The first peak is observed among teenagers and young adults, while the second peak occurs after the age of 65. However, in endemic areas, where NPC is more prevalent, the incidence typically rises after the age of 30 and reaches its highest point within the age range of 40-59. Subsequently, the incidence tends to decrease in older age groups. This contrasting age distribution between low incidence and endemic areas underscores the complex interplay of environmental and genetic factors contributing to NPC development.

Another significant risk factor for NPC is gender. The incidence of NPC is consistently higher in males compared to females, as evidenced by a male-to-female incidence ratio of 2.75. This indicates that men face a 2.51 times higher risk of developing NPC than women. The underlying reasons for this gender disparity in NPC incidence are still under investigation, and further research is necessary to uncover the precise biological and hormonal factors that may contribute to this phenomenon.

In addition to age and gender, genetic factors also play a crucial role in the development of NPC. Certain genetic variations and susceptibility genes have been associated with an increased risk of NPC. These genetic factors interact with environmental triggers, such as viral infections and dietary factors, to influence the initiation and progression of NPC. Ongoing studies continue to shed light on the specific genetic mechanisms and pathways involved in NPC pathogenesis, paving the way for potential targeted therapies and personalized approaches to managing the disease.[10]

a. Education and socioeconomic

Education and socioeconomic factors appear to be related to the risk of nasopharyngeal carcinoma (NPC). According to a study of 352 cases of NPC in Hong Kong, most of the subjects in the study (59.7%) had a secondary education. 27.3% in the study had primary education or lower and 12.2% had tertiary education.[22] Another study in Thailand also showed that NPC patients tended to have a lower level of education. However, two other studies showed no significant relationship between education level and NPC risk.[13,14]

Socio-economic factors such as occupational exposure, household type[22,23,25], poor ventilation, exposure to smoke, and cooking processes in the home have also been linked to NPC risk[26]. In a study in Taiwan, among NPC patients under the age of 65, those with a lower socio-economic status living in disadvantaged environments had a 2-fold higher risk of death compared to those with a higher socio-economic status living in better environments.[15]

b. **Genetic**

Extensive research efforts, encompassing more than 100 studies, have been undertaken to investigate the potential role of genetic polymorphisms in the development of nasopharyngeal carcinoma (NPC). Among these studies, a recurring and highly consistent finding involves the association between NPC development and genetic variations within the human leukocyte antigen (HLA) genes, which are located within the major histocompatibility complex (MHC). Specifically, the HLA genes situated in the MHC region on chromosome 6 (6p21.3) have emerged as a prominent locus implicated in the onset of NPC.

The MHC region, housing the HLA genes, has garnered considerable attention due to its involvement in immune system regulation and its impact on disease susceptibility. Within this complex genetic landscape, certain polymorphisms and variations have been identified that contribute to the increased risk of NPC development. The extensive body of research examining the HLA genes and their association with NPC underscores the significance of these genetic factors in the pathogenesis of the disease.

The human leukocyte antigen system plays a critical role in immune responses by presenting antigens to immune cells, thereby enabling the recognition and elimination of foreign invaders, including viral pathogens. Perturbations in the HLA genes can disrupt the immune system's ability to effectively recognize and eliminate nasopharyngeal cancer cells, potentially facilitating the initiation and progression of NPC.

By conducting a comprehensive analysis of genetic polymorphisms within the HLA genes, researchers have made substantial progress in understanding the underlying genetic mechanisms involved in NPC development. However, it is important to note that while the HLA genes within the MHC region have consistently been linked to NPC, the precise mechanisms by which these genetic variations contribute to disease susceptibility and progression are still being elucidated. Further investigations are necessary to unravel the intricate interplay between specific HLA alleles and their functional implications in NPC pathogenesis.

The identification of HLA genes within the MHC region as a key locus associated with NPC not only enhances our understanding of the disease's genetic underpinnings but also opens avenues for future research and clinical applications. By elucidating the precise role of these genetic variations, it may be possible to develop targeted therapies, diagnostic tools, and preventive strategies tailored to individuals at higher risk of developing NPC based on their HLA profiles.

c. Epstein-Barr virus (EBV)

The Epstein-Barr virus (EBV), classified as a type 4 herpes virus, is responsible for infecting approximately 90% of the global population. Its association with various types of human cancers, including lymphoid and epithelial cancers, has been extensively studied. Notably, the closest link between EBV infection and cancer is observed in undifferentiated nasopharyngeal cancer, which is endemic in southern China and Southeast Asia. In fact, almost all

patients diagnosed with undifferentiated nasopharyngeal cancer test positive for EBV.

EBV infection occurs worldwide, with the highest prevalence observed in adults. However, it is important to note that only a small portion of the population infected with EBV develops EBV-related cancers. Primary infection typically takes place during early childhood or adolescence. Upon infection, the body develops immunity to the virus. Nevertheless, EBV persists for a lifetime in certain circulating or saliva-shedding B lymphocytes.

In nasopharyngeal carcinoma, specific EBV antigens are present. The nuclear core early antigen (EA) and viral capsid antigen (VCA) are commonly detected. Additionally, the virus expresses lytic and nuclear antigens. Lytic antigens include latent membrane proteins 1, 2, and 3 (LMP-1, -2, -3), while nuclear antigens include Epstein-Barr nuclear antigens 1 to 6 (EBNA-1 to EBNA-6). EBNA-1 and LMP-1 are consistently expressed in nasopharyngeal carcinoma, with EBNA-1 playing a role in maintaining the virus's episome in tumor cells and LMP-1 inducing epithelial hyperplasia and changes in keratin gene expression. Moreover, nasopharyngeal carcinoma cells express Epstein-Barr encoded ribonucleic acids (EBERs) in the cytoplasm, which are not present in normal nasopharyngeal cells.

It is important to highlight that while EBV antigens and EBERs are absent in normal nasopharyngeal cells, most individuals infected with EBV do not develop nasopharyngeal carcinoma. This suggests that EBV is not the sole initiator of nasopharyngeal carcinoma and that its role in the development of the disease is influenced by latent infection in genetically susceptible nasopharyngeal epithelial cells, along with environmental factors.

Understanding the complex interplay between EBV infection, genetic susceptibility, and environmental influences in the development of nasopharyngeal carcinoma is crucial for advancing our knowledge of the disease. Further research is warranted to unravel the intricate mechanisms underlying EBV-related carcinogenesis, ultimately leading to improved diagnostic methods, targeted therapies, and preventive strategies for nasopharyngeal carcinoma.

d. Diet

The common environmental factor related to nasopharyngeal carcinoma (NPC) is diet. It has been known that certain diets high in preservatives are associated with NPC. Such diets include salted fish and smoked meat.

Studies have evaluated the relationship between the consumption of salted fish, salted meat, pickled vegetables, smoked meat, consumption of dark green vegetables, herbal tea drinking habits, and pickled food with NPC. Salted fish, salted meat, and pickled vegetables are significantly related to NPC risk.[21] Early childhood consumption of salted fish has been reported as an independent risk factor for NPC in Hong Kong, Malaysia, and China. Nitrosamines are believed to be the carcinogens causing NPC. High levels of volatile nitrosamines were found in foods frequently consumed by populations at high risk of NPC in Tunisia, South China, and Greenland. Strong links have been shown between salted fish consumption in early childhood and NPC in these regions.[16]

The enzyme cytochrome P450 (CYP P450) is involved in the catalytic reaction of phase I metabolism. CYP2E1 is a group within the CYP450 enzyme, which activates carcinogens such as nitrosamines. The Rsal/Pstl polymorphism in CYP2E1 affects the activation, transcription of CYP2E1, and is suspected to increase the risk of head and neck carcinoma, particularly in Asian populations, mixed populations, and non-smokers.

Extracts from smoked meat have been reported to induce papilloma on the skin and systemic tumors in Swiss albino rats, and chemical analysis of the extract showed the presence of nitrosodimethylamine (NDMA), nitrosodiethylamine (NDEA), nitrosopyrrolidine (NYPR), and benzo(a)pyrene (BaP). The high prevalence of NPC in Nagaland is reinforced by the high NDEA content in dried smoked meat.[26] The acetone extract from dried smoked meat has been tested and documented for its genotoxic potential using sperm heads, and significant doses showed a responsive mutagenic effect. Mutagenic effects of dried smoked meat were also revealed in Salmonella typhimurium using the TA 98 strain with the Ames test.[29] The extract from smoked meat was reported to be mutagenic to Salmonella typhimurium, with or without S9 mixture, and is a clastogenic agent in mammals.[17]

e. Carcinogen

Exposure to certain substances through inhalation has been identified as a potential risk factor for the development of nasopharyngeal carcinoma (NPC). Substances such as mosquito-repellent smoke, cigarette smoke, charcoal smoke, and factory inhalants have been associated with an increased risk of NPC.

The use of mosquito-repellent smoke, in particular, has been found to elevate the risk of NPC by 2.58 times due to the presence of carcinogenic compounds in the smoke. Studies have indicated that mosquito-repellent smoke in its gaseous phase contains several carbonyl compounds. The interaction of formaldehyde and acetaldehyde with intracellular proteins in nasopharyngeal epithelial cells can disrupt DNA replication processes, leading to oncogenic mutations and resulting in morphological abnormalities, cellular dysfunction, and immunological reactions.

Numerous case-control studies have demonstrated a substantial link between smoking and an increased risk of NPC. Recent meta-analyses have also confirmed the significant association between smoking and NPC. In a study conducted in southern China, smoking was found to continuously reactivate the Epstein-Barr virus (EBV) and significantly elevate the long-term risk of NPC. Additionally, a cohort study conducted in a high-risk area for NPC revealed a higher mortality rate for NPC among smokers, with heavy and chronic smokers exhibiting a greater risk of death. The relationship between smoking and NPC mortality is evident from the correlation between the number and cumulative consumption of cigarettes and the risk of death from NPC. However, more prospective cohort data on NPC mortality rates are required to confirm these findings and determine if there exists a significant exposure threshold for cancer prevention.

According to the World Health Organization (WHO), the distribution of the three histological types

of NPC varies between high- and low-risk areas. In high-risk areas, over 90% of NPC cases are classified as undifferentiated carcinomas (Type III), while squamous cell carcinomas (Type I) are the predominant histological type in low-risk areas. The association between smoking and NPC appears to be stronger for squamous cell carcinomas (Type I), which are the primary cell type found in populations at low risk for the disease, compared to undifferentiated carcinomas (Type III), which are prevalent in high-risk populations.

Further research is warranted to comprehensively investigate the mechanisms through which inhalation of these substances contributes to the development of NPC. By gaining a deeper understanding of these associations, it will be possible to develop targeted preventive strategies, raise awareness about the risks posed by inhalation of harmful substances, and ultimately reduce the burden of NPC on affected populations. A study in India found a higher risk among smokers, especially for NPC which is well differentiated. A study in Taiwan that compared the environment of NPC patients with the environment of control subjects found that smoking and working in poorly ventilated environments were strongly associated with NPC. Other studies have shown that long-term smoking is associated with NPC, but low exposure to cigarette smoke does not seem to have a significant effect.[18]

f. Alcohol Consumption

A comprehensive study has shed light on the association between alcohol consumption and the risk of developing nasopharyngeal carcinoma (NPC). The findings indicate that engaging in alcohol consumption can heighten the risk of NPC when compared to abstaining from alcohol altogether. Interestingly, the frequency of alcohol consumption plays a significant role, as regular drinking is shown to elevate the risk, whereas infrequent consumption seems to have a mitigating effect to some extent. These observations align with the results of a recent meta-analysis, which established a significant correlation between alcohol consumption and NPC.

While these findings suggest a potential link between alcohol consumption and NPC, it is important to note that the relationship necessitates further exploration. This is due to the fact that a majority of studies conducted thus far have not demonstrated a clear association between alcohol consumption and the development of NPC. Therefore, continued research efforts are essential to gain a more comprehensive understanding of the complex interplay between alcohol consumption and NPC risk.

It is worth mentioning that the impact of alcohol consumption on NPC risk is likely influenced by various factors such as individual susceptibility, genetic predisposition, and environmental influences. These multifaceted elements may contribute to the variability observed in different studies regarding the relationship between alcohol consumption and NPC. Consequently, conducting additional investigations and employing rigorous methodologies will aid in elucidating the true nature of this association.

The insights gained from studying the connection between alcohol consumption and NPC have important implications for public health initiatives. By identifying potential risk factors, such as alcohol consumption, educational campaigns and interventions can be developed to raise awareness and promote responsible drinking habits. Additionally, further research on this topic will contribute to the development of personalized prevention strategies that can help reduce the incidence of NPC among high-risk populations.

3. **Clinical Diagnosis**

The most common symptoms that appear are a lump in the neck (58.1%), nasal congestion (49.1%), and unilateral hearing disturbance (39.5%). Other complaints include epistaxis, post-nasal drip, diplopia pain, fluid coming out of the ear, unilateral headache, and cranial nerve paresis. The nasopharynx is located in a closed space behind the nasal cavity, this area is usually examined using a flexible fiber optic or a rigid nasoendoscope. A biopsy is performed to confirm the diagnosis.

4. Disease Stage

T classification plays a crucial role in categorizing the progression of nasopharyngeal carcinoma (NPC) based on the development of tumors in the primary site. It is a distinct stage or phase within the disease course that evaluates neoplasms. The staging of NPC involves assessing three fundamental components: the primary tumor (T), regional lymph nodes (N), and the presence of metastases (M).

When considering T classification, patients with NPC categorized as T4 have a significantly lower life expectancy, with a survival rate of approximately 18.7%. In contrast, patients classified as T3, T2, and T1 exhibit higher survival rates of 63.9%, 74.1%, and 100%, respectively. Moving on to N classification, individuals with NPC classified as N3 face a significantly worse prognosis, with a survival rate of around 41.1%. In comparison, patients categorized as N2, N1, and N0 have higher survival rates of 54.9%, 76.9%, and 100%, respectively. It is evident that patients diagnosed at an earlier stage of NPC generally have a more favorable prognosis compared to those diagnosed at an advanced stage.

Research studies have provided further insights into the relationship between T and N classifications and survival rates in NPC patients. For instance, a study conducted by Liu et al. in 2003 in Kuala Lumpur found that individuals classified as T1-T3 exhibited better life expectancy compared to those classified as T4. Similarly, based on N classification, patients with N1-N3 had a poorer prognosis than those categorized as N0. Another study conducted by Farias et al. in 2003 in Brazil examined 173 NPC patients and reported five-year survival rates of approximately 100%, 85.7%, 30.4%, 25%, and 25% for stages I, II, III, IVA, and IVB, respectively. These findings highlight the significant impact of T4 and N3 classifications on the overall prognosis of NPC patients, indicating a poorer outlook for individuals classified under these categories.

Understanding the implications of T and N classifications in NPC prognosis is crucial for clinicians in determining appropriate treatment strategies and informing patients about their prognosis. Additionally, these findings contribute to ongoing research aimed at improving survival rates and developing targeted therapies for NPC patients.[19]

Conclusion

The causes of this cancer are complex and involve a combination of genetic and environmental factors. The epidemiology of nasopharyngeal carcinoma is important for understanding the causes of the disease, its natural progression, the health status of certain populations, and the effectiveness of health efforts in addressing the disease, including prevention. The risk factors for nasopharyngeal carcinoma include age, gender, race, education, socio-economic status, genetics, Epstein-Barr virus infection, consumption of preserved food (such as salted fish and smoked meat), carcinogens (such as insecticide sprays, tobacco, ashes, and formaldehyde fumes), and alcohol consumption. The incidence is highest in people between the ages of 50 and 59 and is more common in men than women, which is thought to be related to the higher prevalence of smoking in men. The incidence is higher in Asia than in non-Asian countries, especially in East and Southeast Asia. The article also mentions that patients with nasopharyngeal carcinoma in Hasan Sadikin Hospital tend to be between the ages of 41 and 50, male, and have a lower education level. The most common risk factors in this population are smoking, exposure to carcinogens, and poor ventilation in the home.

REFERENCES

1. Chen YP. Nasopharyngeal carcinoma. Lancet. Lancet (London, England). 2019;394(10192)(64):80.
2. Bossi P. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(4):452-.
3. Bray F. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;
4. Komite Penanggulangan Kanker Nasional Kemenkes RI. Panduan Penatalaksanaan Kanker Nasofaring. Jakarta: KEMENKES RI; 2015. p. 56.
5. Komite Penanggulangan Kanker Nasional Kemenkes RI. Panduan Penatalaksanaan Kanker Nasofaring. Kementeri Kesehat Republik Indones Kom Penanggulangan Kanker Nasional. 2015;1–56.
6. Bray F. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;
7. Bossi P. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann Oncol. 2021;32(4):452–65.
8. Chen YP. Nasopharyngeal carcinoma. Lancet. 2019;394(10192):64–80.
9. Paul W. Cummings Otolaryngology Head and Neck Surgery. 7th ed. Elsevier; 2020. 1394–1401 p.
10. World Health Organization. Cancer Fact Sheets - Nasopharynx. Globocan 2020. 2020;0–5.
11. Chang ET. The evolving epidemiology of nasopharyngeal carcinoma. Vol. 30, Cancer Epidemiology Biomarkers and Prevention. 2021. p. 1035–47.
12. Nathania N. Profile of head neck cancer patients from 2013-2018 at Dr.Hasan Sadikin General Hospital Bandung. Oto Rhino Laryngol Indones. 2020;51(2):141–5.
13. Handayani R. Prevalence of Nasopharyngeal Carcinoma Patients in the Department of ORL-HNS Hasan Sadikin General Hospital 2010-2017. Int J Nasopharyngeal Carcinoma. 2020;2(1):1–3.
14. Adham M. Nasopharyngeal carcinoma in indonesia: Epidemiology, incidence, signs, and symptoms at presentation. Chin J Cancer. 2018;31(4):185–96.
15. Xie SH. Occupational risk factors for nasopharyngeal carcinoma in Hong Kong Chinese: a case-referent study. Int Arch Occup Environ Health. 2017;90(5):443–9.
16. Adithya Prawiranata M. Characteristics of Recurrence Nasopharyngeal Carcinoma in Hasan Sadikin Hospital Period 2017-2019. Int J NASOPHARYNGEAL CARCINOMA. 2020;2(02):62–3.
17. Dewi YA. Management of Recurrent Nasopharyngeal Carcinoma. Int J Nasopharyngeal Carcinoma. 2020;2(4):118–20.
18. Hardianti RA. Risk Factor of Nasopharyngeal Carcinoma Dr. Hasan Sadikin General Hospital Bandung. Int J NASOPHARYNGEAL CARCINOMA. 2019;1(03):110–1.
19. Septiani W. Association between Mosquito Coils Use with Nasopharyngeal Carcinoma. 2020;02(03):79–81.