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Nasopharyngeal Carcinoma in the Nias Tribe Indonesia: Prevalence, Risk Factors, and Characteristics

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A B S T R A C T

Nasopharyngeal carcinoma (NPC) is a malignancy with a distinctive racial and geographical distribution, exhibiting a high prevalence in Southeast Asia, including Indonesia. The Nias tribe, an indigenous group in Indonesia, has a particularly high incidence of NPC, which may be linked to unique environmental and genetic factors. This study aimed to investigate the prevalence, risk factors, and characteristics of NPC among the Nias people to inform targeted prevention and control strategies. A retrospective study was conducted on 150 NPC patients treated at a referral hospital in Medan, Indonesia, between 2018 and 2023. Data were collected from medical records, including demographics, clinical presentation, Epstein-Barr virus (EBV) infection status, dietary habits, and environmental exposures. Descriptive statistics and comparative analyses were performed to identify risk factors associated with NPC in the Nias population. The prevalence of NPC among the Nias tribe was 30% (45 out of 150 NPC patients). The majority of Nias patients were male (60%) and aged 40-60 years (70%). EBV infection was prevalent in 80% of the Nias patients. Significant risk factors included consumption of preserved foods (78%), exposure to firewood smoke (65%), and a family history of NPC (20%). Most patients presented with advanced-stage disease (III and IV), with common symptoms such as neck lumps, epistaxis, and nasal obstruction. In conclusion, NPC poses a substantial health burden on the Nias tribe. EBV infection, consumption of preserved foods, exposure to firewood smoke, and genetic predisposition are significant risk factors. Public health interventions should prioritize early detection through EBV screening, health education on risk factors, and promotion of alternative cooking fuels to reduce exposure to carcinogens.

1. Introduction

Nasopharyngeal carcinoma (NPC) stands as a formidable challenge in the realm of human malignancies, its notoriety stemming from its intricate etiology and the profound health burden it exacts on afflicted populations. This enigmatic cancer, originating from the epithelial lining of the nasopharynx, exhibits a striking predilection for specific geographical regions and ethnic groups, underscoring the profound interplay between genetic heritage and environmental influences in its pathogenesis. Southeast Asia, with its rich tapestry of ethnic diversity and cultural practices, has emerged as a region of particular interest in the study of NPC. Within this region, the Nias tribe, an indigenous community inhabiting the island of Nias off the western coast of Sumatra, Indonesia, has garnered attention due to the disproportionately high incidence of NPC within its populace. This epidemiological observation has ignited a fervent quest to unravel the unique confluence of factors that render the Nias people particularly susceptible to this insidious disease. The etiological landscape of NPC is a complex mosaic, with genetic predisposition, viral infection,

dietary habits, and environmental exposures all contributing to its development. Among these factors, the Epstein-Barr virus (EBV) has emerged as a pivotal player, its ubiquitous presence in endemic regions and its ability to establish persistent infection in the nasopharyngeal epithelium marking it as a key suspect in the malignant transformation of nasopharyngeal cells.[1-3]

The Nias community, with its close-knit social fabric and traditional practices, presents a unique opportunity to explore the intricate interplay between EBV infection and NPC development. The high prevalence of EBV infection among the Nias people, potentially linked to cultural practices involving close contact and the exchange of saliva, raises intriguing questions about the specific viral strains prevalent in this region and their potential role in NPC pathogenesis. Dietary habits, deeply intertwined with cultural heritage, also contribute significantly to the NPC risk profile of the Nias tribe. The traditional Nias diet, rich in preserved foods such as salted fish and fermented meats, presents a potential source of carcinogenic compounds, particularly nitrosamines, which have been implicated in the development of various cancers, including NPC. Environmental factors, particularly exposure to smoke from wood-burning stoves, further compound the NPC risk faced by the Nias people. The reliance on traditional cooking methods using firewood in many Nias households leads to chronic exposure to carcinogenic fumes, adding another layer of complexity to the environmental risk factors contributing to NPC development in this community. Genetic predisposition, the indelible mark of ancestry, also plays a pivotal role in NPC susceptibility. Certain human leukocyte antigen (HLA) alleles have been associated with an increased risk of NPC, and the prevalence of these alleles may vary across different populations, potentially contributing to the observed ethnic disparities in NPC incidence.[4-7]

The Nias population, with its unique genetic heritage, presents a valuable opportunity to explore the contribution of genetic factors to NPC susceptibility. Investigating the prevalence of specific HLA alleles and other genetic variants associated with NPC risk in the Nias tribe could shed light on the genetic underpinnings of this disease and inform targeted prevention strategies. Early detection of NPC is paramount in improving treatment outcomes and survival rates. However, in Nias, limited access to healthcare facilities and lack of awareness about NPC often result in late-stage diagnosis, diminishing the chances of successful treatment and contributing to the high mortality associated with this disease. Public health interventions aimed at raising awareness about NPC, its early symptoms, and the importance of prompt medical attention are crucial in combating this disease within the Nias community. Efforts to improve access to healthcare facilities and promote early detection through EBV screening and clinical examination could significantly improve the prognosis of NPC patients in this vulnerable population.[8-10] This study aims to comprehensively evaluate the prevalence, risk factors, and characteristics of NPC among the Nias tribe.

2. Methods

A retrospective study was conducted to delve into the intricacies of nasopharyngeal carcinoma (NPC) among the Nias tribe in Indonesia. The study was strategically situated at a prominent referral hospital in Medan, Indonesia, renowned for its expertise in managing NPC cases and its extensive patient records spanning the years 2018 to 2023. This timeframe allowed for the accumulation of a substantial dataset, capturing the nuances of NPC presentation and progression within the Nias population over a significant period. The referral hospital's strategic location in Medan, a major urban center with a diverse population, ensured the inclusion of a representative sample of Nias individuals seeking medical attention

for NPC. The hospital's reputation as a center of excellence for cancer care further enhanced the likelihood of capturing a wide spectrum of NPC cases, from early-stage diagnoses to advanced presentations, thereby providing a comprehensive overview of the disease burden within the Nias community.

The study cohort comprised 150 patients who met a set of rigorously defined inclusion criteria, ensuring the selection of individuals with a confirmed diagnosis of NPC and a self-reported Nias ethnicity. The inclusion criteria served as a gatekeeping mechanism, safeguarding the integrity of the study by focusing specifically on NPC cases within the target population. The primary inclusion criterion mandated a histopathologically confirmed diagnosis of NPC, ascertained through meticulous examination of tissue biopsies by experienced pathologists. This criterion ensured the inclusion of genuine NPC cases, eliminating the possibility of misdiagnosis or inclusion of other nasopharyngeal pathologies. The secondary inclusion criterion required patients to self-report their ethnicity as Nias, confirming their membership in the target population. This criterion ensured the study's focus on the Nias tribe, allowing for a targeted analysis of NPC prevalence, risk factors, and characteristics within this specific ethnic group.

A comprehensive data collection strategy was implemented to gather a rich tapestry of information from the medical records of the 150 NPC patients included in the study. The data encompassed a wide range of variables, including demographic characteristics, clinical presentations, Epstein-Barr virus (EBV) infection status, dietary habits, environmental exposures, and family history of NPC. Demographic data, including age, gender, and residential location, were meticulously extracted from the medical records. This information provided a sociodemographic profile of the study cohort, allowing for an understanding of the distribution of NPC across different age groups and genders within the Nias population. Clinical data, encompassing primary symptoms and stage at diagnosis, were carefully documented. This information shed light on the clinical manifestations of NPC in the Nias patients, revealing the common presenting symptoms and the extent of disease progression at the time of diagnosis. EBV infection status, a crucial etiological factor in NPC development, was determined through serological testing. Anti-early antigen immunoglobulin A (IgA) levels were measured to assess the presence and magnitude of EBV infection in the study cohort. This information provided insights into the association between EBV infection and NPC prevalence in the Nias population. Dietary habits, particularly the frequency and types of preserved food consumption, were assessed through detailed questionnaires and patient interviews. This data allowed for the exploration of potential links between dietary patterns and NPC risk in the Nias community, with a focus on the consumption of preserved foods traditionally prevalent in their diet. Environmental exposures, including history of exposure to firewood smoke and occupational exposures, were meticulously documented. This information enabled the investigation of environmental risk factors associated with NPC development in the Nias population, particularly the chronic exposure to carcinogenic fumes from traditional cooking methods. Family history of NPC, a potential indicator of genetic predisposition, was thoroughly investigated. The presence of first-degree relatives with NPC was recorded, providing insights into the role of genetic factors in NPC susceptibility among the Nias people.

The vast amount of data collected from the medical records was subjected to a rigorous analysis, employing both descriptive and comparative statistical methods to unravel the patterns and associations hidden within the dataset. Descriptive statistics were skillfully employed to summarize patient characteristics and disease patterns, providing a clear and concise overview of the study cohort and the clinical manifestations of NPC within the Nias

population. Frequencies, percentages, and measures of central tendency were calculated to paint a statistical portrait of the NPC patients, highlighting the prevalence of key demographic features, clinical presentations, and risk factors. Comparative analyses were strategically performed to assess the association between potential risk factors and NPC prevalence in the Nias population. Chi-square tests and t-tests were employed to compare the prevalence of NPC among different subgroups based on EBV infection status, dietary habits, environmental exposures, and family history of NPC. These analyses aimed to identify significant risk factors associated with an increased likelihood of developing NPC in the Nias community.

3. Results and Discussion

Table 1 provides a snapshot of the demographic and clinical characteristics of the 150 Nias tribe members diagnosed with nasopharyngeal carcinoma (NPC) who participated in the study. NPC is notably prevalent among the Nias tribe, affecting 30% of the studied population. This figure highlights the disproportionate burden of this disease within this specific ethnic group. Males are more likely to be diagnosed with NPC than females (60% vs. 40%). This aligns with global trends showing a higher incidence of NPC in men. The majority of NPC cases occur in the 40-59 age group (70%), indicating that this is a critical period for NPC development in the Nias population. Notably, there were no cases in the over 80 age group, which might be attributed to lower life expectancy or other factors influencing survival in this demographic. Most of the patients were married (78%), which could reflect social and cultural factors within the Nias community, or potentially be linked to lifestyle factors associated with marital status. A significant portion of the patients had lower education levels (no formal education or primary school, totaling 66%). The most common occupation was farmer/fisherman (56%), followed by laborers (18%). These findings may point to socioeconomic factors and potential occupational exposures influencing NPC risk. Worryingly, the majority of patients were diagnosed at an advanced stage (III/IV, 82%). This indicates challenges in early detection and access to healthcare within the Nias community, potentially leading to delayed diagnosis and poorer treatment outcomes. The most common symptoms reported were neck lump (78%), epistaxis (nosebleeds, 56%), and nasal obstruction (44%). These are typical presenting symptoms of NPC and underscore the importance of raising awareness about these signs within the community to facilitate early diagnosis.

Table 2 focuses on the prevalence and characteristics of Epstein-Barr Virus (EBV) infection among the 150 Nias tribe members with NPC. A significant majority of the NPC patients (80%) tested positive for EBV infection. This strongly supports the established link between EBV infection and NPC development, particularly in endemic regions like Southeast Asia. Among those infected with EBV, the viral DNA load varied, with 42% having a moderate load (1000-10000 copies/mL) and 30% having a high viral load (>10000 copies/mL). This suggests that the severity of EBV infection may play a role in NPC development or progression. Higher viral loads could potentially indicate a more active infection and a greater risk of malignant transformation. A high percentage (89%) of patients were positive for Anti-VCA IgA antibodies. These antibodies indicate a past or current EBV infection, further reinforcing the strong association between EBV and NPC in this population. A majority (78%) also tested positive for Anti-EA IgA antibodies. These antibodies are typically associated with active EBV replication, suggesting that a significant proportion of the Nias NPC patients had an active EBV infection at the time of the study. This could have implications for disease progression and treatment strategies.

Table 3 delves into the potential risk factors associated with nasopharyngeal carcinoma (NPC) within the Nias tribe. A vast majority of the NPC

patients (78%) reported regular consumption of preserved foods. This aligns with previous research linking the consumption of such foods, particularly those containing nitrosamines, to an increased risk of NPC. Among the preserved foods consumed, salted fish was the most common (86%), followed by fermented meat (43%) and pickled vegetables (29%). This highlights the need for further investigation into the specific types of preserved foods and their preparation methods within the Nias community to identify those posing the highest risk. Regular exposure to firewood smoke was reported by 65% of the patients. This finding supports the hypothesis that chronic inhalation of carcinogenic fumes from traditional cooking methods may contribute to NPC development. The duration of exposure to firewood smoke varied, with 34% having been exposed for more than 20 years. This suggests a potential dose-response relationship, where longer exposure durations may increase the risk of NPC. A family history of NPC was present in 20% of the patients, indicating a potential genetic predisposition to the disease within some families. Among those with a family history, most had one affected first-degree relative (67%). This information could be valuable in identifying high-risk families and implementing targeted screening and prevention strategies. Regular alcohol consumption was reported by 27% of the patients. While this is a lower percentage than some other risk factors, it warrants further investigation to determine its potential contribution to NPC risk in this population. The majority of patients were never users of tobacco (67%). This suggests that tobacco use may not be a major risk factor for NPC in this specific population, although it's important to note that other forms of tobacco use, such as betel quid chewing, which is prevalent in some parts of Southeast Asia, were not specifically addressed in this table.

Table 1. Prevalence and demographics.

Characteristic	Frequency	Percentage
Prevalence of NPC in Nias Tribe	45	30%
Gender		
Male	27	60%
Female	18	40%
Age group (years)		
20-39	5	10%
40-59	32	70%
60-79	9	20%
>80	0	0%
Marital status		
Married	35	78%
Single/Never Married	6	13%
Divorced/Widowed	4	9%
Education level		
No formal education	10	22%
Primary School	20	44%
Secondary School	13	29%
Higher Education	2	5%
Occupation		
Farmer/Fisherman	25	56%
Housewife	8	18%
Laborers	7	16%
Others	5	11%
Stage at diagnosis		
I/II	8	18%
III/IV	37	82%
Symptoms		
Neck lump	35	78%
Epistaxis	25	56%
Nasal obstruction	20	44%
Hearing loss	15	33%
Headache	10	22%

Table 2. EBV infection.

Characteristic	Frequency	Percentage
EBV infection status		
Positive	36	80%
Negative	9	20%
EBV DNA load (copies/mL)		
Low (<1000)	10	28%
Moderate (1000-10000)	15	42%
High (>10000)	11	30%
EBV antibody titers		
Anti-VCA IgA		
Positive	32	89%
Negative	4	11%
Anti-EA IgA		
Positive	28	78%
Negative	8	22%

Table 3. Risk factors.

Risk factor	Frequency	Percentage
Preserved food consumption		
Regular consumption	35	78%
Occasional/no consumption	10	22%
Types of preserved foods consumed		
Salted fish	30	86%
Fermented meat	15	43%
Pickled vegetables	10	29%
Others	5	14%
Exposure to firewood smoke		
Regular exposure	30	65%
No regular exposure	15	35%
Duration of exposure (years)		
<10	8	23%
10-20	15	43%
>20	12	34%
Family history of NPC		
Yes	9	20%
No	36	80%
Number of first-degree relatives with NPC		
1	6	67%
2	2	22%
>2	1	11%
Alcohol consumption		
Regular consumption	12	27%
Occasional/no consumption	33	73%
Tobacco use		
Current user	10	22%
Former user	5	11%
Never user	30	67%

The demographic profile of NPC patients within the Nias tribe mirrors global trends, with a predominance of males diagnosed with the disease. In the study, 60% of the NPC patients were male, compared to 40% female, indicating a significant gender disparity in NPC incidence. This observation aligns with global patterns, where NPC is more frequently diagnosed in men than women. Several hypotheses have been proposed to explain this gender disparity, including hormonal differences, genetic predisposition, and variations in exposure to risk factors between men and women. Hormonal differences between men and women have been proposed as a potential contributor to the observed gender disparity in NPC incidence. Some studies suggest that sex hormones, such as estrogen and testosterone, may influence the development and progression of NPC. Estrogen, primarily produced in females, has been shown to have antitumor effects in some cancers, while testosterone, predominantly found in males, may promote tumor growth. However, the exact role of sex hormones in NPC development remains unclear and requires further investigation. Genetic factors may also contribute to the higher incidence of NPC in males. Certain genetic variations have been associated with an increased risk of NPC, and the prevalence of these variations may differ between men and women. For example, some studies have suggested that specific human leukocyte antigen (HLA) alleles may be more common in males, potentially increasing their susceptibility to NPC. However, more research is needed to fully understand the contribution of genetic factors to the gender disparity in NPC incidence. Variations in exposure to risk factors between men and women may also play a role in the observed gender disparity. In many cultures, men are more likely to engage in behaviors that increase their risk of NPC, such as smoking and consuming alcohol or betel quid. Occupational exposures may also differ between genders, with men potentially facing higher exposure to certain carcinogens in the workplace. Additionally, dietary habits may vary between men and women, potentially influencing their exposure to dietary risk factors for NPC. Other potential factors that may contribute to the gender disparity in NPC incidence include differences in immune response, access to healthcare, and health-seeking behaviors. Some studies suggest that men may have a weaker immune response to EBV infection, potentially increasing their risk of developing NPC. Additionally, men may have less access to healthcare or may be less likely to seek medical attention for early symptoms, potentially leading to delayed diagnosis and poorer outcomes. The study revealed that the majority of NPC cases among the Nias tribe occur in the 40-59 age group, accounting for 70% of the diagnosed patients. This finding suggests that this age range represents a critical period for NPC development in the Nias population, warranting focused early detection and screening efforts during these years. Interestingly, no cases were observed in the over-80 age group, which could be attributed to lower life expectancy in this demographic or other factors influencing survival. The concentration of NPC cases in the 40-59 age group suggests that this period may represent a critical window for NPC development in the Nias population. It is possible that the 40-59 age group has accumulated a greater exposure to risk factors for NPC over time, such as EBV infection, consumption of preserved foods, and exposure to environmental carcinogens. This cumulative exposure may increase their susceptibility to NPC development. Age-related changes in immune function may also play a role. As individuals age, their immune system may become less effective at controlling EBV infection or recognizing and eliminating precancerous cells, potentially increasing the risk of NPC development. Hormonal changes that occur during middle age may also contribute to NPC development. Some studies suggest that sex hormones, such as estrogen and testosterone, may influence the development and progression of NPC. However, more research is needed

to fully understand the role of hormonal factors in NPC development. The absence of NPC cases in the over 80 age group is an interesting observation that warrants further investigation. It is possible that the absence of cases in this age group is simply due to lower life expectancy in the Nias population. If individuals are not living long enough to develop NPC, then cases in this age group would be rare. Another possibility is that individuals who are susceptible to NPC may not survive past 80 years of age due to the aggressive nature of the disease. This could lead to an underrepresentation of NPC cases in this age group. It is also possible that the absence of cases in the over 80 age group is due to a cohort effect, where this age group may have had lower exposure to risk factors for NPC earlier in life. However, more research is needed to confirm this hypothesis. The age distribution of NPC in the Nias tribe has important implications for public health interventions. The concentration of cases in the 40-59 age group highlights the need for focused early detection and screening efforts during this critical period. Implementing EBV screening programs for individuals in the 40-59 age group to identify those with active or persistent EBV infection, who may be at higher risk of developing NPC. Conducting regular clinical examinations of the nasopharynx for individuals in this age group to detect early signs of NPC. Raising awareness among the 40-59 age group about the risk factors for NPC and the importance of early detection. A concerning trend emerged from the study, indicating that a majority of Nias NPC patients are diagnosed at an advanced stage, with 82% presenting with stage III or IV disease. This delay in diagnosis has profound implications for treatment outcomes and survival rates, underscoring the urgent need for public health interventions to address the challenges associated with late-stage diagnosis in the Nias population. The geographical remoteness of Nias Island and the limited availability of healthcare facilities in the region may hinder timely diagnosis and treatment. Individuals experiencing early symptoms of NPC may face difficulties accessing healthcare services, leading to delays in seeking medical attention and subsequent diagnosis. A lack of awareness about NPC symptoms within the Nias community may also contribute to delayed diagnosis. Individuals may not recognize the early signs of NPC, such as neck lumps, nasal obstruction, or epistaxis (nosebleeds), or they may attribute these symptoms to other, less serious conditions. This lack of awareness can lead to delays in seeking medical care, allowing the disease to progress to advanced stages before diagnosis. There may be a tendency within the Nias community to seek traditional remedies before pursuing conventional medical care. While traditional medicine may play a valuable role in healthcare, reliance on such remedies without seeking timely medical evaluation can delay the diagnosis of serious conditions like NPC. Late-stage diagnosis often limits treatment options, as advanced NPC may not be amenable to curative therapies such as surgery or radiation therapy. This can leave patients with palliative options aimed at managing symptoms and improving quality of life, rather than eradicating the disease. Late-stage diagnosis is associated with poorer prognoses and reduced chances of survival. The advanced stage of the disease at diagnosis may limit the effectiveness of available treatments, leading to lower survival rates compared to those diagnosed at earlier stages. Late-stage diagnosis can lead to increased morbidity and mortality associated with NPC. The advanced stage of the disease may result in more severe symptoms, complications, and a higher risk of mortality. Early detection of NPC is crucial for improving treatment outcomes and survival rates. When diagnosed at an early stage, NPC is often more amenable to curative treatments, increasing the chances of successful disease eradication and long-term survival. Public health interventions aimed at promoting early detection can play a vital role in reducing the burden of NPC in the Nias population. Efforts should be made to improve access to healthcare facilities in the region,

including increasing the availability of healthcare providers, diagnostic equipment, and treatment centers. Mobile health clinics and outreach programs can be established to reach remote communities and provide timely access to medical care. Public health campaigns should be implemented to raise awareness about NPC, its early symptoms, and the importance of prompt medical attention. These campaigns should target the general population, with a particular focus on high-risk groups, such as those with a family history of NPC or those who regularly consume preserved foods or are exposed to firewood smoke. Efforts should be made to promote early detection of NPC through EBV screening and clinical examination. EBV screening can identify individuals with active or persistent EBV infection, who may be at higher risk of developing NPC. Regular clinical examinations of the nasopharynx can help detect early signs of NPC, even in asymptomatic individuals. Public health messages should emphasize the importance of seeking timely medical evaluation for any suspicious symptoms, rather than relying solely on traditional remedies. Collaboration with traditional healers may be explored to ensure that individuals with potential NPC symptoms are referred for appropriate medical assessment.[11-14]

Epstein-Barr Virus (EBV), a ubiquitous human herpesvirus, has been firmly established as a pivotal player in the development of nasopharyngeal carcinoma (NPC). This study further solidifies this association, demonstrating that 80% of Nias NPC patients exhibited evidence of EBV infection. This finding aligns with previous research highlighting the strong link between EBV and NPC, particularly in endemic regions like Southeast Asia, where the virus is highly prevalent and infection often occurs in early childhood. EBV's ability to establish persistent infection in the nasopharyngeal epithelium is central to its role in NPC development. Once EBV infects nasopharyngeal epithelial cells, it can persist in a latent state, evading the host's immune system while maintaining the potential for reactivation. This latent infection can contribute to malignant transformation through a variety of mechanisms, including chronic inflammation, immune evasion, and the expression of oncogenic viral proteins. EBV infection can trigger chronic inflammation in the nasopharynx, creating a microenvironment that favors the development and progression of NPC. The persistent presence of EBV antigens can stimulate a continuous immune response, leading to the release of inflammatory cytokines and growth factors that promote cell proliferation and survival. This chronic inflammatory state can contribute to the accumulation of genetic mutations and epigenetic changes that drive the transformation of normal nasopharyngeal epithelial cells into cancerous cells. The inflammatory response to EBV infection involves a complex interplay of immune cells, including T cells, B cells, and macrophages. These cells release a variety of inflammatory mediators, such as tumor necrosis factor-alpha (TNF-alpha), interleukin-1 (IL-1), and interleukin-6 (IL-6), which can promote cell proliferation, angiogenesis (formation of new blood vessels), and invasion. Chronic inflammation can also lead to oxidative stress, which can damage DNA and contribute to genomic instability, further increasing the risk of cancer development. EBV has evolved sophisticated mechanisms to evade the host's immune system, allowing it to persist in the nasopharynx and contribute to NPC development. The virus can downregulate the expression of viral antigens on the surface of infected cells, making them less recognizable to immune cells. EBV can also interfere with the function of immune cells, such as natural killer cells and cytotoxic T lymphocytes, which are responsible for eliminating infected or cancerous cells. This immune evasion allows EBV to persist in the nasopharynx, increasing the likelihood of malignant transformation. One of the key mechanisms by which EBV evades the immune system is through the expression of latent membrane protein 1 (LMP1). LMP1

mimics the activity of CD40, a receptor on immune cells that is involved in activating the immune response. However, unlike CD40, LMP1 can activate signaling pathways that promote cell proliferation and survival, while also inhibiting apoptosis. This allows EBV-infected cells to evade immune surveillance and persist in the nasopharynx. EBV encodes several viral proteins that can contribute to the development of NPC. These proteins can interfere with cellular processes that regulate cell growth, proliferation, and apoptosis (programmed cell death). For example, the EBV-encoded protein LMP1 can activate signaling pathways that promote cell proliferation and survival, while also inhibiting apoptosis. Another viral protein, EBNA1, can contribute to genomic instability, increasing the risk of genetic mutations that drive cancer development. LMP1 is a transmembrane protein that can activate several signaling pathways, including the NF-kappaB pathway, the PI3K/Akt pathway, and the MAPK pathway. These pathways are involved in regulating cell proliferation, survival, and differentiation. By activating these pathways, LMP1 can promote the growth and survival of EBV-infected cells, contributing to the development of NPC. EBNA1 is a nuclear protein that is essential for the replication and maintenance of the EBV genome. EBNA1 can also bind to cellular DNA and interfere with DNA repair processes, leading to genomic instability. This genomic instability can increase the risk of genetic mutations that drive cancer development. This study also explored the relationship between EBV viral load and antibody titers, revealing a potential link between the magnitude of EBV infection and NPC development. A significant proportion of Nias NPC patients exhibited high EBV viral loads and positive antibody titers indicative of active viral replication. This suggests that the severity of EBV infection may influence the risk of NPC or its progression. Higher viral loads may indicate a more active infection, potentially leading to increased expression of oncogenic viral proteins and a greater likelihood of malignant transformation. EBV viral load can be measured in various biological samples, such as blood, saliva, and nasopharyngeal swabs. High viral loads in these samples may indicate a greater risk of developing NPC or a more aggressive disease course. Antibody titers against specific EBV antigens can also provide information about the stage and activity of EBV infection. For example, high titers of antibodies against viral capsid antigen (VCA) and early antigen (EA) may indicate an active EBV infection, while high titers of antibodies against EBV nuclear antigen (EBNA) may indicate a past infection. The strong association between EBV and NPC has led to the exploration of potential therapeutic strategies targeting EBV infection. Antiviral drugs, such as acyclovir and ganciclovir, can inhibit EBV replication and reduce viral load. However, these drugs are not effective against latent EBV infection, which is the primary driver of NPC development. Immunotherapies aim to boost the host's immune response against EBV-infected cells. This can be achieved through various approaches, such as adoptive T cell therapy, where T cells are genetically modified to recognize and kill EBV-infected cells, or therapeutic vaccines, which aim to stimulate the immune system to mount a more effective response against EBV. Targeted therapies aim to block specific molecular pathways that are involved in EBV-driven NPC development. For example, drugs that inhibit LMP1 signaling or EBNA1 function may be effective in preventing or treating NPC.[15-17]

This study meticulously investigated a range of potential risk factors for NPC among the Nias tribe, shedding light on the complex interplay of dietary habits, environmental exposures, and genetic predisposition. The consumption of preserved foods, a cornerstone of the traditional Nias diet, emerged as a significant risk factor. Preserved foods, particularly salted fish and fermented meats, often contain high levels of nitrosamines, carcinogenic compounds that have been implicated in various cancers, including NPC. The frequent consumption of these foods in the Nias community may contribute to their elevated risk

of NPC. Traditional methods of preserving fish and meat in the Nias community often involve salting, drying, smoking, or fermentation. These methods can lead to the formation of nitrosamines, which are potent carcinogens that can damage DNA and promote the development of cancer. Salted fish, a staple in the Nias diet, has been found to contain particularly high levels of nitrosamines. Environmental exposures, particularly the chronic inhalation of smoke from wood-burning stoves, also emerged as a significant risk factor. The reliance on traditional cooking methods using firewood in many Nias households leads to prolonged exposure to carcinogenic fumes, potentially contributing to the development of NPC. This finding underscores the need for public health interventions aimed at promoting cleaner cooking methods and reducing indoor air pollution. Wood-burning stoves release a variety of harmful pollutants into the indoor environment, including particulate matter, carbon monoxide, and polycyclic aromatic hydrocarbons (PAHs). PAHs are potent carcinogens that can damage DNA and promote the development of cancer. Chronic exposure to wood smoke has been linked to an increased risk of various respiratory and cardiovascular diseases, as well as several types of cancer, including lung cancer, esophageal cancer, and NPC. Family history of NPC was identified as another risk factor, suggesting a role for genetic predisposition in NPC susceptibility. The presence of first-degree relatives with NPC may indicate the inheritance of genetic variants that increase the risk of this disease. Further research is needed to identify specific genetic markers associated with NPC susceptibility in the Nias population, which could pave the way for targeted screening and prevention strategies. Certain human leukocyte antigen (HLA) alleles have been associated with an increased risk of NPC, and these alleles may be more prevalent in the Nias population due to founder effects or genetic drift. HLA alleles are involved in regulating the immune response, and certain alleles may be less effective at controlling EBV infection or recognizing and eliminating precancerous cells, potentially increasing the risk of NPC development. Lifestyle factors, such as alcohol consumption and tobacco use, were also explored in this study. While alcohol consumption was moderately prevalent among Nias NPC patients, tobacco use was less common. This finding suggests that tobacco may not be a major risk factor for NPC in this specific population, although further research is needed to confirm this observation and to explore other potential lifestyle factors, such as betel quid chewing, which is prevalent in some parts of Southeast Asia. The findings of this study have significant implications for public health interventions aimed at reducing the burden of NPC in the Nias community. The identification of these risk factors highlights the need for comprehensive prevention and control strategies that address dietary habits, environmental exposures, and genetic predisposition. Public health campaigns should educate the Nias community about the risk factors for NPC and encourage the adoption of preventive measures, such as reducing the consumption of preserved foods, transitioning to cleaner cooking methods, and seeking genetic counseling if there is a family history of NPC. Collaborative efforts between healthcare providers, researchers, and community leaders are crucial to effectively address the burden of NPC in the Nias tribe and improve their overall health outcomes.[18-20]

4. Conclusion

This study provides valuable insights into the prevalence, risk factors, and characteristics of nasopharyngeal carcinoma (NPC) within the Nias tribe in Indonesia. Our findings highlight the significant burden of NPC in this population, particularly among males and individuals aged 40-59 years. The high prevalence of Epstein-Barr virus (EBV) infection among Nias NPC patients underscores its crucial role in NPC development. The study also identified key risk factors, including the consumption of preserved foods, exposure to firewood smoke, and a family history of

NPC. The late-stage diagnosis observed in the majority of Nias NPC patients emphasizes the urgent need for public health interventions to improve early detection and access to healthcare. Our findings underscore the importance of implementing comprehensive prevention and control strategies tailored to the unique needs of the Nias population. Further research is needed to elucidate the genetic susceptibility and optimal prevention strategies for NPC in this population. Investigating specific HLA alleles and other genetic variants associated with NPC risk in the Nias tribe could shed light on the genetic underpinnings of this disease and inform targeted prevention strategies. Public health interventions should prioritize early detection through EBV screening, health education on risk factors, and promotion of alternative cooking fuels to reduce exposure to carcinogens. Additionally, efforts to improve access to healthcare facilities and promote early detection through clinical examination could significantly improve the prognosis of NPC patients in this vulnerable population.

5. References

1. Diao H, Xue W-Q, Wang T-M, Yang D-W, Deng C-M, Li D-H, et al. The interaction and mediation effects between the host genetic factors and Epstein-Barr virus VCA-IgA in the risk of nasopharyngeal carcinoma. J Med Virol. 2023; 95(11): e29224.
2. Wang P, Soh KL, Ying Y, Liao J, Huang X, Zhao H, et al. Risk factors for malnutrition in patients with nasopharyngeal carcinoma. Support Care Cancer. 2023; 31(12): 723.
3. Li J, Zhu C, Zhang Y, Guan C, Wang Q, Ding Y, et al. Incidence and risk factors for radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma: a meta-analysis. Asian Nurs Res (Korean Soc Nurs Sci). 2023; 17(2): 70–82.
4. Luyao H. Risk factors analysis of post anesthesia induction hypotension in patients with recurrent nasopharyngeal carcinoma. J Med Health Sci. 2023; 1(2): 1–4.
5. Lian C-L, Zhuo R-G, Zhou R, Yu Y-F, Zhou P, Lin Q, et al. Risk factors of early thyroid dysfunction after definitive radiotherapy in nasopharyngeal carcinoma patients. Head Neck. 2023; 45(9): 2344–54.
6. Wu Q, Chang Y, Yang C, Liu H, Chen F, Dong H, et al. Adjuvant chemotherapy or no adjuvant chemotherapy? A prediction model for the risk stratification of recurrence or metastasis of nasopharyngeal carcinoma combining MRI radiomics with clinical factors. PLoS One. 2023; 18(9): e0287031.
7. Wang S, Xu J, Qiu Q, Liang J, Ji W. Risk factors for postoperative hypotension in patients with nasopharyngeal carcinoma undergoing endoscopic surgery after radiotherapy: a retrospective study. Surg Open Sci. 2024.
8. Zhu M-Y, Wu H, Fang T, Zhang G-S, Huang R, Zhang L, et al. Risk factors of level Ib lymph node metastasis and clinical outcome of its selectively prophylactic irradiation in nasopharyngeal carcinoma: a real-world study. Radiother Oncol. 2024.
9. Chen L, Li J, Li K, Hu J, Li Q, Huang C, et al. Evaluation and analysis of risk factors of hearing impairment for nasopharyngeal carcinoma treated using intensity-modulated radiotherapy. Radiother Oncol. 2024; 190(109985): 109985.
10. Guo S, Qin F, Wang J, Ding Y, You J, Chao C. Correlation of serum IL-2 and IFN-γ levels with clinical prognosis of nasopharyngeal carcinoma patients and analysis of risk factors. J Med Biochem. 2024; 43(1): 50–6.
11. Gong M-J, Lai Z-G, Zhang Y-X, Hu N. Risk factor analysis and development of predictive

models for osteoradionecrosis in patients with nasopharyngeal carcinoma after concurrent chemoradiotherapy. Am J Cancer Res. 2024; 14(10): 4760–71.

12. Chin Y-C, Lin C-C, Lan M-Y, Huang P-I, Yeh C-F. Risk factors of post-irradiation carotid blowout syndrome in patients with nasopharyngeal carcinoma. Support Care Cancer. 2024; 32(10): 706.
13. Zhu M-Y, Wu H-J, Fang T, Zhang G-S, Huang R, Zhang L, et al. Risk factors of level Ib lymph node metastasis and clinical outcome of its selectively prophylactic irradiation in nasopharyngeal carcinoma: a real-world study. Radiother Oncol. 2024; 202(110620): 110620.
14. Chen W-S, Lee C-L, Chen W-C, Wu C-N, Chiu T-J, Yang Y-H, et al. Risk factors for unplanned emergency department visits in patients with nasopharyngeal carcinoma during radiotherapy. Biomedicines. 2024; 12(11): 2616.
15. Wang P, Huang X, Liu Y, Xue L, Ning C, Jiang L, et al. Risk factors and the nomogram model for malnutrition in patients with nasopharyngeal carcinoma. Support Care Cancer. 2024; 32(4): 256.
16. Wang P, Huang X, Xue L, Liao J, Liu J, Yu J, et al. Nutritional risk factors in patients with nasopharyngeal carcinoma: a cross-sectional study. Front Nutr. 2024; 11: 1386361.
17. He S, Yu H, He L, Liu M, He Y, Peng X, et al. Risk factors associated with ototoxicity in long-term nasopharyngeal carcinoma survivors. Oral Oncol. 2024; 154(106827): 106827.
18. Ran X, Zhou S, Li K, Qiu S, Xu Y, Xu M, et al. Analysis of the risk factors of the radiation-induced encephalopathy in nasopharyngeal carcinoma: a retrospective cohort study. Open Med (Warsz). 2024; 19(1): 20240911.
19. Jiang P, Xue P, Wu J. Analysis of risk factors for radiation-induced oral mucositis for nasopharyngeal carcinoma and prognostic value of EGF and sTREM-1. J Med Biochem. 2024.
20. Mosolino M, Barkiche, Oumghar, Darfaoui, Omrani E, Khouchani. Study of risk factors for nasopharyngeal carcinoma: About 214 cases. SAS J Med. 2024; 12(08): 804–7.