



Clinicopathological Characteristics of Nasopharyngeal Carcinoma Patients Based on WHO Classification at Dr. Mohammad Hoesin General Hospital Palembang 2020–2024

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ABSTRACT

Introduction. Nasopharyngeal carcinoma is one of the major head and neck cancers with a heavy burden of illness in Southeast Asia, especially in Indonesia. The World Health Organization (WHO) recognizes the three main types of nasopharyngeal carcinoma histopathologically as keratinizing squamous cell carcinoma, non-keratinizing squamous cell carcinoma, and basaloid squamous cell carcinoma. This article describes the clinicopathological features of nasopharyngeal carcinoma patients diagnosed at Dr. Mohammad Hoesin General Hospital (RSMH), Palembang, from 2020 to 2024. **Methods.** A retrospective descriptive observational study was conducted using total sampling method. Clinical and histopathological information was obtained from medical records and pathology archives from patients diagnosed from January 2020 through December 2024. Variables including age, sex, smoking history, clinical stage, operative procedure, and WHO histopathological classification were studied. **Results.** Out of the 138 cases, 56 were diagnosed in 2024 alone, the highest annual number. Majority of nasopharyngeal carcinoma patients were males (71%), less than 50 years old (50.7%), smokers (63%), and primarily presented with stage III (53.6%) disease. Biopsy dominated as the operative procedure with majority (79.7%) of the cases. Non-keratinizing squamous cell carcinoma was the main tumor type with the differentiated subtype being the most common histopathological identification. **Conclusion.** These results indicate that nasopharyngeal carcinoma at RSMH mostly involved male patients who had a history of smoking, most of them were diagnosed at an advanced clinical stage, with non-keratinizing squamous cell carcinoma subtype being the most common histological type.

1. Introduction

Nasopharyngeal carcinoma (NPC) is an epithelial malignancy arising from the squamous epithelium of the nasopharynx, with the most common site of origin being the fossa of Rosenmüller.^{1,2} Despite being a relatively rare tumor worldwide, NPC is endemic in East and Southeast Asia as well as parts of North Africa, regions where it accounts for public health problems.^{3,4} According to GLOBOCAN 2022, NPC is the 23rd most common cancer worldwide. Among countries in the world, Indonesia recorded the highest number of NPC cases with an estimated 13,177 new cases annually and a significant male predominance.³

NPC development is a complex process resulting from the interplay of various factors including Epstein-Barr virus (EBV) infection, genetic factors, environmental agents, and lifestyle elements. A substantial body of evidence indicates that tobacco smoking serves as a determinant risk factor for NPC especially for the non-keratinizing histologic subtype,

whereas ingestion of nitrosamine-rich preserved foodstuffs is considered responsible for exposure in endemic area.^{4,5}

The WHO Classification of Head and Neck Tumours recognizes three main histopathological types of NPC: keratinizing squamous cell carcinoma (KSCC), non-keratinizing squamous cell carcinoma (NKSCC), and basaloid squamous cell carcinoma. NKSCC is subdivided into differentiated and undifferentiated categories. This type is the most common histologic form found in populations living in HPV-endemic regions and is strongly linked to EBV infection.^{2,5}

In addition to histopathological tumor typing, age, sex, history of smoking, and stage of disease at presentation are clinicopathological factors that are regarded as crucial parameters for the therapeutic decision-making and prognostication of the patient.

The clinical stage based on the 8th edition of the American Joint Committee on Cancer (AJCC) TNM

staging system is currently the most widely used prognostic factor for patients with nasopharyngeal carcinoma (NPC).⁴ Obtaining an early diagnosis is warranted due to the fact that advanced-stage patients generally have a worse clinical outcome even with the continuous advancement of radiotherapy and systemic treatment.^{6,7}

Even though the incidence of NPC is high in Indonesia, clinicopathological findings at regional level are still very few, especially in South Sumatra. Most studies published about this area are from major referral centers outside Sumatra or mostly focused on treatment outcome and prognosis and clinicopathological profile of patients has been rarely described.^{1,8,9} This paper presents a study to provide more comprehensive data on the clinicopathological features of NPC patients at RSMH, which is the main tertiary referral hospital in South Sumatra. This type of local epidemiological data is of great significance as patient characters may be influenced by demographic factors, environment, and health care factors, resulting in variations in disease presentation and management.

The main goal of this research was to delineate the clinicopathological features of patients with nasopharyngeal carcinoma at RSMH, Palembang, Indonesia, over the period of 2020-2024. Besides offering essential epidemiological data for the region, the findings might also help in enhancing early detection and timely diagnosis, as well as lay the groundwork for future investigations into NPC in Indonesia.

2. Methods

This retrospective descriptive study was undertaken in the Department of Anatomical Pathology, Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. The study participants were all patients diagnosed histopathologically with nasopharyngeal carcinoma (NPC) from January 1, 2020, to December 31, 2024. A total sampling method was applied. Inclusion criteria were basically availability of complete clinicopathological data: age, sex, clinical stage, smoking history, method of specimen collection, and histopathological diagnosis. Cases with incomplete medical records were excluded.

The clinicopathological data were extracted from patient medical records and histopathology report archives. Tumors were classified as per the Classification of Head and Neck Tumours by WHO, 5th Edition. Clinical staging was performed by referring

to the AJCC (8th Edition) TNM Staging System. Age at diagnosis was divided into <50 years and ≥50 years groups for descriptive analysis based on earlier epidemiological studies. Smoking history was considered positive if patient had smoked cigarettes at any time prior to diagnosis. Statistical analysis of the collected data was carried out using IBM SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA). Data for categorical variables were presented as counts and percentages.

An Ethical Exemption certificate was obtained from the Health Research Ethics Committee of Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia in relation to this study (Reference No. DP.04.03/D.XVIII.06.08/ETIK/313/2025). This study had been led to obtain the exemption from health research ethics as the source of data came from anonymized medical records and archived histopathological specimens. The data presented in this article was collected retrospectively from medical records and pathology archives.

3. Results

Distribution of Nasopharyngeal Carcinoma Patients by Year at RSMH, Palembang, 2020–2024

The total number of patients with NPC in this study was 138. The trend in annual incidence of NPC during the study period has shown a continuous increase till the last year.

The distribution of NPC patients in Table 1 shows the distribution by year during the study period. The number of cases identified shows an upward trend from year to year. In 2020, there were 8 cases (5.7%), which increased to 14 cases (10.14%) in 2021 and 25 cases (18.11%) in 2022. An increase in the number of cases was again observed in 2023 with 35 cases (25.36%), and reached the highest number in 2024, namely 56 cases (40.57%).

Distribution of Nasopharyngeal Carcinoma Patients by Age, Sex, Operative Procedure, Clinical Stage, and Smoking History at RSMH, Palembang

Nasopharyngeal carcinoma (NPC) is an uncommon malignancy worldwide, with an annual incidence of fewer than 1 case per 100,000 population. In the present study, 138 patients with NPC were identified at RSMH, Palembang, between 2020 and 2024. The clinicopathological characteristics of these patients are summarized in Table 2.

Table 1. The annual distribution of NPC cases at RSMH, Palembang.

Year	Cases	Distribution (%)
2020	8	5.7
2021	14	10.14
2022	25	18.11
2023	35	25.36
2024	56	40.57

Table 2. Clinicopathological characteristics of NPC patients

Characteristic	n	%
Age <50 years	70	50.7
Age ≥50 years	68	49.3
Male	98	71
Female	40	29
Smoking history	87	63
No smoking history	51	37
Stage I	23	16.6
Stage II	33	23.9
Stage III	74	53.6
Stage IV	8	5.7
Biopsy	110	79.7
Resection	28	20.3

Table 3. Histopathological distribution based on WHO classification

Histopathological subtype	n	%
Keratinizing squamous cell carcinoma	1	0.7
Non-keratinizing squamous cell carcinoma differentiated subtype	136	98,6
Basaloid squamous cell carcinoma	1	0.7

Table 4. Clinicopathological Characteristics of Nasopharyngeal Carcinoma Patients at RSMH Palembang During 2020–2024

Variable	Total	Diagnosis					
		Keratinizing Squamous Cell Carcinoma			Non-Keratinizing Squamous Cell Carcinoma		Basaloid Squamous Cell Carcinoma
		(n = 1)			(n = 136)		(n = 1)
		WD	MD	PD	Differentiated	Undifferentiated	
Age							
<50 years	70	0 0%	0 0%	0 0%	39 -55,70%	31 -44,28%	0 0%
≥50 years	68	1 -1,47%	0 0%	0 0%	40 -57,14%	26 -38,23%	1 -1,47%
Sex							
Female	40	1 -2,50%	0 0%	0 0%	26 -65%	12 -30%	1 -2,50%
Male	98	0 0%	0 0%	0 0%	53 -54,08%	45 -45,91%	0 0%
Smoking history							
Non-smoker	51	1 -1,96%	0 0%	0 0%	34 -66,60%	15 -29,41%	1 -1,96%
Smoker	87	0 0%	0 0%	0 0%	45 -51,72%	42 -48,27%	0 0%
Clinical stage							
Stage I	23	0 0%	0 0%	0 0%	18 -78,26%	5 -21,73%	0 0%
Stage II	33	0 0%	0 0%	0 0%	18 -54,54%	15 -45,45%	0 0%
Stage III	74	1 -1,35%	0 0%	0 0%	38 -51,35%	34 -45,94%	1 -1,35%
Stage IV	8	0 0%	0 0%	0 0%	5 -62,50%	3 -37,50%	0 0%
Operative procedure							
Biopsy	110	1 -0,90%	0 0%	0 0%	64 -58,18%	45 -40,90%	0 0%
Resection	28	0 0%	0 0%	0 0%	15 -53,57%	12 -42,85%	1 -3,50%

*Note: WD: well differentiated, MD: moderately differentiated, PD: poorly differentiated

The clinicopathological characteristics of NPC patients at RSMH, Palembang, 70 patients (50.7%) were younger than 50 years, 98 patients (71%) were male, and 87 patients (63%) had a history of smoking.

Most patients presented with stage III disease (74 patients; 53.6%), while biopsy was the most frequently performed procedure, accounting for 110 cases (79.7%).

Distribution of Nasopharyngeal Carcinoma Patients by Histopathological Type at RSMH, Palembang

The histopathological spectrum of nasopharyngeal carcinoma (NPC) comprises three major types recognized by the World Health Organization (WHO): KSCC, NKSCC, and basaloid squamous cell carcinoma.² The histopathological distribution in this study is presented in Table 3.

Non-keratinizing squamous cell carcinoma (NKSCC) was the most histopathological type in this study, accounting for 136 of 138 cases (98.6%). Among these, the differentiated subtype was more frequent, identified in 79 cases (57.3%), whereas the undifferentiated subtype was observed in 57 cases (41.3%). Keratinizing squamous cell carcinoma (KSCC) was identified in only one case (0.7%), which was well differentiated, with no moderately or poorly differentiated cases observed. Similarly, basaloid squamous cell carcinoma was rare, occurring in only one case (0.7%).

Clinicopathological Characteristics of NPC Patients at RSMH Palembang

The clinicopathological characteristics of NPC patients at RSMH Palembang during 2020–2024 showed variations based on several clinical factors, including age, sex, smoking history, clinical stage, and operative procedure, will presented in Table 4. Patients with NPC according to age distribution, most of patients were <50 years old (70 patients, 50.7%), while 68 patients (49.3%) were ≥50 years old. The most common histopathological type was the differentiated subtype of NKSCC, with 39 cases in patients under 50 years of age (28.6%) and 40 cases in patients aged 50 years or older (29.4%). The undifferentiated subtype of NKSCC was found in 31 cases in patients under 50 years old (22.8%) and 26 cases in patients aged 50 years or older (19.2%). Keratinizing squamous cell carcinoma was found in patients aged ≥50 years in the well-differentiated subtype, while no cases of the moderately differentiated and poorly differentiated subtypes were found in this study. Pearson's Chi-square analysis showed no statistically significant association between smoking history and histopathological subtype ($p = 0.177$). Likewise, no statistically significant association was observed between clinical stage and histopathological subtype ($p = 0.941$).

4. Discussion

Distribution of NPC Patients per Year at RSMH Palembang During the 2020–2024 Period

We have found an increasing trend in the study results regarding the annual number of nasopharyngeal carcinoma (NPC) patients at RSMH. The number of patients grew from 8 cases (5.8%) in 2020 to 56 cases (40.6%) in 2024. This rising pattern, however, should be considered as an increase in hospital-registered cases rather than in the

population incidence of NPC, as this was a single-center retrospective study.

Indonesia is among the countries with a substantial burden of nasopharyngeal carcinoma (NPC), where the disease remains an important head and neck malignancy. The persistently high occurrence of NPC in endemic populations is thought to result from complex interactions among Epstein-Barr virus (EBV) infection, genetic predisposition, tobacco smoking, and environmental exposures, particularly dietary intake of nitrosamine-containing foods. The interplay of these viral, genetic, lifestyle, and environmental factors may contribute to the continued burden of NPC observed in Indonesia and other endemic regions.¹⁰

A decrease in the number of the 2020 cases was attributed to the Covid-19 pandemic. In the pandemic period, some patients were unable to make it to healthcare services resulting in delayed referrals and cases being neglected due to patients' reluctances. Therefore, a significant reduction in the number of head and neck cancers was observed in spite of the bias of this kind.¹¹

After COVID-19 restrictions were lifted, the number of newly diagnosed NPC cases gradually rose from 2021 to 2024. This trend probably indicates the restoration of healthcare services, greater capacity to diagnosis, and the detection of cases that had been hidden during the pandemic. These results show that NPC is still a major clinical problem in the biggest tertiary referral hospital in South Sumatra and that it is urgent to reinforce early detection and prompt diagnosis in this province.

Frequency Distribution of NPC Patients at RSMH Palembang Based on Age, Sex, Operative Procedure, Clinical Stage, and Smoking History.

The distribution of age in NPC patients was approximately equal with 70 patients (50.7%) aged <50 years, and 68 patients (49.3%) aged ≥50 years. These findings indicate that NPC affects both younger and older adults, although the disease is generally diagnosed during middle adulthood. Previous studies have reported similar findings, with a median age at diagnosis of 52 years (range 32–77 years) in patients with de novo metastatic NPC and 47.3 years (range 9–83 years) in a large retrospective cohort.^{6,9} The relatively high proportion of patients younger than 50 years observed in this study may reflect the endemic nature of NPC in Southeast Asia, where early exposure to EBV infection, genetic susceptibility, and environmental factors contribute to disease development at a younger age than that reported in non-endemic populations.

Male patients comprised 71% of the total number of reported cases, resulting in a male-to-female ratio of around 2.5:1. This result aligned with studies conducted previously in China which also demonstrated a distinct male prevalence.^{6,9} The higher incidence of NPC among men is likely

multifactorial. Men are more frequently exposed to established risk factors such as cigarette smoking, occupational carcinogens, and alcohol consumption, all of which may interact with EBV infection to promote nasopharyngeal carcinogenesis. In addition, sex hormones may contribute to this difference. Experimental studies suggest that estrogen may exert a protective effect against tumor development, whereas androgen signaling has been associated with tumor progression and poorer oncological outcomes.^{12,13}

A history of tobacco smoking was noticed in 63% of the patients which again confirmed the role of cigarette smoking as one of the main modifiable risk factors for NPC. Similar findings have been reported in an Indonesian study from Makassar, where more than half of NPC patients had a smoking history.¹⁴ Tobacco smoke contains numerous carcinogenic compounds, particularly tobacco-specific nitrosamines, which induce DNA damage, oxidative stress, and chronic inflammation of the nasopharyngeal epithelium. Persistent exposure to these carcinogens may promote genetic and epigenetic alterations that facilitate malignant transformation, especially in individuals with latent EBV infection.^{7,14}

More than half of the patients (53.6%) were diagnosed with stage III disease, indicating that most patients presented with locally advanced NPC. Similar observations have been reported in many endemic countries, where delayed diagnosis remains a major challenge. NPC often develops in an anatomically concealed location, and its early manifestations including nasal obstruction, epistaxis, hearing impairment, or cervical lymphadenopathy are frequently nonspecific and easily mistaken for benign upper respiratory tract conditions. Consequently, many patients seek medical attention only after symptoms become more severe. Limited public awareness, delayed referral, and restricted access to specialized diagnostic services may also contribute to the predominance of advanced-stage disease at diagnosis.⁹

Biopsy has been the most common tissue collection method which constitutes 79.7% of the cases. This observation reflects clinical practice where primary NPC surgical resection is hardly ever carried out due to the nasopharynx's complicated location and its close proximity to the cranial nerves, skull base, and main blood vessels. Endoscopic biopsy is an assurance for a histopathological diagnosis based on which treatment is planned. Radiotherapy, both alone and in combination with chemotherapy, remains the standard of care for NPC and is, therefore, surgery is generally limited to diagnostic biopsy.⁴

Frequency Distribution of NPC Patients at RSMH Palembang Based on Histopathological Findings

The present study showed that NKSCC was the predominant histopathological type, accounting for

98.6% of all NPC cases. Within this category, the differentiated subtype was more common than the undifferentiated subtype. In contrast, KSCC and basaloid squamous cell carcinoma were each identified only in a single case, highlighting their rarity in this cohort.

The predominance of NKSCC is consistent with previous studies conducted in endemic regions, including China and Southeast Asia, where this subtype represents the vast majority of NPC cases. A large retrospective study from Shaanxi, China, reported that only 0.4% of patients had KSCC, whereas more than 99% were classified as NKSCC.^{5,9} These findings support the well-established epidemiological pattern of NPC in endemic populations.

The predominance of NKSCC is closely associated with latent Epstein-Barr virus (EBV) infection, which plays a central role in NPC carcinogenesis. EBV contributes to malignant transformation through the expression of viral oncogenes, promotion of genomic instability, and modulation of the host immune response. In endemic populations, the interaction between EBV infection, genetic susceptibility, and environmental exposures including dietary factors and cigarette smoking creates a favorable environment for the development of NKSCC.^{5,9}

The differentiated subtype was more frequently observed than the undifferentiated subtype in the present study. This distribution differs from several studies conducted in highly endemic regions, where the undifferentiated subtype generally predominates. The discrepancy may be related to differences in patient characteristics, regional epidemiological patterns, referral systems, or histopathological interpretation. In addition, the relatively limited sample size and single-center design may have influenced the observed subtype distribution.

The extremely low frequency of KSCC is also consistent with previous reports indicating that this subtype is uncommon in endemic Asian populations but occurs more frequently in Western countries, where it has been associated with cigarette smoking and is less strongly linked to EBV infection. Basaloid squamous cell carcinoma is another rare histological subtype of NPC and is generally associated with more aggressive biological behavior and a poorer prognosis than conventional NPC.^{5,9}

Clinicopathological Characteristics of NPC Patients at RSMH Palembang

The clinicopathological characteristics of patients with nasopharyngeal carcinoma (NPC) according to histopathological subtype are presented in Table 4. Generally, NKSCC was the predominant histopathological type in this study, particularly the differentiated subtype, whereas KSCC and basaloid squamous cell carcinoma were identified only in one cases. This distribution is consistent with the epidemiological pattern of NPC in endemic regions,

where NKSCC represents the vast majority of cases and is closely associated with Epstein-Barr virus (EBV) infection.

Based on age, both differentiated and undifferentiated NKSCC were observed in patients younger than 50 years as well as those aged 50 years or older, indicating that these histopathological subtypes may occur throughout adulthood. This finding is in agreement with previous studies reporting that NPC affects a broad age range in endemic populations. The occurrence of NPC across different age groups is thought to reflect the combined influence of EBV infection, genetic susceptibility, and environmental exposures rather than age itself.⁶

Male patients predominated in both differentiated and undifferentiated NKSCC subtypes. This observation is consistent with previous reports demonstrating a male-to-female ratio of approximately 2–3:1 among NPC patients. The higher frequency of NPC in men has been attributed to greater exposure to environmental and lifestyle-related risk factors, including cigarette smoking, occupational carcinogens, and alcohol consumption. In addition, hormonal differences have been proposed as contributing factors, with estrogen potentially exerting a protective effect against tumor development.^{6,15}

Most patients had a history of cigarette smoking, and both differentiated and undifferentiated NKSCC were commonly identified among smokers. Although smoking is recognized as an important risk factor for NPC, the distribution of histopathological subtypes among smokers in this study appeared relatively similar. Cigarette smoke contains numerous carcinogenic compounds capable of inducing DNA damage, oxidative stress, and chronic inflammation of the nasopharyngeal epithelium. These mechanisms are considered to increase the overall risk of NPC development, while the histopathological subtype is likely influenced by additional factors, particularly latent EBV infection and host genetic susceptibility.¹⁴

The majority of patients were diagnosed with stage III disease, regardless of histopathological subtype. This finding suggests that differentiated and undifferentiated NKSCC share a similar pattern of clinical presentation at diagnosis. The predominance of advanced-stage disease is more likely related to delayed diagnosis because early symptoms of NPC are often nonspecific and easily mistaken for benign upper respiratory tract disorders. Limited public awareness and delayed referral to specialized healthcare facilities may further contribute to late-stage presentation.

Biopsy was the most frequently performed specimen collection technique across all histopathological subtypes. This finding reflects current clinical practice, as biopsy remains the standard diagnostic procedure for obtaining tissue confirmation before definitive treatment. Owing to

the anatomical location of the nasopharynx and the high radiosensitivity of NPC, surgery is generally not considered the primary treatment modality and is usually limited to diagnostic biopsy or selected recurrent or persistent cases.^{4,16}

Overall, the findings of this study demonstrate that NKSCC, particularly the differentiated subtype, was the predominant histopathological type among NPC patients treated at RSMH, Palembang. Patients were predominantly male, younger than 50 years, had a history of smoking, presented at stage III disease, and most commonly underwent biopsy for histopathological diagnosis. These findings further support the characteristic clinicopathological profile of NPC in endemic populations, where EBV-associated NKSCC represents the dominant histological subtype.

5. Conclusion

This study provides a comprehensive overview of the clinicopathological characteristics of patients with nasopharyngeal carcinoma (NPC) treated at RSMH, Palembang, between 2020 and 2024. Most patients were males younger than 50 years with a history of smoking and were diagnosed at stage III disease. Histopathologically, NKSCC, particularly the differentiated subtype, was the most common type observed.

The increasing number of diagnosed cases after the COVID-19 pandemic and the predominance of advanced-stage presentation emphasize that nasopharyngeal carcinoma remains an important health problem in South Sumatra. These findings provide valuable baseline data for the region and may support the development of strategies aimed at improving early detection, timely diagnosis, and patient management. Further multicenter studies incorporating Epstein-Barr virus status and other environmental and genetic risk factors are warranted to better understand the epidemiological and clinicopathological characteristics of nasopharyngeal carcinoma in Indonesia.

6. Author Contribution

F.A. carried out data collection, data analysis, literature review, and manuscript writing. S. had the original idea for the project and supervised it, she also contributed to study design, gave the manuscript critical intellectual content revisions, and approved the final version. Both authors have read and consented to the final manuscript.

7. Acknowledgements

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