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Epidemiological and Clinical Profile of Nasopharyngeal Carcinoma in Indonesia: A Nationwide Descriptive Study

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Abstract

Background: Nasopharyngeal carcinoma (NPC) is now the fifth leading cause of cancer death in Indonesia, with most cases diagnosed at advanced stages due to nonspecific early symptoms. This study describes the epidemiological, clinical, and pathological profiles of NPC in Indonesia.

Methods and Results: This descriptive study used data from the NPC-Indonesia registry between January 2019 and December 2022. It included newly diagnosed NPC patients who visited ENT outpatient clinics and underwent treatment—either single or multimodality regimens—at 16 participating hospitals. The data was collected from the NPC-Indonesia registry data system. Whole data was extracted and sorted into excel sheet, only those cases with confirmed diagnosis and treatment of cancer were analyzed according to age, sex, home province, chief complaint, histopathology subtypes, staging, treatment modality, response to therapy, and distant metastasis. A total of 545 patients 67.7% male and 32.3% female were recorded. The average age was 48 years, ranging from 4 to 80. The most common chief complaint was a neck lump. Most patients were from West Java and were presented with advanced-stage disease. The majority had WHO type 3 histology.

Conclusion: Nasopharyngeal carcinoma in Indonesia commonly presents at an advanced stage, likely due to nonspecific early symptoms. This study is the first large-scale research providing comprehensive NPC data in Indonesia, emphasizing the need for improved early detection and public health awareness.(**International Journal of Biomedicine. 2025;15(3):517-522.**)

Keywords: nasopharyngeal carcinoma • epidemiology • histopathology • metastasis

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Introduction

Nasopharyngeal carcinoma (NPC) is distinctive among head and neck malignancies based on several aspects, such as its epidemiology, clinical manifestations, molecular biomarkers, carcinogenic predisposing factors, as well as prognostic variables. NPC induces a dismal prognosis and becomes endemic in some parts of the globe, particularly Southeast Asia. The mean prevalence of NPC cases in Indonesia reaches 6.2/100,000, with 13,000 additional cases reported each year.[1] Nasopharyngeal carcinoma remains a global burden. In 2019, the incidence of NPC reached 176,500 cases globally; meanwhile, Indonesia achieved the third highest mortality rate due to NPC, with 3,220 deaths in 2019 only.[2] In contrast to other types of cancers, NPC has a unique distribution pattern. In 2018, 129,000 new cases and 73,000 mortality cases were announced globally. The geographic distribution of these cases was highly uneven. Over 70% of additional cases were detected in East and Southeast Asia, while in most other regions, the age-standardized incidence of NPC in both males and females was under 1 per 100,000 person-years. Based on investigations on most populations, the incidence of NPC was two to three times higher in men than in women.[2,3] Comparable to other chronic diseases, NPC presents numerous challenges beyond just treatment. Patients with NPC frequently experience one or multiple symptoms affecting the nasal area, ears, cranial nerves, neck lymph nodes, and distant metastases. It is difficult to establish the early stage of this carcinoma due to the secluded emergence of the nasopharynx itself, with indistinct clinical complaints. Many cases that were then referred to the hospital were already presented at an advanced stage, primarily because of the inadequate awareness of the patient and the doctors at the primary care level. The clinical stage was assessed using the TNM classification released in the American Joint Committee of Cancer (AJCC) 8th edition.[2,4]

It is essential to know the description of nasopharyngeal cancer patients among the Indonesian population, so that it becomes a reference for early diagnosis to provide appropriate treatment to those patients.

Materials and Methods

A retrospective analysis was carried out on all NPC cases that presented to the 16 affiliated hospitals of this research (Dr. Soetomo Regional Hospital, Hasan Sadikin Hospital, M. Djamil Hospital, Pelamonia Hospital, Persahabatan Hospital, Saiful Anwar Hospital, Unhas Hospital, Wahidin Soedirohusodo Hospital, Dharmais Cancer Hospital, Gatot Soebroto Army Hospital, AW Sjahranie Regional Hospital, Arifin Ahmad Regional Hospital, Provinsi NTB Hospital, Dr. Sardjito Public Hospital, Sanglah Public Hospital, and Ciptomangunkusumo National Hospital) from January 2019 to December 2022, who had completed the therapy course and undergone response examination. The data was collected from the NPC-Indonesia registry data system. Whole data was extracted and sorted into excel sheet, only those cases with confirmed diagnosis and treatment of cancer were analyzed according to age, sex, home province, chief complaint, histopathology subtypes, staging, treatment modality, response to therapy, and distant metastasis.

As many as 895 cases were extracted from the database collection, 350 of which were rejected due to incomplete histopathology reports, treatment information, and response therapy data. Therefore, the final data included reached 545 cases. Details of the number of patients from each hospital are outlined in Figure 1.

Statistical analysis was performed using SPSS software, version 16 (SPSS Inc., Chicago, USA).

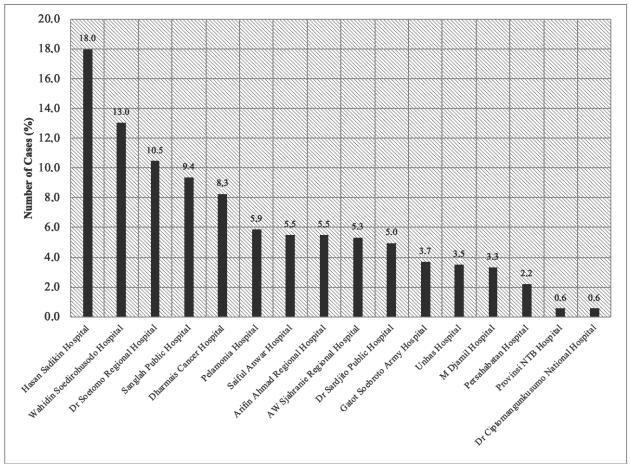

Figure 1. *Distribution of NPC cases by hospitals.*

Results

Male patients were more predominant than female ones, at a ratio of 2.1:1, with 369(67.7%) male subjects and 176(32.3%) female subjects. In terms of age, patients were divided into several age groups with a 10-year gap for each group. Most patients were found in the age group of 50-60 – 166(30.5%), followed by the age group of 40-50 – 15(28.4%), the age group of 30-40 – 84(15.4%), the age group of 60-70 – 78(14.3%), the age group of 20-30 – 32(5.9%), the age group of 70-80 – 19(3.5%), the age group of 10-20 – 9(1.7%), and only 2(0.4%) patients were in the age group under 10. Overall, the mean age was 48 years, with the youngest being 4 and the oldest being 80 years.

Most cases of NPC were from West Java (126/23.1%) cases, followed by South Sulawesi (92/16.9%), and East Java (85/15.6%), Bali (50/9.2%), Riau (33/6.1%), East Kalimantan (30/5.5%), DKI Jakarta (21/ 3.9%), Banten (18/3.3%), DIY (18/3. %), South Sumatra (13/2.4%), Central Java (11/2%), Central Sulawesi (10/1.8%), Southeast Sulawesi (10/1.8%), Jambi (4/0.7%), West Sulawesi (4/0.7%), Lampung (3/0.6%, West Nusa Tenggara (NTB) (3/0.6%), North Maluku (2/0.4%), and Papua (2/0.4%). The provinces with the lowest cases of NPC include Bengkulu, Gorontalo, West Kalimantan, Central Kalimantan, North Kalimantan, Bangka Belitung, East Nusa Tenggara (NTT), West Papua, South Sumatra, and North Sumatra, each of which had only one case (0.2%) (Figure 2).

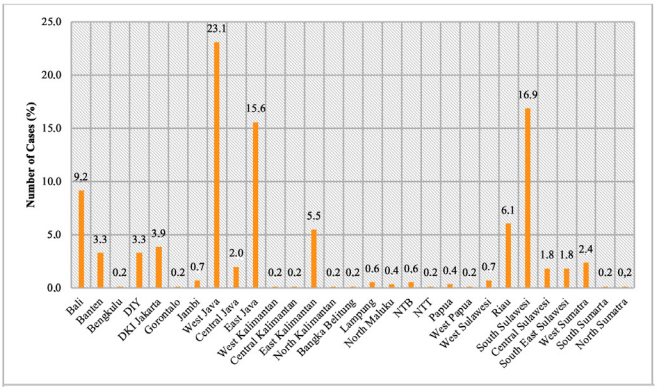

Figure 2. *Distribution of NPC cases by home provinces.*

Most cases emerged with a neck lump, accounting for up to 53.9% of all cases. The second most common complaint was nasal congestion, which accounted for 16.9% of cases. Other symptoms contributed less than 10% each, such as nosebleeds (8.3%), blood-stained discharge (3.9%), tinnitus (5.7%), headaches (4.2%), double vision (2%), and chronic colds (2%), and impaired vision (1.3%); the rest of the complaints were less than 1% each, including neck pain (0.6%) and difficulty swallowing (0.4%). Cheek lump, sore throat, dyspnea, and dysphonia were 0.2% each (Figure 3).

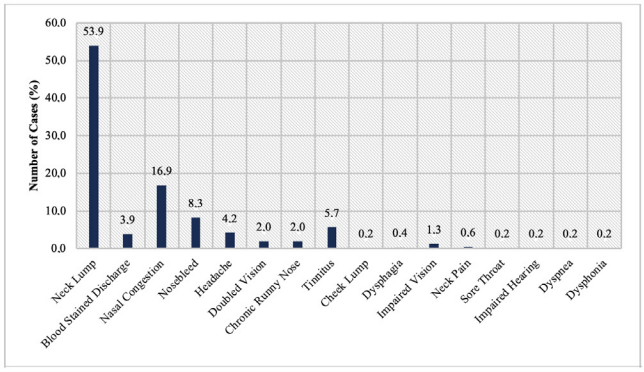

Figure 3. *Complaints and symptoms.*

Histopathological subtype analysis revealed that 378(69.4%) cases were WHO type 3, 155(28.4%) were WHO type 2, and 12(2.2%) were WHO type 1. Notably, 43.5% of patients presented at stage IVA, followed by stage III (27.5%) and stage IVB (16.9%); 9.4% of patients were stage II and only 2.8% stage I.

Based on the tumor extension, most cases found were T4 (33%) characterized by the tumor extension intracranially, spread to the cranial nerves, orbit, hypopharynx, parotid glad and/or broad soft tissue, surpassing the lateral pterygoid muscle outer surface. Those cases were followed by T3 (30.5%) characterized by tumor spread to bony structures, including skull base, pterygoid, cervical vertebrae, and the paranasal sinuses. T1 (10.6%) and T2 (25.9%) were the two least common cases in this study. The N classification for the spreading to surrounding lymph nodes mainly consists of N2 (36%), followed by N3 (29.4%), N1 (21.2%), and N0 (13.6%). The number of M0 cases, where there is no distant metastasis, constituted most cases (83.1%).

The data extracted showed that 92 patients had stage IVB and experienced remote metastases to other organs, such as the lung, bones, liver, and brain. Among all NPC stage IVB patients, the highest incidence of distant metastases was bone (42/45.6%), followed by lung (22/23.9%), liver (17/18.5%), and brain (1/1.1%). This study also found distant metastases to multiple organs, namely 5(5.4%) patients for bone and lung, 4(4.3%) patients for bone and liver, and 1(1.1%) patient for bone and brain (Figure 4).

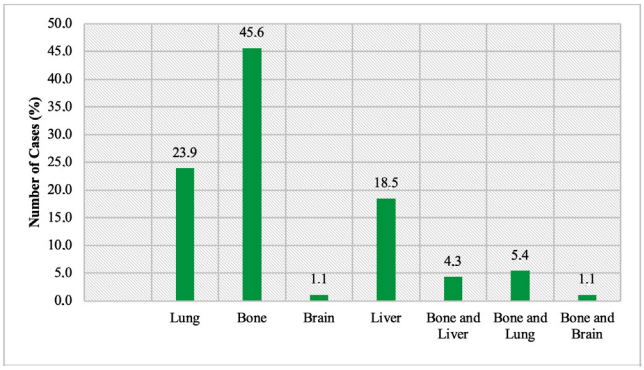

Figure 4. *Distant metastases.*

Discussion

Nasopharyngeal carcinoma has become endemic in Southeast Asia. Indonesia has limited clinical evidence related to this malignancy, as it is the most populous country in Southeast Asia. A review of national NPC registry data using a retrospective method was performed to assess the epidemiological profile of 545 patients with recently diagnosed NPC undergoing both completed and uncompleted treatments due to mortality during or after completing treatment. Our study provided patient demographics in terms of age, male-to-female ratio, and WHO cancer subtypes, which are consistent with the typical nasopharyngeal cancer patient demographics in Southeast Asia.

An epidemiological study of NPC cases in Southeast Asia conducted by Lao et al.[6] reported 34,681 new NPC cases in total, with 25,895(74.7%) cases comprised of male patients and 8,786 of female patients: a ratio of 2.91:1. The study also showed that among the countries of Southeast Asia, the three highest incidences of NPC were identified in Indonesia with 17,992 cases, Vietnam with 6,212 cases, and Philippines with 2,913 cases with the same order of mortality of 11,204 cases, 4,232 cases and 1,899 cases, respectively. This was possibly due to the environmental influence, with relatively harmful predisposing factors associated with development of carcinogenesis, and a lack of budget allocated for health cases and public health initiatives, including incomes, health services, and education within the community. Another study by Adham et al.[6] also found the ratio of male-to-female NPC cases from 1995 to 2005 to be 2.37:1, with the peak

age incidence of 40-49; as many as >80% of the cases were within the age group of 41-50. A significant number, 20%, of NPC cases were contributed by patients under 30 with no bimodal age distribution. As in our study, the male-to-female ratio reached 2.1:1, with the mean age of 48, and the highest incidence was within the age group of 50-60. On the other hand, only 8% of juvenile cases were identified from our study. The lack of awareness in young age cases could cause the difference between these results. Almost all of the pediatric and adolescent patients as well as their parents or guardians were neither aware of the early clinical symptoms of NPC nor even thinking that cancer might occur at their age. Hence they assumed that such a condition as they endured was normal or just a glimpse of a disturbance that later would cause a delay in having a screening or an examination until the condition became more severe or already at an advanced stage.[5,7] In a study by Susetiyo et al.[8] at Dr. Soetomo General Hospital, the ratio of male to female patients was 2.7:1, with the peak age group of 41-50. Each gender, lifestyle, and biological factors were believed to contribute to the difference in NPC incidence. Males are more prone than females to being exposed to carcinogenic substances from the workplace or the habit of smoking; otherwise, females have estrogen, which tends to protect them from NPC due to its NAG7 repressor negative regulator activity of tumor growth [8,9]

The NPC-Indonesia registry allowed us to study the incidence of this disease in several provinces of Indonesia served by 16 different university hospitals. Based on the data, we required the distribution of NPC in 29 provinces in Indonesia. West Java had the highest incidence of NPC, followed by South Sulawesi and East Java. Our results differed from those previously reported by Adham et al.,[1] in which the highest incidence was found in East Java, based on the regional data provided by Malang (9.19/100.000) and Surabaya (7.23/100.000). Nevertheless, as mentioned in the study, the data acquired for the result was extracted from the mean regional incidence based on a few cities in Indonesia. In general, NPC incidence is 5.66/100.000, with approximately 1,000 new NPC findings each month, indicating a prominent challenge in Indonesia.[1,5]

In our study, the result showed that the most common presentation of NPC is in the form of a neck lump and nasal congestion, followed by ear and eye symptoms, as well as throat and breathing symptoms, as the less common complaints. Although neck lump was the most common complaint among the subjects, a previous study by Adham et al.[1] noted that this finding suggested an advanced stage of NPC. Mostly, patients might not notice the early symptoms of NPC, which were unilateral ear problems in 60.6% of the patients, according to the previous study. Still, in our study, ear problems, such as tinnitus and impaired hearing, were some of the less common symptoms identified from NPC patients. Susetiyo et al.[8] also found that the most common clinical symptoms of NPC were due to nearby metastasis, such as neck masses, followed by local infiltration symptoms, including ear and nasal complaints. The neck mass often emerges unilaterally and is painless unless accompanied by inflammation or infection. This could be the main trigger for the advanced stage of NPC diagnosis. Pain causes discomfort in patients, which eventually drives patients to attend an examination.

The reason for this finding in our study is correlated with our results of TNM classification and staging. Most patients in our study suffered from T4 stage. They were also aware that this stage was characterized by the broad extension of the tumor already taking place, which caused major symptoms to the patient with some form of metastasis, both regional and distant. Most regional neck lymph node metastases were identified at the N2 stage, in which the clinical enlargement was already significant, compared to N1, hence a very aggravating symptom endured by almost all patients due to its change in anatomical appearance. Faisal et al.[5] evaluated the results of 428 patients in a single institution study and discovered that T4 and N2 were the most common, with percentages of 63.8% and 39.7% respectively. Furthermore, the nasopharynx's proximity to a dense lymphatic network creates a higher possibility for poorly differentiated and undifferentiated NPCs to metastasize than it does for the other squamous cancers of the head and neck.

Regarding the NPC stage at the time of diagnosis, 43.5% of our cases were at stage IVA. If the advanced stage versus the early stage were also calculated and compared, it would result in 87.8% and 12.2%, respectively. The study by Fles et al.[7] may shed light on this finding regarding Indonesian patients' health attitudes, since, according to this study, most patients with NPC have limited knowledge about NPC and its etiology. Half of the patients have a six-month delay in diagnosis since the symptom's onset. It is mainly due to the patient's lack of awareness, as well as influences from the environment, economic situation, and social aspects, including family, tradition, and religion. Perceived barriers to medical assistance and healthcare include direct non-medical costs not covered by health insurance, complex and prolonged insurance processes, referral systems, and negative past experiences. [7,11]

According to the WHO classification, NPC is classified into three types based on its histopathology, which consists of keratinizing squamous cell carcinoma (1), non-keratinizing squamous cell carcinoma (2), and undifferentiated carcinoma (3). The most abundant type in Southeast Asia is the third WHO type, which is commonly related to EBV infection. Unlike type 3, WHO type 1 is mainly found in non-endemic regions, resulting from tobacco and alcohol consumption. [1,12] Our study also showed WHO type 3 as the most frequent subtype. Approximately 69.4% of cases were undifferentiated carcinoma, and only 2.2% were contributed by WHO type 1 NPC. Most previous studies analyzing NPC cases in Indonesia have also shown that the most common subtype is WHO type 3, consistent with this country being an endemic region of NPC.[1,4,8,13-16] The predisposition for NPC development is EBV infection at a young age, along with chronic viral reactivation in the epithelial tissue of the nasopharynx caused by local inflammation. Nearly all the children in the NPC endemic region become EBV carriers at the age of five. [17]

Moreover, NPC tends to have a propensity for distant metastasis with a higher possibility, unlike the other types of head and neck cancer. Based on the descending incidence, metastasis tends to emerge in bones, liver, lungs, and distant

lymph nodes. In our study, of all 545 patients 92 cases were found to have distant metastasis. Most patients experienced single organ metastasis, with the remainder developing multiple metastases that occurred either simultaneously or sequentially. An earlier study by Qu et al.[10] indicated that bone metastasis occurred in approximately 64%-67% of cases, making it the most common site of metastasis, while brain involvement was the least common among all subtypes of NPC. According to their findings, 332 out of 2758 patients (12.0%) had distant metastases, with 325 out of these 332 patients (97.9%) showing metastases in five specific organs: bone, brain, liver, lung, and distant lymph nodes. In addition, stage N3 is characterized by the highest incidence of metastasis involving the five mentioned organs. Based on the baseline clinicopathological characteristics, distant metastasis is associated to tumor dimension, lymph node contribution, and lymph node size. Frequently, it is found in cases where the tumor was biopsied, but the lymph nodes aren't removed, as well as in subjects with T4 and N3 stages.[10,12] Distant metastasis is the leading trigger of a reduction in patients' survival. A study conducted by Yang et al.[19] identified that 51.1% patients experienced multiple organ metastasis and 59.6% patients had suffered from more than three remote metastatic lesions by the time they were diagnosed. In those cases, bone, liver, and lung were the organs most affected by metastasis. Meanwhile, in our study, 16.9% showed distant metastasis at the time of diagnosis, 89.1% of which involved single organ metastasis, and 10.9% of which included multiple organs. Bone was the most common organ affected by single organ metastasis (45.6%), followed by the lungs and liver, and the least common was the brain. Our study reported that multiple organ metastasis involving bone and lung was identified the most.

Conclusion

Our study concluded that NPC cases are more often found in males than in females, with a ratio of 2.1:1, and frequently occur within the age group of 50–60, with a mean age of 48. The home province for the highest NPC cases was West Java, followed by South Sulawesi and East Java. Overall, the pathologic findings of WHO type 3 with IVA stage, T4 tumor, and N2 node were the most dominant variable findings in this study, almost aligning with those identified in the endemic area of Southeast Asia, specifically in Indonesia. However, NPC is still one of the most perplexing and easily misdiagnosed pathologies. Both patients and physicians often neglect many unspecified early clinical manifestations. Most patients in our study have already shown local metastasis and local infiltration symptoms, such as a lump in the neck and nasal congestion, the two most frequent chief complaints among all subjects. Bone was the most common metastatic organ in this study in terms of single organ metastasis, whereas multiple metastases commonly affect bone and lung as the most common target organs. The findings of this study should be implemented as a basis to encourage awareness and early testing for any suspected case of NPC. Further research is recommended to be conducted with more sufficient data to enhance follow-up from several centers involving the entire home provinces in Indonesia, as well as the use of more accurate and thorough data entry, so that better and more comprehensive results can be gained in the future.

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Ethical Statement

This study was approved by the Medical and Health Research Ethic Committee (MHREC) of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, with the registration number.KE/FK/0001/EC/2024.

Competing Interests

The authors declare that they have no competing interests.

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