Profile of Nasopharyngeal Cancer Patients who Underwent Radiotherapy in Dr. Hasan Sadikin General Hospital Bandung

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INTRODUCTION

Nasopharyngeal cancer (NPC) is a malignant epithelial tumor located in the nasopharynx and is the most common head and neck malignancy [1]. The incidence of this malignancy depends on geographical and racial distributions and is often found in endemic countries such as Southern China, Southeast Asia, North Africa, and the Arctic [2]. According to the data from GLOBOCAN 2018, NPC is the fifth most common cancer with an incidence rate of 5.2 per 100,000 population or 18,000 cases per year. Additionally, NPC accounts for approximately 11,204 cases of death per year in Indonesia [3].

Definitive therapy for NPC is radiotherapy. Some radiotherapy equipment can be used like Cobalt-60 (60Co) and Linear Accelerator (LINAC) which is a newer models and more popular in developed countries. Meanwhile, in developing countries, 60Co is still the main equipment [4]. Other treatment choices include chemotherapy, a combination of chemotherapy and radiotherapy, and supporting treatment such as symptomatic therapy [5,6]. Since NPC is mostly found in an advanced stage, the combination of radiotherapy and chemotherapy is mainly chosen as a treatment for the patients because of its effectiveness in treating cancer cells and is proven to have an excellent overall survival rate [7]. Current staging in NPC was based on The American Joint Committee on Cancer (AJCC) 8th edition which evaluates three categories such as Tumor (T) size, Nodes (N) involvement, and Metastasis (M) or no metastasis [8].

ABSTRACT

Background: Nasopharyngeal cancer (NPC) is a malignant epithelial tumor located in the nasopharynx and is the most common head and neck malignancy. This study aimed to find and describe the profile of NPC patients who undergo radiotherapy at Dr. Hasan Sadikin General Hospital, Bandung.

Methods: This study was a descriptive study conducted at the Department of Radiology of Dr. Hasan Sadikin General Hospital, Bandung. This study employed a total sampling method and was done by observing patients’ status/medical records from January 1, 2018, to December 31, 2019, which was registered based on the Hospital-Based Cancer Registry (HBCR). The inclusion criteria were all patients diagnosed with NPC and undergone radiotherapy.

Results: There were 274 records (19.74%) included as NPC from 1,388 records. This cancer was more frequent in men (70.4%), in the age group of 45–54 years (35.0%), non-active smokers (58.8%), entrepreneurs (23.0%), and those who came from West Priangan (36.1%). The most common chief complaint was an enlargement of neck lymph nodes (55.1%) at stage IVB (42.8%). Histopathological findings were dominated by undifferentiated squamous cell carcinoma (WHO III) (74.4%). Most of the patients were treated with chemoradiation (64.3%).

Conclusions: NPC could happen to anyone with different background. This study found it was more frequent in men than women (2.3:1), in the fourth and fifth decade of life, in entrepreneurs followed by housewives, and even in non-active smokers. It also could happen in children to the elderly. Most patients came with an enlargement of neck lymph nodes as their chief complaint in the advanced stage and need chemoradiation as their treatment.
Information about the profile of NPC patients in recent years is limited. This study aimed to find and describe the profile of NPC patients who underwent radiotherapy Dr. Hasan Sadikin General Hospital, Bandung, from 2018 to 2019.

METHODS

This was a descriptive study conducted at the Department of Radiology of Dr. Hasan Sadikin General Hospital, Bandung. This study used total sampling method by observing patients’ status/medical records from January 1, 2018, to December 31, 2019, which was registered based on the Hospital-Based Cancer Registry (HBCR). The inclusion criteria were all patients diagnosed with NPC previously and performing radiotherapy treatment in 2018 or 2019, and the exclusion criteria were incomplete and missing medical record data.

For each medical record observed, there were three types of profiles consisting of sociodemographic, disease, and management. The sociodemographic profile consists of sex, age, smoking status, occupation, and region. The disease profile consists of chief complaint, cancer cell morphology or histopathology, and staging. The management profile consists of treatment delivery equipment, completeness of therapy, and management type. For smoking status, the patients were asked whether they are active smokers or smoke cigarettes every day or not. There are five populated regions based on West Java Health Profile in 2016 [9]. The staging was based on the AJCC 8th edition [8]. Completeness of therapy was based on the fulfillment of the radiotherapy schedule that had been appointed for the patient by the doctor in charge.

The data were recaptured and processed with Microsoft® Excel 2019 and IBM® SPSS® version 25 software. This study had been approved by the Research Ethics Committee of Universitas Padjadjaran number 811/UN6.KEP/EC/2020.

RESULTS

In total, 273 medical records were included, and 1 was excluded due to its benign characteristics of the total of 1,388 patients from all cases who underwent radiotherapy in HBCR medical records of the Department of Radiology from 2018 to 2019. Based on Table 1, NPC patients are more frequent in men than in women with 193 cases (70.4%) and 81 cases (29.6%). The age median was 48 years, ranging from 11 to 77 years, and the most common age group was the 45–54 age (35.0%). Most patients were not active smokers (58.8%). The most common occupation was entrepreneurs (23.0%), followed by housewives (22.3%). Most patients came from West Priangan (36.1%) and Cirebon (21.0%).

Table 1. Distribution of sociodemographic patient

| Categories             | n = 273 | %  |
|------------------------|---------|----|
| Sex                    |         |    |
| Male                   | 192     | 70.4|
| Female                 | 81      | 29.6|
| Age groups (years)     |         |    |
| 05–14                  | 4       | 1.5 |
| 15–24                  | 23      | 8.8 |
| 25–34                  | 21      | 7.7 |
| 35–44                  | 60      | 21.9|
| 45–54                  | 96      | 35.0|
| 55–64                  | 52      | 19.0|
| 65–74                  | 15      | 5.5 |
| ≥ 75                   | 2       | 0.7 |
| Smoking Status         |         |    |
| Yes                    | 113     | 41.2|
| No                     | 160     | 58.8|
| Region                 |         |    |
| Bogor                  | 36      | 13.1|
| Purwakarta             | 40      | 15.0|
| Cirebon                | 55      | 20.1|
| East Priangan          | 26      | 9.5 |
| West Priangan          | 99      | 36.1|
| Outside west Java      | 17      | 6.2 |
| Occupation             |         |    |
| Entrepreneur           | 63      | 23.0|
| Housewife              | 61      | 22.3|
| Office Staff           | 40      | 15.0|
| Labour                 | 37      | 13.5|
| Farmer                 | 21      | 7.7 |
| Student                | 14      | 5.1 |
| Others                 | 10      | 3.6 |
| Retired                | 8       | 2.9 |
| Unknown                | 7       | 2.6 |
| Military/Police        | 5       | 1.8 |
| Unemployed             | 4       | 1.5 |
| Teacher                | 3       | 1.1 |

Based on the disease profile in Table 2, the most common chief complaint was an enlargement of neck lymph nodes (55.1%). Histopathological findings were dominated by undifferentiated squamous cell carcinoma.
(WHO III) (74.4%), followed by non-keratinizing squamous cell carcinoma (WHO II) (19.3%). The most common stage was stage IVB (42.8%). However, other types of cells were found in this study other than those mentioned in Table 2, such as T Cell lymphoma (n = 2), clear cell carcinoma (n = 1), and B Cell lymphoma (n = 1).

Based on the management profile in Table 3, Most NPC patients completed their therapy (87.6%). External Beam Radiotherapy (EBRT) Linear Accelerator (LINAC) (53.6%) was insignificantly more frequent than other equipment, followed by EBRT 60Co (42.3%), and all of them used 2-dimensional conventional therapy techniques. The most common management type was chemoradiation (77.3%) by chemotherapy during radiation (83.4%). Chemotherapy pre-radiation means the patient started chemotherapy until finished their session and then started radiotherapy later. Meanwhile, chemotherapy during radiation means the patient was treated with chemotherapy and radiotherapy (chemoradiation) at the same time, and chemotherapy post-radiation means the patient finished radiotherapy based on the schedule before being treated with chemotherapy.

**DISCUSSION**

This study found that the male-to-female ratio was 2.3:1 in line with previous studies in Indonesia and worldwide [7,10,11]. The majority of patients were of productive age. NPC mostly occurred in the 45–54-year age group (35%), followed by the 35–44-age group (21.9%). The age distribution of NPC patients differs substantially in areas of varying incidence [11]. Based on the previous study, more than 80% of the NPC patients diagnosed were over the age of 30 and peaked around the age of 40 to 49 years [11,12]. Similar results were found in a study conducted by Diniati et al. [10] which showed that most NPC occurred in the age group of 45–54 years, followed by the 35–44 age group. NPC was mostly found in these age groups due to the development of cancer cells needing several years after exposure to carcinogens in early life [10]. NPC also could happen in children. This study found 1.5% of the cases in children. In line with the study in China, children under the age of 16 accounts for 1–2% of NPC in China [13]. Another study by Jayalie et al. [12] in Indonesia showed that NPC in pediatric patients accounted for 2% of all child malignancies in 2004–2009 with a median age of 12 years, ranging from 7 to 17 years. NPC in pediatrics is associated with Epstein-Barr virus infection [14].

NPC is a multifactorial disease. Many factors could contribute like the environment, diet, and occupation. One of the environmental factors which could contribute to NPC risk in patients is cigarette smoking [15,16]. Exposure to tobacco smoke is associated with Epstein-Barr virus infection, increasing the risk of NPC [17].

**Table 2. Distribution of disease profile**

| Categories                        | n = 273 | %  |
|-----------------------------------|---------|----|
| **Chief Complaint**               |         |    |
| Nasal Symptoms                    | 64      | 23.5|
| Ear Symptoms                      | 16      | 5.9 |
| Neurology Symptoms                | 14      | 5.1 |
| Enlarged Neck Lymph Nodes         | 151     | 55.3|
| Headache                          | 15      | 5.5 |
| Dysphagia/Odynophagia             | 5       | 1.8 |
| Unknown                           | 8       | 2.9 |
| **Morphology Cell**               |         |    |
| Undifferentiated Carcinoma (WHO III) | 204   | 74.4|
| Non-keratinizing SCC (WHO II)     | 53      | 19.3|
| Keratinizing SCC (WHO I)          | 3       | 1.1 |
| Squamous Cell NOS                 | 7       | 2.6 |
| Adenocarcinoma                    | 2       | 0.7 |
| **Stage**                         |         |    |
| I                                 | 10      | 3.7 |
| II                                | 26      | 9.6 |
| III                               | 52      | 19.1|
| IVA                               | 53      | 19.8|
| IVB                               | 116     | 42.6|
| IVC                               | 13      | 4.8 |
| Unapplicable (recurrent case)     | 3       | 0.4 |

WHO, World Health Organization; NOS, not otherwise specified.

**Table 3. Distribution of management profile**

| Categories                        | n = 273 | %  |
|-----------------------------------|---------|----|
| **Completeness**                  |         |    |
| Complete                          | 240     | 88.0|
| Incomplete                        | 33      | 12.0|
| **Treatment delivery equipment**  |         |    |
| EBRT 60Co                         | 115     | 42.0|
| EBRT LINAC                        | 147     | 54.0|
| 60Co and Brachytherapy            | 3       | 1.1 |
| LINAC and Brachytherapy           | 8       | 2.9 |
| **Management type**               |         |    |
| Radiotherapy Only                 | 62      | 22.7|
| Radiotherapy + Chemotherapy       | 211     | 77.3|
| Chemotherapy pre-Radiation        | 33      | 15.6|
| Chemotherapy Durante (Chemoradiation) | 176  | 83.4|
| Chemotherapy Post Radiation       | 2       | 0.9 |

EBRT, External Beam Radiotherapy; LINAC, Linear Accelerator.
However, in this study, the number of non-smoker patients is more than that of active smokers. This result might show there was another factor that could contribute patients to having NPC like habit, diet, or occupation.

The highest incidence of NPC in Indonesia, according to the previous publication by Adham et al. [11], was in Malang, followed by Denpasar, Surabaya, and Bandung. In this study, most patients came from West Priangan (36.1%), followed by Cirebon (20.1%) and Purwakarta (15%). The high accessibility of West Priangan to Dr. Hasan Sadikin Hospital could contribute to the high number of cases from this region. Meanwhile, Cirebon and Purwakarta also show a high number of cases because these regions are in coastal regions. Some studies stated that people with high preserved foods and salted fish diet, especially local people who lived in coastal regions with higher consumption or early exposure to salted fish, had a higher risk of having NPC [7,18,19].

The occupational factor may contribute to the development of NPC, including formaldehyde and wood dust exposure [7]. This study found that most patient occupations were entrepreneurs (23%), followed by housewives (22.3%). A previous study conducted in Pekanbaru City Hospital showed a different result in which NPC mostly occurred in farmers and housewives [10]. Another study by Christian et al. [20] showed that most NPC patients were laborers (53.3%). Entrepreneur was the most frequent occupational possibly because of the correlation with low socio-economic status. In one study, lower socioeconomic status is related to patients’ behavior for seeking medical treatment by delaying healthcare utilization [21]. In addition, the dietary pattern of people with low socio-economic status is associated with the high consumption of preserved foods, increasing the risk of NPC [22].

Most patients came with a chief complaint of neck lymph node enlargement (55.1%), followed by nasal symptoms, ear symptoms, neurological symptoms, headache, and dysphagia. This finding is in line with the previous study that most patients came with enlarged neck lymph nodes, followed by nose disorders [12,23,24]. Besides neck enlargement, the nasal disorder is also one of the most common complaints in NPC patients. In this study, this complaint was the second most common (23.7%), which includes epistaxis and nasal congestion. Nasal disorders were the result of tumor extension to the anterior nasal cavity. Besides neck and nasal symptoms, there was ear symptom (5.8%) that occurred unilaterally and caused the hearing defect or tinnitus due to the blockage of the Eustachian tube in NPC patients [25]. Most NPC patients experienced unilateral hearing loss as an early sign and symptom of NPC, but doctors and patients do not pay attention to this condition until there is an enlarged neck lymph node which is a sign of an advanced stage of NPC [11,12]. This study found some patients came with neurological symptoms (5.1%) like diplopia and loss of facial sensation as chief complaints due to the involvement of cranial nerves III, IV, and VI, which indicate the infiltration and extension of tumor to the cranial area [23].

This study found the most common histopathologic cell type was undifferentiated squamous cell carcinoma (WHO III) (74.4%), followed by non-keratinizing squamous cell carcinoma (WHO II) (19.3%). This finding is in line with the previous publication by Lu et al. [7] in South China, Hongkong, Taiwan, and Singapore, and by Sekarutami et al. [26]. This classification was based on WHO 1978 classification which is more commonly used than WHO 2017. According to the WHO 2017, NPC is divided into three main groups, namely keratinized squamous cell carcinoma, non-keratinized carcinoma, and squamous basaloid carcinoma. Meanwhile WHO 1978 classification divided three histopathologic types into keratinized squamous cell carcinoma (WHO type I), nonkeratinizing carcinoma (WHO type II), and undifferentiated carcinoma (WHO type III) [25].

Unfortunately, most patients came in an advanced stage. This study found that most patients (42.8%) were diagnosed with stage IVB, followed by stage IVA (19.9%). Similar results were shown in studies by Sekarutami et al. [26] and Sriwijaya et al. [27] which stated most patients were diagnosed in stage IV. This is mainly caused by the delayed diagnosis because doctors and patients do not pay attention to early signs of this malignancy such as hearing defect until there is an enlarged neck lymph node which is a sign of an advanced stage of NPC [11,12]. Long waiting time before radiation treatment and poor handling and communication efficiency between hospital departments also could contribute to delayed treatment [28–30]. More cases were handled by LINAC due to cobalt-60’s equipment error in 2018, so the number of patients that could be handled decreased especially by 16CO, and it was also marked that no patients were treated with Cobalt-60 from March 2018 to July 2018.

Patients who registered and did not complete their treatment could be due to various factors, from the patient’s issue or health facilities’ issue. In terms of patients, it could be due to fear or occurring side effects and complications that can arise from therapy such as chemotherapy toxicity, radiotherapy dermatitis, lack of money for non-medicine costs like transportation, inn, and the condition of patients who have been too weak or already died before having time to finish their treatment [31–33]. The health facility is also responsible for the large number of patients who do not get radiotherapy. The cause is an imbalance of supply (competent human resources and adequate facilities or equipment in terms of number and quality) and demand.
(increasing number and complexity of cancer patients every year) of health facility sources [29,30].

The main treatment for NPC is chemoradiation, and surgery is not recommended for this cancer, unlike other solid tumors due to their anatomical characteristics [6,7]. Radiotherapy was chosen as the definitive treatment for NPC due to its high radiosensitive tumor in addition to chemotherapy drugs to make tumor cells more sensitive or smaller before radiation [25,34]. However, not every case of NPC must be treated with chemoradiation, for example, in early-stage patients [6]. This study found chemoradiation as the most treatment type (64.3%) because most patients came in stage IV condition.

This study has several limitations, including inadequate or lost information due to the input data only from one hospital and a 2-year data period. This study cannot state the outcome of patients after radiotherapy treatment. Certain variables could be biased such as occupation and region as the collected data is secondary.

CONCLUSIONS

In conclusion, NPC could happen to anyone with different background. This study found it was more frequent in men than women (2.3:1), in the fourth and fifth decade of life, in entrepreneurs followed by housewives, and even in non-active smokers. It also could happen in children to the elderly. Most patients came with enlargement of neck lymph nodes as their chief complaint, in an advanced stage, and needing chemoradiation as their treatment.

DECLARATIONS

Ethics Approval
This study had been approved by the Research Ethics Committee of Universitas Padjadjaran number 811/UN6. KEP/EC/2020.

Competing of Interest
The authors declare no competing interest in this study.

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