

# PATHOLOGICAL PROFILE OF NASOPHARYNGEAL CARCINOMA IN ANATOMICAL PATHOLOGY OF DR SOETOMO GENERAL ACADEMIC HOSPITAL DURING 1 JANUARY 2016 – 31 DECEMBER 2018

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## Abstract

Nasopharyngeal carcinoma (NPC) is a malignancy that has unique epidemiological characteristics, which incidence varying according to race and geographical differences. The early stage of NPC is often difficult to diagnose clinically because of its hidden location in the nasopharynx and because the initial symptoms resemble an upper respiratory tract infection. Most of the patients diagnosed at an advanced stage. The aim of this study was to determine the profile nasopharyngeal carcinoma in anatomical pathological Dr. Soetomo General Academic Hospital during 1 January 2016 – 31 December 2018. This study used a descriptive observational study with a retrospective approach. The data were presented in tables of the distribution of the number of cases, histopathological diagnosis, sex group, age, chief complaints and follow-up based on histopathology. The data was obtained from the electronic medic record (EMR) of Dr. Soetomo General Academic Hospital. There were 431 cases, the most age was 41-50 years, namely 146 cases (33,9%), the most gender was male consist of 302 cases (70%), the most common complaint was a neck lump, 202 cases (47%), non keratinizing squamous cell carcinoma, undifferentiated subtype was the most histopathological type, namely 398 cases (92,3%), and there were 118 cases (27,3%) who were followed up biopsy, 86 patients (20%) with good respon biopsy results, 21 patients (4,9%) with poor respon biopsy results and 11 patients (2,5%) recurrences.

*Keywords:* profile of pathological, nasopharyngeal carcinoma, NPC

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## 1. Introduction

Nasopharyngeal carcinoma is a malignancy that has unique epidemiological characteristics, with an incidence that varies according to race and geographical differences

(Tan et al., 2016). Nasopharyngeal carcinoma (NPC) is an epithelial carcinoma that arises in the nasopharyngeal mucosa and microscopically or ultrastructurally shows evidence of squamous differentiation (El-nagar et al., 2017). Nasopharyngeal carcinoma is common among several ethnic groups, including Inuit, North African, and Chinese from Southeast Asia (El-nagar et al., 2017 ; Wei et al., 2017). Nasopharyngeal carcinoma is mainly found in men of reproductive age (the ratio of male and female patients is 2.18:1) and 60% of patients are between 25 and 60 years old (Chang et al., 2006).

Nasopharyngeal carcinoma is the most common cancer in Indonesia due to the close associations between EBV infection and NPC risk (Adham et al., 2012). Plasma Epstein-Barr virus (EBV) DNA has been used for population screening, prognostication, predicting treatment response for therapeutic adaptation and disease surveillance. Early stages of NPC are often difficult to diagnose clinically because of their hidden location in the nasopharynx and because the initial symptoms resemble those of an upper respiratory tract infection. This has resulted in most NPC patients being diagnosed at an advanced stage (Chen et al., 2019). The existence of knowledge about nasopharyngeal carcinoma ranging from prevention, early detection, appropriate treatment will be able to help overcome the problems caused by nasopharyngeal carcinoma

## 2. Material and Methods

### Study design

The research design used was descriptive observational with a retrospective approach, because observations were made on events that had occurred previously using secondary data.

### Statistical analysis

This study used descriptive analysis of pathological characteristics of nasopharyngeal carcinoma patients which included age, gender, histopathological diagnosis, subtypes of nasopharyngeal carcinoma, and histopathological follow-up. This study used data from histopathological examination of nasopharyngeal carcinoma biopsy specimens at the Anatomical Pathological of Dr. Soetomo General Academic Hospital during the period 1 January 2016 – 31 December 2018. The results of the histopathological examination of nasopharyngeal carcinoma which was diagnosed early in 2016, 2017, 2018 and had followed-up for a maximum of 3 years after being diagnosed.

## 3. Result

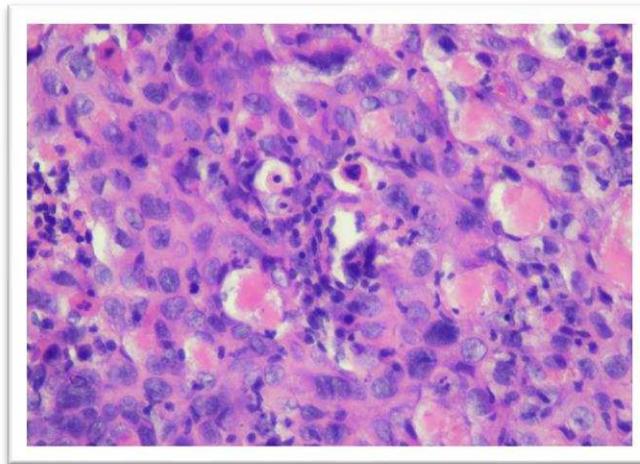
In this study, during 1 January 2016 – 31 December 2018, there were 431 cases diagnosed with nasopharyngeal carcinoma based on the results of histopathological examination at the Anatomical Pathological of Dr. Soetomo General Academic Hospital. The most cases were in 2018 with 148 cases followed by 2016 as many as 142 cases.

**Table 1.** Profile of nasopharyngeal carcinoma during 1 January 2016 – 31 December 2018 in Dr. Soetomo General Academic Hospital

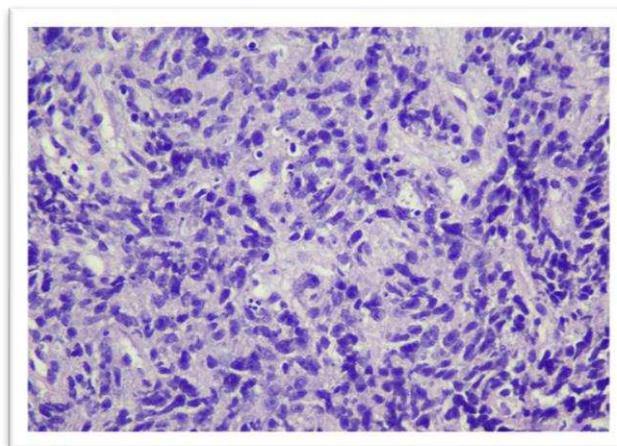
	Total	Percent (%)
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<b>Gender</b>		
Male	302	70
Female	129	30
<b>Age Group</b>		
11-20 y.o	20	4,6
21-30 y.o	28	6,5
31-40 y.o	64	14,9
41-50 y.o	146	33,9
51-60 y.o	113	26,2
61-70 y.o	47	10,9
>70 y.o	13	3
<b>Chief Complain</b>		
Neck lump	202	47
Headhache	7	2
Epistaxis	13	3
Diplopia	2	0
Referred hospital	73	17
No data	134	31
<b>Histopathological Subtype</b>		
Keratinizing squamous cell carcinoma	10	2,3
Non keratinizing squamous cell carcinoma, differentiated subtype	23	5,3
Non keratinizing squamous cell carcinoma, undifferentiated subtype	398	92,4
Basaloid squamous cell carcinoma	0	0
<b>Followed up</b>		
Good respon	86	20
Poor respon	21	4,9
Recurrent	11	2,5
No followed up	313	72,6

Nasopharyngeal carcinoma divided into 3 subtype based on histopathological feature: Keratinizing squamous cell carcinoma, Non keratinizing squamous cell carcinoma differentiated and undifferentiated subtype, and Basaloid squamous cell carcinoma. Histopathological feature of nasopharyngeal carcinoma in Anatomical Pathological of Dr. Soetomo General Academic Hospital during 1 January 2016 – 31 December 2018.



**Figure 1** Histopathological feature of keratinizing squamous cell carcinoma (HE staining 400x magnification)



**Figure 2** Histopathological feature of non keratinizing squamous cell carcinoma, undifferentiated subtype (HE staining 400x magnification)

#### 4. Discussion

Nasopharyngeal carcinoma is a rare malignancy in most of the world, with a prevalence of usually less than 1/100,000. Nasopharyngeal carcinoma is the most common cancer in Indonesia, ranks fourth as the most common tumor after cervical cancer, breast cancer, and skin cancer, and is the most common malignancy in the head and neck (El-nagar et al., 2017 ; Bray et al., 2018). This research was conducted at Anatomical Patological of Dr. Soetomo General Academic Hospital during 1 January 2016 – 31 December 2018 was resulted 431 cases.

Epidemiologically, NPC is an interesting cancer because it is related to geographical conditions and racial distribution, so that the causes of tumors can be seen from genetic, social, and environmental factors (Adham et al., 2012). Most cases were male in this research. The ratio of male and female patients is 1.2 : 1. In the United States, the ratio is 2:1 (Globocan, 2011). Nasopharyngeal carcinoma is always higher in male. It has not been found the cause of the higher male than female for this cancer. Men tend to be more often exposed to carcinogenic substances in their work environment than women, so they were more at risk for suffering from cancer (Adham et al., 2012; Chen et al., 2019). The disease is 100% associated with Epstein Barr virus (EBV) infection, especially the most common type of undifferentiated NPC (WHO type III) (Adham et al, 2012 ; El-nagar et al., 2017). Many environmental factors are considered important for risk factors for nasopharyngeal carcinoma. Dried salted fish which is usually a menu of Indonesian people is reported to cause NPC because of its nitrosamine content. Chronic exposure and intake of chemical carcinogens, formalin and phorbol esters, which are also widespread in Indonesia, are also considered as important risk factors, although the details are not yet known (Wang et al., 2016).

In this study, the mean age was 48 years, the youngest age at diagnosis was 14 years while the oldest age was 79 years. Research data in Indonesia 100 percent of children aged 5 years infected with EBV. Primary infection occurs in childhood, presents with symptoms of upper respiratory infection or mild inflammation, even without symptoms. In Hong Kong, 80% of children are infected by 6 years of age, almost 100% are seroconverted by 10 years of age. EBV infection begins in the oropharyngeal epithelium from saliva transmission. During infection, B lymphocytes are the main target of EBV. The EBV virus alters the submucosa of B lymphocytes and spreads the infection to the distal surface of the nasopharyngeal epithelium. EBV infection alone cannot cause NPC, because a person's genes, the way the body deals with infection also contribute to the development of NPC. Increased titers of immunoglobulin G and A antibodies (IgG and IgA) against viral capsid antigens were found in NPC patients (Brays et al., 2008). The existence of genetic, environmental and living habits, and infection as the dominant contributor to the incidence of NPC still requires further research (Sultan et al., 2010). In this study, the highest number of patients was found in the age group of 41-50 years with 146 patients (33.9%). This is in accordance with a study conducted by Wicaksana and colleagues in 2019, which stated that the incidence of nasopharyngeal carcinoma mostly occurred in the fifth decade of life. The incidence of nasopharyngeal carcinoma in this age range is increasing due to the influence of genetic factors, environmental factors, or exposure to carcinogenic materials at a previous age. This shows that from the first exposure to carcinogenic materials until the onset of cancer it takes a long time (Wicaksana et al., 2019).

The chief complaint of most patients in this research was preceded by a lump neck, as many as 202 patients (47%). According to a previous study conducted by Marlinda Adham, neck mass was the most common clinical symptom found in patients with 46%. Enlarged lymph nodes are the closest lymphogenous spread of nasopharyngeal cancer cells. Lymphatic drainage from the Rossemuller fossa drains into the nodes of Rouvier to the retropharyngeal space and continues to the deep upper neck lymph nodes. Tumor metastases to cervical lymph nodes may be unilateral or bilateral. So this is the reason for the patient to go to the doctor in the advanced stage (Adham et al., 2012 ; Alan et al., 2013).

Most of patient in this case had no follow up, there was many factors cause patients not to be followed-up. The majority of patients diagnosed with advanced nasopharyngeal carcinoma are people who come from the lower middle class economy. Radiotherapy can only be done at a tertiary hospital or a referred hospital that is far from patient's house. This is in accordance with the condition of Dr. Soetomo General Academic Hospital which is a tertiary hospital, the majority of patients being referred from outside the city. According to a previous study conducted by Chen et al, China in 2010, another factor that causes patients to drop out of follow-up is discomfort due to the acute side effects of radiotherapy. These include dry mouth, fatigue, sore throat, skin injury, taste changes, decreased appetite, otitis and hearing loss. These complaints could bring great physical stress and mental anxiety to patients, creating tremendous fear in the minds of patients and families (Chen et al., 2014).

Most cases were non-keratinizing squamous cell carcinoma, undifferentiated subtype as many as 398 patients (92.3%) in this research. NPC is broadly divided by the World Health Organization into keratinizing and nonkeratinizing subtypes. The histologic features of keratinizing NPC are similar to those of conventional squamous cell carcinomas arising elsewhere in the aerodigestive tract. These features include abundant keratinization, eosinophilic glassy cytoplasm, keratin pearls, and intercellular bridging. Nonkeratinizing NPC, characterized by solid sheets, irregular islands, or trabeculae of carcinoma with an absence of keratinization, is further subclassified into differentiated and undifferentiated subtypes. The differentiated subtype demonstrates some level of cellular stratification and paving, often described as resembling transitional cell carcinoma of the bladder. The undifferentiated subtype, such as the case presented here, has a characteristic syncytial growth pattern consisting of large cells with round to oval vesicular nuclei and prominent nucleoli. In addition to its histologic characteristics, nonkeratinizing NPC has several key clinical features which distinguish it from keratinizing NPC. Nonkeratinizing NPCs are relatively more frequent in high-incidence areas, where they represent >95 % of all NPCs (compared with approximately 75 % of NPCs in low-incidence areas). Nonkeratinizing NPCs also have a high association with positive EBV serologies, are more radiosensitive, and are more frequently associated with lymph node and distant metastasis (Peterson et al., 2012).

## 5. Conclusion

Non keratinizing squamous cell carcinoma were the most common histopathological sub type. Nasopharyngeal carcinoma were most common among persons aged 41-50 years. Most patients are male. The most common main complaint were lump in the neck.

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