The Association Between Clinical Characteristics and Histopathology of Nasopharyngeal Carcinoma at Dr. Mohammad Hoesin General Hospital, In 2019-2020

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A B S T R A C T

Introduction. Nasopharyngeal carcinoma is a cancer originating from the nasopharyngeal epithelium. Clinical characteristics such as age, gender, and risk factors are believed to influence the incidence of this cancer. Patients suffering from nasopharyngeal cancer may have certain clinical symptoms and provide certain histopathological features. **Methods.** The method used in this research were analytic observational with a cross sectional design using secondary data in the form of medical records from the Department of Anatomical Pathology section and the Central Medical Record section of RSUP Dr. Mohammad Hoesin Palembang as the research subject. Sixty-four (64) samples were obtained, then data were managed using the SPSS application. **Results.** The highest age group was 35-55 years old, which amounted to 44 people (68.8%). According to gender, the most common were males with 53 people (82.8%). According to clinical symptom, the most common were non-epistaxis with 33 people (51.6%). According to risk factors, the most were smokers with 36 people (56.3%). According to histopathology, the most common features were differentiated non-keratinized squamous cell carcinoma with 40 people (62.5%). From the statistical test, it resulted that p > 0.05 for all variables (age, gender, clinical symptoms, and risk factors) that associated with histopathology of nasopharyngeal carcinoma. **Conclusion** There was no significant association found between clinical characteristics and histopathology of nasopharyngeal carcinoma.

1. Introduction

Nasopharyngeal carcinoma (NPC) is a cancer arising from the nasopharyngeal epithelia. This tumor is most frequently located in the Rosenmüller fossa.[1] According to the International Agency for Research on Cancer, in 2018, there were about 129,000 new NPC cases, accounting or only 0.7% of all cancer diagnoses. In spite of this, the globally geographical distribution of these cases is highly imbalanced, with >70% of cases diagnosed in East and Southeast Asia.[2]

In Indonesia, NPC is the fifth most frequent cancer, right after carcinomas of the breast, cervix, lungs and liver, with 19,943 new NPC cases diagnosed in 2020.[3]

The incidence of NPC is believed to be affected by clinical characteristics, such as age, sex, and existing risk factors, such as smoking. Patients suffering from NPC may also show certain clinical symptoms, such as epistaxis, and show certain histopathological characteristics. Presently there is a lack of previous research associating clinical characteristics with the histopathological features of NPC. Thus, this study aims to determine the association of clinical characteristics with histopathological features of NPC.

2. Methods

This study was an analytical, observational study, with cross sectional design. The data used in this study were secondary data obtained from medical records at the Anatomical Pathology Department and Medical Records Center of Dr. Mohammad Hoesin General Hospital, Palembang. All complete medical records of patients with NPC at the Anatomical Pathology Department and Medical Records Center of Dr. Mohammad Hoesin General Hospital, Palembang, from the year 2019 to 2020, were included in this study. The sampling method used in this study was purposive sampling.

Data obtained from the medical records included age, sex, epistaxis as clinical symptom, smoking as risk factor, and histopathology of NPC. The data were then processed and statistically analyzed by using SPSS 26.0 software. The statistical analysis used in the study was Chi-square, and if the data were not eligible for parametric analysis, the Mann-Whitney and Fisher's Exact tests were used. The analyzed data were then presented as tables and narration.

3. Results

Out of the 182 medical records, 64 were included as samples in this study, of which 40 samples were from the year 2019 and 24 samples were from the year 2020. The majority of NPC patients were aged 35 to 55 years (n = 44, 68.8%) (Table 1).

In this study, there were more male NPC patients (82.8%) than female patients (17.2%). (Table 2). In this study, there were 31 patients (48.4%) with epistaxis as clinical symptom, while 33 others (51.6%) did not present with epistaxis (Table 3). Based on smoking history, out of 64 NPC patients, 36 (56.3%) were smokers (Table 4.). Based on histopathological features, there were no NPC patients with keratinizing squamous cell carcinoma (SCC) and basaloid SCC. There were 40 (62.5%) patients with well-differentiated non-keratinizing SCC and 24 (37.5%) patients with undifferentiated non-keratinizing SCC (Table 5).

Table 1. Age distribution of NPC patients

Age	n	%
<35 years	9	14.0
35-55 years	44	68.8
>55 years	11	17.2
Total	**64**	**100.0**

Table 2. Sex Distribution of NPC Patients

Sex	n	%
Male	53	82.8
Female	11	17.2
Total	**64**	**100.0**

Table 3. Distribution of Epistaxis as Clinical Symptom in NPC Patients

Clinical Symptom	n	%
Epistaxis	31	48.4
No Epistaxis	33	51.6
Total	**64**	**100.0**

Table 4. Smoking as Risk Factor in NPC Patients

Risk Factor	n	%
Smokers	36	56.3
Non-smokers	28	43.7
Total	**64**	**100.0**

Table 5. Histopathological characteristics of NPC patients

Histopathological features	n	%
Keratinizing SCC	0	0
Well-differentiated non-keratinizing SCC	40	62.5
Undifferentiated non-keratinizing SCC	24	37.5
Basaloid SCC	0	0
Total	**64**	**100,0**

In this study, chi-square analysis was not performed because 2 cells did not fulfill the expected cell count of 5. Instead, Mann-Whitney test was performed, and the obtained p value was 0.912 (p > 0.05). This indicated there was no significant association between age and histopathological NPC diagnosis (Table 6).

Well-differentiated non-keratinizing SCC was more frequent in male patients (31 patients, 48.4%), and undifferentiated non-keratinizing SCC was more frequent in female patients (9 patients; 14.1%). In this study, chi-square analysis was not performed because 1 cell did not fulfill the expected cell count of 5. Instead, Fisher's exact test was performed, and the obtained p value was 0.186 (p > 0.05), indicating no significant association between sex and

histopathological diagnosis of NPC (Table 7).

Well-differentiated non-keratinizing SCC was most frequent in both patients presenting with epistaxis (21 patients, 32.8%) and without epistaxis (19 patients; 29.7%). Chi-square analysis was performed, and the obtained p value was 0.401 (p > 0.05), indicating no significant association between epistaxis as clinical symptom and histopathological diagnosis of NPC (Table 8).

Well-differentiated non-keratinizing SCC was most frequent in both smokers (21 patients, 32.8%) and non-smokers (19 patients; 29.7%). In this study, chi-square analysis was performed, and the obtained p value was 0.435 (p > 0.05), indicating no significant association between epistaxis as clinical symptom and histopathological diagnosis of NPC.

Table 6. Association between age and histopathological NPC diagnosis

Age	Histopathological feature of NPC						p
	Well-differentiated non-keratinizing SCC		Undifferentiated non-keratinizing SCC		Total		
	n	%	n	%	n	%	
< 35 years	6	9.4	3	4.6	9	14.0	
35-55 years	27	42.2	17	26.6	44	68.8	
> 55 years	7	10.9	4	6.3	11	17.2	0.912
Total	**40**	**62.5**	**24**	**37.5**	**64**	**100.0**	

*Mann-Whitney test, p = 0.05

Table 7. Association between sex and histopathological diagnosis of NPC

Sex	Histopathological feature of NPC						p
	Well-differentiated non-keratinizing SCC		Well-differentiated non-keratinizing SCC		Total		
	n	%	n	%	n	%	
Male	31	48.4	22	34.4	53	82.8	
Female	9	14.1	2	3.1	11	17.2	**0.186**
Total	**40**	**62.5**	**24**	**37.5**	**64**	**100.0**	

*Fisher's Exact test, p = 0.05

Table 8. Association between epistaxis as clinical symptom and histopathological diagnosis of NPC

Clinical symptom	Histopathological feature of NPC						p
	Well-differentiated non-keratinizing SCC		Well-differentiated non-keratinizing SCC		Total		
	n	%	n	%	n	%	
Epistaxis	21	32.8	10	15.6	31	48.4	
No epistaxis	19	29.7	14	21.9	33	51.6	0.401
Total	**40**	**62.5**	**24**	**37.5**	**64**	**100.0**	

`*Chi-square test, p = 0.05

***Table 9.* Association between smoking history and histopathological diagnosis of NPC**

Risk factor	Histopathological feature of NPC						p
	Well-differentiated non-keratinizing SCC		Well-differentiated non-keratinizing SCC		Total		
	n	%	n	%	n	%	
Smokers	21	32.8	15	23.4	36	56.2	
Non-smokers	19	29.7	9	14.1	28	43.8	
Total	**40**	**62.5**	**24**	**37.5**	**64**	**100.0**	**0.435**

*Chi-square test, p = 0.05

4. Discussion

According to age, the largest number of data obtained is in the 35-55 years age group as many as 44 of 64 people. The results of this study are in line with research by Wira, et al. (2019) at Sanglah Hospital Denpasar in 2014-2016 where the most were in the 35-55 years age group as many as 97 out of 171 people. The results of this study are also almost in line with the research of Faiza, et al. (2016) at RSUP Dr. M. Djamil Padang in 2010-2013 where the most were in the 41-65 years age group as many as 30 out of 44 people. According to research Dawolo et al. (2017) at RSUP Dr. Mohammad Hoesin Palembang, the most data were found in the 46-55 years age group as many as 34 out of 110 people.

According to WHO, the incidence of NPC increases in their 30s and peaks until the age of 40-60 years and most patients diagnosed with this cancer have reached an advanced stage (stages III and IV) so that the mortality rate due to NPC increases in this age group.[5] This is because When a person has reached productive age (30-50 years), risk factors such as smoking habits and consumption of salted fish from an early age can trigger the occurrence of NPC because starting from the first exposure to carcinogenic substances until the onset of cancer takes a long time.[6]

According to gender, in terms of numbers, the most data was found in the male sex as many as 53 out of 64 people. The results of this study are in line with research by Wira, et al. (2019) at Sanglah Hospital Denpasar in 2014-2016 where the most were males as many as 114 out of 171 people, then Faiza, et al. (2016) at RSUP Dr. M. Djamil Padang in 2010-2013 where the majority were male as many as 23 out of 44 people, and Dawolo et al. (2017) at RSUP Dr. Mohammad Hoesin Palembang where the most found in the male sex as many as 80 out of 110 people. According to WHO, NPC can occur two to three times higher in men than women.[5] This happens because men's lifestyles are different from women's, such as smoking habits where the number of smokers in men is higher than women and men. more easily exposed to carcinogenic substances (vapours, fumes, flammable products, cotton dust or solvents such as phenoxy acids and chlorophenols) which tend to cause NPC when working.[7]

According to clinical symptoms in the form of epistaxis, in total, the highest data was found in clinical symptoms not epistaxis as many as 33 out of 64 people. The results of this study are related to research by Faiza, et al. (2016) at RSUP Dr. M. Djamil Padang in 2010-2013 where the clinical symptom of epistaxis was not the dominant clinical symptom of nasopharyngeal carcinoma because according to this study nasal obstruction was the dominant clinical symptom with 35 of 44 people at least having this symptom. Based on research conducted by Dawolo et al. (2017), out of 110 cases, the most common clinical symptoms of NPC were nasal congestion (49.09%), a lump in the neck (43.64%), and nosebleeds (epistaxis) (36.36%). According to WHO, epistaxis is one of the most common symptoms of patients with NPC.[5] Epistaxis in cancer occurs due to the fragility of the tumor wall so that stimulation and touch can cause nosebleeds or nosebleeds. This blood discharge is usually repeated, the amount is small and often mixed with mucus, so it is pink in color. Epistaxis can also be caused by the spread of the tumor to the mucous membranes of the nose which can injure the walls of the blood vessels in this area.[5]

According to history of smoking, in total, the most data obtained were on the risk factors of smokers as many as 36 of 64 people. The results of this study are in line with research by Wira, et al. (2019) at Sanglah Hospital Denpasar in 2014-2016 where the most risk factors were smokers as many as 90 out of 171 people. The content of carcinogens in cigarette smoke can weaken the immune system, making it difficult for cancer cell phagocytosis. When this happens, the cancer cells continue to grow without stopping. The toxins in tobacco smoke can damage or alter cell DNA. DNA is a cell's "instruction guide" that controls the normal growth and function of cells. When DNA is damaged, cells can start to grow out of control and produce cancerous tumors.

In total, the highest data was found in undifferentiated squamous cell carcinoma of 40 out of 97 people. The results of this study are not in line with Wira, et al. (2019) at Sanglah Hospital Denpasar in 2014-2016 and Faiza, et al. (2016) at RSUP Dr. M. Djamil Padang in 2010-2013 where the two research results obtained the most data found in undifferentiated undifferentiated squamous cell carcinoma with 163 out of 171 people in Sanglah Hospital, Denpasar and 33 out of 44 people in Dr. M. Djamil Padang. By number, keratinized squamous cell carcinoma accounts for 20 to 30 percent of NPC, undifferentiated undifferentiated squamous cell carcinoma 30 to 40 percent, and undifferentiated undifferentiated squamous cell carcinoma 40 to 50 percent. The frequency of histologic types varies by geographic area. In the United States, the majority of NPCs have histological findings of keratinized squamous cell carcinoma, whereas in Asia, the histological findings of undifferentiated and undifferentiated squamous cell carcinoma are the most

common.[7] According to WHO, tobacco smoking and alcohol consumption are factors that may contribute to the formation of the histopathological picture of keratinized squamous cell carcinoma and consumption of foods containing high nitrosamines contributes to the formation of the histopathological picture of undifferentiated and undifferentiated squamous cell carcinoma. In NPC endemic populations, undifferentiated and undifferentiated squamous cell carcinomas have a multifactorial etiology, such as genetic susceptibility, EBV infection, and consumption of salted fish.[5,7]

The results of the study of the distribution of the association between age and histopathology of nasopharyngeal carcinoma obtained a p value of 0.912 (p > 0.05), this indicates that age does not have a significant effect on differences in the histopathological picture of cancer. This result is in line with the research of Xuemei et al. (2017) which states that there is no significant association between age and NPC histopathology with a p value of 0.207 (p > 0.05).[9]

Based on the association between age and cancer histopathology, WHO states that the histopathological picture of squamous cell carcinoma, both keratinized and non-keratinized, most often appears in the 30s and peaks until the age of 40-60 years and various other research results show that aging only affects a person's risk for developing cancer. cancer and does not affect the histopathological picture of cancer.[15,16,17]

At the cellular level, aging is associated with impaired stem cell communication between cells. These events result in the accumulation of irreparable damage to important processes in the body. Stem cells affected by increasing age can be a source of tissue/organ failure or even cancer formation. Aging has a role in increasing the incidence of cancer in the population because the number of stem cell divisions is higher in the elderly compared to young people. It also underscores the proposed role of cancer stem cells in tumor formation and spread. The number of cell mutations acquired during aging is also very high. This can lead to the accumulation of tissue changes in aberrant cells that can develop into malignant tumors.[13]

The results of the study of the distribution of the association between sex and histopathology of nasopharyngeal carcinoma obtained a p value of 0.186 (p > 0.05), this indicates that there is no significant association between sex and histopathology of nasopharyngeal carcinoma. These results are in line with the research of Xuemei et al. (2017) which states that there is no significant association between gender and NPC histopathology with a p value of 0.719 (p > 0.05).[9] Based on the association between sex and cancer histopathology, WHO states that the histopathological features of squamous cell carcinoma, both keratinized and non-keratinized, can occur in both males and females. cancer because most of the results of previous studies only showed differences in the incidence of NPC based on gender.[7,8,9,13]

The results of the study of the distribution of the association between clinical symptoms of epistaxis and histopathology of nasopharyngeal carcinoma obtained a p value of 0.401 (p > 0.05), this indicates that there is no significant association between clinical symptoms of epistaxis and histopathology of nasopharyngeal carcinoma. Based on the association of clinical symptoms in the form of epistaxis with histopathology of cancer, WHO states that the histopathological picture of squamous cell carcinoma, both keratinized and non-keratinized macroscopically, can cause necrosis and bleeding. mucous membranes of the nose that injure the walls of blood vessels.[4] The fragility of the tumor walls is mostly caused by external factors such as direct physical contact (excessive palpation of the outer layer of the tumor) and bacterial contact from outside the tumor. In general, epistaxis is not used as a factor that determines the histopathological picture of cancer and is only used as a common clinical symptom in NPC.[12]

The results of the study of the distribution of the association between smoking risk factors and histopathology of nasopharyngeal carcinoma obtained a p value of 0.435 (p > 0.05), this indicates that there is no significant association between smoking risk factors and histopathology of nasopharyngeal carcinoma. This result is not in line with the research of Feng et al. (2009) which states that there is a significant association between smoking risk factors and the histopathology of NPC with a p value of 0.002 (p < 0.05).[17] Based on the association between smoking risk factors and cancer histopathology, WHO states that smokers are more at risk of developing NPC and most of the histopathological features of NPC obtained in patients with risk factors for smoking are creatinine squamous cell carcinoma.[5] Feng et al. (2009) stated in his research in North Africa that cigarette consumption and snuff (tobacco powder with addictive substances) were significantly associated with the formation of histopathological features of keratinized squamous cell carcinoma. The content of carcinogens in cigarettes and snacks can weaken the immune system and damage DNA cells. This can cause cancer cells to continue to grow without stopping and produce cancerous tumors. The resulting cancer tumor then gives a histopathological picture in the form of keratinized squamous cell carcinoma.[17]

5. Conclusion

The cases of nasopharyngeal carcinoma in the Anatomical Pathology section and the Central Medical Record section, Dr. Mohammad Hoesin Palembang according to age were mostly found in patients aged 35-55 years old. According to gender, the majority of NPC patients were male. According to clinical symptoms, patients commonly presented without epistaxis. According to risk factors, most NPC patients were smokers. The most common histopathological features of nasopharyngeal carcinoma patients were undifferentiated squamous cell carcinoma.

There was no significant association between age, gender, clinical symptoms of epistaxis, and smoking risk factors with histopathological diagnosis of nasopharyngeal carcinoma.

6. References

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