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Differences in Carcinogenic Risk Factors for Histopathological Types of Nasopharyngeal Malignancies Based on WHO Classification

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ABSTRACT

Nasopharyngeal carcinoma (NPC) remains a major malignancy in Southeast Asia, including Indonesia. Variations in histopathological types are suspected to be influenced by carcinogenic risk factors such as smoking, consumption of grilled foods, preserved foods, and alcohol intake. This study aims to analyze differences in the dominant histopathological types of NPC—Keratinizing Squamous Cell Carcinoma (KSCC), Non-Keratinizing Squamous Cell Carcinoma (NKSCC), and Undifferentiated Cell Carcinoma—based on major risk factors in Medan. An analytical observational study with a cross-sectional design was conducted using 75 eligible medical records of NPC patients (2020–2025) from Royal Prima Ayahanda Hospital Medan and Dr. Pirngadi General Hospital Medan. Data were analyzed using Chi-Square or Fisher's Exact Test and Odds Ratio. Results indicate that Undifferentiated Cell Carcinoma is the most prevalent type (61.3%), followed by NKSCC (29.3%) and KSCC (9.3%). No significant association was found between smoking, grilled food consumption, preserved food intake, or alcohol use and the histopathological types ($p > 0.05$). However, a higher risk tendency was observed for preserved food consumption toward KSCC (OR = 6.00) and grilled food consumption toward KSCC (OR = 2.98). These findings provide preliminary insight into how carcinogenic exposures may shape histopathological patterns of NPC and support future prevention and screening strategies in endemic regions.

Keywords: *nasopharyngeal carcinoma; carcinogenic risk factors; histopathology; smoking; preserved foods*

INTRODUCTION

The nasopharynx is the cavity behind the nose that has a complex structure and plays an important role in the upper respiratory system (Devine & Zur, 2020). *Nasopharyngeal carcinoma* (KNF

) is a malignant tumor that originates from nasopharyngeal epithelial cells and has the ability to spread to surrounding tissues or metastasize to other organs. Globally, *KNF* remains a significant health problem. Based on GLOBOCAN 2022 data (World Health Organization, 2023), there are approximately 133,000 new cases and 80,000 deaths due to *KNF* worldwide. In the Southeast Asian region, including Indonesia, *KNF* ranks fourth among cancers after breast, cervical, and lung cancers. *KNF* lesions are most commonly found in the Rosenmüller fossa, the transitional area between columnar epithelium and squamous epithelium, which is particularly susceptible to malignant transformations caused by carcinogen exposure.

In Indonesia, *KNF* cases are still widely reported, including in North Sumatra Province. According to reports from Dr. Pirngadi Hospital Medan and Haji Adam Malik Hospital (2020–2023), the number of cases shows an increasing trend, with 150–200 new cases annually in the Medan area. This rise is thought to be related to exposure to environmental carcinogenic risk factors such as cigarette smoke and the consumption of preserved foods. Data from the Ministry of Health of the Republic of Indonesia (2023) indicate that the incidence of *KNF* in North Sumatra reaches 2–3 per 100,000 population, making it a regional health priority.

The risk factors contributing to *KNF* are not only genetic but are also greatly influenced by exposure to carcinogenic substances from the environment and lifestyle. Carcinogenic substances are chemical or physical agents that can cause DNA damage and induce genetic alterations in cells. Exposure sources include active and passive cigarette smoke, motor vehicle emissions, burnt food, salted fish, preserved foods, and alcohol consumption (Zevanya & Iswarini, 2023). According to Guo et al. (2025), consumption of high-salt foods such as salted fish produces nitrosamines, chemical compounds that are carcinogenic and play an important role in the transformation of epithelial cells into malignant cells. Furthermore, cigarette smoke contains over 70 carcinogenic substances, including benzopyrene and tobacco-specific nitrosamines, which trigger genetic mutations in cells (Al-Anazi et al., 2023).

Histopathologically, the World Health Organization (WHO, 2022) classifies *nasopharyngeal carcinoma* into two main groups: *Keratinizing Squamous Cell Carcinoma* (KSCC) and *Non-Keratinizing Squamous Cell Carcinoma* (NKSCC). The *Non-Keratinizing* subtype can be further divided into differentiated and undifferentiated types. For analysis purposes, this study categorizes the histopathological types into three groups: Keratinizing squamous cell carcinoma (Keratinizing SCC), Non-keratinizing squamous cell carcinoma (Non-keratinizing SCC), and Undifferentiated cell carcinoma.

Several studies highlight how the distribution of histopathological types of *nasopharyngeal carcinoma* (*KNF*) varies based on exposure to specific risk factors. For example, an international study by Cut Vani & Andrian (2023) found that approximately two-thirds of keratinizing squamous cell carcinoma (KSCC) cases are associated with smoking, whereas non-keratinizing carcinoma (NKC) types occur more frequently in non-smoking individuals. In Indonesia, Ramelan et al. (2022) reported that the undifferentiated subtype predominates in hospitals, likely influenced by consumption of preserved foods and environmental factors. This is supported by Romdhoni et al. (2023), who linked foods high in nitrosamines, such as salted fish and processed meats, to an increased risk of *KNF* in Southeast Asia.

However, limited research has specifically identified the dominant histopathological type of *KNF* associated with each carcinogenic risk factor, especially in the Medan area. Therefore, this study aims to determine the most dominant histopathological type of *nasopharyngeal carcinoma* in relation to carcinogenic risk factors such as smoking habits, consumption of burnt food, preserved food, and alcoholic beverages in patients at regional hospitals in Medan. The findings are expected to provide a scientific basis for *KNF* prevention and early detection strategies tailored to community exposure patterns in North Sumatra, as well as to support the achievement of health-related Sustainable Development Goals (SDGs).

The study's problem formulation focuses on whether there is a difference in the dominance of histopathological types of *nasopharyngeal carcinoma*—including keratinizing squamous cell carcinoma, non-keratinizing squamous cell carcinoma, and undifferentiated carcinoma—based on exposure to various carcinogenic risk factors such as smoking, burnt food, preserved food, and alcoholic beverages among patients in Medan hospitals. The general objective is to determine differences and dominance in the histopathological types of *nasopharyngeal carcinoma* based on carcinogenic risk factors in several Medan hospitals. Specific objectives include identifying the most dominant histopathological types in patients with a history of smoking, consumption of burnt or baked foods, preserved foods, and alcoholic

beverages. Additionally, the study aims to analyze the distribution differences in histopathological types of *nasopharyngeal carcinoma* within each risk factor category.

This research is expected to offer several benefits. For the general public, it can provide insights into the relationship between carcinogenic risk factors and variations in histopathological types of *nasopharyngeal carcinoma*, raise awareness to reduce carcinogen exposure in daily life, and encourage the implementation of targeted screening programs in high-risk areas such as North Sumatra. For researchers, the study will serve as a scientific reference for understanding connections between carcinogen exposure and histopathological variation and as a foundation for further studies on environmental and lifestyle influences, including biomarker discovery and prevention strategies. For students, it will deepen understanding of the diverse histopathological types of *nasopharyngeal carcinoma* and their associated risk factors, support academic research in anatomical pathology and oncology, and stimulate interest in tropical oncology research in Indonesia.

METHOD

This study was an analytical observational study with a cross-sectional design aimed at analyzing the relationship between various carcinogenic risk factors—including smoking habits, consumption of burnt foods, preserved foods, and alcohol consumption—and the histopathological type of nasopharyngeal carcinoma in patients in the Medan area. The research was conducted from March to September 2025 at Royal Prima Ayahanda Hospital Medan and Dr. Pirngadi Hospital Medan, involving a population of 145 patients diagnosed with nasopharyngeal carcinoma through histopathological examinations during the 2020–2025 period. The sample size was determined using the Slovin formula with a 10% margin of error, resulting in a required sample of 60 patients. Sampling was performed using a simple random sampling technique based on medical records that met the inclusion criteria, which included patients with a histopathologically confirmed *KNF* diagnosis and complete risk factor data. Patients with metastasis, recurrent *KNF* history, or incomplete medical records were excluded from the study.

The independent variables consisted of smoking behavior, consumption of burnt foods, preserved foods, and alcohol, while the dependent variables were the histopathological types of *KNF* according to the 2022 WHO classification—Keratinizing SCC, Non-Keratinizing SCC, and Undifferentiated Carcinoma. Data collection involved securing ethical permission, coordinating with medical record officers, selecting data based on inclusion criteria, recording risk factors, and verifying data accuracy before inputting into SPSS. Univariate analysis was presented as frequency distributions, followed by bivariate analysis conducted using the Chi-Square or Fisher's Exact test with odds ratio calculations to assess risk trends. When necessary, multivariate analysis in the form of multinomial logistic regression was employed to identify the risk factors that most significantly influenced the histopathological type of *KNF*. All procedures were carried out in accordance with research ethics standards, maintaining patient data confidentiality and obtaining ethical approval from relevant institutions.

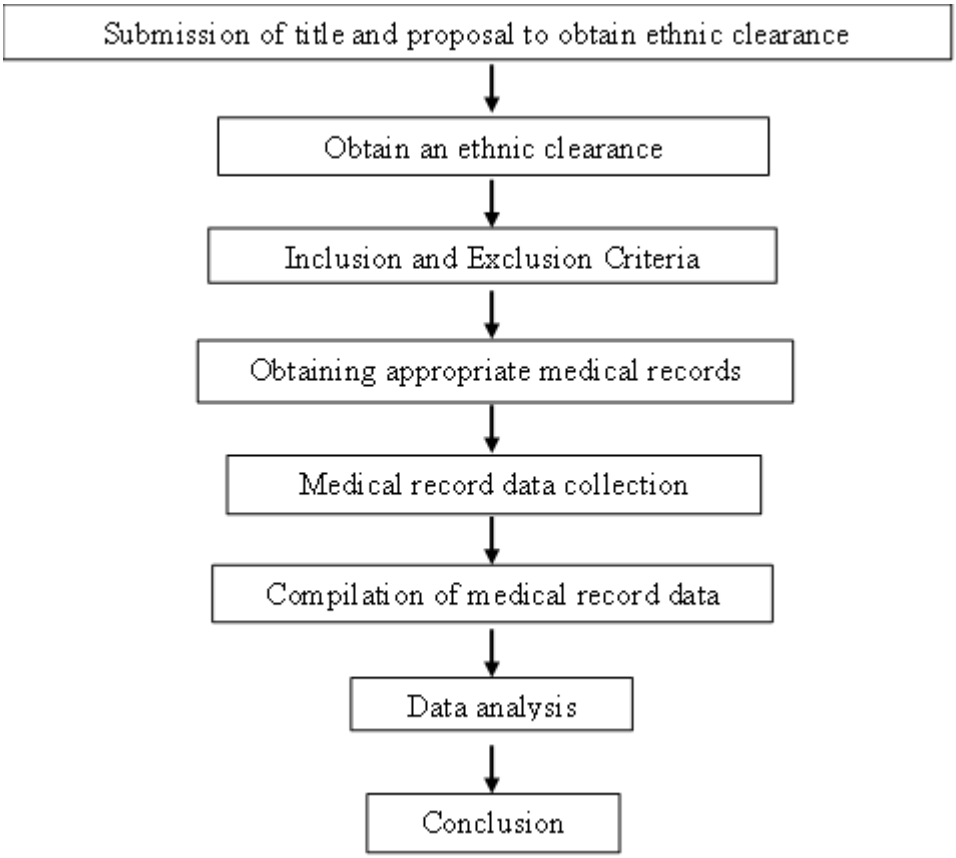

Figure 1. Research Methodology Flowchart
Source: Researcher's Conceptualization, 2025

RESULTS AND DISCUSSION

This research was conducted at Royal Prima Ayahanda Hospital in Medan and Dr. Pirngadi Hospital in Medan City. Data were collected from the results of the medical records of patients who experienced nasopharyngeal carcinoma at Royal Prima Ayahanda Hospital Medan from January 2020 to April 2025 and Dr. Pirngadi Hospital Medan City from January 2020 to August 2025. Based on the medical record data, as many as 75 patient data were obtained that met the inclusion and exclusion criteria of this study.

Univariate Analysis

Frequency Distribution Based on Risk Factors

Smoke

Table 1. Frequency Distribution by Smoking Risk Factors

Risk factor	Category	Frequency	Percentage (%)
Smoke	No	35	46,7
	Ya	40	53,3
Total		75	100

Source: Medical record data from Royal Prima Ayahanda Hospital and Dr. Pirngadi General Hospital Medan, 2020-2025

Based on Table 1, out of 75 respondents, as many as 35 patients (46.7%) did not smoke while 40 patients (53.3%) had a history of smoking before being diagnosed with nasopharyngeal carcinoma**.**

Baked Goods

Table 2. Frequency Distribution by Risk Factors for Burned Food

Risk factor	Category	Frequency	Percentage (%)
Baked Goods	Infrequently	39	52,0
	Often	36	48,0
Total		75	100

Source: Medical record data from Royal Prima Ayahanda Hospital and Dr. Pirngadi General Hospital Medan, 2020-2025

From Table 2, most of the patients before being diagnosed with nasopharyngeal carcinoma in this study were included in the category of rarely consuming burnt foods, namely 39 patients (52%), while 36 patients (48%) were classified as frequently consuming burned foods.

Preserved foods

Table 3. Frequency Distribution by Risk Factors of Preserved Food

Risk factor	Category	Frequency	Percentage (%)
Preserved foods	Infrequently	35	46,7
	Often	40	53,3
Total		75	100

Source: Medical record data from Royal Prima Ayahanda Hospital and Dr. Pirngadi General Hospital Medan, 2020-2025

The results of table 3 show that the results of the frequency distribution in this study show that patients diagnosed with nasopharyngeal carcinoma rarely consume preserved food, which is 35 patients (46.7%) and those who often consume preserved food are 40 patients (53.3%).

Alcohol

Table 4. Frequency Distribution by Risk Factors for Alcohol

Risk factor	Category	Frequency	Percentage (%)
Alcohol	No	56	74,7
	Ya	19	25,3
Total		75	100

Source: Medical record data from Royal Prima Ayahanda Hospital and Dr. Pirngadi General Hospital Medan, 2020-2025

Based on Table 4, most of the patients diagnosed with nasopharyngeal carcinoma, namely 56 patients (74.7%), did not consume alcohol, while 19 patients (25.3%) had a habit of drinking alcohol.

Frequency Distribution by Histopathological Type

Table 5. Frequency Distribution by Histopathological Type

Histopathological Type	Frequency	Percentage (%)
Keratinizing Squamous Cell Carcinoma	7	9,3
Nonkeratinizing Squamous Cell Carcinoma	22	29,3
Undifferentiated Cell Carcinoma	46	61,3
Total	75	100

Source: Medical record data from Royal Prima Ayahanda Hospital and Dr. Pirngadi General Hospital Medan, 2020-2025

Based on Table 5, the distribution of histopathological types shows that the type of Undifferentiated Cell Carcinoma is the most commonly found, which is as many as 46 cases (61.3%). Furthermore, Non-Keratinizing Squamous Cell Carcinoma was found in 22 cases (29.3%), and Keratinizing Squamous Cell Carcinoma was found in only 7 cases (9.3%).

Bivariate Analysis

The Relationship of Smoking and Histopathological Types

Smoking and Keratinizing Squamous Cell Carcinoma (KSCC)

Table 6 Relationship of Smoking with Keratinizing *Squamous Cell Carcinoma*

Smoke	*Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% Confidence Interval**
No	32 (91,4)	3 (8,6)	1,000	1,185	0,246 – 5,702
Yes	36 (90)	4 (10)			

Source: Processed research data, 2025

Based on Table 6, for the relationship between smoking and the type of Keratinizing Squamous Cell Carcinoma, in the non-smoking group, 3 people (8.6%) experienced Keratinizing Squamous Cell Carcinoma. Meanwhile, in the smoking group, 4 people (10.0%) experienced Keratinizing Squamous Cell Carcinoma. When the Chi-square test was performed, the results of 2 cells (50%) expected count < 5 were obtained, so Fisher's Exact Test was used. The test results showed p value = 1,000 (p > 0.05), which means that there was no significant

association between smoking and the incidence of Keratinizing Squamous Cell Carcinoma. An Odds Ratio (OR) value of 1.185 with a 95% Confidence Interval (0.246–5.702) indicates that smokers have a 1.18 times greater risk of developing Keratinizing Squamous Cell Carcinoma compared to non-smokers, but this result is not statistically significant.

Smoking with Non-Keratinizing Squamous Cell Carcinoma (NKSCC)

Table 7. Relationship of Smoking with *Non-Keratinizing Squamous Cell Carcinoma*

Smoke	*Non-Keratinizing Squamous Cell Carcinoma n (%)*				
	No	Yes	*p-value*	OR	95% *Confidence Interval*
No	24 (45,3)	11 (31,4)	0,709	0,828	0,306 – 2,239
Yes	29 (54,7)	11 (27,5)			

Source: Processed research data, 2025

In the Non-Keratinizing type of Squamous Cell Carcinoma, as many as 11 people (31.4%) experienced the occurrence of Non-Keratinizing Squamous Cell Carcinoma but did not smoke. Meanwhile, in the smoking group, 11 people (27.5%) experienced Non-Keratinizing Squamous Cell Carcinoma. Because the expected count < 5, the Chi-Square test was used. These results showed a p-value = 0.709 (p > 0.05), which means that there was no significant association between smoking and the incidence of Non-Keratinizing Squamous Cell Carcinoma. An Odds Ratio (OR) value of 0.828 with a 95% Confidence Interval (0.306 – 2.239) indicates that smokers have a 0.828 times lower chance of developing Non-Keratinizing Squamous Cell Carcinoma than non-smokers, but these results are also not statistically significant.

Smoking and Undifferentiated Cell Carcinoma

Table 8. Relationship of Smoking with *Undifferentiated Cell Carcinoma*

Smoke	*Undifferentiated Cell Carcinoma n (%)*				
	No	Yes	*p-value*	OR	95% *Confidence Interval*
No	14 (40)	21 (60)	0,824	1,111	0,438 – 2,819
Yes	15 (37,5)	25 (62,5)			

Source: Processed research data, 2025

For the type of Undifferentiated Cell Carcinoma, from Table 8, it was found that 21 people (60.0%) who did not smoke, had Undifferentiated Cell Carcinoma. Meanwhile, in the smoking group, 25 people (62.5%) experienced Undifferentiated Cell Carcinoma. Since the expected cell met the analysis requirements, which is more than 20% expected count < 5, the Chi-Square test was used. The results showed a p-value = 0.824 (p > 0.05), which means that there was no significant association between smoking and the incidence of Undifferentiated Cell Carcinoma. An Odds Ratio (OR) value of 1.111 with a 95% Confidence Interval (0.438 –

2.819) indicates that smokers have a 1.11 times greater risk of developing Undifferentiated Cell Carcinoma than non-smokers, but the association is not statistically significant.

Overall, the results of this study show that smoking does not have a significant effect on all three types of nasopharyngeal carcinoma. However, in the types of Keratinizing Squamous Cell Carcinoma and Undifferentiated Cell Carcinoma, patients who smoke have higher risk factors compared to those who do not smoke.

The Relationship of Burned Food to Histopathological Type

Foods Burned and Keratinizing Squamous Cell Carcinoma (KSCC)

Table 9. Relationship of Burned Foods with *Keratinizing Squamous Cell Carcinoma*

Baked foods	*Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	37 (94,9)	2 (5,1)	0,250	2,984	0,541–16,462
Often	31 (86,1)	5 (13,9)			

Source: Processed research data, 2025

Based on the results of bivariate analysis between the habit of consuming burned food and the histopathological type of Keratinizing Squamous Cell Carcinoma (KSCC), the group that often-consumed burnt foods were 5 people (13.9%) who experienced Keratinizing Squamous Cell Carcinoma. Meanwhile, in the group that rarely consumed burned food, only 2 people (5.1%) experienced Keratinizing Squamous Cell Carcinoma. Since 2 cells (50%) expected count < 5, the relationship analysis uses the Fisher's Exact Test. The test results showed a p-value of 0.250 (p > 0.05), which means that there was no significant association between the habit of eating burned food and the incidence of Keratinizing Squamous Cell Carcinoma. However, an odds ratio (OR) value of 2.984 with a 95% Confidence Interval (0.541–16.462) indicates a tendency that respondents who frequently eat burned foods have a nearly 3 times greater risk of developing Keratinizing Squamous Cell Carcinoma than the infrequent group, but this difference is not statistically significant due to the p> value of 0.05.

Foods Burned and Non-Keratinizing Squamous Cell Carcinoma (NKSCC)

Table 10. Relationship of Burned Foods with *Non-Keratinizing Squamous Cell Carcinoma*

Baked foods	*Non-Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	29 (74,4)	10 (25,6)	0,465	1,150	0,534 – 3,935
Often	24 (66,7)	12 (33,3)			

Source: Processed research data, 2025

In Table 10, namely the type of Non-Keratinizing Squamous Cell Carcinoma (NKSCC), in the group that rarely consumed burnt food (n = 39), there were 10 people (25.6%) who experienced Non-Keratinizing Squamous Cell Carcinoma. Meanwhile, in the group that often-consumed burnt food (n = 36), there were 12 people (33.3%) who experienced Non-Keratinizing Squamous Cell Carcinoma. The results of the Chi-Square test showed a p-value of 0.465 (p > 0.05), which means that there was no significant relationship between the habit of eating burned food and the incidence of Non-Keratinizing Squamous Cell Carcinoma. An odds ratio of 1.450 with a 95% Confidence Interval (0.534 – 3.935) showed a 1.15-fold increased risk in the group that often-consumed burnt foods, but this result was also not statistically significant.

Foods Burned and Undifferentiated Cell Carcinoma

Table 11. Relationship of Burned Food with *Undifferentiated Cell Carcinoma*

Baked foods	***Undifferentiated Cell Carcinoma n (%)***				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	12 (30,8)	27 (69,2)	0,144	0,497	0,193–1,276
Often	17 (47,2)	19 (52,8)			

Source: Processed research data, 2025

Meanwhile, in the type of Undifferentiated Cell Carcinoma, namely in Table the group rarely consumed burnt food (n = 39), as many as 27 people (69.2%) experienced Undifferentiated Cell Carcinoma. Meanwhile, in the group that often-consumed burnt food (n = 36), there were 19 people (52.8%) who experienced Undifferentiated Cell Carcinoma. The results of the Chi-Square test showed a p-value of 0.144 (p > 0.05), which means that there was no significant association between the consumption of burnt food and the incidence of Undifferentiated Cell Carcinoma. An odds ratio of 0.497 with a 95% Confidence Interval (0.193–1.276) showed that the group that frequently consumed burnt foods had a 0.497 lower chance of developing Undifferentiated Cell Carcinoma than the infrequent group, but this difference was also not statistically significant.

Overall, the results of this study show that the consumption of burnt foods does not have a significant effect on the three types of nasopharyngeal carcinoma. However, in the types of Keratinizing Squamous Cell Carcinoma and Non - Keratinizing Squamous Cell Carcinoma, patients who ate burned foods had higher risk factors compared to those who did not eat burned foods.

The Relationship of Preserved Food with Histopathological Types

Foods preserved and Keratinizing Squamous Cell Carcinoma (KSCC)

Table 12. Relationship of Preserved Foods with *Keratinizing Squamous Cell Carcinoma*

Preserved foods	*Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Ya**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	34 (97,1)	1 (2,9)	0,113	6,000	0,685 – 52,535
Often	34 (85)	6 (15)			

Source: Processed research data, 2025

In Table 12, the type of Keratinizing Squamous Cell Carcinoma (KSCC), the number of patients was higher in the group that often-consumed preserved food, which was 6 out of 40 patients (15%), compared to the group that rarely consumed, which was 1 in 35 patients (2.9%). When the Chi-square test was performed, the results of 2 cells expected count < 5 were obtained, so the Fisher's Exact Test was used. The test results showed p-value = 0.113, which means that there was no significant association between the consumption of preserved foods and the incidence of Keratinizing Squamous Cell Carcinoma. However, there is a tendency to increase the risk in individuals who consume these foods more often. Odds Ratio (OR) = 6,000; 95% CI (0.685 – 52.535) indicates that individuals who frequently consume preserved foods have an approximately 6 times greater risk of developing Keratinizing Squamous Cell Carcinoma. Although not statistically significant, these results still show clinically relevant indications of the potential role of preserved food consumption in increasing the risk of Keratinizing Squamous Cell Carcinoma.

Foods preserved with Non-Keratinizing Squamous Cell Carcinoma (NKSCC)

Table 13. Relationship of Preserved Foods to *Non-Keratinizing Squamous Cell Carcinoma*

Preserved foods	*Non - Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	23 (65,7)	12 (34,3)	0,378	0,639	0,685–52,535
Often	30 (75)	10 (25)			

Source: Processed research data, 2025

Meanwhile, in Table 13 for the type of Non-Keratinizing Squamous Cell Carcinoma (NKSCC), respondents who rarely consumed preserved and exposed food were 12 patients (34.3%), while the group that consumed frequently was 10 patients (25%). The results of the Pearson Chi-Square test showed a p-value = 0.378 with OR = 0.639 (95% CI: 0.685 – 52.535), indicating the absence of a significant association and no increased risk of Non-Keratinizing Squamous Cell Carcinoma due to the consumption of preserved foods. Even numerically, the group that consumed frequently appeared to have a 0.639 times lower risk, although the difference was not statistically significant.

Foods preserved with Undifferentiated Cell Carcinoma (NKSCC)

Table 14. Relationship of Preserved Foods with *Undifferentiated Cell Carcinoma*

Preserved foods	*Undifferentiated Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
Infrequently	13 (37,1)	22 (62,9)	0,800	0,886	0,349–2,253
Often	16 (40)	24 (60)			

Source: Processed research data, 2025

As for the type of Undifferentiated Carcinoma, the results of the crosstab showed that the number of patients diagnosed with the type of Undifferentiated Cell Carcinoma was relatively balanced between the group that rarely and often consumed preserved food, namely 22 people (47.8%) and 24 people (52.5%) respectively. The Pearson Chi-Square test yielded a p-value = 0.800 with OR = 0.886 (95% CI: 0.349 – 2.253), indicating that the group that frequently ate preserved foods had a 0.886 lower chance of developing Undifferentiated Cell Carcinoma than the infrequent group, but this difference was also not statistically significant.

Overall, the results of this study show that the consumption of preserved foods does not have a significant effect on all three types of nasopharyngeal carcinoma. However, in the Keratinizing type of Squamous Cell Carcinoma, patients who eat preserved foods have higher risk factors compared to those who do not eat preserved foods.

The Relationship of Alcohol to Histopathological Types

Alcohol and Keratinizing Squamous Cell Carcinoma

Table 15. Relationship of Alcohol to *Keratinizing Squamous Cell Carcinoma (KSCC))*

Alcohol	*Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
No	49 (87,5)	7 (12,5)	0,181	0,875	0,793 – 0,966
Yes	19 (100)	0 (0)			

Source: Processed research data, 2025

From Table 15, in the type of Keratinizing Squamous Cell Carcinoma, the respondent who did not consume alcohol had an incidence rate of 12.5% (7 out of 56 patients), while in the group that consumed alcohol there were no cases at all (0%). The results of the Fisher's Exact Test ($p = 0.181$; $p > 0.05$), did not find a significant association between alcohol consumption and the incidence of Keratinizing Squamous Cell Carcinoma. The use of the

Fisher's Exact test was chosen because there is 1 cell expected count < 5 so that the Chi-Square test does not meet the analysis assumptions. The Odds Ratio (OR) = 0.875 (95% CI: 0.793 – 0.966) indicates that individuals who do not consume alcohol have a lower risk of Keratinizing Squamous Cell Carcinoma, but this difference is not statistically significant. Thus, alcohol consumption was not shown to significantly affect the incidence of Keratinizing Squamous Cell Carcinoma in this study.

Alcohol and Non-Keratinizing Squamous Cell Carcinoma

Table 16. Relationship of Alcohol to *Non-Keratinizing Squamous Cell Carcinoma (KSCC))*

Alcohol	*Non - Keratinizing Squamous Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
No	41 (73,2)	15 (26,8)	0,405	1,594	0,529 – 4,809
Yes	12 (63,2)	7 (36,8)			

Source: Processed research data, 2025

In the non-keratinizing type of squamous cell carcinoma, respondents who did not drink alcohol had an incidence rate of 26.8% (15 out of 56 patients), while those who consumed alcohol reached 36.8% (7 out of 19 patients). The results of the Chi-Square test obtained p - value = 0.405 (p > 0.05), indicating that there was no significant association between alcohol consumption and the incidence of NKSCC. The Odds Ratio = 1.594 (95% CI = 0.529 – 4.809) also suggests that individuals who consume alcohol have about 1.6 times greater chance of developing NKSCC than those who do not, but the wide range of confidence indicates that these results are statistically unstable.

Alcohol and Undifferentiated Cell Carcinoma

Table 17. Relationship of Alcohol to *Undifferentiated Cell Carcinoma (KSCC)*

Alcohol	*Undifferentiated Cell Carcinoma n (%)*				
	No	**Yes**	***p-value***	**OR**	**95% *Confidence Interval***
No	22 (39,3)	34 (60,7)	0,850	1,109	0,378 – 3,251
Yes	7 (36,8)	12 (63,2)			

Source: Processed research data, 2025

Meanwhile, in the type of Undifferentiated Cell Carcinoma, it can be seen in Table 17 that the group that did not consume alcohol experienced Undifferentiated Cell Carcinoma, amounting to 34 out of 56 patients (60.7%). Meanwhile, in the group that consumed alcohol it was slightly lower, namely 12 out of 19 patients (63.2%). Chi-Square results with p-value = 0.400 (p > 0.05) showed that there was no significant association between alcohol consumption and the incidence of Undifferentiated Cell Carcinoma, with an OR value = 1.109 (95% CI =

0.378 – 3.251) indicating that individuals who consumed alcohol had an approximately 1.109 times greater chance of developing Undifferentiated Cell Carcinoma Compared to those who did not, however, a wide range of confidence indicated that these results were statistically unstable.

Overall, the results of this study show that alcohol consumption does not have a significant influence on all three types of nasopharyngeal carcinoma. However, in the Non - Keratinizing Squamous Cell Carcinoma and Undifferentiated Cell Carcinoma types, patients who eat preserved foods have higher risk factors compared to those who do not eat preserved foods.

Univariate Analysis

Frequency Distribution Based on Risk Factors

a. Smoke

Based on Table 4.1, out of a total of 75 respondents, it is known that as many as 40 people (53.3%) have a smoking habit, while 35 people (46.7%) do not smoke. These results suggest that most patients with nasopharyngeal carcinoma (KNF) have a history of smoking. Smoking has long been known as one of the main risk factors in the development of KNF due to the content of carcinogenic substances such as nicotine, tar, and nitrosamines that can cause oxidative stress, genetic mutations, as well as changes in the nasopharyngeal epithelial tissue. Chronic inflammatory processes due to exposure to cigarette smoke also accelerate DNA damage and trigger the transformation of normal cells into malignant cells.

The results of this study are in line with a prospective cohort study in Vietnam involving 20,144 men, in which 44.2% of respondents had a history of smoking and 55.8% did not smoke. The smoking group was reported to have a higher tendency to develop nasopharyngeal carcinoma than those who did not smoke (Nguyen et al., 2023). These findings are supported by an international meta-analysis study by Liu et al. (2023) that analyzed 46 studies and concluded that smoking habits are consistently associated with an increased risk of developing nasopharyngeal carcinoma in various world populations.

In addition, the results of this study are also consistent with the findings of Alfiyana Alimin et al. (2024) at Pelamonia Makassar Hospital which reported that out of a total of 45 KNF patients, as many as 25 people (55.56%) had a history of smoking and 20 people (44.44%) did not smoke. This proportion is almost the same as the results of this study, which also shows that more than half of KNF patients are smokers. The similarity of these results reinforces the suspicion that smoking habits play an important role as a risk factor in the incidence of nasopharyngeal carcinoma, especially in the Southeast Asian region where the prevalence of smoking is still high.

b. Baked foods

Based on Table 4.2, it can be seen that 39 individuals (52.0%) rarely consume baked goods, while 36 individuals (48.0%) do so frequently. This data indicates that the number of respondents who are used to eating baked goods and who rarely do so are almost balanced. Carcinogens, such as polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs), can appear when food is burned, especially in meat and fish. These compounds are formed when proteins and fats react at high temperatures, which can lead to genetic changes in the nasopharyngeal tissue as well as epithelial cells in the upper respiratory tract.

Previous research has also produced similar findings regarding the consumption habits of baked goods among patients with nasopharyngeal carcinoma (KNF). One study mentioned that out of 20 KNF patients, 11 individuals (55%) regularly consumed fish or grilled meat more than three times a month, while 9 individuals (45%) rarely did so. Another study at Abdul Moeloek Hospital indicated that out of 45 respondents, there were 21 patients (84%) who often consumed fish or grilled meat, while 9 patients (45%) did so rarely. A similar study also reported that about 37 patients (71.2%) had a routine habit of eating grilled foods compared to 15 patients (28.8%) who rarely or never did so. These findings further reinforce the suspicion that exposure to the carcinogen from burned foods may contribute to an increased risk of nasopharyngeal carcinoma.

c. Preserved foods

Based on the data in Table 4.3, out of the 75 people who were made respondents, it is known that 43 individuals (57.3%) belong to the group that often consumes preserved food, while 32 individuals (42.7%) are included in the group that rarely consumes it. These findings indicate that the majority of respondents tend to have the habit of consuming preserved foods on a regular basis.

The habit of consuming preserved foods such as salted fish, processed meat products, and foods that go through the fermentation process is at risk of increasing the likelihood of nasopharyngeal carcinoma (KNF). Preservation methods such as salting, fermentation, or the use of chemicals such as nitrites can produce carcinogenic compounds such as N-nitrosamine and Polycyclic Aromatic Hydrocarbons (PAHs), which have the potential to damage DNA and trigger genetic changes in nasopharyngeal tissue.

Research conducted by Huang et al. (2021) in the journal Nutrients also revealed that out of a total of 220 respondents, 126 people (57.3%) who regularly consumed preserved foods showed a greater risk of developing nasopharyngeal carcinoma compared to 94 people (42.7%) who rarely engaged in such consumption. In addition, Putri and Rahmadani's (2023) study in Indonesia found that out of 100 respondents, 58 people (58.0%) often ate preserved foods, while 42 people (42.0%) rarely did.

The findings of this study are in line with the results obtained by Huang et al. (2021) and Putri & Rahmadani (2023), who emphasized that respondents who had the habit of eating a preserved food showed a higher proportion of the incidence of nasopharyngeal carcinoma. These similarities in results corroborate the argument that exposure to carcinogenic compounds found in preserved foods contributes to a high risk of nasopharyngeal carcinoma.

d. Alcohol

Based on Table 4.4, it was revealed that the majority of participants, with a total of 56 people (74.7%), did not consume alcohol, while 19 people (25.3%) had consumption behavior. Although the prevalence of alcohol drinkers in this study was lower, the habit still contributed to an increased risk of developing cancer, including nasopharyngeal carcinoma. Alcohol can cause chronic irritation of the mucosal lining in the upper respiratory tract and produce acetaldehyde, a harmful compound capable of causing oxidative stress and interfering with DNA repair in epithelial cells in the nasopharynx. In the body, alcohol is converted into acetaldehyde, a harmful compound that induces lipid peroxidation as well as damages oxidative DNA, leading to a decrease in epithelial regenerative ability and leading to abnormal cell proliferation (National Cancer Institute, 2024; PubMed, 2022; PMC, 2023).

The findings of this study are in line with a study conducted by Li et al. (2021) in the South China region involving 2,441 cases of nasopharyngeal carcinoma and 2,546 controls, where alcohol consumption was more common in the patient group compared to the control group. Another study by Zhang et al. (2022) involving 1,923 male patients also noted that 364 of them were alcoholics, while 1,559 did not behave as such. In addition, a study by Wang et al. (2023) that included 377 NPC patients found that 149 people (39.5%) had a history of drinking alcohol, while 228 people (60.5%) did not. The similarity of the results of this study suggests that although the proportion of alcohol drinkers does not necessarily dominate, persistent patterns of alcohol consumption are associated with a higher risk of developing nasopharyngeal carcinoma through the mechanism of DNA damage caused by acetaldehyde exposure as well as oxidative stress.

Bivariate Analysis

The Relationship of Smoking with Histopathological Types

The results of the bivariate analysis showed that there was no significant association between smoking behavior and histopathological type of nasopharyngeal carcinoma (KNF), because the total p-value > 0.05. Although the Odds Ratio (OR) for Keratinizing SCC (1.185) and Undifferentiated Carcinoma (1.111) indicates a tendency to increase the risk, these values are not statistically significant due to the wide 95% confidence interval and crossing the 1 mark. These findings indicate that smoking plays a greater role in cancer initiation than determining the morphological variations of cells that affect histopathological type.

The results of this study are consistent with Liang et al. (2021) and Putri and Kurniawan (2021) who reported that smoking increases the risk of KNF, but did not specifically determine its histopathological type. Similar consistency was also found by Romdhoni et al. (2023) and Ramelan et al. (2022), who concluded that smoking was not significantly associated with variation in histological type of KNF. The weak link is thought to be related to the small sample size, the lack of data on smoking duration and intensity, and limitations on secondary data.

Thus, although smoking does not directly affect the histopathological type, this habit remains an important risk factor in the process of nasopharyngeal carcinogenesis. Efforts to prevent smoking behavior still need to be prioritized to reduce the incidence of KNF, especially in populations with high EBV exposure.

The Relationship of Burned Food to Histopathological Type

The results of bivariate analysis showed that the consumption of grilled foods did not have a significant relationship with the histopathological type of nasopharyngeal carcinoma, as seen from the p value for all types of cancer that was above 0.05. However, there is a tendency to increase the risk for Keratinizing Squamous Cell Carcinoma with an OR of 2.984, but this outcome is unstable due to the very wide confidence interval (95% CI = 0.541–16.462). These findings are consistent with research by Zhang et al. (2023) and Lin et al. (2024) which showed that consumption of burned foods increases the risk of head-neck cancer and nasopharyngeal carcinoma through exposure to polyaromatic hydrocarbons (PAHs) and nitrosamines. However, the main difference is that the results of this study are not statistically significant, likely influenced by small sample sizes, variations in food types, baking methods, and frequency of consumption.

Other factors such as Epstein–Barr Virus (EBV) infection can also affect the outcome because EBV has a dominant role in the development of Non-Keratinizing and Undifferentiated types, so the effects of burning food consumption are less visible. Consistent with Rahmawati et al. (2022) and Huang et al. (2023), consumption of burnt foods can indeed increase the risk of KNF in general, but is not specific to variations in histopathological type. Thus, although the statistical relationship is not significant, the results of this study still confirm the importance of reducing the consumption of burnt foods to avoid chronic exposure to carcinogenic compounds that support the process of nasopharyngeal carcinogenesis.

The Relationship of Preserved Food with Histopathological Types

The results of the bivariate analysis showed that the consumption of preserved foods was not significantly related to the histopathological type of nasopharyngeal carcinoma, indicated by the p-value for all types of cancer (0.113; 0.378; 0.800) greater than 0.05. However, there is a tendency to increase the risk for Keratinizing Squamous Cell Carcinoma with an OR of 6,000, but this outcome is unstable due to the very wide confidence interval (95% CI: 0.685–52.535). Biologically, preserved foods can contribute to carcinogenesis through the formation of mutagenic N-nitrosamines, as well as high salt content that causes mucosal irritation and chronic inflammation. Exposure to the chemical in preserved foods also has the potential to amplify the activity of the Epstein–Barr virus through increased expression of LMP1 and LMP2A.

These findings are in line with the research of Wang et al. (2017) and Kurniawati (2020) which both showed a positive but insignificant relationship between the consumption of preserved foods and the histopathological type of KNF, with OR values in a similar range. Additional support from the Chang et al. (2019) and Nguyen et al. (2021) studies shows a consistent pattern of increased risk, although it does not reach statistical significance. Thus, although a direct link to histopathological type is not proven, the consumption of preserved foods remains considered a potential risk factor in the long term, especially in individuals with EBV infection.

The Relationship of Alcohol to Histopathological Types

The results showed that alcohol consumption was not significantly related to the histopathological type of nasopharyngeal carcinoma (KNF), marked with a p-value for all types of cancer that was above 0.05. Although there is a tendency to increase the risk of about 1.6 times in the Non-Keratinizing type and 1.1 times in the Undifferentiated type, all of these values are not statistically significant. These findings are in line with global studies that show that alcohol only slightly increases the risk of KNF, especially in heavy consumption, while low consumption such as in Indonesia generally does not have a significant effect. Cultural factors and low alcohol consumption patterns in Indonesia also explain the insignificance of the relationship.

Although not significant as a single factor, alcohol is still recognized as a group 1 carcinogen by the IARC and may increase the risk of cancer if it interacts with other factors, such as smoking and Epstein–Barr Virus (EBV) infection. Research by Wang et al. (2023) and Simanjuntak et al. (2022) also confirms this synergistic nature. In addition to alcohol, three other risk factors—smoking, burnt food, and preserved foods—also showed a p-value of > 0.05, so it was not shown to be associated with differences in histopathological types of KNF.

Thus, the zero hypothesis was accepted and no direct influence of carcinogenic risk factors on histological type variation was found.

However, this insignificance does not negate the biological role of such factors in the process of carcinogenesis. Recent scientific literacy shows that exposure to nitrosamines, PAHs, and EBV activation (LMP1, LMP2A) has an effect on tumor initiation, but does not always determine the type of histological morphology. Genetic and immunological factors, such as variations in HLA and detoxifying genes (CYP2E1, GSTM1), are thought to play a greater role in determining the histological type of KNF. Methodological limitations, such as small sample sizes, inaccurate exposures, uneven sample distribution, and incomplete medical record data, also affect outcomes.

Overall, this study confirms that KNF is a multifactorial disease that is influenced by a combination of environmental factors, viral infections, and genetic predispositions, rather than by a single lifestyle factor. These findings remain of epidemiological value and could be the basis for future research with larger sample counts and stronger analytical designs.

CONCLUSION

The study found that Undifferentiated Cell Carcinoma was the most common histopathological type of nasopharyngeal carcinoma in patients from the Medan area, followed by Non-Keratinizing and Keratinizing Squamous Cell Carcinomas. No statistically significant association was identified between carcinogenic risk factors such as smoking, burnt food, preserved food, or alcohol consumption and the variations in histopathological types, although preserved food consumption showed a tendency to increase the risk of Keratinizing SCC. The findings underscore that nasopharyngeal carcinogenesis is multifactorial, involving interactions between Epstein-Barr Virus (EBV) infection, genetic predispositions, and environmental exposures, making carcinogenic risk factors clinically relevant despite lacking a direct link to histopathological differences. It is recommended that healthcare professionals intensify education and prevention efforts focusing on risk factor exposure and early screening, supported by standardized prevention programs and enhanced diagnostic capacities. Future research should include larger samples, incorporate variables like EBV infection, genetic factors, and intensity of risk exposure, and apply multivariate analysis to control confounders. Increasing public awareness about healthy lifestyles, nutrition, and the importance of routine check-ups is also vital to improve early detection and treatment outcomes in nasopharyngeal carcinoma.

REFERENCES

Al-Anazi, A., Rahman, S., & Al-Mutairi, F. (2023). *Tobacco-derived carcinogens and nasopharyngeal carcinoma: Molecular mechanisms and epidemiologic insights. Journal of Head and Neck Oncology, 45*(2), 134–142.

Cut Vani, A., & Andrian, E. (2023). *Laporan kasus karsinoma sel skuamosa nasofaring. Jurnal Riset Rumpun Ilmu Kedokteran, 2*(2), 163–191. https://doi.org/10.55606/jurrike.v2i2.2009

Devine, C., & Zur, K. (2020). Upper Airway Anatomy and Physiology. *Diagnostic and Interventional Bronchoscopy in Children*, 17–37.

Guo, Q., Zhang, L., & Chen, Y. (2023). *Environmental carcinogens and nasopharyngeal carcinoma in Southeast Asia: A meta-analysis. Asian Pacific Journal of Cancer Prevention, 24*(5), 1567–1575.

Huang, J., Li, X., Chen, Y., & Zhao, M. (2021). *Association between preserved food consumption and nasopharyngeal carcinoma risk: A systematic review and meta-analysis. Nutrients, 13*(4), 1109–1118. https://doi.org/10.3390/nu13041109

Li, X., Zhang, Y., & Chen, W. (2023). *Clinicopathological features and updated insights into nasopharyngeal carcinoma origin and spread patterns*. *Frontiers in Oncology*, 13, 1124507. https://doi.org/10.3389/fonc.2023.1124507

Liang, Z., Wang, Y., Chen, D., & Xu, X. (2021). *Cigarette smoking and risk of nasopharyngeal carcinoma: Evidence from epidemiological studies. Cancer Epidemiology, 74*, 102004. https://doi.org/10.1016/j.canep.2021.102004

Lin, Z., et al. (2024). EBV DNA detection in nasopharyngeal carcinoma biopsy specimens. Journal of Medical Virology, 96(2), 305–312.

Liu, Q., et al. (2022). *Cigarette smoking, EBV reactivation, and nasopharyngeal carcinoma risk. Cancer Science, 113*(2), 689–699.

Putri, A. D., & Kurniawan, H. (2021). *Hubungan kebiasaan merokok dengan kejadian karsinoma nasofaring di RSUP Dr. Kariadi Semarang. Jurnal Kedokteran Diponegoro, 10*(2), 75–83.

Putri, S. R., & Rahmadani, E. (2023). *Konsumsi makanan awetan sebagai faktor risiko kanker kepala dan leher di daerah pesisir Sumatera Barat. Jurnal Kesehatan Andalas, 12*(1), 55–63. https://doi.org/10.25077/jka.12.1.55-63.2023

Rahmawati, I., Suryani, D., & Utami, F. (2022). *Hubungan konsumsi ikan dan daging bakar dengan kejadian karsinoma nasofaring di wilayah pesisir Sulawesi Selatan. Jurnal Gizi dan Kesehatan Indonesia, 5*(3), 145–153.

Ramelan, R., Shoffi, M. N., Halim, A. S., & Diarsvitri, W. (2022). *Karakteristik klinis dan histopatologi karsinoma nasofaring. Jurnal Kedokteran Syiah Kuala, 22*(3), 106–110. https://doi.org/10.24815/jks.v22i3.21689

Ramelan, S., Widodo, A., & Pratiwi, D. (2022). *Faktor risiko lingkungan terhadap insidens karsinoma nasofaring di Indonesia: Studi kasus-kontrol di Jawa dan Sumatera. Jurnal Epidemiologi Indonesia, 16*(1), 112–120.

Romdhoni, A., et al. (2023). Environmental and dietary risk factors of nasopharyngeal carcinoma in Indonesia. Asian Oncology Research Journal, 12(4), 180–191.

Romdhoni, R., et al. (2023). *Correlation between smoking and histopathologic types of nasopharyngeal carcinoma. Jurnal Ilmu Kedokteran Klinis, 11*(4), 221–230.

Simanjuntak, H. B., Lubis, A. R., & Siregar, R. (2022). *Hubungan konsumsi alkohol dengan kejadian karsinoma nasofaring di RSUP H. Adam Malik Medan. Jurnal Onkologi Klinik Indonesia, 8*(1), 33–40.

Wang, Y., Lin, Z., & Chen, L. (2023). Serological detection of EBV markers in nasopharyngeal carcinoma. Virology Journal, 20(1), 55–63.

Wang, Y., Liu, F., Zhang, T., & Chen, J. (2023). *Alcohol consumption and risk of head and neck cancers: A dose–response meta-analysis. BMC Public Health, 23*(1), 122–132. https://doi.org/10.1186/s12889-023-16045-9

World Health Organization. (2023). GLOBOCAN 2022: Nasopharyngeal Cancer Fact Sheet. Geneva: WHO.

World Health Organization. (2025). Guidelines for the Diagnosis and Treatment of Nasopharyngeal Carcinoma. Geneva: WHO.

Zevanya, E., & Iswarini, B. (2023). *Peran paparan karsinogenik makanan diawetkan dalam etiologi karsinoma nasofaring di Asia Tenggara. Indonesian Journal of Cancer, 17*(3), 200–210.

Zhang, L., et al. (2023). *Environmental exposure, EBV infection, and nasopharyngeal carcinoma in Chinese population: A population-based study. Cancer Medicine, 12*(7), 3456–3467.

Zhang, L., Huang, W., & Chen, X. (2023). *Intake of grilled and smoked food and risk of upper respiratory tract cancer: A population-based case-control study. Frontiers in Oncology, 13*, 1012456. https://doi.org/10.3389/fonc.2023.1012456