

Salted Fish Consumption Factors on the Incidence of Nasopharyngeal Cancer: A Systematic Review

Faktor Konsumsi Ikan Asin terhadap Kejadian Kanker Nasofaring: Systematic Review

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ABSTRACT

Nasopharyngeal cancer (NPC) is a squamous cell cancer that originates from the epithelial lining of the nasopharynx. The issue of salted fish consumption is a concern because the salt preservation process can produce carcinogenic nitrosamine compounds. The nitrosamine content is formed from the reaction between nitrite, nitrate, and secondary amines, which has the potential to cause cell changes to become malignant if consumed in the long term, especially from an early age. This study aimed to systematically review the consumption pattern of salted fish based on age, frequency of consumption, and its potential risk of NPC and to identify gaps in the results of previous studies. The method used was a *systematic review* by searching the literature on *online databases* such as Scopus, PubMed, ScienceDirect, and Garuda. A total of 126 articles were obtained, and 11 articles met the criteria. The results of the analysis showed that there are differences in salted fish consumption patterns based on age and frequency that may increase the risk of NPC, especially in individuals who started consuming in childhood and high amounts. This study highlights the need for further research that considers genetic aspects, types of salted fish, and processing methods in different regions to clarify the causal relationship.

Keywords: Risk factors, salted fish, nasopharyngeal cancer

ABSTRAK

Kanker nasofaring (NPC) merupakan kanker sel skuamosa yang berasal dari lapisan epitel di nasofaring. Masalah konsumsi ikan asin menjadi perhatian karena proses pengawetan dengan garam dapat menghasilkan senyawa nitrosamin yang bersifat karsinogen. Kandungan nitrosamin tersebut terbentuk dari reaksi antara nitrit, nitrat, dan amina sekunder, yang berpotensi menyebabkan perubahan sel menjadi ganas jika dikonsumsi dalam jangka panjang, terutama sejak usia dini. Tujuan dari studi ini adalah untuk mengulas secara sistematis pola konsumsi ikan asin berdasarkan usia, frekuensi konsumsi, dan potensi risikonya terhadap kejadian NPC, serta untuk mengidentifikasi kesenjangan dari hasil-hasil studi sebelumnya. Metode yang digunakan adalah *systematic review* dengan menelusuri literatur pada *database online* seperti Scopus, PubMed, ScienceDirect, dan Garuda. Sebanyak 126 artikel diperoleh, dan 11 artikel memenuhi kriteria. Hasil analisis menunjukkan bahwa terdapat perbedaan dalam pola konsumsi ikan asin berdasarkan usia dan frekuensi yang dapat meningkatkan risiko NPC, terutama pada individu yang mulai mengonsumsi sejak masa kanak-kanak dan dalam jumlah yang tinggi. Studi ini menyoroti perlunya penelitian lanjutan yang mempertimbangkan aspek genetik, jenis ikan asin, serta metode pengolahan di berbagai wilayah untuk memperjelas hubungan kausal tersebut.

Kata Kunci: Faktor risiko, ikan asin, kanker nasofaring

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INTRODUCTION

Nasopharyngeal cancer is endemic in parts of Asia and Africa, with the highest incidence in Southern China at 25-50 cases per 100,000 population.¹Data from GLOBOCAN in 2020 showed that the incidence of nasopharyngeal cancer reached 133,354 cases with a distribution of 96,371 cases in men and 36,983 cases in women, and with 80,008 new deaths.² And increased by 120,434 new cases in 2022.³

Risk factors associated with the disease include consumption of salt-cured foods, such as smoked meat, salted vegetables, salted meat, and salted fish, exposure to carcinogens, smoking, and alcohol consumption.⁴Excessive consumption of nitrosamines and nitrates contained in salted fish may increase the risk of developing the disease.⁵In Indonesia, salted fish production reached 175,522 tonnes in 2017 and continued to increase until the following year.⁶

The prevalence of nasopharyngeal cancer in Indonesia is 6.2 per 100,000 population, with 13,000 new cases per year. ⁷ Based on GLOBOCAN data in 2022, the incidence of the disease was 18,835 cases, with 14,497 cases in men.³ Research by Sitepu *et al.* (2023) stated that there was an association between individuals who consumed salted fish and the incidence of nasopharyngeal cancer ($p < 0.05$).⁸ However, a study suggested that there was inconsistency in the results of the relationship between consuming salted fish and the incidence of nasopharyngeal cancer. A significant association was only seen in a study conducted in Southern China. The inconsistency may be due to differences in population and the type of salted fish consumed.⁹ Because of this, this study aims to systematically

review the factors of salted fish consumption on the incidence of nasopharyngeal cancer.

MATERIALS AND METHODS

The research method used was a *systematic review* using secondary data from *online databases*, namely Scopus, Pubmed, Science Direct, and Garuda. The keywords for searching articles in the *database* used a combination of MeSH keywords with *salted fish* and *nasopharyngeal carcinoma* and used the principle of Boolean Operators to narrow the search. In the Scopus, Pubmed, and ScienceDirect *databases*, the keywords ("Salted Fish" OR "Dried Salted Fish" OR "Preserved Fish") AND ("Nasopharyngeal Neoplasms"[MeSH] OR "Nasopharyngeal Carcinoma" OR "Nasopharyngeal Cancer") were used. In contrast, Garuda used "Salted fish" and "Nasopharyngeal Carcinoma."

To screen appropriate articles, the PRISMA (*Preferred Reporting Items for Systematic Review*) method was used with inclusion criteria, including articles that discuss the relationship of salted fish consumption to nasopharyngeal cancer, published in the range of 2015-2025, and are *free access*. Articles that do not discuss the relationship of salted fish consumption to nasopharyngeal cancer are *reviewed* in nature, in languages other than Indonesian and English, and will be included in the exclusion criteria.

To focus the study, a PECO (Population, Exposure, Comparison, Outcome) approach was used with the following criteria: Population; Individuals who consume salted fish. Exposure; Salted fish consumption. Comparison; Individuals who do not consume salted fish. Outcome; Effect of population and frequency of salted fish



consumption on the incidence of NPC.

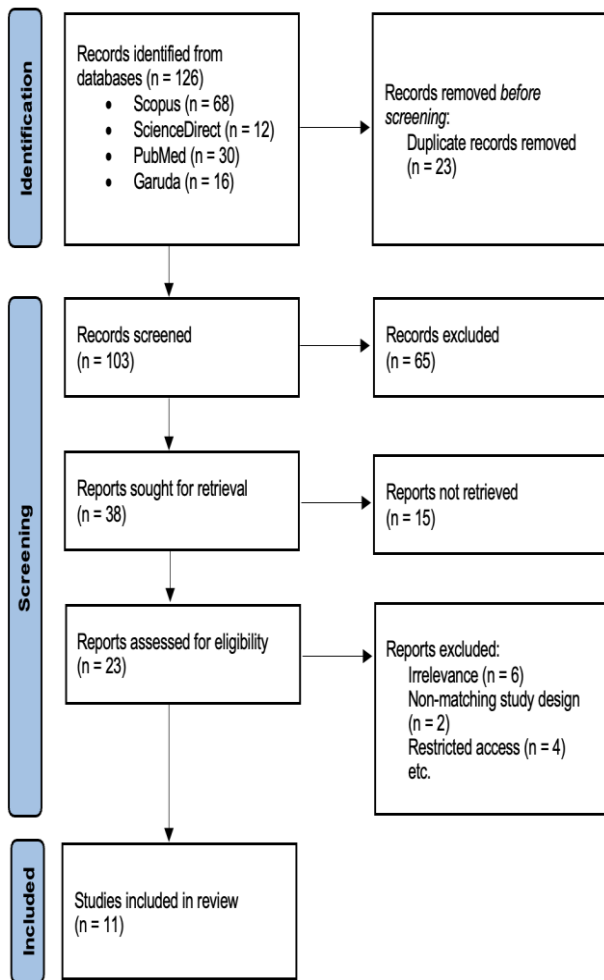


Figure 1. Flow of Article Screening

Articles that passed the selection were then extracted using an extraction table that included the name of the researcher, year of publication, research title, method, research population, frequency of salted fish consumption, and research results. The extracted data were then analyzed descriptively by two independent authors.

RESULTS

Article search results from four online databases, namely PubMed (n=30), ScienceDirect (n=12), Scopus (n=68), and Garuda (n=16), resulted in a total of 126 articles. A total of 23 articles were excluded due to duplication, and 65 articles were excluded because they were published before 2015. After a screening process through title, abstract, methods, and accessibility, 11 articles met the inclusion criteria and were used in this systematic review.

Systematic review.

Table 1. Results of Article Search

No.	Author/ Year	Title	Method	Age of Population	Consumption Frequency	Research Results
1.	Nuaba <i>et al.</i> (2020) ¹⁰	Correlation of Cigarette Smoking and Salted Fish Consumption with Nasopharyngeal and Its Clinical Stage in ORL-HNS Outpatient, Sanglah General Hospital	Case-control	Mean age 47.35 years	History of salted fish consumption	Salted fish consumption increased the risk of NPC by 2.4 times (OR = 2.4, P = 0.036) but was not significantly associated with the clinical stage of NPC (AOR = 2.288, P = 0.148).



No.	Author/ Year	Title	Method	Age of Population	Consumption Frequency	Research Results
2.	Chen <i>et al.</i> (2022) ¹¹	Environmental Factors for Epstein-Barr Virus Reactivation in a High-Risk Area of Nasopharyngeal Carcinoma: A Population-Based Study	Case-control	Adults and adolescents	Weekly	Not significantly associated with Epstein-Barr virus (EBV) reactivation, which is a major risk factor for nasopharyngeal cancer, with an OR of 1.01 (95% CI = 0.77-1.34)
3.	Ban <i>et al.</i> (2017) ⁽¹²⁾	Haplotype CGC of XPD, hOGG1, and ITGA2 polymorphisms Increases the Risk of Nasopharyngeal Carcinoma in Malaysia.	Case-control	Mean age 52.8 years	Salted fish consumption before the age of 10 years	Associated with increased risk of NPC with OR of 1.77 (95% CI = 1.30-2.42)
4.	Kasim <i>et al.</i> (2020) ⁽¹³⁾	Consumption of Salted Fish and Smoked Meat with Incidence of Nasopharyngeal Carcinoma	Cross-sectional	46-55 years old	>3 times a month	There is an association between salted fish consumption and the incidence of nasopharyngeal cancer (<i>p-value</i> : 0.038)
5.	Sulaksana & Kadriyan (2019) ¹⁴	Characteristics and Risk Factors of Patients with Nasopharyngeal Carcinoma in West Nusa Tenggara Hospital	Descriptive Cross-sectional	46-55 years old	History of salted fish consumption	A total of 29 cases (15.6%) of nasopharyngeal cancer due to consumption of salted fish
6.	Nathania <i>et al.</i>	Profile of Head and Neck Cancer	Retrospective Descriptive	Mean age 47.45 years	There was a history of	The highest case of <i>head</i>



No.	Author/ Year	Title	Method	Age of Population	Consumption Frequency	Research Results
	(2020) ⁽¹⁵⁾	Patients at Hasan Sadikin Hospital in 2013-2018			salted fish consumption	and neck cancer, nasopharyngeal cancer (31.20%), and salted fish consumption as the second highest risk factor (23.31%)
7.	Barret <i>et al.</i> (2019) ⁽¹⁶⁾	Past and Recent Salted Fish and Preserved Food Intakes Are Weakly Associated with Nasopharyngeal Carcinoma Risk in Adults in Southern China	Population-based Case-control	20-74 years	Weekly	Eating salted fish since childhood increases the risk of NPC (OR = 1.56 (1.24-1.97); p-trend = 0.01)
8.	Rizal & Utama (2019) ⁽¹⁷⁾	Role Of Dietary Intake As Risk Factor For Nasopharyngeal Carcinoma In Muhammadiyah Hospital Palembang June 2017-September 2018	Descriptive Cross-sectional	41-60 years	Salted fish consumption $\geq 3x/week$ for >3 years	Of the total 17 cases, 11 cases of NPC were caused by salted fish consumption (64.70%).
9.	Fitria <i>et al.</i> (2020) ⁽¹⁸⁾	Association Between Risk Factors with The Event of Nasopharynx Carcinoma in Soebandi Hospital Period Of January 2017- March 2019	Observational Analytic with Case-control Design	40 samples; not specific about age	There is a history of salted fish consumption	Salted fish consumption affects the risk factor of NFC with a value of (p = 0.004)
10.	Lye <i>et al.</i> (2015) ⁽¹⁹⁾	Homozygous Wildtype of XPD K751Q	Matched Case-control	Mean age 53.17 years	History of salted fish consumption	Individuals who consume salted fish are



No.	Author/ Year	Title	Method	Age of Population	Consumption Frequency	Research Results
		Polymorphism Is Associated with Increased Risk of Nasopharyngeal Carcinoma in Malaysian Population			n	more susceptible to NPC (OR = 1.75)
11.	Kurnia <i>et al.</i> (2021) ²⁰	Young Woman with Early Stage Nasopharyngeal Carcinoma: A Rare Case	Case Report	1 female NPC patient, 27 years old	Eating salted fish since childhood	The patient had early-stage NPC

Based on the results of the analysis, it can be observed that there are variations in salted fish consumption patterns associated with nasopharyngeal cancer incidence based on the age of the population and the frequency of consumption. The age pattern of the population in the analyzed studies generally ranged from 20 to 74 years, with the mean age predominantly in the 40-55 years range. However, it is important to note that some studies showed a greater risk when exposure to salted fish occurred from childhood, as reported by Ban *et al.* (2017), where salted fish consumption before the age of 10 years was significantly associated with an increased risk of NPC (OR = 1.77; 95% CI = 1.30-2.42).¹²

Frequency of consumption also plays a major role as a risk factor. For example, in the study by Kasim *et al.* (2020), the consumption of salted fish more than three times a month was significantly associated with the incidence of NPC ($p = 0.038$).¹³ Another study by Rizal & Utama (2019) showed that consumption ≥ 3 times per week for more than three years resulted in 64.70% of NPC cases in the studied population.¹⁷

These findings suggest that the more frequent and earlier one is exposed to salted fish, the greater the risk of NPC. Thus, high and long-term consumption patterns, especially from an early age, are important risk factors to be aware of, especially in populations with a strong culture of salted fish consumption.

DISCUSSION

Nasopharyngeal cancer (NPC) is a type of squamous cell cancer that originates from the epithelial cell layer in the nasopharynx and has three main types, namely keratinized type with an incidence of 20-25%, differentiated non-keratinized type with a percentage of 10-15% and undifferentiated non-keratinized type with a percentage of 60-65%. Eating foods containing nitrosamines is one of the risk factors for the disease.¹ There are two types of nitrosamine compounds, namely nitrosamines, which are direct carcinogens, and nitrosamines, which are carcinogens that require metabolic processes in the body. Several compound substances participate in forming nitrosamines, namely nitrates, nitrites, and



secondary amines, that can react easily in the stomach.²¹ The study explained that each salted fish from different regions has a different nitrite compound. Salted fish from the Belawan market contains nitrite of 40.34 mg/kg, Sibolga of 30.58 mg/kg, and Medan of 21.32 mg/kg. The nitrite compound content is still included in the safe limit by Permenkes No. 722/Menkes/Per/IX/88.²²

The consumption habits of salted fish in the population are closely related to the socio-demographic conditions of the community. Reflected in the *demand* for salted fish is influenced by family income, location of residence in coastal areas, and the price of salted fish.^{23,24} People's preferences for salted fish consumption are influenced by various factors, both from the aspect of taste, price, and cultural and socio-economic habits. A study by Haque *et al.* (2019) in Dhaka, Bangladesh, showed that out of 120 respondents, 95.83% chose *Tenualosa Elisha* and 91.67% chose *Pampus Sinensis* for taste reasons, while salted fish such as *Pama pama* (33.33%) was preferred because of its lower price. In addition, the average household consumption of marine fish (including salted fish) was also recorded at 5.49kg per month.²⁵

Long-term exposure to salted fish, especially from an early age, may increase the risk depending on other biological factors. One such factor is the genetic role of the XPD K751Q gene variation that shows different levels of susceptibility in each individual. This gene plays a role in the DNA repair system through the nucleotide excision repair (NER) pathway. It is known that certain variants, such as the Lys/Lys genotype, can lead to decreased DNA damage repair efficiency.¹⁹ When individuals with this gene variant consume foods

high in nitrosamines repeatedly, it is more difficult for their body's system to correct the mutations that occur, resulting in a significantly increased risk of malignant cell transformation.

Poor preservation techniques are also a risk factor for NPC.²⁶ Dry salted fish processing is at risk of being contaminated with sand or dirt because it uses drying techniques that are spread on mats.²⁷ In Indonesia, some policies regulate standards in fish processing, including salted fish. In the Decree of the Minister of Marine Affairs and Fisheries Number 8/KEPMEN-KP/2014 concerning the Enforcement of the Implementation of the Indonesian National Standard for Fishery Products, there are several SNI numbers related to dried salted fish, namely SNI 2721.1: 2009 in the specification section, SNI 2721.2: 2009 in the raw material requirements section, and SNI 2721.3: 2009 in the handling and processing section.²⁸ Another policy, which regulates the fish processing business, is the Regulation of the Minister of Maritime Affairs and Fisheries Number 5 of 2021 concerning Fish Processing Business in article 26 paragraph (1) that "Business Actors who already have a SIUP in the field of Fish Processing are required to have SKP in the process of Fish Processing within a maximum period of 3 (three) months from the time the SIUP in the field of Fish Processing is effectively issued."^{11,29}

The lack of knowledge about NPC is a challenge in dealing with the incidence of the disease. The results of a study explained that a villager in the North Lombok area did not know much about NPC, including risk factors and prevention methods.³⁰ Lack of knowledge can contribute to delays in diagnosis, especially in populations that have a habit of consuming salted



fish. A study by Sulaiman (2022) showed that in RSUD Sayang, Cianjur, salted fish consumption was the highest risk factor for nasopharyngeal cancer (57.5%). Most patients presented with complaints of a lump in the neck, which is a common indicator of advanced stages 31 in line with the study by Ren *et al.* (2017) in China, who found that weekly salted fish consumption correlated with an increased risk of advanced stage diagnosis.³² Due to increased complaints, it is common for new patients to present to ENT specialists making treatment more difficult.²⁰

Efforts can be made to increase *awareness* about NPC, namely through education. Intervention through seminars on NPC can increase awareness by 32.3%.³³ This is in line with research by Wedayani *et al.* (2023) that the *posttest* results regarding NPC increased to 18 people who scored > 50 after receiving a seminar intervention compared to the *pretest* results, which only contained eight people with a score > 50.³⁴ In addition to education, *early diagnosis* can be done to be able to carry out early treatment and prevent changes in cancer cells into advanced stages.

CONCLUSIONS AND SUGGESTIONS

Salted fish consumption is a potential risk factor for nasopharyngeal cancer, especially if consumed at an early age and in high frequency. However, not all studies show the same results. This difference is influenced by many factors, such as genetic background, living habits, environment, and salted fish processing techniques that vary from region to region. On the other hand, the lack of public knowledge related to NPC also contributes to delays in treatment, so more serious efforts are needed to deal with the problem, both in

terms of education and *early diagnosis*, to reduce the incidence and advanced stages of NPC.

If the causal relationship is stronger, further research is needed to design and evaluate health education and intervention programs that aim to reduce the consumption of unsafe salted fish or promote healthier processing methods in high-risk communities. This may help to identify more effective prevention strategies.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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