

Relationship Between Salted Fish Consumption and Nasopharyngeal Carcinoma: An Evidence-based Case Report

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ABSTRAK

Tujuan: mengetahui hubungan antara konsumsi ikan asin dengan kejadian karsinoma nasofaring (KNF). **Metode:** pencarian artikel dilakukan di PubMed® dan ScienceDirect® sesuai pertanyaan klinis. Setelah dilakukan penapisan dengan kriteria inklusi dan eksklusi, penulis menemukan enam artikel tentang karsinoma nasofaring dan konsumsi ikan asin dengan desain kasus-kontrol. Keenam artikel tersebut kemudian dilakukan penilaian kritis terhadap validity, importance, dan applicability-nya. **Hasil:** tidak ditemukan hubungan yang konsisten antara konsumsi ikan asin dengan KNF. Terdapat tiga penelitian yang menunjukkan hubungan antara konsumsi ikan asin dan KNF dan ketiga penelitian tersebut dilakukan pada populasi China Selatan yang memang memiliki insidens KNF yang sangat tinggi dan terkait dengan jenis ikan asin Chinese-style yang dikonsumsi. **Kesimpulan:** tidak terdapat hubungan konsisten antara konsumsi ikan asin dengan karsinoma nasofaring.

Kata kunci: ikan asin, faktor risiko, karsinoma nasofaring.

ABSTRACT

Aim: to know the relationship between salted fish consumption and nasopharyngeal carcinoma (NPC). **Methods:** we searched for the articles from PubMed® and ScienceDirect® based on our clinical question. After filtered with our in- and exclusion criteria, we had six articles about this topic, all of them were case-control studies. All articles were then critically appraised for their validity, importance, and applicability. **Results:** there was no consistent relationship between salted fish consumption and NPC. Worth to note that those studies who showed the firm relationship were conducted in Southern China, where the incidence of NPC was extremely high and related to specific Chinese-style salted fish consumption. **Conclusion:** there was an inconsistent relationship between salted fish consumption and NPC.

Key words: salted fish, risk factor, nasopharyngeal carcinoma.

INTRODUCTION

Nasopharyngeal carcinoma is the most common malignancy in ear, nose and throat (ENT) division. To date, there was a geographic discrepancy in the prevalence of NPC. Asian

ethnicity, including South East Asia, had higher risk of NPC. Globally, NPC had low incidence (around 1/100 000 people per annum),¹ ranked 24th and considered to be a rare malignancy. However, in Indonesia, NPC was ranked as

the 4th most common tumour among males. The incidence of NPC in Indonesia was about 6.2/100 000 people per annum. The diagnosis was considered difficult and frequently patients came in late stage of the disease.²

Host related factors, genetic variation, and environmental exposure had been reported to influence those numbers. Beside the well known Epstein-Barr virus, salted fish consumption remained environmental factors related to this malignancy. N-nitrosamine had been proposed to have a role in the relationship between salted fish and NPC. However, it remains unclear why this cancer would only develop in specific anatomical area.³⁻⁵

Fish products, including salted fish, are an important source of animal protein. In 2010, Indonesia was rank second as a capture fish producer in the world.⁶ Traditional processing of marine fish such as drying and salting were considered the safe and cost-effective method to deliver protein to the population.⁷ Thus, the knowledge about salted fish long term consumption effect, especially its relation with NPC is essential. The most frequently asked question regarding its consumption is whether salted fish consumption has a relationship with adulthood NPC. This study aimed to answer this question.

CLINICAL QUESTION

A male patient, 55 years old came to clinic with tinnitus, nose bleed, and lumps in the neck. The patient had been diagnosed with NPC based on histological examination and already treated by his previous doctor. From early childhood, this patient regularly consumed salted fish. Patient then asked to the doctor in the office whether there was a relation between salted fish consumption and NPC. Thus, we formulate the following clinical question: Is there a relationship between salted fish consumption and adulthood NPC?

METHODS

The literature searching was done in two large databases: PubMed® and Sciencedirect® on May 22nd, 2014. The keywords were “salted fish” and “nasopharyngeal carcinoma” or “nasopharynx cancer”. We then set further article selection

with criteria: Publication within last 10 years, human subject, and research conducted among adult (more than 19 year old) population as we want to exclude factors related to NPC among children or adolescence that might differ with adulthood NPC. Lastly, we appraised articles using case control or cohort method with salted fish as an exposure for NPC. One article was being appraised by two reviewers for its validity, importance and applicability using standardised criteria for etiologic research critical appraisal.

RESULTS

After conducting literature searching in those two large databases, we found 113 articles related to our terms. Nineteen articles matched the searching strategy using criteria as described above (17 articles from PubMed® and 2 articles from Sciencedirect®). Finally, there were six articles that relevant for our clinical question: Ekburanawat et al.⁸, Jia et al.⁹, Ren et al.¹⁰, Guo et al.¹¹, Yang et al.¹², dan Hsu et al.¹³ (**Figure 1**)

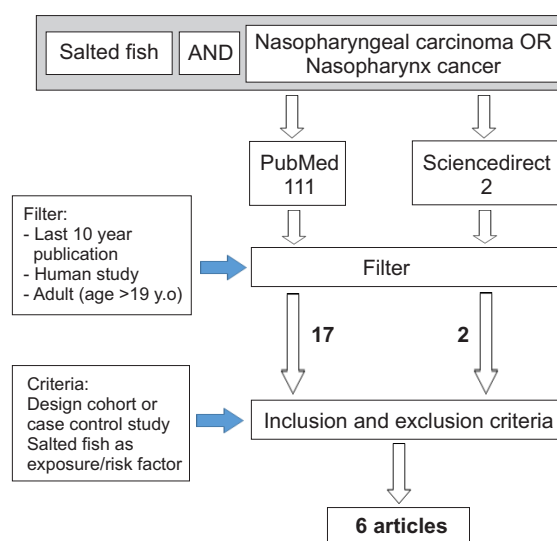


Figure 1. Flow chart of literature searching

On the **Table 1**, all of six articles were valid based on validity critical appraisal aspect. All of included studies were case control and used questionnaire to recall subjects' salted fish eating habits.

Jia et al.⁹ conducted a case control study to evaluate the relationship between Cantonese

Table 1. Result of critical appraisal for validity, importance and applicability aspects (6 articles)

Articles	Study design	Number of subjects	Validity								Importance		Applicability	
			Two groups similar?	Measured the same way?	Adequate follow up?	Exposure preceded the onset?	Dose-response gradient	Dechallenge?	Consistent association?	Biological sense?	Salted fish comparison	Crude OR (95% CI)		Adjusted OR (95% CI)
Ekburanawat et al (2010)	CC	327 cases; 327 controls	+	+	#	+	#	#			<1 time/week ≥1 time/week	1 1.39 (0.91-2.14)	1 1.38 (0.84-2.25)	+
Jia et al (2010)	CC	1387 cases; 1459 controls	+	+	#	+	-	#			less than monthly monthly weekly or more	1 2.39 (1.80-3.17) 1.58 (1.20-2.09)	1 2.42 (1.65-3.54) 1.57 (1.16-2.13)	-
Ren et al (2010)	CC	1845 cases; 2275 controls	+	+	#	+	+	#			Never or rarely ≥1/month ≥4/week	1 2.47 (2.16-2.84)	1 2.54 (2.20-2.94) (category 2 and 3 combined)	-
Guo et al (2009)	CC	1049 cases; 785 controls	+	+	#	+	+	#	-	+	Never <3 times/month ≥3 times/month	1 1.59 (1.27-1.99) 2.03 (1.27-3.19)	1 1.23 (0.83-1.81) 1.90 (1.05-3.47)	-
Yang et al (2005)	CC	502 cases; 1942 controls	+	+	#	+	+	#			Never <1/week >1/week	1 0.81 (0.44-1.47) 1.37 (0.69-2.71)	1 0.65 (0.31-1.35) 1.78 (0.82-3.89)	?
Hsu et al (2012)	CC	375 cases; 327 controls	+	+	#	+	#	#			Not eating Eating	1 0.54 (0.23-1.27)	1 0.88 (0.35-2.21)	?

CC: Case-control. + Yes, stated clearly; - negative finding; # not applicable; ? not sure

traditional diet and NPC, one of the main food being investigated was salted fish. Cases were recruited from hospital patients confirmed by histo-pathological examination while its controls were recruited from general check-up patients in the same hospital. Controls were matched based on sex, age, dialect, and residency. In that study, subjects with monthly regular salted fish consumption had higher risk to NPC (adjusted OR 2.42, CI 95%: 1.65-3.54).

Meanwhile, Ren et al.¹⁰ also conducted a case control study to investigate environmental factors attributed to NPC in patients with previous family history with one of the exposures was salted fish consumption. Cases were NPC patients whom diagnosed in a cancer center, lived in Guangdong at least for five years and did not have other cancer history. Controls were general check up patients and matched for sex, age and residency. In this study, salted fish consumption minimally once a month had higher risk of NPC (adjusted OR 2.54, CI 95%: 2.20-2.94).

Guo et al.¹¹ also conducted a case control study to investigate the relationship between non viral risk factors and NPC in the high risk Guangdong population, Southern China. Cases were recruited based on confirmed histo-pathological examination of NPC while controls were healthy people matched for age, sex and residency. Similar with two previous reports, this study confirmed the relationship between salted fish consumption with NPC. Salted fish consumption more than three times a month was a risk factor of NPC (adjusted OR 1.90, CI 95%: 1.05-3.47).

However, the three other reports had conflicting results. There was no association between salted fish consumption and NPC found in Yang et al.¹², Hsu et al.¹³, and Ekburanawat et al.⁸ studies. Yang et al.¹² conducted the case control study in high risk people living in Taiwan. Even in people with salted fish consumption more than once a week, there was no relationship between salted fish consumption and NPC with adjusted OR 1.78 CI 95%: 0.82-3.89.

In lined with Yang et al.¹² who performed study outside Southern China, Hsu et al.¹³ conducted study also in Taiwan. Cases were recruited from NPC patients whom diagnosed was confirmed by

histo-pathological examination. Controls were then matched for age, sex, and residency. Salted fish consumption more than three times a month did not associated with NPC (adjusted OR 0.88, CI 95%: 0.35-2.21).

Ekburanawat et al.⁸ conducted study in Thailand population from National Cancer Institute in Bangkok. Controls were healthy subjects from the same place. There was no relationship between salted fish consumption and NPC (adjusted OR 1.38, CI 95%: 0.84-2.25).

After appraising the validity and importance of all studies, we look for the clinical application. The most similar spectrum of patients with our population was a study conducted in Thailand. However the studies showed significant relationship between salted fish consumption and NPC only from all studies being conducted in Southern China. The Chinese population might be different from Indonesian based on genetic variation and race.

DISCUSSION

The relationship between salted fish consumption and adulthood NPC was still inconsistent as previous reports suggested.^{1,2} There are three main factors strongly suggested to have association with NPC: Epstein-Barr virus, genetic susceptibility, and environmental factors.^{1,14} The worldwide incidence for NPC was quiet low, however, several Asian continent countries had relatively higher incidence, especially in Southern China and South East Asia. In Southern China, NPC incidence was extremely high.¹ Jia et al.⁹, Ren et al.¹⁰, and Guo et al.¹¹, clearly showed that there were significant relationship between salted fish consumption with NPC in that population (Guangdong). However, the other three studies conducted not in Southern China failed to show such relationship.

Based on International Agency for Research on Cancer (IARC), salted fish was divided into Chinese-style and other-style. Chinese-style salted fish are known containing high level of N-nitrosamine. However, to date there was still no article about the level of N-nitrosamine in other style salted fish and the relationship of its consumption with NPC still remain unclear.⁴ There were some different methods in processing

the Chinese-style and other style salted fish. The Chinese-style salted fish was made frequently with removing internal organ from the throat of the fish, while the other style removed it from an incision of the abdomen. Salted fish then was immersed and weighted for salting in a wooden vats. After finishing the process, the Chinese-style salted fish usually stored for about 4-5 months before being ready for consumption. This is not common in Indonesian salted fish. Thus, this might explain why Chinese-style salted fish contained such high level of N-nitrosamine.^{1,4} Southern China population, in which the three studies that have significant results of the relationship between salted fish consumption and NPC, consumed the Chinese-style salted fish.

In Indonesia, the incidence of NPC was higher than the overall global report but not as high as Guangdong, Southern China population. The reporting cases of NPC in Indonesia might be underestimated as this disease had lack medical awareness and thus still did not properly registered.² To the best of our knowledge, there was no study reporting the relationship between salted fish consumption and NPC in Indonesia. In addition, we also had scarce data about the level of nitrosamine consisted in Indonesian salted fish. Further, we could assumed that there was no relationship between salted fish consumption and NPC in population outside Southern China who do not consume Chinese-style salted fish.

CONCLUSION

In the answer to our clinical question, we found that the relationship between salted fish consumption and nasopharyngeal carcinoma was not consistent. Such relationship was shown only in studies conducted in Southern China setting, in which the incidence of nasopharyngeal carcinoma was extremely high and the salted fish that being consumed is Chinese-style salted fish. The differences in the nasopharyngeal carcinoma incidence and salted fish being eaten in different population might contribute to this inconsistent result.

To find a better evidence, we recommend using the systematic review. Current systematic review did not answer the relationship between salted fish and nasopharyngeal carcinoma as it

ignored the evidence from non-Chinese study population in their conclusion.⁵ Thus, the result could not be extrapolated in different setting, including our patient in Indonesia, and could not firmly conclude that salted fish consumption generally link to nasopharyngeal carcinoma. Our study would also recommend the study of N-nitrosamine level consisted in salted fish in Indonesia. Salted fish is an important source of protein and thus the evidence about its harm would be important for our public health issue.

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