

Histamine Fish Poisoning (HFP) in Indonesia: Current status and challenges.

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Abstract. Histamine fish poisoning (HFP) is one of many global food safety issues experienced by fish industries in both developed and developing countries, in which temperature abuse and mishandling during processing, storage, and distribution were identified as the main sources of histamine formation and accumulation in the products. In Indonesia, official reports on HFP are limited, however, mass media documented HFP cases and outbreaks which occurred every year, from different regions of Indonesia. The Scombroid fish, including Bullet and Frigate Tuna locally named as *Tongkol* (*Auxis rochei*, *A. thazard*), was reported as the main food vehicle causing the majority of HFP cases. The maximum allowable level of histamine for fresh and processed fish marketed in Indonesia is 100 mg/kg, except for fresh tuna for sashimi (50 mg/kg), based on Indonesian National Standard (SNI). The results from official control and monitoring programs by Indonesian's government as well as published studies reported the presence of elevated levels of histamine in fish sold at domestic markets, hence implementing the cold-chain system during post-harvest stages is still a challenge. Evaluation of the current national requirement for histamine testing for fish products also important, to ensure product safety prior to consumption.

Keywords: *tongkol; domestic market; national standard; temperature; fish products safety*

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1. Introduction

Histamine is one of many global food safety issues affecting both developed and developing countries. In Indonesia, the consumption of tuna (*tuna*), mackerel or bullet tuna (*tongkol*) and skipjack (*cakalang*) which domestically named as TTC, was commonly associated with histamine fish poisoning (HFP) or previously named as Scombroid fish poisoning [1]. Fish with naturally high level of histidine, which generally belong to family Scombridae, including tuna and albacore (*Thunnus*), skipjack (*Katsuwonus*), mackerel (*Scomber*), and bonitos [2] were likely contained a high level of histamine that may lead to HFP cases. Histamine formation and accumulation in fish products occur due to a combination of temperature abuse and mishandling of Scombroid fish during processing, storage and distribution [2-6]. Hence, as far as misconduct on the handling and processing practices of Scombroid fish still found in fish industries, the risk of HFP still present globally in both developed and developing countries.

Histamine in fish is produced through decarboxylation of histidine by bacteria which naturally present in fish or as a result of contamination. This catabolism process is catalysed by histidine decarboxylase (*hdc*) enzyme [7]. Enterobacteriaceae species such as *Morganella morganii*, *Raoultella planticola*, *R. ornithinolytica*, *Hafnia alvei*, *Klebsiella pneumonia*, *Citrobacter freundii*, *Enterobacter aerogenes* and *Proteus vulgaris* are known as prolific histamine producing bacteria and are usually implicated to HFP cases [8-12].

2. Current status of HFP cases/outbreaks in Indonesia

Official reports on HFP cases/outbreaks in Indonesia, providing information such as the implicated food (fish product), the histamine level, the presence of histamine producing bacteria, the reported symptoms, and the number of patients, are still limited. The Indonesian Ministry of Health together with the National Agency of Drug and Food Control are the competent authorities responsible for investigation and countermeasures of outbreaks related to infectious disease and food poisoning at local and national levels (Ministry of Health Regulation 2/2013).

A systematic review on published and unpublished investigation reports and studies about foodborne outbreaks in Indonesia reported 1.176 foodborne outbreaks occurred during 2005 – 2015 [13]. As defined in the Indonesian Health Ministry Regulation No. 949/MENKES/SK/VII/2004, a case with patients/affected people between 10 to more than 300 people is categorized as an outbreak. However, only 175 of these reports have completely identified the food vehicles and the poisoning agents causing the outbreaks. Pathogenic bacteria such as *Eschericia coli*, *Bacillus cereus* and *Staphylococcus* sp. were amongst the most common causes of poisoning, with more than 15% of the total cases were due to contamination of these pathogens. While chemically, histamine was reported as the major cause of the reported foodborne poisoning outbreaks (6.7%). To date, the most available information on the reported HFP cases is mainly obtained from the newspaper. In the last five years, more than 800 people suffered from HFP, with 25% of the patients were hospitalized (Table 1).

Table 1. HFP cases in Indonesia reported from local newspapers during 2015 – 2020.

Number of affected consumers (patients)	Location	Suspected fish vehicle	References
34 hospitalized	Malang (East Java)	Frigate/bullet tuna	[14]
10 hospitalized	Cilacap (Central Java)	Frigate/bullet tuna	[15]
200 (86 hospitalized)	Aceh (Special Region of Aceh)	Frigate/bullet tuna	[16]
37 hospitalized	Tenggarong (East Kalimantan)	Frigate/bullet tuna	[17]
14 (5 hospitalized)	Jambi	Frigate/bullet tuna	[18]
>100 received treatment in local health facilities	Kolaka (Southeast Sulawesi)	Skipjack tuna	[19]
300 received treatment in local health facilities	Jember (East Java)	Frigate/bullet tuna	[20]
50 (3 hospitalized)	Pasaman (West Sumatera)	Frigate/bullet tuna	[21]
53 (21 hospitalized)	Pemalang (Central Java)	Frigate/bullet tuna	[22, 23]
19 received treatment in local health facilities	Batang (Central Java)	Frigate/bullet tuna	[24]

Note: Frigate/bullet tuna (Local name: Tongkol); Skipjack tuna (Local name: Cakalang)

In all reported cases, symptoms such as nausea, vomiting, dizziness, skin rash, breath difficulties (dyspnea), and diarrhoea appeared shortly up to 2 hours after fish consumption. These symptoms corresponded with published reports on HFP clinical symptoms (Table 2). Most people also recovered within 24 hours, thus cases involved one to few persons are usually remain unreported [6, 25]. HFP symptoms are known to be mild and self-limited, thus patients usually self-medicated. These factors contribute to the low reports of HFP cases in Indonesia.

Table 2. Published clinical symptoms of HFP.

Clinical symptoms of HFP	Reference
A peppery taste, numbness of the tongue, headache, flushing and sweating, dizziness, nausea, diarrhoea, and dyspnea	[26]
Skin rashes, mouth tingling, vomiting, dyspnea (difficulty breathing)	[27]
Diarrhoea, rash, nausea, vomiting, fever, abdominal pain	[25]
Nausea, vomiting, headache, skin rashes	[14]

Frigate/bullet tuna (*Auxis* sp., *Euthynnus affinis*) was identified as the most common source of poisoning from these reports, which can be related to the availability of this product in domestic market all year round. In addition, the average national price of frigate/bullet tuna at producer level was relatively cheaper (IDR 23,838 -24,666/kg), compare to tuna (IDR 31,647 – 32,834) and skipjack (IDR 24,607 – 26,082) [28]. Tuna and tuna-like fish (TTC) are amongst the most popular and economically important capture commodities in Indonesia. From 7.2 million tonnes of total Indonesian capture fisheries production in 2018, the production of TTC composed 306; 492 and 488 thousand tonnes, respectively [29].

Amongst other seafood, TTC were the most commonly consumed fish by Indonesian’s household. According to the survey of household consumption on animal-based sources in Indonesia in 2014, TTC were consumed by 24% of all respondents which was higher than other types of seafood. In addition, the calculated TTC consumption for urban and rural consumer in 2014 were 3.4 and 4.1 (National);14.5 and 17.2 (Household) kg/cap/year,

respectively [30]. In general, the preference of Indonesian's consumer at rural area to allocate their consumption expenditure to buy seafood product (including TTC) caused by its budget priority for animal-based protein source [31]. Seafood product are cheap and accessible for consumer at rural area (especially in coastal area). Hence, the seafood consumption is higher for consumer at rural than urban area.

However, in domestic market, these commodities are often distributed with minimum or no cooling system, providing suitable environment for microbial growth, including histamine producing bacteria, and trigger histamine formation/accumulation. Histamine is a heat-stable protein which cannot destroyed by common cooking practices such as boiling, steaming, heating or freezing [1, 32], therefore its formation should be prevented prior to further processing and consumption by applying proper cold chain system.

3. Regulation regarding histamine limit in fish products in Indonesia

The National Standardization Body of Indonesia has published 92 national standards (Standar Nasional Indonesia-SNI) regarding the minimum quality and safety requirements for fish products (Table 3), including frozen, dried, boiled, fermented, fresh and cold, canned, and live fish as well as surimi-based product. These standards aimed to improve product competitiveness, to maintain fair trade as well as to provide consumer protection.

For fresh fish (SNI 2729:2013), the maximum allowable level of histamine is 100 mg/kg; and histamine testing is required for fish belong to family *Scombridae*, *Clupeidae*, *Pomatomidae*, and *Coryphaenidae* [33]. This level is similar to the level set by Canadian authority for canned, fresh and frozen Scombroid fish including tuna, mackerel and mahi-mahi [34]. Australia set higher maximum limit, i.e. 200 mg/kg of histamine as a natural toxin in fish and fish product [35]. The European Commission (EC) orders a three class sampling for fish species which naturally have high level of histamine (Reg. EC 2073/2005) where amongst nine sets of samples, no more than two samples may exceed 100 mg/kg histamine ('m'), and no sample may exceed 200 mg/kg histamine ('M') [36].

Table 3. Maximum level of histamine in different fish products as required by the SNI.

SNI number	Type of product	Histamine concentration (mg/kg)
SNI 2729:2013	Fresh fish	100
SNI 2693:2014	Fresh tuna for sashimi	50
SNI 7530:2018	Fresh tuna loin	100
SNI 2696:2013	Frozen fish fillet	100
SNI 4110:2014	Frozen fish	100
SNI 7968:2014	Frozen cooked tuna loin	100
SNI 4104:2015	Frozen tuna loin	100
SNI 8271:2016	Frozen fish steak	100
SNI3 7263:2018	Frozen marlin loin	100
SNI 2725:2013	Hot-smoked fish	100
SNI 8269:2016	Rendang tuna	100
SNI 2691:2017	Katsuobushi	100
SNI 8645:2018	Fish jerky	100
SNI 2717:2017	Salted-boiled fish	100
SNI 8222:2016	Canned sardine and mackerel	100
SNI 8223:2016	Canned tuna	100
SNI 8377:2017	Fish sauce	40 mg/100 g
SNI 7266:2017	Fish ball	100

4. Evaluation of histamine sampling monitoring plan and national standard on histamine testing

The Indonesian Fish Quarantine and Inspection Agency (FQIA) is the competent authority to monitor the quality and safety of fish landed in fishing ports or fish landing areas as well as fish sold in the markets in Indonesia. More than 3,000 fish samples were collected within the period of 2013 – 2018, which consisted of fresh and processed fish (Table 4). More than 50% of the total samples were fish which naturally have high histidine content. However, only 23.8% of these families (385 samples) were tested for histamine content including tuna and tuna-like fish (local names: tongkol, cakalang, deho, madidihang), scad, mackerel (local names: salem, gindara, kembung), sardines, trevallies, mahi-mahi, and marlin.

During the period of 2013-2018, no fresh fish tested were exceeded the allowable level of histamine (100 mg/kg) as required by National Standard of Indonesia SNI 2729:2013, however samples contained more than 50 mg/100 were still found (Table 4). For processed fish, the highest level of histamine detected during this period was 151,42 mg/kg from salted-boiled tuna in 2014. However, since 2015 no processed fish were tested for histamine, which may lead to underreporting data. Although the monitoring results showed that no fresh fish samples tested exceed 100 mg/kg, the low percentage of sample tested for histamine might causes underestimation of the real figure of histamine contamination in fish marketed domestically. Also, samples with histamine more than 50 mg/kg might pose significant risk to consumer if these samples were not handled properly following the good handling practices (GHP). To enable more valid assessment on the histamine level in fish sold in the

domestic markets, it is suggested to perform an evaluation on the fish sampling plan and to update the targeted fish which represent more high-risk groups/fish.

Table 4. The number of fish with high histidine content collected and tested for histamine during monitoring and surveillance program by the Indonesian FQIA*

Year collected	Fresh fish			Processed fish	
	Sample collected	Sample tested for histamine	Samples >50 mg/kg histamine	Sample collected	Sample tested for histamine
2013	52	19	Samples contained 65.5 and 71.5 mg/kg histamine	15	7
2014	45	24	None	25	11
2015	102	54	Samples contained 66.1; 70; 72.7; 73.3; 84.2; 85.2 and 98.8 mg/kg	0	0
2016	31	12	None	0	0
2017	770	101	Samples contained 52.2; 63.7; 70.1; 82.6; 86.9 and 92.7 mg/kg	9	0
2018	567	157	79.9 mg/kg	0	0
Total	1567	367		49	18

*Data provided by the Indonesian FQIA

Within sampling monitoring plan, the type of fish collected should adequately represent the “high-risk” fish, i.e., fish with naturally high histidine content or fish implicated to HFP cases/outbreaks. The majority of samples tested for histamine content reported in Table 4 belong to family *Scombridae* (79%), followed by *Carangidae* (11.17%), *Clupeidae* (4.16%) and small proportion of *Coryphaenidae* and *Gempylidae*. As mentioned earlier, SNI 2729:2013 required histamine testing for fresh fish from family *Scombridae*, *Clupeidae*, *Pomatomidae*, and *Coryphaenidae* [33].

To provide detail information on “high-risk” fish which can be used to evaluate the SNI reference list, literature search on fish implicated to HFP cases worldwide between 2000 – 2020 (Table 5) as well as reported cases in the US and EU were done (Table 6-7). Data on histamine-related foodborne outbreaks in the US during 2000 – 2017 was collected from the US CDC web-based National Outbreak Reporting System (NORS) (<https://www.cdc.gov/norsdashboard/>), while reports on food with risk of histamine contamination which are distributed in the EU markets during 2000 - 2020 was obtained from the EU Rapid Alert System for Food and Feed (RASFF) portal (<https://webgate.ec.europa.eu/rasff-window/portal/>). The majority of fish from family *Scombridae*, such as tuna (Yellowfin, Bigeye, Skipjack) were reported to have elevated histidine content (exceeded the recommended level) and/or associated to HFP cases/outbreaks.

Table 5. Reported HFP cases (2000 - 2020) and histamine levels of the associated fish.

Fish name	Histamine level (mg/kg)	References
Billfish (<i>Makaira niglicans</i>)	2,570	[37]
Billfish (<i>Xiphias gladius</i>)	1,570 – 2,695	[37]
Escolar (<i>Lepidocybium flavobrunneum</i>)		
Cooked, marinated, smoked	400-7,300	[26, 38, 39]
Fish cube (<i>Tetrapturus angustirostris</i>)	523	[40]
Herring (semi dried-whole)	2,800 - 4,800	[41]
Marlin (<i>Makaira nigricans</i>)		
Filleted	435-478	[42]
Fried striped marlin	620, 896	[43]
Mackerel (<i>Scomberomorus</i>)		
Canned	612-1,539	[44]
Fried Japanese Spanish mackerel (<i>Scomberomorus niphonius</i>)	3,318	[45]
Raw Japanese Spanish mackerel (<i>Scomberomorus niphonius</i>)	1,906	[45]
Mackerel (saba)	1,266 - 2,423	[41]
Milkfish (<i>Chanos chanos</i>)	616 - 2,350	[46, 47]
Mahi-mahi (<i>Coryphaena hippurus</i>)	113-377; 2,000	[48-50]
Saury paste (<i>Cololabis</i> sp.)	320	[51]
Swordfish (<i>Xiphias gladius</i>)		
Filleted, fried, cooked	280-7,600	[39, 52, 53]
Frozen	6,700	[53]
Sardine		
Canned, dried	144.8 - 1,700	[10, 54]
Dumpling	958	[41]
Tuna		
Cold-smoked	914-4,550	[39]
Fresh, raw	35; 96-1,738	[39, 55]
Processed or prepared products (burger, canned, dumpling, fermented, fried, mayonaise, patties. ready to heat packed, salad, sandwich)	3,860 - 4,710, 6,432; 86-1,608; 446.2; 350; 1,824; 1,000	[27, 39, 49, 56-61]
Yellowfin tuna (<i>Thunnus albacares</i>)	470 - 4,900	[62-64]
Raw	1,720	[65]
Vacuum packed	7,100 - 9,100	[66]
Steak	290	[67]
Saute	3,100	[63]
Cooked	3,720	[65]

Table 6. Outbreaks in the US due to histamine contamination in fish during 2000 – 2017.

Fish name	Number of reports
Ahi	6
Blue marlin	3
Escolar	9
Mahi-mahi	8
Marlin	1
Salmon	1
Tuna	9
Unspecified	1
Wahoo	1
Yellowfin tuna	2

Note: identified outbreaks setting were prison/jail, private home/residence, restaurant (dine-in, take away), grocery store.

Table 7. RASFF notifications of food consignments (suspected and confirmed) with potential risk to cause HFP during 2000 – 2020.

Fish name	Product type	Histamine level (mg/kg)
Anchovies (<i>Engraulis encrasicolus</i>)	Fillet, in oil	290 – 4,200
Atlantic pomfret (<i>Brama brama</i>)	Chilled	
Butterfish/Escolar (<i>L. flavobrunneum</i>)	Fillet	208 – 1,000
Marlin	Fillet, loin	400 - 690
Sardines	Canned fillet in oil, chilled	220.3 – 1,323
Albacore (<i>Thunnus alalunga</i>)	Frozen whole	3,110 – 3,698
Atlantic Bluefin Tuna (<i>Thunnus thynnus</i>)	Fresh	1,000 – 3,603
Bigeye tuna (<i>Thunnus obesus</i>)	Vacuum-packed loin	565
Tuna	Canned, chilled, defrosted, fresh, frozen, raw, thawed, vacuum packed	5 - 10,000
Yellowfin tuna (<i>T. albacares</i>)	Chilled (fillet, loin, smoked), defrosted, fresh, frozen, marinated, thawed, vacuum packed	1 - 5,100
Yellowtail amberjack (<i>Seriola lalandi</i>)	Fresh	1,000

Based on data in Table 5-7, the following suggestions can be made to evaluate the groups of fish which currently required histamine testing as defined by SNI.

1. Published data/reports/cases listed families such as *Scombridae*, *Clupeidae* and *Coryphaenidae* as group of HFP implicated fish and/or fish with high level of histamine. Therefore, SNI recommendation to test these families was appropriate, but family *Pomatomidae* should no longer be included in the SNI, since no HFP reports/cases were associated with this family.

2. Families such as *Carangidae*, *Xiphiidae*, and *Gempylidae* were reported as fish associated with HFP cases and/or found to contain high level of histamine, therefore these families should be included in the list of fish family to be analysed for histamine content in the SNI recommendation.
3. Apart from the above-mentioned families, other families including *Dussumeridae*, *Engraulidae*, *Bromidae*, and *Istiophoridae* were also reported as group of HFP-associated fish and/or fish with high level of histamine. However, these families were not presence in Indonesian water, therefore were not recommended to be included in the list of fish family to be analysed for histamine content in the SNI recommendation., especially when local raw material is used during fish processing.

5. Future directions

Although the maximum allowable level of histamine in fish as regulated by the Indonesian government is below the toxic level (200 mg/kg) suggested by the FAO/WHO [5], conditions such as tropical environment and potential contamination during handling and processing could rapidly elevate the level of histamine in fish sold in Indonesian market. Studies suggested that the formation of histamine in fish product correlates with the growth of histamine producing bacteria (HPB), where toxic concentrations (>200 mg/kg) were observed during middle or exponential phase of bacterial growth [68, 69].

At the end of fish distribution chain in domestic market in Indonesia, fish were marketed to fish processors or food service providers and sold directly for household consumption. In 2017, 48.57% (8.4 million tonnes) of total domestic fish consumption was accounted from the household, followed by processing industries (36.74%) and food service providers such as hotels and restaurants [70]. Following this trend, controlling fish temperature at consumer's hand also plays an important role to keep the safety and quality of fish. Fish for direct consumption in the household were generally purchased from traditional or modern markets, in which controlling the cold-chain system could be a challenge by retailers or consumers. Thus, consumer education on how to safely handle fish, especially Scombrotoxic fish, become critical. This effort should be supported by collaboration between government and private sectors to provide adequate information (i.e., education and extension), tools and infrastructures such as ice making machine for traditional fish seller in traditional market. Apart from that, the current maximum allowable level of histamine in fresh fish for direct consumption should be reviewed, to provide the highest protection for consumer.

Whilst the recommended level of histamine in fish is still applicable for fish intended as raw material in the fish processing facilities or food service providers such as restaurant or caterer, fish in this category is usually purchased directly from fish landing place or wholesales, where the cold-chain system is better managed as part of the seller good handling practices (GHP) required by the food authorities.

This review includes primary data from routine monitoring of histamine in fish products in Indonesia and secondary information from the scientific literature on HFP report worldwide, thus provides reliable science-based information to be used by the competent authority to review the present regulations related to histamine in fish. However, more recent data on histamine in fish are still needed. To improve the current status of HFP cases in Indonesia, a comprehensive and real-time platform to report HFP cases that is accessible for everyone needs to be developed by Indonesian Government (i.e. Ministry of Health, Indonesian FDA, Local Authorities). In addition, consumer awareness and their involvement to prevent HFP cases should be further investigated.

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