IMPACT FACTOR

2.429

Reviews on Environmental Health

Volume 35 (2020): Issue 3 (Sep 2020): Special Issue: Assessing and mitigating environmental exposures in early life; Issue Editors: Sharon Brabon and Zahir Islam

ORIGINAL ARTICLES

Human health risk assessment of heavy metals via consumption of fish from Kao Bay

Hasnawati Amqam, Dahlan Thalib, Daud Anwar, Saifuddin Sirajuddin, and Anwar Mallongi

Article Category: Research Article | Pages: 257–263 | Published online: 29 Jun 2020

Mini Review

Hasnawati Amqam*, Dahlan Thalib, Daud Anwar, Saifuddin Sirajuddin and Anwar Mallongi

Human health risk assessment of heavy metals via consumption of fish from Kao Bay

https://doi.org/10.1515/reveh-2020-0023
Received February 18, 2020; accepted May 10, 2020

Abstract: Water pollution by heavy metals due to discharge from gold mining activity has threatened the aquatic environment and human health of the community around Kao Bay. This report review explores the level of mercury and arsenic in the fish and the health risk of fish consumption within the community around Kao Bay. Fish from 10 spots in the bay were analyzed for mercury and arsenic using Atomic Absorption Spectrophotometry. Community members around Kao Bay were interviewed for details of their fish consumption. Daily intake of metals and health risk level were also calculated. All of the fish caught contained mercury (mean of 0.2110 ug/g) and arsenic (mean of 0.422 ug/g). This heavy metal concentration exceeds the allowable level for food standard. The human health risk assessment showed that the fish caught from Kao Bay were not safe for human consumption (RQ>1). The hazard risk quotient based on cancer and non-cancer was more than one. As many as 49 of 52 people living around Kao Bay have a risk from mercury and arsenic exposure via fish consumption. The magnitude of HQ and ECR values for most fish indicates that it is not safe for consumption.

Keywords: arsenic; hazard; mercury; pompano; rabbitfish; snapper.

Introduction

The application of heavy metals in industries has resulted in severe environmental pollution through the discharge of effluents into the environment [1–3]. One of the sectors that contribute to this is gold mining. Water pollution by heavy metals due to discharge from gold mining activity has threatened the aquatic environment and human health of the surrounding community. Because of potential toxic effect and ability to bioaccumulate in marine ecosystems, heavy metals have been a global interest. Mercury (Hg) and Arsenic (As) are categorized as toxic heavy metals, and maximum residual levels in the environment and food have been defined for humans [4–6]. Heavy metals bioaccumulation in organisms and biomagnifications delineate the processes and pathways of xenobiotics in a food chain from one trophic level to another. Heavy metals enter the food chain after the consumption of water or organisms caught as food (i. e., zooplankton and phytoplankton) [7]. Considering their sensitivity to contamination, fish have been well documented as good bio-indicators for measuring the quality of the aquatic environment [8–10]. They are involved in varying trophic levels and show different sizes [11]. In many parts of Indonesia, fish and other water organism have been consumed daily by the community, indicating that the community have a high risk of heavy metals exposure from fish consumption. Consumption of heavy metal-contaminated fish for protract periods lead to the accumulation of heavy metals in human.

Kao Bay is located on the northern part of Halmahera Island. There are many gold mines operated legally or illegally around Kao Bay. Thus, artisanal gold mining has been the primary income source for thousands people and also has been the main source of mercury (Hg) and arsenic (As) pollution. The discharge from mining tailing has increased the Hg and As contamination in Kao Bay. A previous study found Hg of 0.12–0.23 ppm in red snapper, 0.03–0.51 ppm in mullet fish, 0.002 ppm in white shrimp, and liver of Goldband goatfish (0.02 ppm) [12]. The finding of heavy metal content in the fish led to the importance of health risk assessment, exploring the risk level in the community from fish consumption. Thus, this study aims to assess human health risk from fishes consumption within the community around Kao Bay.

***Corresponding author: Hasnawati Amqam**, Environmental Health Department, Public Health, Universitas Hasanuddin, Makassar, Indonesia, E-mail: hasnawati.amqam@unhas.ac.id. https://orcid.org/0000-0003-4961-8517
Dahlan Thalib: Health Agency Office, Halmahera Tengah Regency, Indonesia
Daud Anwar and Anwar Mallongi: Environmental Health Department, Public Health, Universitas Hasanuddin, Makassar, Indonesia
Saifuddin Sirajuddin: Nutrition Department, Public Health, Universitas Hasanuddin, Makassar, Indonesia

Methods

Research site

The research was conducted in Kao Bay. It is located on the northern part of Halmahera Island at the position of 1‖25 ‘U – 0‘50‘U and 127‘40 ‘T 128‘10‘T. This bay is a basin of two northern arms of Halmahera Island, through a threshold approximately 40 m deep. The western and northern part of the bay is a vast expanse in the shape of a lowland which is overgrown with mangrove trees and consists of sandy beaches. Kao Bay has characteristics of a bag-like shape with a diameter of 15 km^2. This bay is a fishing ground for local fishers and is famous for a relatively large producer of shrimp and anchovy. Kao Bay located at five sub-district of North Halmahera Regency (Malifut, Kao, Kao Teluk, West Kao, and North Kao) and two others Regencies (East Halmahera and West Halmahera). The coastal area includes the estuary of the Dum-Dum, Manuasa, Sai, Taolas (Kobok), Akesone, Tabobo, Papaya, and Sommi Rivers. The mining sites of PT. Nusa Halmahera Minerals (NHM) and some artisanal gold mines which have the potential to release heavy metal waste from industrial activities are upstream from these rivers. The map of Kao Bay and the sampling site is shown in Figure 1.

Sample

a. Fish sample

Fish were caught along Kao bay waters 10 m from the coast, at 10 different points (Figure 1). The fish include snapper (*Lutjanus griseus*), rabbitfish (*Siganus* sp) and pompano fish (*Caranx sexfasciatus*) and are the most consumed fish by coastal communities in the two villages around Kao Bay. Each fish sample was put in a plastic bag, sealed, and stored in a cool box with ice and cool packs. Samples were stored in the 0–5 °C temperature freezer.

b. Human

Fifty-two fishermen living in the coastal area of Kao Bay; Dum-Dum Village, Kao Bay District and Tabobo Village, Malifut District agreed to participate in this study. Fishermen who have lived for a minimum of 5 years in the coastal areas were chosen with consideration for the chronic effects of Hg and As. Consuming fish from the study area were also taken as an inclusion criterion. The fishermen were interviewed about their socio-economic characteristic by means of a questionnaire. Food Frequency Questionnaire (FFQ) and food pictures were

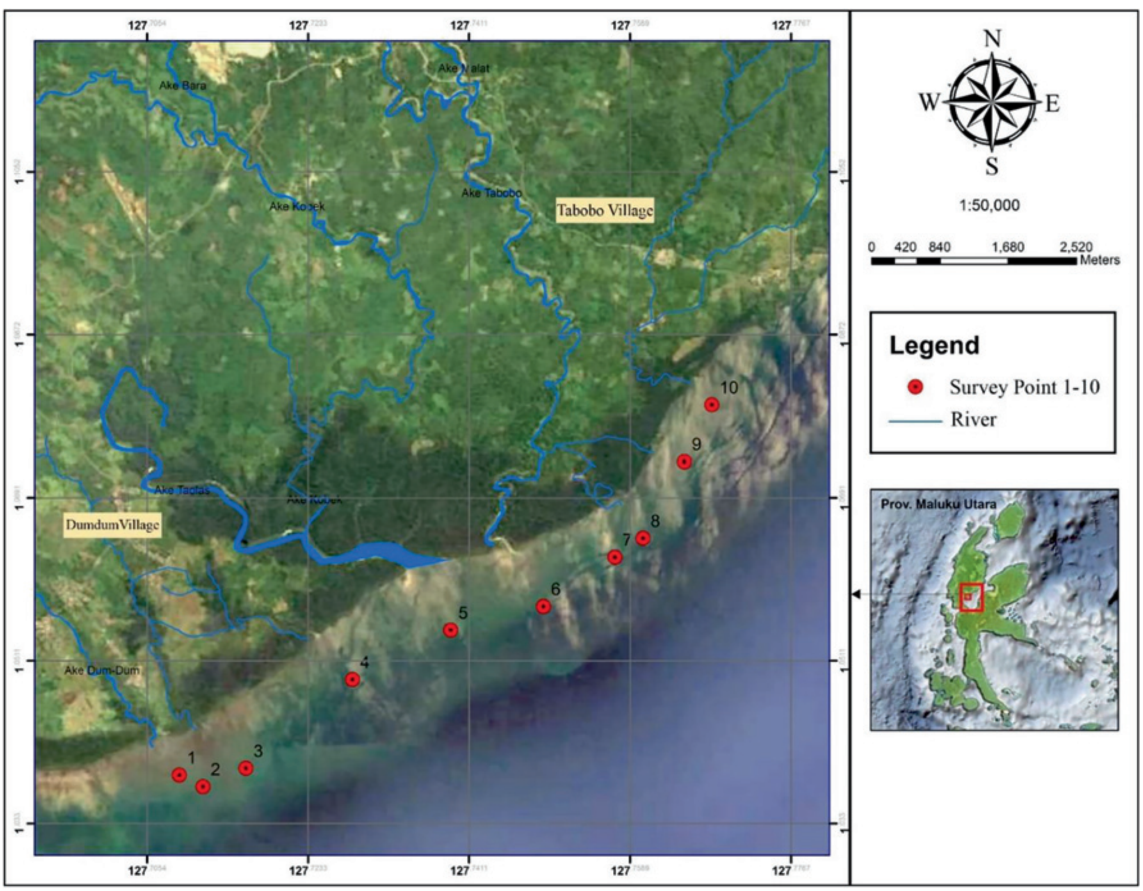

Figure 1: Map of Kao bay and sampling site (point 1–10).

used to define their fish consumption. For ethical consideration, informed consent were obtained from all of the participants involved in this study before interview.

Fish analysis

Arsenic measurement: Fish samples, weighing 10–15 g each, were taken from research locations. The fish meat was put into a volumetric flask. As much as 50 mL of HNO_3 and 5 mL of $HClO_2$ solution were added until the sample was submerged, then the sample was put in a heater for 30 min for destruction until clear and completely dissolved. After cooling, the completely dissolved sample was filtered into a 50 mL volumetric flask then piped into 20 mL tubes and was put on Auto Sampler Set. Sample was mixed with As reductant solution called $NaBH_4$ 1.5% and NaOH 0.2% and moved into Microwave Plasma Atomic Emission Spectrometer (MP-AES). The sample analysis results were displayed on a computer.

Hg measurement: Approximately 10–15 g of fish sample was put in a volumetric flask. Acids ($HClO_4$, HNO_3) were added with a ratio of 1:4 to each volumetric flask, shaken and left it for one night. Initially they were heated with 100 °C temperature until the brown steam from the nitrate disappears, then raised to 200 °C until the solution was clear with a volume of approximately 1.2 mL. The sample is then removed out and diluted to 20 mL using aquades. The solution was shaken and left for one night until it settles, and the solution was clear. The heavy metal content is then measured using Atomic Absorbance Spectrophotometer (AAS).

Data analysis

The human health risk was assessed using the formulas for intake calculation, non-carcinogenic and carcinogenic risk.

Intake rate calculation:

$$I = \frac{CxRctExfExDt}{Wb \quad x \quad tavg}$$

Risk calculation for non-carcinogenic:

$$\mathrm{RQ} = \frac{I}{\mathrm{RfD}}$$

Carcinogenic risk calculation:

$$\mathrm{ECR} = 1xSF$$

Notes:

I (Intake) : Risk agent concentration consumed by human (mg/kg/day)

C (Concentration) : Risk agent concentration in food (mg/kg)

R (Rate) : Consumption rate or number of consumption everyday (gr/day)

tE (time of exposure) : Duration or number of hours of exposure each day (24 h/day) in a settlement)

fE (frequency of exposure) : Length or number of days of exposure each year (day/year)

Dt (Duration time) : Length or number of years of exposure

Wb (Weight of body) : Weight of a person (kg)

tavg : time average period, 30 years X 365 days/year = 10.950 days (non-carcinogenic)

RQ : Risk Quotient for exposure to ingestion pathways

RfD : Reference dose, risk agent reference value for ingestion exposure (mg/kg/day)

0.0003 for As and 0.0001 for MeHg

ECR : Excees Cancer Risk, the risk level of individual experience cancer

SF (slope factor) : Reference values for risk agents with carcinogenic effects

Result

Characteristics of Respondents

Table 1 showed that the majority of respondents were >40 years old (67.31%). Most of the respondents received elementary school as their highest level of education, indicating that the majority of them had a low level of education. Mostly, respondents have lived in the village for more than 40 years. Their time living in Kao Bay area was the same as their age as they have never left the village. The most frequent fish to be consumed were snapper fish (*L. griseus*), mostly consumed twice a day (90.38%) or 14 times a week with the amount of more than 100 g/day (51.92%). The people mostly had refill water for drinking (59.62%) and piped water for bathing.

Risk assessment

In the risk assessment of mercury, Rfd of methylmercury (MeHg) was used considering that around 95% of total mercury will be transformed to MeHg through methylation process [13]. Figure 2 shows that the level of risk (RQ) for average consumption of fish containing mercury and arsenic were more than one (RQ>1). This result indicated that consumption of the fish containing mercury and arsenic is not safe for public consumption.

Conclution from the result of the RQ value >1 is that mercury in *L. griseus* with an average level of 0.0002293 mg/g is a high risk for people weighing up to 62 kg when consuming Snapper fish as much as 360 g/day for 365 days/

Table 1: Characteristic of respondents.

Variable	n	%
Age (years)		
<30	6	11.54
30–40	11	21.15
>40	35	67.31
Education		
No School	3	5.77
Elementary school	34	65.38
Junior high school	10	19.23
Senior high school	5	9.62
Length of stay (years)		
<30	13	25.0
30–40	10	19.23
>40	29	55.77
Drinking water source		
Refilled container water	31	59.62
River	15	28.85
Artesian well	3	5.77
Piped Water	2	3.85
Deep earth Well	1	1.92
Clean water source		
River	18	34.62
Artesian well	3	5.77
Piped Water	51	59.62
Consumed Fish		
Siganus Sp	40	76.92
Caranx sexfasciatus	6	11.54
Lutjanus griseus	6	11.54
Health problems		
Influenza/Headache	38	73.08
Itchy	5	9.62
Rheumatism	5	9.62
Toothache/gum pain	1	1.92
Hypertension	1	1.92
Others	2	3.85
Health problem characteristic		
Continuous	1	1.92
Intermittent	51	98.08
Health problem treatment		
Self-treatment	14	26.92
Health facilities	38	73.08

year for a period of 30 years. These risk estimates were calculated for the default lifetime duration of 30 years thus effects of mercury toxicity may be experience in the next 30 years. With an RQ value >1, risk management is needed to reduce perceived health risks. Figure 3 showed that the highest ECR value for As resulted from the consumption of *Caranx sexfasciatus*, reached a maximum of 0.0026 and the mean of 0.0014. The values were more than the ECR of 10^{-4}, the indicator unit for a chemical result in a carcinogenic effect. Meanwhile, the consumption of other fishes resulted in ECR lower than 10^{-4}.

Discussion

Minimum, maximum, mean concentrations and standard deviation of heavy metals in fish *L. griseus, Siganus* sp, *C. sexfasciatus* caught from Kao Bay are presented in Table 2. The heavy metal Hg and As recorded 100% incidence in the 10 fish samples. Insignificant variations were observed in the concentration of heavy metals among different species due to the slight difference size among the species. Furthermore, feeding habits and accumulation capacities also contribute to the concentration variations. Mercury concentrations in fish tissue are affected by age, length, and weight of the fish [14].

Mean Hg concentration was as high as 0.108 ± 0.006 mg/kg in *L. griseus* from Dum-Dum Village and 0.350 ± 0.311 mg/kg in same fish species from Tabobo Village. The lowest Hg accumulation (0.097 mg/kg) was in *Siganus* sp from Dum-Dum Village. While the highest Hg concentration was observed in *L. griseus* caught from Tabobo, as high as 0.570 mg/kg. This highest concentration was because the size of the fish was larger than the others. The size indicated that this fish was more mature than the other species. Thus, the accumulation of heavy metals in its tissues had been occurring for longer and resulted in higher mercury. Some studies have reported mercury levels in the range of 0.05–0.32 mg/kg in *L. griseus*, 0.03–0.20 mg/kg in *Lutjanus campechanus* from Coastal Louisiana [15], 0.01 mg/kg in *L. griseus* from Gorontalo river [16], 0.193 mg/kg and 0.409 mg/kg in *L. griseus* from marine area and estuarine area of Florida Bay respectively [17]. Maximum limit of mercury contamination in food set by the National Government of Indonesia is 0.5 mg/kg [18]. Thus, the Hg levels in most fish samples were still lower than the standard set, except in *L. griseus* from Tabobo which slightly higher than the standard. A study in Totok Bay showed that Hg was detected in fish (0.804 mg/kg) and gastropods (1.02 mg/kg) which were also exceeded the maximum limit. Total levels of As in gastropods were seven times higher than the maximum level of that standard [19].

Another study in Ranayapo Amurang River, North Sulawesi, showed that Hg and As concentrations in sediments from four villages around the river were approximately 0.05–1.3 ppm and 2–100 ppm respectively. The sediments from the river estuary contained 0.18 ppm Hg and 1 ppm Ass. The highest level of both of these heavy metals come from Karinbow village, which was an area of artisanal mining [20]. Another study at Kao Bay region; around Balaotin, Cibok and Kobok rivers found that exposure to Hg-contaminated snails (*Trachus telescopium Linnaeus*) has exceeded the maximum limit exposure of >1 ppm/kg/day for

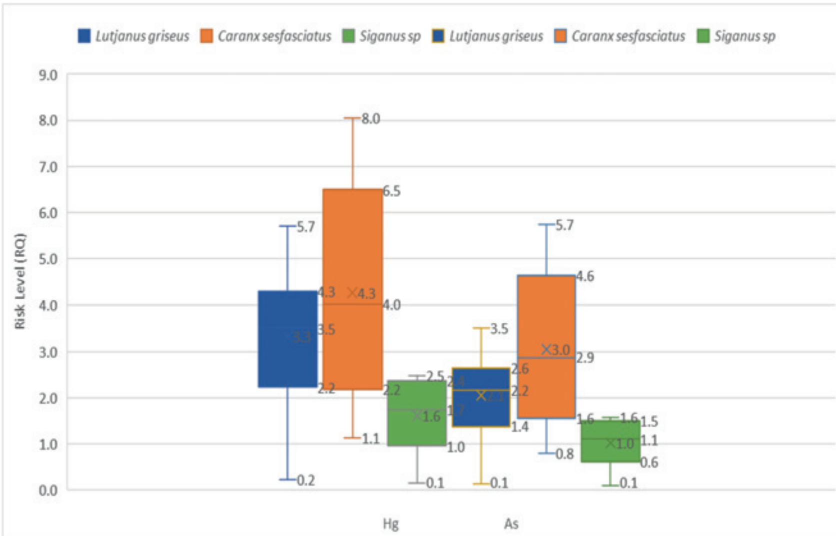

Figure 2: Non carcinogenic risk level (RQ) from consumption of fish contain mercury and arsen in the community of Kao Bay coastal area.

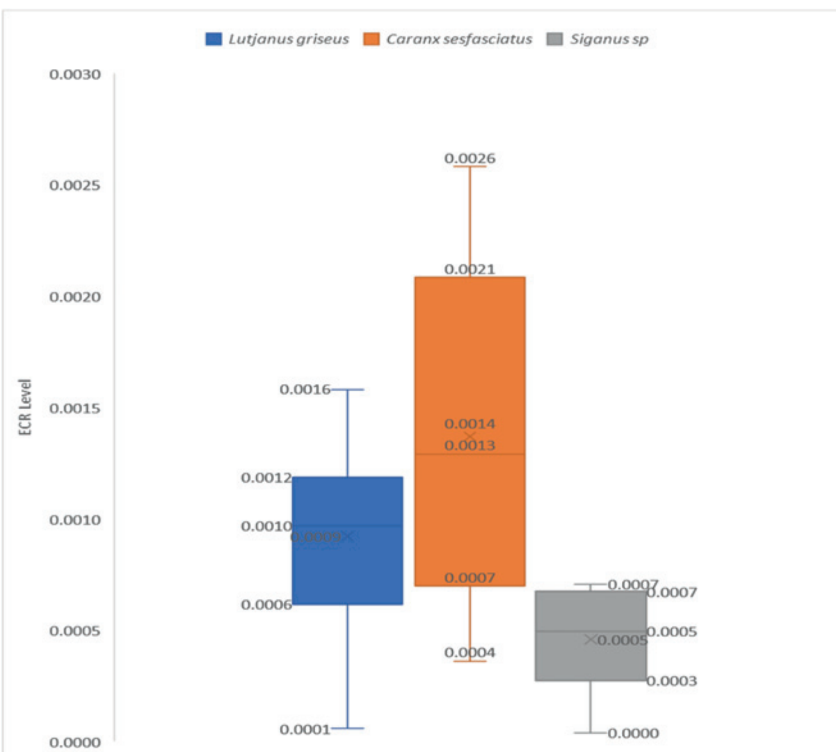

Figure 3: Carcinogenic risk level (ECR) from consumption of fish contained arsen in the community of Kao Bay coastal area.

Table 2: Mercury and arsenic concentration in Kao Bay.

Village	Fish	Hg (mg/kg)			As (mg/kg)		
		Min	Max	Mean ± SD	Min	Max	Mean (SD)
Dum-Dum	*Lutjanus griseus*	0.104	0.113	0.108 ± 0.006	0.232	0.239	0.235 (0.045)
	Caranx sexfasciatus	0.198	0.212	0.205 ± 0.093	0.467	0.502	0.484 (0.025)
	Siganus sp	0.097	–	–	0.187	–	–
Tabobo	*Lutjanus griseus*	0.130	0.570	0.350 ± 0.311	0.203	1.019	0.611 (0.576)
	Caranx sexfasciatus	0.200	0.246	0.228 ± 0.024	0.146	0.939	0.458 (0.422)

children and <1 ppm/kg/day for adults. Also, for weekly Hg exposure, it was at a high range of >3.5 ppm/kg/week [21]

Mercury is a systemic poison and is accumulated in the liver, kidneys, spleen, and bones. In the body, mercury is excreted through urine, faeces, sweat, saliva, and milk. Mercury poisoning will cause symptoms in the central nervous system such as personality abnormalities and tremors, convulsions, senility, insomnia, loss of self-confidence, irritation, depression, and a sense of fear. Mercury poisoning can also cause gastrointestinal symptoms such as stomatitis, hypersalivation, colitis, chewing pain, gingivitis, black lines on the gums (leadline), and loose and skin problem such as dermatitis and ulcers/wounds.

The mean concentrations of As were highest in *L. griseus* and *C. sexfasciatus* from Dum-Dum that reached 0.186 mg/kg and 0.484 mg/kg, respectively. The highest mean concentration for *Siganus* sp was from Tabobo with the level of 0.611 mg/kg. This level was still below the Indonesian National Standard for As contamination in food (1.0 mg/kg) [18]. Maximum levels for As in certain foods have been established by the European Commission Regulation via benchmark dose lower confidence limit (BMDL01) values between 0, 3 and 8 μg/kg BW/day [22]. FAO and WHO recommend the maximum limit in permitted in food for As is 0.35 mg/kg BW [23]. The USA sets the amount of As in food that can be consumed is less than 0.04 mg/day of seafood, while for the total amount of As that can be consumed is 0.2 mg/day [24]. The total As exposure from food without industrial As exposure should be less than 0.3 mg/day. Arsenic affects the body, especially the blood which can affect the bone marrow and change the composition of blood cells, on the liver causing central necrosis and cirrhosis of the liver. The effect of arsenic on the kidneys is vessel damage, tubules and glomerular kidneys. The kidneys first affected by arsenic are glomerular so proteinuria occurs. The effect of arsenic on the cell system can cause damage to cell mitochondria which causes a decrease in cell energy causing cell death [24].

Health risk estimation

The consumption of 200 g of fish containing 500 p.g mercury/kg will result in the intake of 100 p.g mercury, predominantly methylmercury (MeHg). This amount is one-half of the recommended provisional tolerable weekly intake [25]. The level of mercury in fish, even for humans consuming only small amounts (10–20 g of fish/day), can markedly affect the intake of MeHg. Mercury in fish may be in the form of methylation because of the bioaccumulation and biomagnification process in the food chain. Fish also not only accumulates mercury metal in water but can convert organic mercury to metal mercury in their bodies through biomethylation. Mercury contaminates in fish are accumulated and biomagnified and more than 90% will be transformed to MeHg [26]. Thus, instead of RfD total mercury, RfD of MeHg was used in the risk estimation.

Risk level (RQ) more than 1 or ECR $>10^{-4}$ indicate the fish are not safe for consumption by the people living in the Kao Bay area due to the risk of emerging adverse health effects. People who consumed the lowest level of fish containing Hg (0.0001142 mg/kg) resulted in RQ of 1.054. Meanwhile, consumption of the highest level of Hg (0.0004770 mg/kg) raises this to RQ of 3.924. Thus, the community around Kao Bay who consumed contaminated fish has a risk level of more than one. Similarly with the consumption of fish contained As, except for the lowest level of As contained fish.

ECR of more than 10^{-4} indicated that arsenic in *C. sexfasciatus* with a maximum level of 0.00046854 mg/kg increases the risk to a person with a bodyweight of 57 kg if he consumes it up to 300 g/day for 365 days/year within 70 years. ECR of 0.001585 means that there are 1.585 cases within a million people which may develop cancer or there are 1.58 people with increased risk for developing cancer in a million persons.

The level of risk is greatly influenced by the amount of Hg and As intake. Several factors influence the intake, such as the concentration of chemicals in fish, body weight, duration of exposure, intake rate, and frequency of exposure [11]. Risk is a probability. It does not mean that individual with RQ>1 will definitely experience adverse health effects. The value shows that individuals with RQ>1 have a higher probability of experiencing adverse impacts than individual with RQ=1. Thus, risk management is necessary to control and minimize the estimated risk within the community.

The research conducted at the Kenjeran Beach in Surabaya showed that respondents who consumed contaminated fish with an average mercury concentration of 99.11 g/day had a mercury concentration in their hair of 0.5 ppb [27]. Mercury in fish may be in the form of methylation because of the bioaccumulation and biomagnification process in the food chain. Fish also not only accumulates mercury metal in water but can convert organic mercury to metal mercury in their bodies through biomethylation.

Conclusion

Mercury and arsenic concentration in the fish from Kao Bay have been documented as exceeding the allowable level for the food reference standard. The magnitude of Hazard Quotient (HQ) values for most fish was still more than one, which indicates they are not safe for consumption. The accumulation and biomagnifications process in the living aquatic habitats of Kao Bay produce hazard for contaminated fish consumption in long period.

Acknowledgments: The authors wish to thank the Central Halmahera District Health Office and Government of North Maluku Province for supporting the study.
Research funding: Research reported in this article was supported partly by the Governor of North Maluku Province(No. 221/KPTS/MU/2015), the period of 2014–2019. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Governor.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Conflict of interest: Authors state no conflict of interest.
Informed consent: Informed consent was obtained from each participant included in the study.
Ethical approval: This study was approved by the Ethical Committee of Medical Faculty of Hasanuddin University.

References

1. David IG, Matache ML, Tudorache A, Chisamera G, Rozylowicz L, Radu GL. Food chain biomagnification of heavy metals in samples from the Lower Prut Floodplain Natural Park. Env Eng Manag J 2012; 11:69–73.
2. Hall RJ, Kolbe E. Bioconcentration of organophosphorus pesticides to hazardous levels by amphibians. J Toxicol Environ Heal Part A Curr Issues 1980;6:853–60.
3. Batvari B, Prabhu D, Kamalakannan S, Krishnamurthy RR. Heavy metals accumulation in two fish species (*Labeo rohita* and *Cirrhina mrigala*) from Pulicat Lake, North of Chennai, Southeast Coast of India. J Chem Pharm Res 2015;7:951–6.
4. Nauen CE. Compilation of legal limits for hazardous substances in fish and fishery products. FAO Fish Circ (FAO) no 764;1983.
5. Commission regulation No. 466/2001. Official Journal of European Commission, 1.77/1. 2011.
6. Administration F and D. Fish and fishery products hazards and controls guidance, 4th ed. US Department of Health and Human Services Food and Drug Administration, Rockville 2011.
7. Ahmed MK, Baki MA, Islam MS, Kundu GK, Habibullah-Al-Mamun M, Sarkar SK, et al. Human health risk assessment of heavy metals in tropical fish and shellfish collected from the river Buriganga, Bangladesh. Environ Sci Pollut Res 2015;22: 15880–90.
8. Authman MMN, Zaki MS, Khallaf EA, Abbas HH. Use of fish as bio-indicator of the effects of heavy metals pollution. J Aquac Res Dev 2015;6:1–13.
9. Plessl C, Otachi EO, Körner W, Avenant-Oldewage A, Jirsa F. Fish as bioindicators for trace element pollution from two contrasting lakes in the Eastern Rift Valley, Kenya: spatial and temporal aspects. Environ Sci Pollut Res 2017;24:19767–76.
10. Naigaga I, Kaiser H, Muller WJ, Ojok L, Mbabazi D, Magezi G, et al. Fish as bioindicators in aquatic environmental pollution assessment: a case study in Lake Victoria wetlands, Uganda. Phys Chem Earth, parts A/B/C 2011;36:918–28.
11. Burger J, Gochfeld M, Jeitner C, Pittfield T, Donio M. Heavy metals in fish from the Aleutians: interspecific and locational differences. Environ Res 2014;131:119–30.
12. Simange MS, Simbolon D, Jusadi D. Analisis Kandungan Merkuri (Hg) dan Sianida (CN) Pada Beberapa Jenis Ikan Hasil Tangkapan Nelayan Di Teluk Kao, Halmahera Utara. Repos IPB Bogor 2010:335–353. https://repository.ipb.ac.id/handle/123456789/53762. (Accessed 19 July 2019).
13. Baeyens W, Leermakers M, Papina T, Saprykin A, Brion N, Noyen J, et al. Bioconcentration and biomagnification of mercury and methylmercury in North Sea and Scheldt Estuary fish. Arch Environ Contam Toxicol 2003;45:498–508.
14. WHO. Environmental Health Criteria 101; Methylmercury. World Health Organization, Geneva, 1990;1–144.
15. Bank MS, Chesney E, Shine JP, Maage A, Senn DB. Mercury bioaccumulation and trophic transfer in sympatric snapper species from the Gulf of Mexico. Ecol Appl 2007;17:2100–10.
16. Arifin YI, Sakakibara M, Sera K. Impacts of artisanal and small-scale gold mining (ASGM) on environment and human health of Gorontalo Utara Regency, Gorontalo Province, Indonesia. Geosciences 2015;5:160–76.
17. Evans DW, Crumley PH. Mercury in Florida Bay fish: spatial distribution of elevated concentrations and possible linkages to Everglades restoration. Bull Mar Sci 2005;77:321–46.
18. Badan Standardisasi Nasional. Batas Maksimum Cemaran Logam Berat dalam Pangan [Internet]. SNI 7387:2009 2009. Available from: https://sertifikasibbia.com/upload/logam_berat.pdf.
19. Rumampuk NDC, Warouw V. Bioakumulasi total merkuri, arsen, kromium, cadmium, timbal di Teluk Totok dan Teluk Buyat, Sulawesi Utara. J LPPM Bid Sains dan Teknol 2015;2:49–59.
20. Kitong MT, Abidjulu J, Koleangan HS. Analisis merkuri (Hg) dan arsen (As) di sedimen sungai Ranoyapo kecamatan Amurang Sulawesi Utara. J MIPA 2012;1:16–9.
21. Samman A, Batu DTFL, Setyobudiandi I. Konsentrasi merkuri dan hubungannya dengan indeks kepadatan keong popaco (*Telescopium telescopium*) di Kao Teluk, Halmahera Utara. DEPIK J Ilmu-Ilmu Perairan. Pesisir dan Perikan 2014;3. https://doi.org/10.13170/depik.3.2.1471.
22. European Union. Maximum levels of inorganic arsenic in foodstuffs. Off J Eur Union 2015;L 161/14.
23. FAO. Joint FAO/WHO food standards programme codex alimentarius commission on contaminants in Food. FAO/WHO, Italia. 2016.
24. US EPA, 1997. Arsenic and fish consumption, EPA-822-R-.EPA Dallas, Texas.
25. FAO/WHO. Joint FAO/WHO expert committee on food additives. World Health Organization; 2010, Vol 71.
26. Marrugo-Negrete J, Verbel JO, Ceballos EL, Benitez LN. Total mercury and methylmercury concentrations in fish from the Mojana region of Colombia. Environ Geochem Health 2008;30:21–30.
27. Sudarmaji AHS, Suwarni A, 2004. Contaminated fish consumption in long period. Konsumsi Ikan Laut, Kadar Mercury Dalam Rambut, Dan Kesehatan Nelayan Di Pantai Kenjeran Surabaya. J Manusia Dan Lingkungan 11(2004). https://doi.org/10.22146/jml.18627.