Potential risks of secondary Sideroblastik Anemia due to the lead contaminated fish consumption from Youtefa Gulf in Jayapura, Papua

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Abstract:

The impact of Plumbum (Pb) or lead pollution on aquatic biota can harm environmental humans health. Some research conducted in Youtefa Gulf, Jayapura found that Pb has been polluting the waters and living biota. This study aims to analyze the magnitude of health risk due to exposure to Pb and epidemiological study in how much risk of health problems caused by exposure to Pb. Type of study is observational epidemiological cross sectional analytic approach. Sampling was determined by purposive sampling. Protoporphyrin levels in the urine of 75 respondents found 19 samples (25.3%) that protoporphyrin levels> 30 mg / dl (Secondary sideroblastic anemia) and 56 samples (74.7%) were normal. The risk level of several variables with consecutive secondary sideroblastic anemia due to Pb toxicity was 95% CI = 0:54 (0:26 to 1:13) fish intake rate with risks level = 1.48 95% CI (1.26- 1.75), length of stay = 2 CI 95% (0.9-4.2), sex = 1.18 95% CI (0.52-2.4), age 95% CI 2:32 (1:19 to 4:53), the blood levels of Pb = 0:53 95% CI (0.41-0.73), respectively.

Key words: Secondary sideroblastic anemia, Protoporphyrin, Plumbum

Introduction

Coastal area is an area that is prone to contamination due to errors in its management because it makes the coastal region as a dumping all sorts of waste coming from the mainland [1]. One of the pollutants that often contaminate water and harm marine life is a heavy metal such as plumbum (Pb). The main cause of Pb be dangerous pollutant because it cannot be destroyed (non-degradable) by living organisms in the environment and accumulate in the environment, especially to the bottom waters form a complex compound along with organic and inorganic materials and combinations adsorbs. Biota living in heavy metal polluted waters, can accumulate heavy metals in their tissues. The higher the metal content in the water the higher the content of heavy metals in the body of the animal is accumulated [2].

The impact of waste disposal in the form of heavy metals cause disruption of aquatic biota. Gulf Yotefa can not be separated from the problem of heavy metal pollution, because a part of ragtag Jayapura, the estuary into the Gulf Yotefa. In 2004 a survey Bappedalda Jayapura on water quality parameters Yotefa polluted sea in the Gulf of Pb has reached 0.03 mg / l [3]. Based on the research results Manalu in 2012, found that an index of pollution in the waters of the Gulf of Storet Yotefa based index (a value of raw data about the quality of the water which is then transformed into an index) are in moderate and severe polluted [4].

Pb Exposure to animals and humans and may provide acute toxic effects, sub-acute, and chronic subkronik. Chronic toxic effects occur when chemicals accumulate in biological systems (absorption exceeds excretion biotransformation) or if that does not produce toxic effects or if not recovered sufficiently from biological systems to perform recovery of damages in the frequency interval of exposure, or presentation occurs repeatedly [5]. Such entering pollutant into aquatic system lead to the hazard both to the current human life and environmental ecosystem due to varies heavy metal toxic pollution [6]. There are several studies that have been conducted in the Gulf Yotefa associated with environmental pollution, such as research Bappedalda Jayapura City (2004), Manalu [4], but previous studies have not assess epidemiologically about Pb materials with secondary sideroblastic anemia, other than that there is no research the test corpoporphyrin and protoporphyrin. This study attempts to answer those factors associated with the incidence of secondary sideroblastic anemia.

Materials and Methods

This analytic epidemiological study using a cross sectional approach is the approach through the process of calculation or estimate the risk to a target organism, system or (sub) populations by measuring Pb concentrations in humans. After the measurement is done, then calculate the risk to calculate prevalence ratios [7]. The population in this study are all people who live around the Youtefa Gulf. The sample is a portion of the population. The sampling technique was purposive sampling, resulting in the determination of the sample, the researcher establishes the following criteria: a. Willing to be respondent, b. Stay in Yotefa Gulf > 2 years. Exclusion criteria: Not willing to be a respondent and Stay in Yotefa Gulf < 2 years. Number of sample taken were 74. The level of corpoporphyrin and protoporpirin urine using a LCMSMS (Liquid Chromatography Mass Spectrofotometri Detector). The level of blood plumbum using Quantum Resonance Analyze.

Results
a. Pb Poisoning (corpoporphyrin levels) with secondary sideroblastic anemia

Based on the survey results revealed that of the 75 respondents surveyed, 100% of respondents found corpoprphyrin levels above the standard that is> 20 ug / dl. To analyze the epidemiological, then the data is made into a dichotomy by using the median value is> 16.9 mg / dl in categorizing risk. The result is of 75 samples found 33 respondents or 44% of the high corpoporphyrin levels (above the median value and 42 respondents or 56% of the corpoporphrinnya levels below the median. As for the case of secondary sideroblastic anemia, of 75 samples tested found 23 samples or 30, 7% higher protoporphyrinnya levels or secondary sideroblastic anemia. To see whether Pb poisoning is a risk factor for secondary sideroblastic anemia, following the analysis of the epidemiology of these variables:

Table 1: Analysis of risk between levels corpoporphyrin with secondary sideroblastic anemia among community in Youtefa Gulf, Papua, 2014

	Secondary sideroblastic anemia		Not Secondary sideroblastic Anemia		Total	X2 (P value)	Risks level; 0,54	
	n	%	n	%			L	U
Median Corpophyrin (>16,9µg/dl)	8	21,6	29	78,4	37	0,94	0,26	1,13
Corpoporphyrin (≤16,9 µg/dl)	15	39,5	23	60,5	38			
Total	23	30,7	52	69,3	75			

Table shows that of 37 people corpoporphyrinnya levels above the median value (16.5 micrograms /dl) there are 8 people or 21.6% have secondary sideroblastic anemia and of the 38 people below the median values are 15 people or 39.5% anemic secondary. To determine whether there is a relationship between levels with secondary sideroblastic anemia with corpoporphyrin then both variables were analyzed by X2 and it is known that P value is 0.94, because the P value > 0.05 alpha then interpreted that there is no relationship between toxicity Pb with secondary sideroblastic anemia. Then, to determine whether the poisoning risk factors Pb is secondary sideroblastic anemia, the two variables were analyzed by calculating the ratio of prevalence. The analysis showed that Risks level = 0.54 95% CI = 0.26 Lower and Upper = 1.13 Pb then interpreted that poisoning is not a risk factor for secondary sideroblastic anemia, because the lower and upper includes the number 1.

b. Intake Rate Fish with secondary sideroblastic anemia

Table 2: Risks Analysis between fish intake with secondary sideroblastic anemia among communities in Youtefa Gulf, Papua, 2014

	Secondary Sideroblastik Anemia		Not Secondary Sideroblastik Anemia		Total	X2 (P value)	Risk level ; 1,489	
							L	U
	n	%	n	%				
High Intake rate	0	0	5	100	5			
Low Intake rate	23	32,9	47	67,1	70	0.12	1.26	1.75
Total	23	25.3	55	74.7	75			

The analysis showed that Risks level = 1.489 95% CI = 1.26 Lower and Upper = 1.75 for risk greater than the one in which the value of the lower and upper does not include the number 1 then interpreted that the person has a high intake rate risk of Pb with 1,48 times for secondary sideroblastic anemia than people with Pb low intake rate.

c. Length of Stay and secondary sideroblastic anemia

Table 3: Risks analysis of long-lived with secondary sideroblastic anemia among communities in the Youtefa Gulf of Papua, 2014

	Secondary Sideroblastik Anemia		Not Secondary Sideroblastik Anemia		Total	X2 (P value)	Risk level ; 2,0	
							L	U
	n	%	n	%				
Length stay (>40 thn)	16	40	24	60	40	0.61	0.9	4.2
Length stay (< 40 tahun)	7	20	28	80	35			
Total	23	30,7	52	69,3	75			

The analysis showed that risk level = 2.0 95% CI = 0.9 Lower and Upper = 4.2 then it is interpreted that the length of stay in the Youtefa Gulf is not a risk factor for secondary sideroblastic anemia, because risk level <1.

d. Gender and secondary sideroblastic anemia

Table 4: Risk analysis of Gender and secondary sideroblastic anemia among community in the Gulf Youtefa Jayapura, Papua, 2014

	Secondary Sideroblastik Anemia		Not Secondary Sideroblastik Anemia		Total	X2 (P value)	Risk level ; 1,18	
							L	U
	n	%	n	%				
Male	6	33,3	12	66,7	18			
Female	17	29,8	40	70,2	57	0,77	0,52	2,4
Total	23	30,7	52	69,3	75			

The table shows that the secondary sideroblastic anemia prevalence in males was higher (33.3%) than in secondary sideroblastic anemia prevalence in women (29.8%) prevalence of anemia is different from the results of several previous studies. Farihah report that of 205 samples in the know of anemia in men by 32% (151 people) and the female workers by 64% (56 people). Mulyawati report of 72 women were found as many as 56 people (77.7%) are anemic. So also reported Untoro et al, anemia in women by 41.3%, amounting to 62.4% reported Adriani and MOH reports of 56.0% [8].

This research differs from research conducted by Tan Malaka in 2012 which found that there is a relationship between the sexes with hemoglobin levels due to exposure of Pb at the toll booth attendant Jagorawi Jakarta [9]. This study also differs from the results of research Reina Engle Stone, et al, in Cameroon which found that 13.5 times the risk of women with anemia compared with men [10].

5. Age with secondary sideroblastic anemia

Table 5: Risk analysis of age and secondary sideroblastic anemia among communities in Youtefa Gulf , Jayapura, 2014

	Secondary Sideroblastik Anemia		Not Secondary Sideroblastik Anemia		Total	X2 (P value)	Risk level ; 2,32	
							L	U
	n	%	n	%				
Age > 65 y	5	62,5	3	37,5	8			
						0,039	1.195	4,53
Age $\leq$ 65 y	18	26,9	49	73,1	67			
Total	23	30,7	52	69,3	75			

According to the theory of groups at risk of anemia is a group of elderly people and children, but because in this study the respondents aged> 20 years, so their analysis grouped into two groups at risk are elderly and not the elderly.

6. Plumbum levels in the blood with sideroblastic anemia

Table 6: Risk analysis of Pb levels in blood with secondary sideroblastic anemia among communities in Youtefa Gulf of Papua, 2014

	Secondary Sideroblastik Anemia		Not Secondary Sideroblastik Anemia		Total	X2 (P value)	Risks level ; 0.553	
							L	U
	n	%	n	%				
Kadar Pb > 0,64 µg/dl	22	56,4	17	43,6	39	1,0	0.41	0,73
Kadar Pb< 0,64 µg/dl	1	100	0	50	1			
Total	23	57,5	17	42,5	40			

Discussion

a. Relationship with the incidence of Pb poisoning of secondary sideroblastic anemia

Pb in the body can cause acute poisoning and chronic poisoning. Minimum number of Pb in the blood which can cause poisoning range from 60-100 micro-grams per 100 ml of blood. In acute poisoning usually occurs due to the inclusion of lead compounds soluble in acid or inhaling the vapors Pb. The symptoms that arise include nausea, vomiting, intense abdominal pain, abnormal brain function, severe anemia, kidney damage and even death can occur within 1-2 days. Abnormalities of brain function occurs because Pb is competitively displace major minerals such as zinc, copper, and iron in regulating our mental functions. Chronic lead poisoning causes symptoms such as depression, headache, difficulty concentrating, restlessness, decreased memory, insomnia, hallucinations and muscle weakness. Central nervous system is the major target organs of lead. According to Dr. M. Erikson's research shows that pregnant women who have high levels of lead in their blood turned out to be 90% of the deposits of lead in the body is passed to the fetus through the placenta, where fetal toxicity affects intellectual and behavior of the child in later life. From the World Bank notes, URBAIR 1994, it appears that the effects of air pollution by lead in Indonesia has caused 350 cases of heart disease [11].

The relationship between lead poisoning and iron deficiency anemia has been studied, particularly in high-risk populations, such as people living in the area of lead smelting. Previous lead poisoning is associated with neurotoxic effects compared to the

effects on heme synthesis. Several studies have found that lead levels increase with iron deficiency anemia. Other studies show a significant increase in the proportion of Pb in the blood of 100 to 199 mg / dL and> 200 mg / dL with iron deficiency anemia. Increased blood lead levels can interfere with erythropoiesis inhibits the synthesis of protoporphyrin, and interfere with the absorption of iron increases the risk of anemia. On the condition of lead poisoning, the most visible effect is the formation of the heme pathway. Lead inhibits the enzyme δ-aminolevulinic acid and ferrokelatase dehydrate, so the enzyme δ-aminolevulinic acid dehydrate cannot change porphobilinogen, consequently cannot enter the iron heme protoporfirin.Perkursor cycle, protoprofi erythrocytes rin protoporfi changed to zinc, be increased and decreased heme formation, causing severe anemia.

According to WHO, a heavy metal such as Pb is including heavy metals that do not provide biological benefits to the human body. Too many Pb can damage various systems of the body including the nervous and reproductive systems and kidneys, and can cause high blood pressure and anemia. Pb can accumulate in bones and Pb poisoning can be diagnosed from a blue line around the gums and corpoporphyrin levels. Pb is very harmful to the brain development of the fetus and children, and for pregnant women. Pb can interfere with the metabolism of calcium and Vitamin D. Pb high levels in children can cause irreversible consequences may include learning disabilities, behavioral problems, and mental retardation. At very high levels, Pb can cause seizures, coma and death [12].

b. Relationship between intake rate with secondary sideroblastic anemia

The analysis showed that risk level = 1.489 95% CI = 1.26 Lower and Upper = 1.75 for risks level greater than the one in which the value of the lower and upper does not include the number 1 then interpreted that the person has a high intake rate risk of Pb is 1,48 times for secondary sideroblastic anemia than people whose low intake rate. Effect of Pb on haemopoietic system cause a decrease in red blood cell production and decreased survival time (survival time) due to interference with the cell membrane. Nature of anemia is normocytic or normochrom-normochrom-microcytic. However, the incidence of haemopoietic effect as above only occur in chronic exposure to levels in the blood Pb l 50 g / dl or more. Pb suppress heme synthesis through inhibition Ferochelatase, resulting in an increase in erythrocyte protoporphyrin or in the urine [9].

Divalent metal transporter 1 (DMT 1) that serves to transfer the iron passes through the apical membrane of duodenal enterocytes is not only specific to iron. DMT-1 also can transport other divalent metal ions, including manganese, cobalt, copper, zinc, cadmium and lead. Therefore, iron deficiency conditions increase the speed of absorption of other divalent metals, especially lead to iron deficiency conditions increase the incidence of lead poisoning. Conversely the presence of iron can reduce lead poisoning, through direct competition in the binding site. Number Pb absorbed in the gastrointestinal tract depends on several factors, such as particle size, pH, other substances in the gastrointestinal tract, and the status of essential nutrients. Absorption Pb ingested on an empty stomach condition is higher than when ingested with food. The presence of iron may reduce absorption of Pb by way of direct competition on a bond, the condition of iron deficiency causes increased absorption, retention and Pb toxicity. Once absorbed, 99% plumbum bound to the erythrocytes, and 1% free spread into the soft tissues and bone, so that the levels in the blood Pb describe levels in the body. The total load of stored blood Pb in the four compartments, the blood (half-life 35 days), soft tissue (half-life 40 days), trabecular bone (half-life of 3 to 4 years), and a component of the cortical bone (half-life 16 to 20 years) . Pb has various effects on cells, ie Pb bound to the enzyme and can change and eliminate the effects of the enzyme. Pb inhibit the enzyme δ-aminolevulinic acid and ferrokelatase dehidrase, so the enzyme δ-aminolevulinic acid dehidrase (ALAS) cannot change the result porphobilinogen iron protoporphyrin cannot enter the cycle. Heme precursor, erythrocyte zinc protophorphyrin be replaced protophorphyrin, be increased and decreased heme formation.

A study in Jakarta in 2001 showed Pb source mainly from Pb gasoline emissions, evidenced by the finding that levels of blood Pb children living near busy traffic higher than children who live far away from the traffic. Other sources of potentially Pb include city tap water pipes, painted with varnish, exposure in the workplace parents brought home (work in smelting or recycling of metals, welding, related to the car, and printing), recycling battery, Pb ceramic-coated, Pb -coated wires, plastic, toys, cosmetics, soil and dust. Pb can also be sourced from a variety of other products, such as old paint chips, herbal medicine (ayurvedic medications), deodorant, Mexican candies, sauces imports and food imports. (Lopez, et al., 2013).

c. The relationship between length of stay with secondary sideroblastic anemia

The longer people live in an area polluted environment Pb (fish and sea water containing contaminated Pb), the more have a higher risk of contamination is affected. According Indriani Mustaphia, et al in 2006 that we should all be aware of if staying in the area the fish is tainted when consuming the fish, because the fish were taken from a contaminated waters, could cause toxic effects on organisms, especially humans who consume them. An example is Minamata disease happens to the people in Japan who have a penchant for eating raw fish. Humans infected with Minamata disease are those who live long and eat fish caught from heavy metal contaminated waters. Evidence that a long stay in a polluted environment affects the health of living creatures are fish exposed to lead in a long time, the lead content is not only found in the gills but were also found in the gastrointestinal tract, liver and muscles. Lead poisoning can cause effects on rainbow trout after the fish were exposed to lead for 2 hours at a concentration of 7.7 mg / L Pb in fish cyprinidonts whereas the effects seen after exposure for 12 hours at a concentration of 3.0 mg / L Pb. Goldfish is more resistant to organic timbale this is evidenced by the results of studies showing that the fish are dying after exposure to lead at a concentration of 1 mg / L Pb for 60 to 114 hours. While eels dying after exposure to lead for 21 days at a concentration of 3.0 mg / L Pb (Metelev et al, 1983 in Mustaphia, et al., 2006).

Looking at the results of research Metelev, et al, then theoretically the length of stay in a region that is water and contaminated fish have the risk of health effects, however the results of this study differ

from theory and previous research, it is due to the small study sample, cause analysis limited.

d. Relationship between gender with secondary sideroblastic anemia

According to Anaya Mandal [13], women have an increased risk of anemia, especially in girls at puberty, which has just had a menstrual period that a lot of bleed and iron deficiency, so it can be affected by anemia. In addition, women are also in pregnancy where there is a growing demand to iron [11]. The results also differ with Farzin [14], Tehran research found that there are differences in the levels of Pb in both men and women where the levels of Pb in the blood of men was higher than women. The study using the t test with ANOVA: $F = 4.86$; $p < 0.06$ [4].

This difference is due to many factors one of which is a method and tool used to determine the status of the anemia, the study of anemia status determination by using LCMSMS (Liquid Chromatography Mass Spectrofotometri Detector), which of course is much more sensitive compared to using other tools. Besides the type of anemia in this study is more specific in anemia secondary sideroblatisk using protoporphyrin assay which is more sensitive than other diagnostic tools. Results of studies of anemia in Indonesia showed that anemia prevalence in women is higher in women than in men.

The analysis showed that $RP = 2.32$ 95% CI $= 1.195$ and Lower Upper $= 4.53$ then interpreted that persons aged> 65 years (elderly) had 2.32 times the risk of developing secondary sideroblastic anemia than non-elderly. The results of this study together with research conducted on workers at SIH Marice Industrial Estate Pulogadung Jakarta in 2009 which found no significant correlation between age and the incidence of anemia with a P value: 0.006 and RP: 1.7 95% CI (1.1 to 2 , 4) [8]. According to Esther, the effects of exposure to Pb on human health vary significantly depending on the amount and duration of exposure, as well as the health status of people who are exposed. Some people have a very big risk to damage from exposure to heavy metals, for example children and the elderly, those with respiratory disease and heart disease, lung as well as those who actively are a high risk group [15].

Elderly and children are particularly at risk with anemia associated with endurance of both age groups, the reason for the age of the children and the elderly in general, low body immunity so that the absorption of iron or nutritional decline. This will aggravate the condition if they live in a place that

their environment has been polluted by Pb (Lopez, et al., 2013)

e. Relationship Pb levels in the blood with secondary sideroblastic anemia.

The analysis showed that RP = 0553 Lower 95% CI = 0.41 and = 0.73, the Upper interpreted that Pb levels in the blood is not a risk factor for secondary sideroblastic anemia, because RP <1. This study was different from the results with studies conducted in Greenland who discovered that there is a close relationship between how often adults consume wild birds taken during the hunt and the measured blood lead hunter. According to researchers, this situation is quite severe because bullets are used by hunters to contain high Pb so bullets contaminate bodies of birds, and hunters who consume wild birds Pb lead levels in the hunter becomes high [6]. Chemical Forms of Pb is an important factor affecting the properties of Pb in the body. Organic components such tetraethil Pb can be immediately absorbed by the body through the skin and mucous membranes. Organic Pb absorbed mainly through the gastrointestinal and respiratory tracts and is the main source of lead in the body. Not all Pb is sucked or ingested into the body will remain in the body. Approximately 5-10% of the amount ingested will be absorbed through the digestive tract, and approximately 30% of which are inhaled through the nose will be absorbed through the respiratory system will stay in the body because it is influenced by the size of the particles (Lopez, et al., 2013).

The content of lead in the blood represents the balance between the amount of lead taken into the body with a lead that is excreted from the body, which can also describe the presence of lead in soft tissue and hard tissue. It found that the lead content found in the blood and soft tissue component is equal to 1% of the total lead that enters the body, and about 90-99% of lead in the blood contained in the erythrocytes. According to Klaassen (2001) of lead can cause negative effects on hematology, which causes anemia and hypocromic mikrocitic 1). Mikrocitic anemia is anemia characterized by red blood cell size smaller than the size of a normal red blood cells, whereas hypocromic anemia is anemia that is characterized by the declining value of the Mean Corpuscular Haemoglobin Concentration. Anemia hypocromic mikrocitic and this occurs in the red blood cells are deficient in iron can lead to increased reticulosit (Klaassen, 2001). Lead affects the function oxidase enzyme in the synthesis of hemoglobin coproporfirinogen [16]. Lead can increase coproporfirinogen oxidase enzyme activity and decrease the activity ferochetalase catalyzing

iron (Fe) into protoporphyrin (Klaassen, 2001). Protoporphyrin is an organic compound for the formation of heme that binds to Fe and has the ability to bind O2 (Burden, et al., 1998). Lead increases the levels levulinat Amino Acid (ALA) which is required in the synthesis of heme precursors porphobilinogen to form hemoglobin [17].

Increased levels of ALA will affect the formation of porphobilinogen and protoforfirin-9. Protoporpyrin-9 accumulate in the red blood cells can cause a decrease in the number of red blood cells and a reduction in red blood cell age. Along with these phenomena, the hemoglobin synthesis is inhibited [15]. Increased protophorfirin in children occurs when there is a blood lead level of 14-17 micrograms / dl [18]. These results differ from studies in Greenland and in contrast to the existing theory, this is because in this study using a limited sample, of the 75 samples of the study, only 40 people were successfully checked Pb levels in their blood. The limited number of samples examined greatly affect the results of the analysis.

Conclusion
a. Risk level of Pb poisoning secondary sideroblastic anemia is 95% CI 0:54 (0:26 to 1:13) or not a risk factor.
b. Risk level of fish intake with the incidence rate of secondary sideroblastic anemia is 1:48 95% CI (1.26-1.75).
c. Risk level of live longer with secondary sideroblastic anemia is 2 95% CI (0.9-4.2).
d. Risk level of sex with secondary sideroblastic anemia is 1:18 95% CI (0.52-2.4).
e. Risk level of age with secondary sideroblastic anemia is a 95% CI RP 2:32 (1:19 to 4:53).
f. Risk level of in the blood Pb levels with secondary sideroblastic anemia is 0:53 95% CI (0.41-0.73).

Acknowledgement

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