RELATIONSHIP BETWEEN DRINKING WATER WITH BLOOD ARSENIC LEVEL AND SKIN LESIONS OCCURRENCE IN BUYAT VILLAGE NORTH SULAWESI INDONESIA

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Abstrak

Kontaminasi Arsenik pada air tanah merupakan krisis kesehatan masyarakat di daerah Buyat, dimana penduduk yang terkontaminasi arsenik melalui air minum dari sumur gali yang digunakan untuk minum dapat menimbulkan berbagai lesi kulit. Studi kasus control dimaksudkan untuk meneliti faktor risiko air minum dengan konsentrasi arsenik dalam darah dan lesi kulit. Jumlah sampel sebanyak 54 kasus yang menderita lesi kulit dan sebanyak 54 kontrol dengan tidak ada lesi kulit. Kemudian dilakukan analisis risiko dengan menggunakan Odd Rasio (OR). Hasil menunjukkan bahwa konsentrasi arsenik dalam air minum pada sumur gali sekitar 0,01-0,104 mg/L (rata-rata 0,056 mg/L). Analisis risiko antara konsentrasi arsenik dalam air minum dengan konsentrasi arsenic dalam darah didapatkan nilai OR = 19,45 95% CI: 6,52-58,00), kemudian kadar arsenik dalam darah dengan kejadian lesi kulit (keratosis dan hiperkeratosis) didapatkan nilai OR = 15,63, CI 95%: 4,94-49,40). Penelitian Ini menyimpulkan bahwa tingginya kadar arsenik dalam air minum dan darah merupakan faktor risiko terjadinya lesi kulit pada penduduk di daerah Buyat Sulawesi Utara Indonesia.

Kata kunci: arsenik, air minum, darah, kelainan kulit.

1. Introduction

Arsenic is an ubiquitous element with metalloid properties. Its chemistry is complex and there are many different compounds of both organic and inorganic arsenic. In nature, it is widely distributed in rocks, soil and sediments. In water, arsenic occurs in both inorganic and organic forms. The main organic arsenics, methylarsenic acid and dimethylarsenic (WHO, 2003a; 2003b; ATSDR, 2005; 2007; 2007b) in air, particulate matters have been shown to contain both inorganic and organic arsenic compounds. Plants grown on soil, marine algae and seaweed usually also contain considerable amount of arsenic. In industries arsenic compounds are mainly used in agriculture and forestry. Much smaller amount is used in the glass and chemical industries as feet, additive and drugs. Arsenic can be a source of environmental pollution, near sites of coal burning and smelting of metals (Daud, 2009). A study was previously reported the association of levels of arsenic in drinking water and blood with the prevalence of keratoses and hyperpigmentation in West Bengal. Another study also identified cases who apparently consumed low levels of arsenic (10 µg/liter). However, the survey examined only the participants' primary current drinking-water source. Here, we present a nested case-control study to examine the dose-response pattern for the arsenic-induced skin lesions using detailed exposure assessment. The exposure assessment incorporates arsenic concentration data from current and past water sources used in households and work sites (Haque, 2003, Daud, 2009).

Chronic ingestion of inorganic arsenic causes characteristic skin lesions including pigmentation changes, mainly on the trunk and extremities, and keratoses of the palms of the hands and soles of the feet. Hyperpigmentation has been described as raindrop-shaped discoloration spots, diffuse dark brown spots, or diffuse darkening of the skin on the limbs and trunk. Skin lesions due to arsenic ingestion are a problem in themselves, and there is some evidence that those who have them may be at particularly increased risk of arsenic-caused internal cancers. The acute toxicity of arsenic at high concentrations has been known about for centuries. It was only relatively recently that a strong adverse effect on health was discovered to be associated with long-term exposure to even very low arsenic concentrations. Drinking water is now recognised as the major source of human intake of arsenic in its most toxic (inorganic) forms (Daud, 2009). The presence of arsenic in drinking water is difficult to detect without complex analytical techniques. Hundreds of millions of people, mostly in developing countries, daily use drinking water with arsenic concentrations several times higher than the World Health Organization (WHO) recommended limit of 10 millionths of a gram per litre of water (10 µg/L), (WHO_b, 2003).

The most serious damage to health has taken place in Bangladesh and West Bengal, India. In the 1970s and 1980s, UNICEF and other international agencies helped to install more than four million hand-pumped wells in Bangladesh to give communities access to clean drinking water and to reduce diarrhoea and infant mortality. Cases of arsenicosis were seen in West Bengal and then in Bangladesh in the 1980s. By 1993 arsenic from the water in wells was discovered to be responsible. In 2000, a WHO report was addressed for the intended cases (Smith *et al.*, 2000).

2. Methods

This study was intended to examine risk factors of drinking water, blood arsenic levels to skin lesions at peoples in Buyat Areas, North Sulawesi-Indonesia. Prior to the respondents recruitement, shallow water (wells) and Geographics Positional System (GPS) data were obtained for 25 at cases group and 25 at the control group. (some wells is used for more than one participants). For blood samples, we took from two groups whereas cases (n=54) were people who suffering from skin lesion (keratosis or hyperkeratosis) living in Buyat Village (exposure areas) then were frozen at -20^o before shipped and

Table 1. General characteristics of cases and controls in Buyat Areas, North Sulawesi Indonesia

Variabels	Cases N=54		Controls N=54	
	N	%	N	%
Sex				
Female	25	46,3	23	42,6
Male	29	53,7	31	57,4
Age				
20-29	6	9,3	7	16,7
30-39	9	16,7	8	14,8
40-49	10	18,5	9	16,7
50-59	16	29,6	17	31,5
< 60	14	25,9	11	20,4
Education				
Non formal education	6	11,1	4	7,4
Primary	27	50,0	20	37,0
Secondary	15	27,8	23	42,6
College	6	11,1	7	13,0
Occupation				
Farmer	26	48,1	27	50,0
civil servants/military	2	3,7	3	5,6
private employees	4	7,4	7	13,0
Work at house (housewife,maid)	22	40,7	17	31,5

analised in Laboratory of Institute Environmental Health Technical and Communicable Desiase Control (CDC) in Manado, the procedure was approved by the Ethical Clearence of the Medical Faculty of Hasanuddin University Makassar, Indonesia, while control (n=54) were people with no skin lesion who were living in Buyat Village. Inclusion criteria were age more than 10 years and living at the areas more than 7 years. Arsenic levels was analyzed using AAS-GF (Atomic Absorption Spetrometry-Graphite Furnace) while skin lesion diagnosed by a Dermatologist from Medical Hasanuddin University. Data analysis was performed using Odd Ratio (OR).

3. Results

Table 1 provide information of participants characteristics both cases and control groups which consist of sex, age, education and occupation in Buyat area during the period of study. Male participants was higher than female. Then, age between 50-59 years was the major for both groups. Education moreover, the primary school level at case group was the highest while in control group, secondary school was the highest. In term of occupational, the majority participant work as farmer.

Odd Ratio analysis results in Table 2 shown arsenic levels in drinking water provides risk for the presence of arsenic in the blood. There is a statistically significant correlation between arsenic in drinking water with arsenic levels in the blood with p = 0.00 and OR = 19.45 (95% CI. 6.52-58,00). That is, someone who is drinking water arsenic levels exceeding 0.01 ppm, 19.45 times higher risk of experiencing an increase arsenic in their blood than people drinking water at levels below 0.01 ppm.

Table 3 shown the predictor variable levels of arsenic in the blood gives the risk of occurrence of hyperkeratosis. There is a statistically significant correlation between arsenic in the blood with skin disorders (hyperkeratosis) the value $p = 0.00$; OR = 15.63 (95% CI. 4.94 to 49.40). That is, one's levels of arsenic in their blood exceeding the threshold value of 0.7 ppm of 15.63 times the risk of experiencing skin disorders than those levels of arsenic in their blood below 0.7 ppm.

4. Discussion

Since single doses of as are rapidly and extensively cleared from the blood via the kidney, blood As (BAs) concentrations have been considered to reflect only recent exposure. However, with chronic and continuing exposure, steady-state concentrations in blood and urine are achieved; these have the potential to serve as biomarkers of past

Table 2. Arsenic Level in Drinking Water as Risk Factor to Arsenic in Blood at People in Buyat Areas North Sulawesi Indonesia

Variable	Concentration of Arsenic in Blood		OR	95% C I.
Consentration of Arsenic in Drinking Water (mg/L)	(+)	(-)		
High	29 (85.3%)	17 (23.0%)	19.45	6.52-58.00
Low	5 (14.7%)	57 (77.0%)		

Table 3. High Level Arsenic in Blood as a Biomarker of Risk Factor to Keratosis and Hyperkeratosis (skin lesion) at People in Buyat Areas North Sulawesi Indonesia

Variable	Keratosis & Hyperkeratosis (skin lesion)		OR	95% C I.
Concentration of Arsenic in blood (mg/L)	(+) (-)			
High	30 (55.6%)	4 (7.4%)	15.63	4.94-49.40
Low	24 (44.4%)	50 (92.6%)		

exposure. Blood As (BAs) has been used in many epidemiological investigations (Hall *et al.,*2006) Results of research conducted in the area of North Sulawesi Buyat found arsenic levels in relation to arsenic levels in water wells and drill. The study found a dose-response relationship between arsenic levels in drinking water and skin disorders (hyperkeratosis). Similar research has reported the relationship of hypertension and diabetes mellitus with arsenic exposure from drinking water (Ahsan *et al,* 2000; Ahsan *et al,* 2006). Another study recently published in the relationship between the prevalence of benign skin diseases (melanosis and keratosis) and exposure to arsenic from drinking water. This cross-sectional design of West Bengal, India studied 7683 subjects and found a dose-response relationship between prevalence of hyperpigmentation and keratoses with dose levels of arsenic in drinking water. The researchers found the prevalence of both conditions is higher in male subjects than female subjects at each dose level. They reported that skin diseases can infect those who consume the water levels of arsenic below 50 ppb (WHO, 2003a).

Ahsan *et al,* (2006) found a significant relationship between arsenic levels in drinking water with a wound in the skin with OR = 1.91 (95% CI, 1.26 to 2.89) at levels between 8.1 to 40.1 ug / l, OR = 3.03 (95% CI, 2.05 to 4.50) at levels between 40.1 to 91.0 g / l, OR = 3.71 (95% CI, 2, 53 to 5.44) at levels between 91.1 to 175.0 ug / l and OR = 5.39 (95% CI, 3.69 to 7.86) at levels of between 175.1 to 864.0 g/l. This research proved levels of arsenic in drinking water increases the risk will be even greater. In Thailand (Siripitayakunkit *et al,* 2003), found an association Arsenic levels in drinking water with the incidence of skin lesions (melanosis and hyperkeratosis) OR = 4.0, (95% CI, 1.80-9.20). Characteristics of skin wounds and skin color changes (hyperpigmentation and hypopigmentation) mostly in the upper chest, back, arms, legs, keratosis palms, and soles of the feet. Examined levels of arsenic in well water used by communities for drinking, 96% have exceeded 0.05 ppm and the highest levels of 1.81 ppm. 1602 population as a sample and control group 126 participant who had been screened for skin wounds. Sample group of 612 residents (35.4%) showed skin injuries associated with Arsenosis (such as hyperpigmentation, depigemntation, keratosis) or skin cancer, in the chest, palms and soles of the feet. |The affected men more than women from drinking water contamination, whereas in the control group did not find any skin lesions. This is in line with research conducted in the area Buyat, from 54 controls found that none having hyperkeratosis (keratosis or hyperkeratosis) (Wang and Wai, 2004).

Found the pump well water is not safe and contain arsenic> 0.05 ppm (52.35%) in the area of Shanxi, 11.30%, near Mongolia, Jilin 12, 21%, Xinjiang, Qinghai 8.33 4.77%, and Ningxia. 1.06%, (Sylvia and Smoller, 2004). Found levels of arsenic in drinking water in the Southwest region levels of 10-40 ppb. In areas close to the industry in ground water (drilled wells) was found even 80 ppb to 300 ppb. Arsenic levels in ground water (water supply) in Vietnam about 0.9 to 321 ppb (Sun, 2004). There are 27% of wells exceeded the WHO standard, which is 10 ppb (Pfeifer *et al.*, 2002).

Arsenic is a constituent of drinking water naturally occurring in various parts of the world. Although arsenic has been considered a major public health problem in Indonesia, particularly in the Buyat, still few researchers conducted a systematic study of public health impact of exposure to arsenic. One recent study examined hyperkeratosis Buyat population and assess the prevalence. Another study found the prevalence of skin diseases around 0.37% in people exposed to arsenic below 0.005 ppm, 0.63% at levels of 0.006 to 0.050 ppm, and 6.84% at levels of 0.081 ppm. Case-control analysis, relative risk of skin diseases increased three-fold in levels above 0.05 ppm ($p < 0.05$) (Shinkai, 2007). Rahman 1999 found about 29% had skin lesions due to high arsenic drinking water levels. then continued relationship test and the results are of significance between the groups exposed to the group not exposed to arsenic in drinking water values ($p < 0.01$) (McDonald *et al*., 2007). The same thing is found in Nepal (Adamsen, K.R |and Pokhrel, A, 2002), then in the state of West Bengal, India, which borders to Bangladesh (Rahman *et al.*, 1999).

The results of these studies provide a deeper understanding, which has been in the term of arsenic in drinking water such as in Bangladesh, namely 0.5 ppm is still very risky to cause. This research study is first in Indonesia to examine the relationship between arsenic levels in fish, rice, drinking water, blood, and urine with skin disease (hyperkeratosis). This study used a case control study and found 54 cases (hyperkeratosis). amounted to 20.22% of 267 study participants who have skin diseases in the village of Buyat. The estimated prevalence is likely to increase because people who experience skin lesions have the family members who drink water from the same source. By chronic exposure to arsenic in food and beverages can cause various diseases, including skin lesions, cardiovascular, neurological, hepatic, hematological, endocrine, and renal systems. Arsenic is classified as a Class I human carcinogen by the WHO. Arsenic associated with skin cancer, lung, bladder, kidney, and liver cancer. The skin is the main organ of accumulation of arsenic and chronic exposure produces characteristic changes in pigmentation (hyperpigmentation and hypopigmentation), hyperkeratosis, and after a long exposure causes skin cancer (Wu *et al.*, 2001, Hall *et al,* 2006,). High arsenic levels in the blood is a manifestation of interference with the organs, like liver, lung, pancreas, heart, reproductive, nervous, endocrine, and skin and other organs. Liver disorders may occur when contaminated with high levels of arsenic via oral 0.01-0.1 ppm/day (ATSDR,2005). After contamination Arsenal-Sodium (20-85 ppm) in drinking water for 6 weeks experienced heam Hepatic synthesis and delta-aminolaevulinic acid (ALA) and neuroblastoma cells found in mice after exposure to arsenic for 24 h,(Kapaj *et al.,* 2006). A study was explains 6 million residents of the 9 districts in West Bengal, India are exposed to high levels of arsenic through drinking water. More than 300,000 people showed arsenic caused skin lesions. Arsenicosis chronic hyperkeratosis caused many variations, such as pigmentation changes, hyperkeratosis, non-melanoma skin cancer. The high incidence of opportunistic infection due to the individual arsenic exposure. The study also found no significant differences between the exposed population and unexposed to arsenic with values ($p < 0.001$), (WHO, 2001).

The Study describes a typical such as hyperkeratosis of the skin (especially on the palms and soles of the feet), a double form of hyperkeratosis appeared like corn and warts, as compared with a prospective analysis of cross-sectional analysis. Arsenic exposure changes during the period of follow-up could affect the estimate of the ratio, especially with regard to low-level arsenic exposure. However, in a separate analysis, the estimated OR with additional adjustment for arsenic urine measured at the time of follow-up remained almost the same, (Haque, 2003). Arsenic contamination in Buyat problems have been reported more than 10 national and international institutions in the past. The views given different from each other as well as solutions. Now these two sources of arsenic beleve derived from shallow wells and aquifers that are used as sources of drinking water and compared with the Maximum Concentration Levels (MCL) 0.01 ppm (WHO, 2003a).

Better biomarkers are needed to help elucidate mechanistic knowledge of As toxicity and for risk assessment Biswas, 2008, Tchounwou *et al,* 2004). In applying The National Academy of Science risk assessment/management paradigm to As toxicity, described the need for better dose-response assessment, exposure assessment and risk characterization, in order to realistically make risk management decisions (Tchounwou *et al,* 2004, Biswas, 2008).

Total Blood Arsenic levels can contribute to these efforts because they represent a measure of internal dose. Blood Arsenic metabolite data may provide insight into metabolic differences that lead to differences in susceptibility to arsenicosis but, because Blood Arsenic metabolites are non-detectable in the low exposure range, they have limited utility in risk assessment studies. Accordingly, dose–response studies of individuals with ongoing chronic exposure, over a wide range of exposures are best served by analyzing total Blood Arsenic concentrations. Comparative analyses of Blood Arsenic levels with biomarkers of early biologic effects due to As toxicity, such as DNA damage or markers of oxidative stress, will likely shed light on the biological variations that render some more vulnerable (Wu *et al.*, 2001). Indeed, using atomic absorption spectrophotometry reported positive associations between Blood Arsenic and plasma reactive oxidants, and an inverse relationship with plasma antioxidant capacity (Smith *et al*., 2000, Rahman *et al*., 1999).

5. Conclusion

High Arsenic levels in drinking water is a risk factor for occurrence high arsenic in blood with the risk 15.45 times greater than low levels of arsenic in drinking water that consumed by people in Buyat area. High Arsenic levels in blood is a risk factor for keratosis and hyperkeratosis (skin lesions) with the risk 16 times greater than the low levels of arsenic in the blood at people in Buyat Areas.

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