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Analysis of High Levels of Urine Proteins as a Sign of Impaired Kidney Function in Communities Around a Nickel Mining Industry in Morosi District, Southeast Sulawesi

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SUMMARY

The study is proposed to analyse the influence of individual and environmental factors on urine proteins levels as a parameter for impaired kidney function in the community around Nickel mining industry in Morosi Sub-District, Southeast Sulawesi Indonesia. This quantitative study used a cross sectional study design. The population was people in 3 villages around the nickel mining industry aged 20-59 years. The sample size was 61 people using simple random sampling technique. Independent variable was age as representation of individual factor and environmental factors including housing condition, water quality, waste management and household liquid waste. Urine proteins as a parameter for impaired kidney function was the dependent variable. Data were collected by questionnaire and taking urine samples. Data were analysed using the multinomial logistic regression test with a significance level of 95%. The results show that age, water source quality, solid waste management and waste water management can be associated with proteinuria in communities around the Morosi nickel mining industry.

Keywords: Kidney disease; age; water; environment; waste; liquid.

SUMMARY

The existence of the nickel mining industry in Morosi District, Southeast Sulawesi, has had both positive and negative impacts on the surrounding community [1,2]. The positive impacts of the existence of the mining industry include opening up opportunities for small and micro businesses in the community and agricultural products such as vegetables which are also marketed to the mining industry environment. In this way, the income of people around the industry increases by around 20.5% [1]. Furthermore, there are job opportunities for people living around the mining industry [3]. Meanwhile, the negative impact of the presence of the nickel mining industry is its contribution to the low quality of the environment, including the quality of water, land and air sources for the surrounding community [4,5]. The Pollution Index at locations closed to the mining industry was identified to be in the range of 7.20 PI. The nickel mining industry has carried out nickel and nickel ore (smelter) processing and refining activities. Emissions from nickel mine management include dust or ash and also gases such as CO, SO_x and NO_x [6].

The air pollution which contains dangerous toxins, especially fine particles, can stay in the air longer. People living in this environment will inhale these toxic fine particles (directly without realizing it. These fine particles disrupt and damage the blood circulation system and the first organ affected is the kidneys. Disorders of the circulatory system become very vital for the continued function of other body organs, including the condition of the kidneys. Therefore, hypertension is often suggested to be the main cause in

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chronic kidney sufferers [7]. Furthermore, people who use contaminated water sources for their daily needs can also infect body organs, including the kidneys. If the human kidney organ damage, the glomerulus cannot filter and reabsorb food substances, including. As a result, food substances cannot become energy or repair cells in the human body. The substances which cannot be absorbed will be excreted in the urine, resulting in high urine proteins levels. Therefore, high urine protein reflects impaired kidney function [8].

The seriousness of kidney disease can also be seen from changes in the frequency of urination in a day, blood in the urine, nausea and vomiting and swelling, especially in the feet and ankles [8]. Several previous studies stated that high levels of urine proteins could be caused by exposure to cadmium (Cd) originating from various sources including food or inhalation of small doses of Cd over a long period of time [9]. Cadmium can accumulate in the body, especially the liver and kidneys [9]. Cadmium is a type of heavy metal that is dangerous because this element can cause vascular and kidney damage. High levels of cadmium in human blood may result in high levels of urine proteins [10]. Through disruption in the balance of calcium and phosphate in the kidneys among other pathogenetic mechanisms. The existence of the nickel mining industry in Morosi has contributed to increasing levels of heavy metals, including cadmium.

The degree of exposure to hazardous materials of people around the industry is of course related to several factors. For example, the longer people live around the mining industry, the higher the level of exposure to these dangerous substances will be. The amount of time a person has lived around the mining industry is proportional to an individual's age. However, it can also be said that if someone moves to an area near the industry at some point in their life, the amount of time spent will be shorter compared to someone of the same age who has always lived in that area.

Previous studies stated that the worse the home conditions and environmental sanitation of individuals around the mining industry, the higher their serum creatinine levels compared to those with good home conditions and environmental sanitation [11]. High serum creatinine levels are also an indicator of the level of kidney damage. However, is the effect the same when using urine protein chemical parameters to see the influence of age and environmental conditions on the level of kidney damage in the community around the Morosi nickel mining industry? Therefore, the aim of this research is to analyze the effect of age and environmental conditions on urine protein in communities around the Morosi Nickel mine, Southeast Sulawesi Province, Indonesia. Environmental conditions include housing conditions, water quality, solid waste and liquid waste management. Meanwhile, the age shows how long the individual has lived in that environment.

METHODS

Research Design

This research uses quantitative methods with an analytical observational approach with a cross sectional study design. This research was conducted in 3 villages around the nickel mining industry, namely Tanggobu, Porara and Morosi Villages, Morosi District, Konawe Regency, Southeast Sulawesi Province from July to August 2022.

Population and samples

The population of this study is formed by adults in Tanggobu Village, Morosi, Porara, Morosi District aged 20-59 years. The sample size was 61 subjects selected using simple random sampling technique. The sample inclusion criteria were adults aged 20-59 years who were willing to be respondents, could communicate well, and had lived in the research location for at least 1 year.

Research variables

In our research the dependent variable is represented by urine protein levels. This variable (y) is divided into 4 categories, namely undetectable (0-0.1 g/L), low (0.1 g/L $\leq$ y < 1 g/L), moderate (1 g/L $\leq$ y < 3 g/L), and high (y $\geq$ 3 g/L) [12]. The independent variables are age and, among environmental factors, house condition, water sources, waste management and household waste management. Age is divided into 2 categories, namely early adulthood (20-39 years) and advanced adulthood (40-59 years) [13]. All environmental factor variables are divided into 2 categories, namely good and bad, according to whether or not the environmental conditions meet the health standards set by the Ministry of Health of the Republic of Indonesia [14].

Data collection and analysis

There were 61 respondents interviewed with a questionnaire and their urine samples taken. We collected spot urine samples and used the dipstick urinalysis method to determine urine protein levels using urine Reagent Strips (URIT 13G Brand). Then, the data were processed with SPSS version 25 using the multinomial logistic regression test with a significance level of 0.05.

Research Ethics

This research was conducted after obtaining approval from the Mandala Waluya University research ethics committee no. 039/KEP/UMW/V/2022 dated 16 May 2022. Respondents' participation in this research was based on their informed consent and was voluntary.

Table 1. Characteristics of respondents in three villages in the Morosi Nickel Mine Industrial area

Respondent's Characteristics		Frequency	Percent (%)
Sex	Female	43	70.5
	Male	18	29.5
Marital status	Single	5	8.2
	Married	51	83.6
	Widow widower	5	8.2
Education	No school	2	3.3
	Elementary school	28	45.9
	Junior high school	11	18.0
	Seniour high school	15	24.6
	Diploma	1	1.6
	Bachelor	4	6.6
	Total	61	100.0

RESULTS

Respondent Characteristics

This research recruited 61 respondents, most of whom were female (43 people, 70.5%). There were only 18 male respondents (29.5%) (Table 1). The majority of respondents were married (83.6%). However, there were few single people and widows/widowers, namely 5 people each (8.2%). The education level of respondents was mostly elementary school (45.9%). There were also quite a lot of respondents with a high school education, namely 24.6%. However, there were a small number of respondents who had a diploma (1.6%) and bachelor's degree (6.6%). There were also some respondents who participated in this research who had never been to school, namely 3.3%.

Urine proteins Levels

There were only 8.2% respondents whose urine protein levels was low. However, there were 88.5% respondents whose urine protein levels were undetectable (0-0.1 g/L). Respondents whose protein levels were medium and high, there were only 1.6% (Table 2).

Table 2. Urine Proteins Levels, Individual and Environmental Factors in three Villages in the Morosi Nickel Mine Industrial Area

Factors	Variables	Frequency	Percent
Urine proteins Levels	Undetectable (0 – 0.1 g/L)	54	88.5
	Low (from >0.1 g/L to ≤ 1 g/L)	5	8.2
	Moderate (from >1 g/L to < 3 g/L)	1	1.6
	High (≥ 3 g/L)	1	1.6
Individual	**Age group: Years old**		
	Early adulthood (20-39)	26	42.6
	Advanced adulthood (40-59)	35	57.4
Environment	**Quality of Water sources:**		
	Good	49	80.3
	Bad	12	19.7
	Housing condition:		
	Good	31	50.8
	Bad	30	49.2
	Household Solid waste management:		
	Good	24	39.3
	Bad	37	60.7
	Household WaterWaste Management:		
	Good	39	63.9
	Bad	22	36.1

Table 3. Parameter Estimates of low urine proteins vs undetectable urine proteins for individual and environmental factors

Urine Proteins	B	Std. Error	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B)	
							Lower Bound	Upper Bound
Intercept	24.449	3.802	41.343	1	0.000			
Age	0.053	0.069	0.586	1	0.444	1.054	0.921	1.206
Water Source	-29.158	1.192	598.179	1	0.000	2.171	2.099	2.247
Housing condition	-0.130	1.086	0.014	1	0.905	0.878	0.104	7.381
Solid Waste Management	-28.149	0.000	.	1	.	5.957	5.957	5.957
Waste Water Management	-0.532	1.098	0.235	1	0.628	0.587	0.068	5.053

The reference category of urine proteins is: Undetectable

The reference category of environmental factors (water source, housing condition, solid and water waste management) are: Bad

Individual and Environmental Factors

Individual factors related to age show that the older adult group is the most dominant (57.4%) compared to the early adult group (42.6%) (Table 2). Environmental factors include the quality of water sources used daily, condition of the house, management of solid waste and liquid waste from the house. It was identified that the majority of respondents had a good water source (80.3%), adequate housing conditions (50.8%), and good household wastewater management (63.9%). However, there is still a lot of solid waste management that is not good (60.7%).

Multivariate analysis

Table 3 explains that individual factors (age) and environmental factors have a significant effect on low urine protein levels (>0.1 g/L to <1 g/L). The coefficient value of multinomial logistic regression (B) is 24,449, where this value is positive and significant at p<0.0001. This means that the younger the age and the better the quality of the individual's environment, the probability of having an undetectable urine protein level (0-0.1 g/L) is very high with a standard error of 3,802. Of the several variables, there was only water source which has a very significant effect on low urine protein levels (>0.1 g/L to <1 g/L) compared to age and other environmental factors such as house condition (p=0.905), solid waste management and liquid (p<0.628). The water source coefficient value is -29.158, where this value is negative and significant at p<0.0001. This means that if an individual uses a poor water source, the probability of having undetectable protein levels (0-0.1 g/L) is very low compared to low protein levels (>0.1 g/L to <1 g/L). The Odds Ratio of the water source is 2.171, which means that individuals with a water source which is 1 time worse are estimated to have a low urine protein level (> 0.1 g/L to > 1 g/L) 2.171 times more likely, compared to individuals with the quality of the water source is 1 time better.

Table 4 explains that age and environmental variables do not have a significant effect on medium urine protein levels (>1 g/L to <3 g/L) (p=0.996). However, the coefficient value of the multinomial logistic regression (B) is 191.854, which is positive, but not significant. This means that the younger the age and the better the environmental quality, the probability that an individual will have undetectable urine protein levels (0-0.1 g/L) is very high, with a standard error of 36.551. Of the several variables, there were only house conditions which effected significantly for moderate protein levels (>1 g/L to <3 g/L) with p<0.000, compared to age (p=0.996), water source (p=0.998), solid waste management (p=0.998) and liquid waste management (p=0.997). The coefficient value of house condition is -18,968, where this value is negative and significant at p<0.0001. This means that if an individual lives in poor housing conditions, the probability of having undetectable protein levels (0-0.1 g/L) is very low compared to moderate urine protein levels (>1 g/L to <3 g/L). The odds ratio of the house condition is 5.787. This means that individuals with housing conditions which are 1 time worse are estimated to have medium urine protein levels (>1 g/L to <3 g/L) 5,787 times more likely, compared to individuals with housing conditions that are 1 time better.

Moreover, table 5 also shows that age and environmental variables do not have a significant effect on high urine protein levels (≥3 g/L) (p=0.995). However, the multinomial logistic regression coefficient (B) value is -484,966, which is positive, but not significant. This means that if age gets older and environmental quality gets worse, the probability of

Table 4. Parameter Estimates of medium urine proteins vs undetectable urine proteins for individual and environmental factors

Urine Proteins	B	Std. Error	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B)	
							Lower Bound	Upper Bound
Intercept	191.854	36551.557	0.000	1	0.996			
Age	-5.592	1045.359	0.000	1	0.996	0.004	0.000	.c
Water Source	-59.833	20158.490	0.000	1	0.998	1.035	0.000	.c
Housing condition	-18.968	0.000	.	1	.	5.787	5.787	5.787
Solid Waste Management	43.236	15621.065	0.000	1	0.998	.c	0.000	.c
Waste Water Management	-81.956	22511.427	0.000	1	0.997	2.552	0.000	.c

The reference category of urine proteins is: Undetectable

The reference category of environmental factors (water source, housing condition, solid and water waste management) are: Bad

.C: Constant

an individual having an undetectable urine protein level (0-0.1 g/L) is very low, with a standard error of 84.241. Of the several variables, there was only house condition which effects significantly for high protein levels (≥3 g/L) with p<0.000, compared to the variables age (p=0.996), water source (p=0.997), solid waste management (p= 0.999) and liquid waste management (p=0.998). The coefficient value of house condition is 19,632, where this value is positive and significant at p<0.0001. This means that if an individual lives in good housing conditions, the probability of having undetectable protein levels (0-0.1 g/L) is very high compared to high urine protein levels (≥3 g/L). Meanwhile, the Odds Ratio of housing conditions to high urine protein levels (≥3 g/L) is not readable.

DISCUSSION

This study has shown that the quality of water source and housing condition are determinants of the high levels of urine proteins in the community around the Morosi mining industry. The water sources used by the community there may have been contaminated by heavy metals and waste from both industry and households. There are around 19.7% of households

Table 5. Parameter Estimates of high urine proteins vs undetectable urine proteins for individual and environmental factors

Urine Proteins	B	Std. Error	Wald	df	Sig.	Exp(B)	95% C.I. for Exp(B)	
							Lower Bound	Upper Bound
Intercept	-484.966	84241.777	0.000	1	0.995			
Age	6.783	1343.953	0.000	1	0.996	883.050	0.000	.c
Water Source	62.910	19890.903	0.000	1	0.997	0.000	0.000	.c
Housing condition	19.632	0.000	.	1	.	.c	.c	.c
Solid Waste Management	9.506	13840.769	0.000	1	0.999	13446.440	0.000	.c
Waste water management	36.159	14686.078	0.000	1	0.998	5056116588 144295.000	0.000	.c

The reference category of urine proteins is: Undetectable

The reference category of environmental factors (water source, housing condition, solid and water waste management) are: Bad

.C: Constant

who use dug wells for their daily needs. Dug wells that are exposed to heavy metals such as arsenic, lead and cadmium when someone drinks them will circulate in the blood which is then bound by low-molecular-weight (LMW) proteins. LMW proteins that have bound these heavy metals will be absorbed by the tubules [15]. An increase in the load of such proteins in the tubular lumen leads to saturation of the reabsorption mechanisms by tubular cells, and, in the most severe or chronic conditions, causes toxic damage, which favors increased excretion of all proteins in the urine, including low protein [16,17].

Dug wells are also said to be more susceptible to contamination from various sources, including latrines [18]. The dug wells with polluted water is a source of infection, including Helicobacter pylori infection [19]. Helicobacter pylori disrupts the upper digestive system, especially stomach ulcers, duodenum and certain stomach cancers. In the excavated water from nickel mining fields, it has been identified that there are several indigenous bacteria that are resistant to heavy metal stress. These resistant bacteria include *Escherichia, enterococcus, Bacillus sp., staphylococcus, Klebsiella* and *Pseudomonas* species of bacteria.[20].

Individuals who used contaminated water sources may become infected with the urinary tract. This condition also concerns a person's personal hygiene behaviours. The worse a person's personal hygiene behaviours are, the more likely it is that urinary tract infections will occur. If the urinary tract is infected, it will cause excessive excretion of small proteins. An infected urinary tract can damage the tubules and glomeruli, resulting in impaired proximal tubular reabsorption [21]. An abnormal increase in protein production will exceed the reabsorption capacity of the proximal tubule. Finally, protein levels in the urine will be high and postinfectious glomerulonephritis occurs. Post-infectious glomerulonephritis is caused by an immune response to pathogens [22,23]. These manifestations can be acute or chronic because they depend on the type of microorganisms present in the polluted water. Immune system disorders in chronic kidney disease also increase the individual's susceptibility to virus-related to reduce the body's response to vaccines [23].

This study also shows that poor housing conditions are also a cause of high proteinurine levels. The mechanism of influence of poor housing conditions on proteinurine levels and kidney health is through a complex mechanism involving individual and structural factors. Firstly, there is exposure to fine particles in the house. These fine particles can affect kidney health [24, 25, 26]. Individuals living in homes with poor conditions are also more susceptible to heat, lower water availability, and poor water quality, resulting in acute kidney injury, chronic kidney disease, and nephrolithiasis [27, 28,29, 30].

Furthermore, inadequate housing conditions can also affect health through neurohormonal mechanisms, including stress. Acute stress is thought to cause kidney disease through increased blood pressure, heart rate, and decreased vascular reactivity, mediated by the autonomic nervous system, hypothalamic-pituitary-adrenal axis, inflammatory cytokines, and endothelinA [31,32,33,34,35]. Moreover, poor housing conditions also have an impact on social aspects, such as social exclusion which ultimately triggers psychological stress and results in hypertension, sodium and water retention. Stress contributes to increased sympathetic nervous system activity, secretion of glucocorticoids, and inflammatory cytokines, which contribute to higher rates of vascular disease, including risk factors for chronic kidney disease [24].

Finally, it can be said that the mechanism of influence of environmental factors on proteinuria levels is complex and involves factors such as glomerular hemodynamic, tubular absorption, and diffusion gradients. Alterations in multiple pathways and different molecular interactions may lead to the same clinical endpoints of proteinuria and chronic kidney disease. Glomerular diseases encompass a variety of immune and nonimmune disorders that can attack and damage multiple components of the glomerular filtration barrier. In many of these conditions, renal visceral epithelial cells respond to injury along defined pathways, which may explain the resulting clinical and histological changes.

CONCLUSIONS

The quality of water sources and house conditions determine the high levels of protein urine in communities around the Morosi nickel mining industry. The quality of water sources is associated with the inclusion of pollutant sources in the form of heavy metals and solid waste and waste. These two pollutants have a negative impact on a person's body condition, allowing urine protein levels to become high through a complex mechanism. House conditions that do not meet the requirements also have an impact on air circulation and affect aspects of the physical, social and psychological health of the occupants. This condition tends to increase proteinurine levels. The higher levels of urine proteins indicate the level of kidney damage. Therefore, poor water source and housing conditions influenced to the kidney health conditions in people around the nickel mining industry.

Finally, this study can give information for health policy makers and programs to increase community health around the Morosi nickel mining industry. For example, providing piped clean water facilities and improving housing condition and environment can become priority programs in Morosi Sub district.

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CONFLICTING INTEREST

All authors declare no conflicts of interest in this paper.

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