

Determining Kidney Damage Risk Factors Associated with Urine Paraquat Levels and Biochemical Urine Profile of Farmers in Banjarbaru, South Kalimantan, Indonesia

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Abstract

Aim: Kidney damage from paraquat is influenced by several factors, including the duration of work, the span of exposure from the pesticide spraying, and the nutritional status of the farmers. This damage can be indicated by the high levels of paraquat and changes of the biochemical status in the urine. The present study aimed to analyze the relationship between the length of work, duration of spraying, and the nutritional status obtained from the measurement of body mass index (BMI) values, with the paraquat levels and biochemical status of the farmer's urine samples. **Materials and Methods:** This study was a cross-sectional study and was conducted in September 2022 in North Landasan Ulin Village, Banjarbaru City, South Kalimantan, Indonesia. The length of work and spraying duration were obtained from the direct interviews, while the BMI values were calculated by dividing the body weight (kg) by the body's height (m). Analysis of the paraquat levels in the urine was measured using a spectrophotometer, while the urine's biochemical status was obtained using the dipstick colorimetric method. Statistical analysis used: the relationship between each variable is analyzed using the Spearman rank correlation test. **Results:** Results from the study show that the length of work, duration of spraying, and BMI were moderately associated with an increase in the urinary paraquat levels (correlation coefficient [Rs] 0.26–0.50) ($P < 0.05$); although the previous factors did not appear to correlate with any changes in the urine's biochemical status. **Conclusion:** In summary, prolonged exposure to the spray in combination with the farmers' long work hours, and also factoring in the abnormal BMI values, resulted in an increase of paraquat levels in the urine.

Keywords: Farmers, kidney, paraquat, pesticide, toxicology

INTRODUCTION

South Kalimantan is one of the many provinces in Indonesia, whose livelihood is based on agriculture.^[1-3] Data from the Indonesian Central Bureau of Statistics state that the agricultural sector absorbs the most labor, displaying that there was an increase of 35.38% in 2017–35.19% in 2018.^[4]

The increasing growth of agriculture resulted in the rising use of pesticides, like paraquat.^[5,6] Paraquat is a herbicide-type pesticide, which is widely used by horticultural farmers in the South Kalimantan province. Data in 2022 stated that as many as 90% of paraquat-active pesticides were used by vegetable farmers in Sukamara, North Landasan Ulin, South Kalimantan. Prolonged exposure to paraquat can cause a variety of health

problems, thus making farmers a vulnerable group that is susceptible to such problems.^[5]

Paraquat, with the chemical name 1,1-dimethyl-4,4-bipyridylium, is classified as an active ingredient in toxic herbicides. Paraquat enters the body through inhalation, dermal, and oral routes;

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furthermore, it is metabolized through xenobiotic metabolism and excreted through urine with a half-life of 12 h.^[7] Data show that 90% of the metabolized paraquat will be secreted as much as 90% in the kidneys,^[8] thus making the kidneys prone to high levels of paraquat and resulting in damage to them. Research results have proven that paraquat triggers damage to the proximal tubules in the kidneys.^[9]

Kidney damages caused by paraquat exposure, especially of those in the tubules, will result in a decrease in its excretion further increasing the accumulation of paraquat in the kidneys. Accumulation and kidney damage due to paraquat have been proven by the results of a study conducted on a 12-year-old child living in an agricultural area located in Iran. The results of the study concluded that the child had impaired kidney functions, due to paraquat exposure.^[10] Results of another test done on rats, exposed to the pesticide, showed also an impaired kidney function, which was characterized by an increase in the weight of the rat's kidney.^[11] The findings of this study are also reinforced by the results of another research conducted by Neghab *et al.*,^[12] the results proved that pesticide exposure can cause renal excretion disorders seen from the changes in urine biochemical components.

The toxicity of paraquat is influenced by several factors such as age, gender, use of personal protective equipment (PPE), frequency and duration of exposure, spraying direction, spraying area, and time affected,^[13] and another key factor is also nutritional status. Nutritional status and a good diet have been shown to reduce the body's susceptibility to a number of toxic compounds.^[14]

Research on the influence of factors related to paraquat toxicity and also the toxic effects of it on the kidney have been widely conducted. On the other hand, research that links the factors of the duration of work as a farmer, frequency of exposure to paraquat, and the nutritional status of a person, to the paraquat levels in urine and impaired kidney function caused by the paraquat, has never been done. It is important to understand the profiles of environmental exposure to parabens in vulnerable populations, especially in developing countries where exposures remain largely uncharacterized, and the relationship of these compounds with various factors is unclear.^[15] Based on these circumstances, this study was conducted to analyze the relationship between the previous factors and the impacts of paraquat on the urine, and also the damage done on the kidneys. In addition, nutritional status was also measured using the body mass index (BMI), and impaired renal function will be known through changes in urine biochemistry from urinalysis results.

MATERIALS AND METHODS

Research design

This study was an analytical observational study with a cross-sectional approach. Ethical approval for this study (Ethical Committee No. 450/KEPK-FKULM/EC/X/2022) was provided by the Ethical Committee of Medical Research, Lambung Mangkurat University, South Kalimantan, Indonesia, on 13 October 2022.

The research was conducted in September 2022, with the research location being in North Landasan Ulin Village, Liang Anggang Subdistrict, Banjarbaru City, of the South Kalimantan Province. The subjects of the research were 55 farmers who worked in the area. The selection of the subjects was based on the inclusion and exclusion criteria of the research subjects. The inclusion criteria of the research subjects were: (a) vegetable farmers of the male gender; (b) the pesticide used contains the active ingredient of paraquat; (c) pesticide spraying is done in the morning; (d) collection of the urine samples were done 6 h after coming into contact with the paraquat spray; and finally, (e) the willingness of the individual to being a research subject. Meanwhile, the exclusion criteria for research subjects were individuals who had a history of acute kidney injury, chronic kidney disease, or other severe diseases that may disrupt with the quality of the urine samples.

Data taken from each subject included the duration of spraying, the working period of the farmer, height (BL) in centimeters (cm), weight (BW) in kilograms (kg), and BMI. Data on the duration of spraying and work were obtained from the direct interviews with the farmers, while data on BW, BL, and BMI were obtained from the direct measurements. Furthermore, each farmer provided a urine sample to measure the paraquat levels and analyze the urine's biochemistry. The urine sample was collected in sterile plastic bottles. The urine sample was stored at room temperature (RT; 20°C–25°C) in the Chemical/Biochemical Laboratory, Lambung Mangkurat University, Banjarbaru, South Kalimantan, Indonesia. We assessed all the parameters immediately after collection.

Measurement of paraquat concentration in urine

Analysis of paraquat concentration in the urine was carried out using the method proposed by Rai *et al.*^[16] This analysis was conducted by taking 1 ml of urine sample, which was then placed into a test tube, and is added 1 ml of 5% EDTA and 1 ml of 1% trichloroacetic acid (CCl₃COOH). The mixture was then centrifuged at 1850 rpm for 10 min. Afterward, 1 ml of 1% sodium borohydride (NaBH₄) solution and 1 ml of 2M sodium hydroxide (NaOH) were added. Next, deionized water was added to the mixture until the volume of the mixture was 10 ml. The mixture was subsequently placed into a thermostat at a temperature range of 35°C–40°C for 5 min. Finally, the absorbance of the mixture was measured with a spectrophotometer at a wavelength of 600 nm.

Urine biochemical analysis

Urine biochemical analysis was performed using the dipstick colorimetric method (Convergys® Urine Matrix Test Strips, Convergent Technologies, Coelbe, Germany).^[17] The test began by putting a urine sample into a test tube. The test strip was then dipped into the test tube containing the sample for approximately 2 s; it was then taken out and left for 60 s. The color results produced by the test urine strip will be matched with the available indicators. The results of biochemical analysis consist of pH value, specific gravity, glucose, protein, blood, ketones, nitrites, bilirubin, urobilinogen, leukocytes, and ascorbic acid. The pH value and specific gravity will be assessed quantitatively, while the other parameters will be assessed qualitatively.

Data analysis

Data on subject characteristics and urine biochemical analysis results will be presented in tabular form and analyzed descriptively in terms of number and frequency (%). In addition, the analysis of the relationship between each variable of work duration, spraying duration, and BMI with paraquat concentrations in the urine will be analyzed using the Spearman rank correlation test. The Spearman rank correlation test analysis was conducted with the help of a web-based statistical application at <https://www.socscistatistics.com/tests/spearman/default2.aspx>. The results of the analysis will obtain the value of the correlation coefficient (R_s). The value of R_s will be classified into several categories, including (1) $R_s = 0.00-0.25$ meaning that the relationship is very low; (2) $R_s = 0.26-0.50$, the relationship is moderate; (3) $R_s = 0.51-0.75$, there is a strong relationship; (4) $R_s = 0.76-0.99$ means that there is a very strong relationship; and (5) $R_s = 1.00$ signifies a perfect relationship. In addition, the relationship between these variables is said to be meaningful if $P < 0.05$.^[18]

Data on the results of work duration, spraying duration, and BMI will also be analyzed for their relationship with urine biochemical profiles, to determine the damage to the kidney's function. This relationship analysis was carried out using the Chi-square test. Variables are said to be related if $P < 0.05$.

RESULTS

The research was conducted in North Landasan Ulin Village, Liang Anggang Subdistrict, Banjarbaru City, South Kalimantan Province [Figure 1]. The selection of the research site was based on the fact that this area is the center of vegetable plantations in Banjarbaru City. This village has the highest number of vegetable farmers compared to other villages in Banjarbaru City, totaling about 862 farmers and then divided into 35 farmer groups. By calculating with Slovin's formula

and matching subjects to the inclusion and exclusion criteria, a total of 55 subjects were obtained. Data on the characteristics of the 55 research subjects are presented in Table 1.

Table 1 shows that 96.36% of the study subjects were more than 25 years old. Vegetable farmers in North Landasan Ulin Village, on average, spray paraquat-based pesticides with a duration of ≤ 60 min (87.23%). The results of Table 1 also display that 80% of the farmers worked > 5 years. 69.10% of farmers had normal BMI and 30.90% of farmers had abnormal BMI. The results of Table 1 also show that 60% of vegetable farmers do not use PPE.

The results of the work duration data were then analyzed for their relationship with the measurement results of paraquat concentrations in urine. The results of this study are presented in Table 2. The results in Table 2 show the value of $R_s = 0.50416$ with $P < 0.05$. Based on the data, the length of work is moderately and significantly related to paraquat concentrations in urine; such results were obtained due to the differences between the R_s and P values. This result means that the longer a farmer's work duration, the concentrations of paraquat in urine will increase.

The results of the analysis of the relationship between the duration of pesticide spraying and paraquat concentrations in urine are presented in Table 2. The results of the analysis showed a value of $R_s = 0.30526$ with $P < 0.05$. This means that the length of spraying is also moderately and significantly related due to the differences between values. The results concluded that the longer the farmers had contact with paraquat through spraying, the more elevated paraquat concentrations will be in the urine.

The results of the analysis of the relationship between BMI and paraquat concentrations in urine are presented in Table 2. The results of the analysis show the value of $R_s = 0.30313$ with $P < 0.05$. This shows that BMI has a moderate and significant

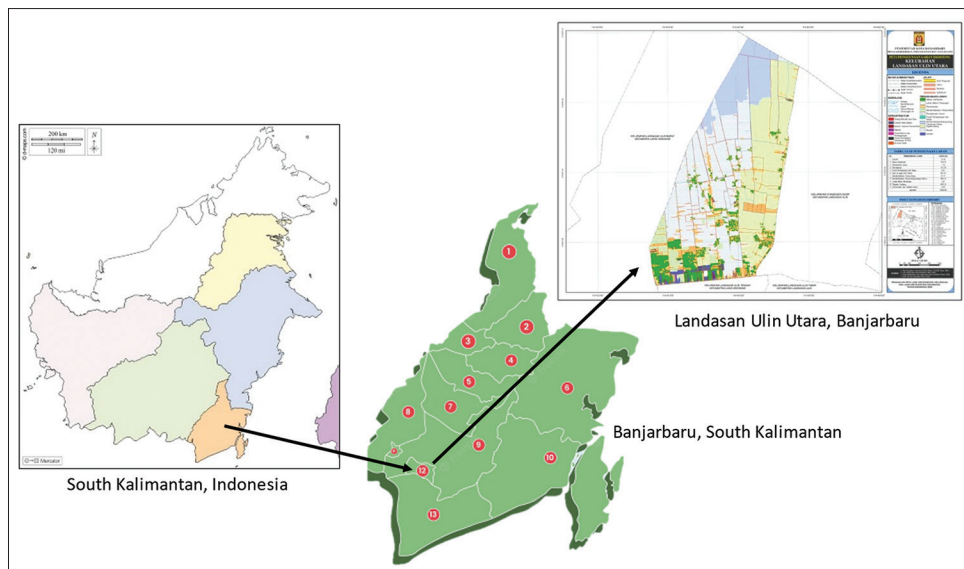


Figure 1: Location of North Landasan Ulin Village

Table 1: Characteristics of the research subjects

Characteristics	Total	Frequency (%)
Age (years)		
≤25	2	3.64
>25	53	96.36
Mean	48.73	
Maximum	70	
Minimum	22	
Spraying duration (per week)		
≤60 min	48	87.23
>60 min	7	12.77
Mean	49.91	
Maximum	180	
Minimum	10	
Length of work as a farmer (years)		
≤5	11	20
>5	44	80
Mean	14.66	
Maximum	37	
Minimum	1	
BMI		
Normal (18.5–24.9)	38	69.10
Not normal (<18.5 or > 24.9)	17	30.90
Mean	22.11	
Maximum	32.04	
Minimum	15.71	
Uses of mask		
Used	22	40
Not used	33	60

BMI: Body mass index

Table 2: Correlation between the length of work, pesticide-spraying duration, and body mass index with urine paraquat concentrations

Parameters	Urine paraquat level	
	Rs	P
Length of work	0.50416	0.00000
Pesticide-spraying duration	0.30526	0.02343
BMI	0.30313	0.02447

BMI: Body mass index

relationship with paraquat concentrations in urine; once again, the results correspond to the difference of values between the Rs and P values.

The results of the urine biochemical analysis of the study subjects are presented in Table 3. The results in Table 3 show that most of the subjects' urine biochemical parameters appeared normal. Biochemical parameters that looked positive in most farmers were seen in the bilirubin parameter. A total of 69.10% of subjects were detected positive for bilirubin in urine. In addition, urine protein parameters were also mostly positive in the urine of the subjects. The results in Table 3 show that 90.90% of the subjects contained protein in their urine. Other parameters such as leukocytes, ketones, nitrites,

Table 3: Urine biochemical status of pesticide-spraying farmers

Parameters	Total	Frequency (%)
Leukocyte		
Negative	48	87.27
Positive	7	12.73
Ketones		
Negative	53	96.36
Positive	2	3.64
Nitrite		
Negative	51	92.72
Positive	4	7.28
Urobilinogen		
Negative	53	96.36
Positive	2	3.64
Bilirubin		
Negative	17	30.90
Positive	38	69.10
Protein		
Negative	5	9.1
Positive	50	90.90
Glucose		
Negative	51	92.72
Positive	4	7.28

urobilinogen, and glucose did not appear to be detected in the subjects' urine. The results of the status of urine biochemical parameters were also analyzed for their relationship to working period, length of spraying, and BMI using the Chi-square test. The results concluded that said factors did not associate with the biochemical status of the urine in the subjects.

DISCUSSION

The results of this study show that the paraquat concentrations in urine are related to the length of work of the farmers in a day. These results are in line with the results of several previous studies which also stated that the period of work is associated with an increase of pesticide poisoning.^[6] The longer a vegetable farmer works, the higher the paraquat concentrations in the farmer's urine. The duration of the farmer's work leads to a more prolonged and greater contact between the farmer and the pesticide. This results in the process of paraquat bioaccumulation in the kidneys, which in turn causes higher concentrations of paraquat in the urine.^[9]

Another conclusion of this study was that the duration of the farmer's contact with the pesticide, through spraying, was related to the concentrations of paraquat in the urine. The longer the spraying time, the higher the amount of paraquat in the urine. The length of spraying can increase the risk of paraquat entering the body due to continuous exposure. Paraquat that enters the body is distributed to the lungs, liver, and kidneys, and stored in the muscle tissue. Low concentrations of paraquat can be maintained in the muscle tissue and slowly released into the blood and excreted through

urine. The small proportion of paraquat distributed to deeper compartments can only be eliminated slowly by the kidneys over days to weeks or even longer. This may explain the persistence of paraquat in both plasma and urine. In addition, the persistence of paraquat in the kidneys can cause further kidney damage, resulting in acute kidney injury, renal tubular necrosis, renal azotemia, alkaline urine, proteinuria, and mild systemic hypertension.

This study also examined the relationship between BMI and paraquat concentrations in urine. The analysis showed that BMI was associated with the paraquat concentrations in urine, showing that if a farmer's BMI is deemed abnormal, the level of paraquat in the urine will increase. BMI is a picture of a person's nutritional status. A person's nutritional status is related to several factors, including nutritional intake, diet, physical activity, lifestyle, socioeconomic status, education level, knowledge level, environmental conditions, exposure to chronic diseases, and fat percentage. A normal BMI illustrates that a person's nutritional status is good so that the metabolic process and elimination of toxic substances are able to function properly. An abnormal BMI will result in the disruption of these processes so that the body cannot perform these processes optimally. Thus, the better the BMI, the more toxic substances can be eliminated and excreted into the urine.^[6]

This study also examined the relationship between urine biochemical status with working time, pesticide-spraying duration, and BMI. The results showed that there was no relationship between the urine's biochemical status with said factors. The results showed that the vegetable farmers in this study did not experience kidney problems. This is thought to be due to the duration of spraying of most of the farmers which is ≤ 60 min and the good nutritional status of the farmers which can be seen through the normal BMI statuses of almost all the farmers.

The results of previous studies prove that the duration of spraying greatly affects the accumulation and concentrations of paraquat in the urine. The results of Konthonbut *et al.*'s^[19] study proved that the duration of the research levels in urine in his study was still lower than Malaysian farmers. Farmers in the study used paraquat with an average duration of 6–66 min/day compared to the 135–254 min of the Malaysian farmers. This is also reinforced by the results of Ramdan *et al.*'s research^[13] which stated that the pesticide concentrations in the body are strongly influenced by the duration of spraying and the concentration of pesticides sprayed, both factors increasing the risk of pesticide poisoning. Though, this was not mentioned in the previous study.

CONCLUSION

The results of the study have proven that certain factors such as the length of the farmer's work time, duration of the time spraying, and BMI values of the farmers have a correlation with paraquat concentrations in the urine, although it appears that these factors have no effect on the biochemical status of the

urine. The results of this study also shows that the concentration of paraquat in urine will increase with an increase in several factors such as length of work and duration of pesticide spraying, except BMI. While the exact values of when the span of work, duration of spraying, and BMI values until the farmer experiences kidney problems and when changes will occur in the urine's biochemical status cannot be clearly determined. There are still several factors that may influence the results of this study. Further research with a larger number of subjects and with diverse characteristics such as longer working hours, longer spraying duration, spraying dose, abnormal BMI, type of sprayer, and other factors may be needed so that the exact number of working hours, spraying duration, and BMI values that can trigger kidney disorders in farmers will be known.

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Conflicts of interest

There are no conflicts of interest.

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