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SUBCLINICAL RENAL DYSFUNCTION IN HORTICULTURAL FARMERS: EARLY DETECTION IN HIGH PESTICIDE EXPOSURE AREAS

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Abstract

Introduction: *Globally, Chronic Kidney Disease of Unknown etiology (CKDu) poses a growing medical and social challenge, particularly in agrarian countries with a high prevalence of pesticide exposure. Indonesia, is one of the countries with a dominant agricultural sector. Tanjungsari and Glonggong villages in Wanasari subdistrict, Brebes Regency, are agricultural areas with a high intensity of pesticide use.* ***Methods:*** *This research aimed to identify the prevalence of subclinical renal dysfunction and associated risk factors in horticultural farmers in areas with high pesticide exposure. This research applied a cross-sectional method involving 40 farmers aged 26-65 years from two villages in Wanasari District, Brebes Regency. Data collection was carried out through interviews, and examination of kidney function biomarkers (serum creatinine and eGFR). Statistical analysis was conducted using Logistic Regression tests.* ***Results and Discussion:*** *The study revealed that 37.5% of participants exhibited eGFR values <90 ml/min/1.73 m2, indicating subclinical impairment of kidney function. Employment duration >20 years (p=0.024; OR=6.000; 95% CI:1.263-28.498) and daily working hours >6 hours (p<0.001; OR=69.279; 95% CI:6.423-756.965) showed a significant association with reduced eGFR values. Occupational health interventions should prioritize managing the duration and intensity of exposure to hazardous substances in the workplace, regardless of the workers' gender.* ***Conclusion:*** *The conclusion is that the daily working hours and the employment duration of the farmers are significantly associated with impaired kidney function, potentially acting as an initial marker of CKDu.*

INTRODUCTION

On a worldwide scale, Chronic Kidney Disease (CKD) is considered one of the most pressing public health challenges, commonly associated with metabolic disorders such as diabetes mellitus (1). Nevertheless, in recent years, a subgroup of CKD, referred to as CKDu, has emerged, which lacks a clearly defined cause. Several reports have indicated a rising number of CKDu cases in countries, including India, Pakistan, and Srilanka (2-3). One of the most affected areas is Tierra Blanca, where rapid declines in kidney function are especially prevalent among agricultural workers (4). In Central America, Mesoamerican Nephropathy, the term used to describe this condition, has resulted in widespread mortality with thousands of reported deaths (5). Additionally, pesticide exposure has been associated with other health consequences, such as a higher prevalence of dyslexia in children (6).

Although the precise etiology of CKDu has not yet been fully established, numerous studies have indicated a strong association with pesticide exposure (7). The incidence of CKDu appears to rise in tandem with intensive insecticide usage in agricultural practices (8-9). Prolonged pesticide exposure may adversely

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affect health, as indicated by elevated serum alanine aminotransferase enzyme activity (10). Moreover, chemical exposure, even at minimal levels, may disrupt endocrine regulation and contribute to an increased mortality risk (11). Persistent exposure to elevated temperatures and long-term pesticide use are also believed to increase the probability of CKDu (12).

Indonesia is an agrarian country, with the majority of its population working in the agricultural sector spread across all provinces in Indonesia. East Java, Central Java, and West Java are the provinces with the highest number of farmers, totaling 3,263,708 (East Java), 2,614,608 (Central Java), and 2,210,568 (West Java) (13). Indonesia is a major player in the agricultural sector, which contributes to its relatively high level of pesticide use. According to the Ministerial Decree No. 379/KPTS/SR.330/M/6/2020, 153 pesticides, including insecticides, fungicides, and herbicides, are officially approved for use in Indonesia (14).

To date, no research has specifically examined the distribution of CKDu cases and their underlying risk factors among shallot farmer communities in Indonesia, particularly in Brebes Regency. Tanjungsari and Glonggong Villages, located in Wanasari District, Brebes Regency, Central Java, Indonesia, are known as areas with intensive use of pesticides. Although several studies on the health impacts of pesticide exposure have been conducted in Indonesia, the primary focus of these studies has not been on CKDu, but rather on the general health effects of individuals with prolonged and continuous pesticide exposure. Given the higher prevalence of CKDu observed in Asian populations (12,15-16), this research aims to analyze the association between related risk factors and the occurrence of CKDu among shallot farmers.

METHODS

Research Design

This cross-sectional research involved shallot-spraying farmers from Tanjungsari and Glonggong Villages, Wanasari District, Brebes Regency. These areas were selected due to their intensive use of pesticides in agricultural activities. Geographically, Tanjungsari and Glonggong Villages are located in Wanasari District, located between 6049’-6053’ South Latitude and 108053’-109011’ East Longitude. Wanasari District covers an area of 144.92 hectares and consists of 20 villages (17). This research was carried out from April to June 2025. Ethical clearance was obtained from the authorized institutions, with approval granted by the Health Research Ethics Committee of the Faculty of Public Health, Universitas Diponegoro, No. 157/EA/KEPK-FKM/2025.

Respondents

All respondents were aged 26-65 years. Research sampling was conducted randomly and based on respondents’ willingness to be involved in this research. All respondents had no prior diagnosis of hypertension, diabetes, or other conditions classified under CKD categories. Additionally, none of the respondents were taking hypertension or diabetic medications at the time of the research data collection.

Laboratory Analysis

Blood samples were labeled and centrifuged in the laboratory to separate the serum. Each sample was analyzed for Serum Creatinine (SCr) and estimated Glomerular Filtration Rate (eGFR). The SCr and eGFR examinations were measured and analyzed based on clinical guidelines by employing standard methods using the enzymatic calculation method.

Key Results

Kidney function was assessed using SCr levels and estimated eGFR. A decrease in kidney function was indicated by reduced eGFR values, based on a chosen cutoff point of 60-89 ml/min/1.73 m^2, which reflects the early stages of renal function decline.

Statistical Analysis

To examine differences between the normal group and the reduced eGFR group, a statistical approach was taken to analyze categorical variables using the Chi-square test and Fisher’s exact test, with non-normally distributed continuous variables assessed using the Mann-Whitney test. Kidney biomarkers, serum creatinine, and eGFR were used as indicators of kidney function decline. To assess the association between working hours and employment duration with eGFR, a logistic regression model was applied.

RESULTS

This research involved as many as 40 respondents aged 26-65 years, with a median age of 50 years (IQR: 39.25-61.75). The majority of respondents were male (90%), and most had attained only Basic Education (82.5%). Based on the employment duration (52.5%), of the farmers had worked for more than 20 years, and as many as 72.5% of the respondents worked more than 6 hours per day. Respondents were evenly distributed in two villages, Tanjungsari Village and Glonggong Village, with each village contributing 50% of the total sample. Based on the results of renal biomarker measurements, the average SCr level was 0.88±0.15 mg/dl. Based on eGFR estimates, 62.5% of respondents had values

≥90 ml/min/1.73 m², while 37.5% of them showed lower values, indicating subclinical renal dysfunction.

Based on eGFR stratification, individuals with eGFR ≥90 mL/min/1.73 m² had a median age of 106 (range 90-128), whereas those with eGFR <90 mL/min/1.73 m² presented a lower median age of 84 (64-89). The Mann-Whitney test showed a value of p=0.090, indicating that the difference in age between the two groups was not statistically significant.

Most respondents in this research were male (90%), while only 10% were female. Among respondents within the eGFR group <90 ml/min/1.73 m², the majority were male (75%), while only 25% were female. However, the results of the farmer's exact test showed no significant difference (p=0.139). Exposure to pesticides is known to have adverse health effects. The high percentage of male respondents with decreased kidney function in this research can provide an early picture that there is a tendency to associate pesticide exposure with sex/gender, although the results are not significant. This is likely due to unequal distribution of the number of samples between males and females. Therefore, additional research with a more balanced sample distribution is recommended.

Most respondents had basic education levels (82.5%). Results from Fisher's Exact test demonstrated the absence of a statistically significant association between educational attainment and eGFR values (p=0.691). A limited educational background is associated with insufficient knowledge regarding personal protective equipment and occupational safety practices. Consequently, it can indirectly increase the long-term risk of impaired kidney function, even though it is not significantly noticeable.

As many as 52.5% of respondents had a duration of >20 years. Chi-square analysis revealed a significant association between employment duration and eGFR (p=0.007), with farmers working >20 years having a 3.6-fold higher risk of decreased kidney function (Prevalence Rate (PR)=3.61; 95% Convidence Interval (CI): 1.13-11.5) than those with ≤20 years. Most farmers with a working experience of ≤20 years had an eGFR value of ≥90 mL/minute/1.73 m2 (84.2%), while workers with a working experience of >20 years had a higher proportion of decreased kidney function (57.1%).

Based on the research results, 72.5% of respondents reported having daily working hours of ≤6 hours. However, in the group of respondents who worked >6 hours per day, the proportion of eGFR decrease was recorded much higher, i.e., 90.9%, compared to the ≤6-hour group (17.2%). Chi-square analysis demonstrated a highly significant association between working hours and reduced eGFR values (p<0,001) with a prevalence ratio of 5.28 (95% CI:2.13-13.1). Farmers working more than 6 hours daily exhibited a 5.3-fold higher risk of decreased kidney function than those working 6 hours or less. These suboptimal working conditions represent a significant factor that should be considered in formulating strategies aimed at preventing kidney disease among agricultural workers.

Based on this research, half of the respondents (50%) came from Tanjungsari Village and 50% from Gronggong Village. No significant difference in eGFR was found between the two villages (p=0.744), indicating a similar distribution of kidney function decline. Residential locations classified as high-risk areas for CKDu are often associated with agricultural geographic factors.

Table 1. Characteristics of Respondents (26-65 years) based on eGFR

	Overall (n=40)	eGFR, mL/min/1.73 m2		P value	PR (95%CI)
		≥ 90 (n=25)	60-89 (n=15)		
SociodemoFigureics Age, Year, Median (IQR)	50 (39.25-61.75)	106 (90-128)	84 (64-89)	0.090[a]	
Gender Man Woman	36 (90.0) 4 (10.0)	24 (66.7) 1 (25.0)	12 (33.3) 3 (75.0)	0.139[b]	
Education Basic Education Secondary-Higher Education	33 (82.5) 7 (17.5)	20 (60.6) 5 (71.4)	13 (39.4) 2 (28.6)	0.691[b]	
Daily Working Hours >20 Year ≤ 20 Year	21 (52.5) 19 (47.5)	9 (42.9) 16 (84.2)	12 (57.1) 3 (15.8)	0.007[c]*	3.61 (1.13-11.5)*
Daily Working Hours >6 Hour ≤ 6 Hour	11 (27.5) 29 (72.5)	1 (9.1) 24 (82.8)	10 (90.9) 5 (17.2)	0.000[b]*	5.28 (2.13-13.1)*
Residence Tanjungsari Village Glonggong Village	20 (50.0) 20 (50.0)	12 (60.0) 13 (65.0)	8 (40.0) 7 (35.0)	0,744[c]	

eGFR: estimated Glomerular Filtration Rate;; IQR: Inter Quartille Range; [a]Mann Whitney test; [b]Fisher Exact Test; [c]Chisquare Test; PR: Prevalence Rate

Data analysis presented in Table 2 shows that the median serum creatinine concentration was 0.8750 mg/dl, with a mean value of 0.8833 mg/dl (95% CI:0.8395-0.9270). The standard deviation value (SD) of creatinine was 0.1477 mg/dL, with a minimum value range of 0.59 mg/dL and a maximum of 1.21 mg/dL. For the eGFR indicators, the median value was 93.00, with a mean of 95.48 (95% CI:90.85-100.05). Standard deviation of eGFR of 15,818 ml/min/1.73 m^2 with a minimum value of 64 ml/min/1.73 m^2 and a maximum value of 128 ml/min/1.73 m^2. Clinically, elevated SCr levels indicate impaired renal function associated with pesticide exposure. However, based on previous research, increased serum creatinine can also be caused by inaccuracies in extreme muscle function and mass.

Table 2. Serum Creatinine and Estimated Glomerular Filtration Rate (eGFR) Measurements

	Median	Mean (95%CI)	SD	Min	Max
Creatinine (mg/dl)	0.8750	0.8833 (0.8395-0.9270)	0.1477	0.59	1.21
eGFR (mL/menit/1,73 m^2)	93.00	95.48 (90.85-100.05)	15.818	64	128

SD: Standard Deviation; eGFR: estimated Glomerular Filtration Rate

Distribution of eGFR by Gender, Educational Level, Residential Location, Employment Duration, and Daily Working Hours

Figure 1(A) illustrates the distribution of eGFR values by respondents' gender. Generally, the median value of eGFR in the male group is higher than that in the female group. A significant decline in kidney function is frequently observed among farming populations. The distribution of data in the male group seemed to be wider, with the range of eGFR values from approximately 64 to more than 128 ml/minute/1.73 m^2, while in the female group, it ranged narrowly, between 70 and 100 ml/minute/1.73 m^2. This can certainly affect the results.

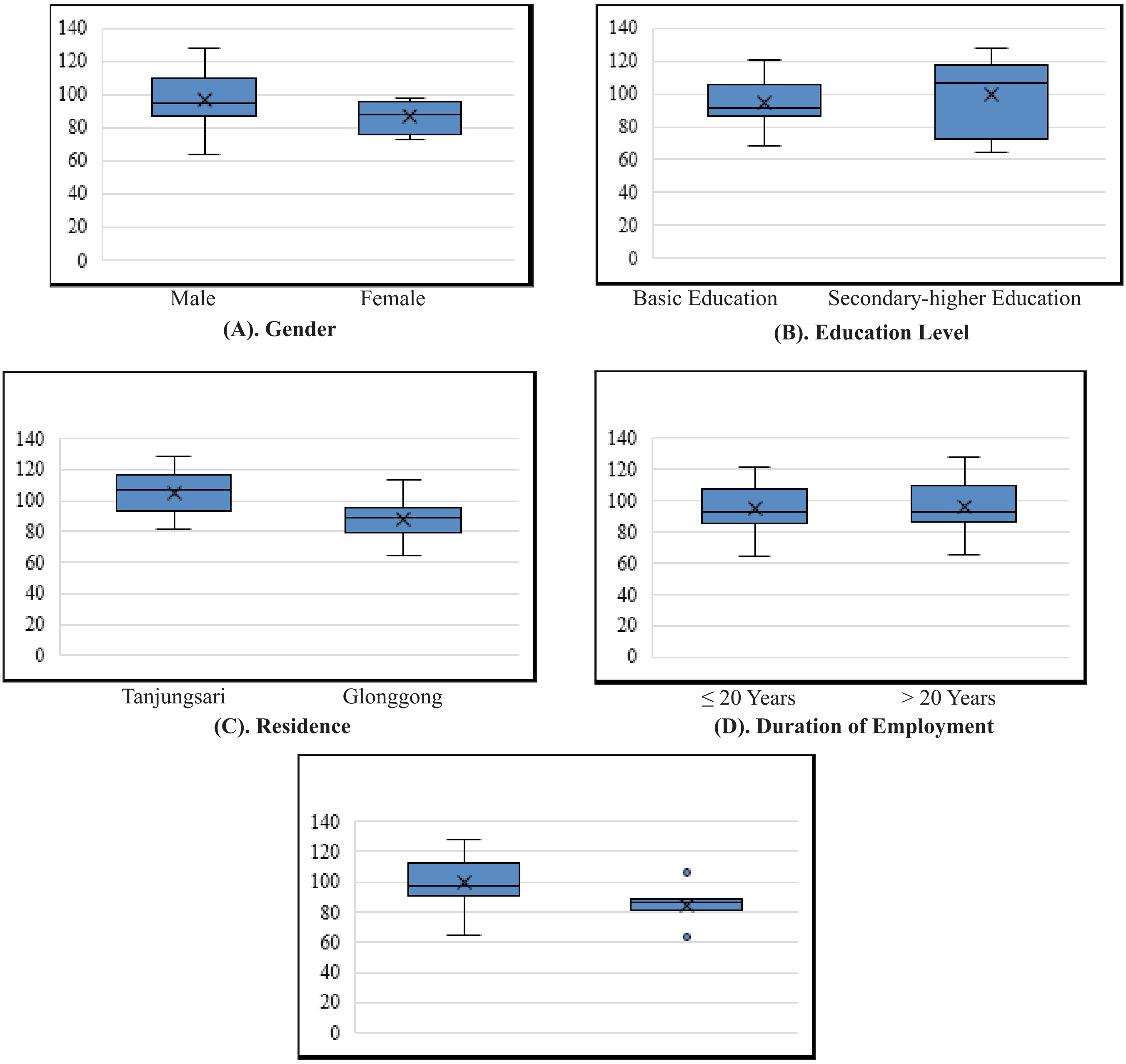
Based on the interpretation of Figure 1(B), which displays eGFR based on the respondents' educational levels, a significant difference was identified between the group with basic education and those with secondary to higher education. Individuals with at least a moderate educational level generally exhibit higher median eGFR values, suggesting a positive association between educational level and kidney function. Farmers who frequently handle agricultural pesticides often show limited awareness of chemical health risks, likely due to lower educational attainment. The group with secondary to higher education also shows a wider distribution of data, as indicated by a large interquartile range as well as lower whiskers reaching about 65 ml/min/1.73 m^2 and upper whiskers exceeding 120 ml/min/1.73 m^2.

Figure 1(C) shows the distribution of eGFR values based on the respondents' residential locations. The distribution of eGFR values among respondents residing in the Tanjungsari and Glonggong areas has a relatively similar pattern. The median positions in the two groups were nearly identical, indicating that the median eGFR values between the two areas did not show significant differences. Several prior investigations have indicated that areas with significant pesticide contamination are associated with decreased kidney function. Specific locations within agricultural zones have also been linked to the occurrence of CKDu in both male and female populations. The average value of eGFR, indicated by an "x", seemed to be slightly greater among respondents in the Glonggong Village compared to the Tanjungsari Village, although the difference appeared to be minimal.

Based on Figure 1(D), the estimated Glomerular Filtration Rate (eGFR) shows a fairly significant difference between groups with employment duration ≤20 years and >20 years. The median eGFR in the ≤20-year working age group was years, indicating that, generally, individuals with shorter working years had better kidney function. The results suggest that increasing years of employment are inversely related to eGFR levels. The average eGFR ("x" mark) appeared higher in the ≤20-year working age group, supporting the finding that kidney function tends to decline with length of employment.

Figure 1(E) illustrates the distribution of eGFR values in the group of workers based on daily working hours (≤6 hours and >6 hours), showing a significant difference in the distribution pattern and median of kidney function. The group with a ≤6-hour working time showed a higher median eGFR, accompanied by a wider range of data. This indicates the diversity of kidney function conditions in the group. Most individuals in this group had an eGFR above the normal threshold (≥90 ml/min/1.73 m^2)

In contrast, the group with a working time of > 6 hours showed a narrower distribution of eGFR and a lower median, indicating a tendency to decline in kidney function. Almost all data distribution was below the value of 90 ml/min/1.73 m^2, with exceptional findings revealing a significant reduction in kidney efficiency.



(E). Daily Working Hours

Figure 1. Distribution of estimated Glomerular Filtration Rate (eGFR) Based on Gender, Educational Level, Residential Location, Employment Duration, and Daily Working Hours.

Association Between Employment Duration and Daily Working Hours With Reduced eGFR Values

The employment duration variable had a statistically significant relationship with a decrease in eGFR, with a value of p=0.024 and an OR of 6,000 (95% CI:1.263–28.498), individuals, with longer work duration had a sixfold higher likelihood of reduced eGFR than those with shorter tenure, after gender adjustment. The gender variable did not show a significant association with a decrease in eGFR, as indicated by values of p=0.434 and OR=2.667 (CI95%): 0.229–31.069).

Table 3 shows that this association is statistically meaningful and clinically relevant. These findings indicate that longer work experience often reflects the duration of chronic exposure to toxic substances, including pesticides, which are important risk factors contributing to the decline in kidney function among farmers. A prolonged duration of employment, especially among females, may contribute to a decline in eGFR values, potentially due to hormonal differences. Prolonged occupational pesticide exposure in long-serving farmers increases the risk of kidney function decline.

Table 3. Results of Logistic Regression Analysis between Employment Duration and Decreased eGFR Values after Gender Adjustment

	p-Value	OR (95% CI)
Gender	0.434	2.667 (0.229 – 31.069)
Duration Of Employment	0.024	6.000 (1.263 – 28.498)

According to the logistic regression analysis presented in Table 3, a significant association was identified between employment duration and gender with the decline in eGFR. In this research, the length of work variable showed a value of $p<0.001$ and an Odds Ratio (OR) of 69.729 (95% CI:6.423–756.965). This shows that individuals with longer working hours have a 69.7 times greater risk of experiencing diminished eGFR in comparison to individuals with shorter working hours, after adjusting for gender.

Table 4. Results of Logistic Regression Analysis between Daily Working Hours and Decreased eGFR Values after Gender Adjustment

	p-Value	OR (95% CI)
Gender	0.044	15.538 (1.074 – 224.825)
Daily Working Hours	0.000	69.729 (6.423 – 756.965)

In addition, in Table 4, gender was also found as a variable that was significantly related to the decrease in eGFR, with values of $p=0.044$ and OR=15.538 (1.074–224.825). This means that both genders are approximately 15.5 times more likely to have decreased kidney function.

DISCUSSION

The evidence from this research indicates that male farmers possess increased eGFR values compared to their female counterparts, implying that despite the elevated eGFR levels, men demonstrate a broader variability in kidney function than women. The relatively similar minimum values between the two groups suggest that the risk of impaired kidney function remains in both. Kidney function, in general, may be modulated by sex hormone levels in both males and females (18). Supporting this, research from the United States found that women over the age of 50 who are exposed to pesticides face elevated health risks (19). Evidence from a study in Spain revealed that early indicators of renal damage, manifested as subclinical tubular injury, underscore the kidney's vulnerability to pesticide exposure (20). Beyond gender, other contributing factors to decreased kidney function among agricultural workers, particularly male farmers, include lifestyle choices, smoking habits, and physical activity (12,20). The prevalence of CKD in Brazil is most commonly observed among relatively young men (22). Nonetheless, clinical assessment revealed that decreased kidney function, with eGFR below 90 mL/min/1.73 m², tends to be more prevalent among older individuals (4). This aligns with previous studies, which have demonstrated that kidney function naturally declines as part of the aging process (21-22). Previous studies indicated that the proportion of adults aged 20-60 years with an eGFR ≤60 ml/min/1.73 m^2 was 3,5%, comprising 1,9% in individuals aged 20-39 years and 4,4% in those aged 40-60 years (4). Factors affecting pesticide toxicity include age, PPE awareness and use, smoking habits, and duration of pesticide application (25). Another study reported that females have the highest odds ratio for CKDu, with an OR of 1,36 (95% CI 1,01-1,84) (26). In addition, gender differences can also be caused by several factors, including physiological differences such as greater muscle mass in men, which affect creatinine levels and eGFR calculations. Environmental factors or different workloads between men and women also have the potential to affect kidney function.

The group with a primary education background exhibited a narrower distribution of eGFR values, with a median approaching the lower threshold of the normal range, approximately 90 ml/minute/1.73 m^{2,} and a limited overall range. This indicates a lower degree of variability in kidney function among individuals within the group, which may adversely affect farmers' health conditions, as urinary pesticide metabolite levels tend to be lower among individuals with higher educational attainment relative to respondents with limited educational backgrounds (27). These findings are aligned with previous research involving female respondents in Chiang Mai, Thailand (28). In addition to impaired kidney function, pesticide exposure may also lead to other adverse health effects, particularly among those with limited educational backgrounds (8,29). These differences may be influenced by factors such as limited knowledge about health, lifestyle habits, access to medical services, and awareness of the importance of personal protection from occupational risks, which are generally better enjoyed by individuals with higher education. The average eGFR value shown by the "x" sign on the Figure looked similar in both groups, but the combination of a higher median and a wider distribution in the middle-upper education group indicated that education could potentially be a protective factor against decreased kidney function.

However, differences were observed in the extreme ranges of eGFR values, specifically in the minimum and maximum levels between the two regions. The Glonggong region shows a higher maximum value of eGFR than the Tanjungsari region; this indicates the existence of individuals with optimal kidney function. In contrast, the minimum values in the Glonggong Region were recorded as lower, which means that there are individuals with more severe kidney function impairments in the region. Areas with certain geographic characteristic, such as agriculture, the use of contaminated well water has the potential to lead to kidney damage (30-31). Prior studies had also indicated that prolonged occupational exposure to pesticides and high temperatures among farmers might contribute to the deterioration of kidney function (32). People who work in agricultural areas have a low risk of eGFR with an OR of 5.19 (95% CI 1.11-24.26) (4). Geographically, the decline in kidney function also affects people who live in agricultural areas (28). Research in India states that the increase in chronic kidney disease, with an unknown etiology, is concentrated in agricultural regions with relatively high levels of pesticide use (16,33). This condition indicates a wider dissemination of data in the Glonggong Region, potentially reflecting differences in risk factors such as environmental exposure, lifestyle behaviors, or diverse health conditions.

Prolonged exposure to pesticides may lead to variations in the concentration of pesticide residues within the human body (9,27). Consistent use over an extended period can also result in the accumulation of heavy metals, which may adversely affect farmers' health conditions (35). Individuals in Sri Lanka with extended durations of occupational engagement in service have exhibited a higher rate of CKDu (31). These results support the importance of early detection and periodic monitoring of workers in the agricultural sector. Reduced eGFR in workers may result from repeated exposure to pesticide-related heavy metals (33-34). The presence of DAP metabolites in urine has the potential to cause subclinical events of kidney injury (38-39). Previous research has suggested that exposure can lead to early signs of kidney injury and increase the risk of developing chronic kidney disease (CKD). These findings lead to the possibility of an accumulation of occupational risk exposures (e.g., exposure to pesticides, toxic chemicals, or work stress) that have an impact on decreased kidney function.

A consistent decline in kidney function is observed among individuals with longer work durations, particularly when combined with exposure to toxic substances, dehydration, or high physical workload, indicating that the longer a person works, the lower her/his eGFR value tends to be. Workers who work in horticultural areas are often exposed to intense sunlight, and combined with longer working hours and pesticide exposures, this can lead to an increase in CKD cases (16,33). Although the OR results show a tendency to increase risk, A notably wide confidence interval indicates estimation uncertainty and the likelihood of the absence of a statistically significant relationship. This can be due to the uneven distribution of samples between genders or a relatively small sample size, thus reducing the power of analytics to detect significant differences. These findings support the notion that prolonged exposure to harmful substances in the workplace significantly contributes to the decline in kidney function (18). Possible biological pathways include the nephrotoxic impact of chemicals on the nephrons, along with oxidative stress and persistent inflammation that may accelerate the deterioration of renal function (6,20,27). With the insignificance of gender in this model, the main focus of occupational health interventions should be on controlling the duration and intensity of exposure to toxic substances in the workplace, regardless of the workers' gender.

The findings underscore the critical need for risk-oriented occupational health surveillance and targeted interventions, particularly in sectors characterized by prolonged pesticide exposure. An initial decline in eGFR values may progress to CKD, potentially diminishing workers' quality of life (20,29-30). Consequently, routine kidney function screening for individuals with extended working hours is essential. Simultaneously, consistent implementation of strategies to minimize exposure, such as mandatory use of personal protective equipment, comprehensive occupational safety training, and regulation of working hours, remains imperative. To maximize the effectiveness of these strategies, continuous environmental assessment and exposure reduction policies should be adopted, ensuring a holistic approach to preventing CKDu and safeguarding worker health.

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CONCLUSION

This research demonstrates that work characteristics, especially employment duration and daily working hours, are significantly associated with decreased kidney function, as indicated by eGFR values. The average eGFR and serum creatinine levels suggest that respondents have decreased renal function, although not yet at an advanced stage.

These results reinforce existing evidence that agricultural workers chronically exposed to environmental risks, such as pesticides and physically demanding working conditions, have the potential to experience impaired kidney function. Therefore, it is essential to implement occupational health-based interventions, such as counseling, screening, the consistent use of personal protective equipment, and regulation of working hours, to mitigate the long-term impacts on renal health.

AUTHORS' CONTRIBUTION

H: Conceptualization, Methodology, Software, Data Curation, Writing-Original draft. MR, S, NEW: Visualization, Investigation, Validation, Reviewing, and Editing

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