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Association Between Cadmium and Nickel Levels in Urine and Cardiovascular Risk in Female Waste Workers

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Keywords

Cadmium; Nickel; subclinical cardiovascular risk; female; waste workers

Abstract

Female waste workers are at risk of exposure to cadmium and nickel, which can affect hematological and inflammatory biomarkers and potentially influence cardiovascular risk. This study aims to analyze the relationship between cadmium and nickel levels in urine and MCV, RDW-SD, and PCT in female waste workers. Using a cross-sectional design and a biomonitoring approach, the analysis was conducted by measuring heavy metal levels in urine and hematological and inflammatory biomarkers through complete blood tests. The results showed that cadmium decreased MCV and RDW-SD, while cadmium and nickel increased PCT as an indicator of systemic inflammation. Thus, although changes in MCV and RDW-SD do not directly increase cardiovascular risk, increased PCT confirms the potential toxic effects of heavy metals on the cardiovascular system.

INTRODUCTION

Heavy metal pollution is a major environmental and public health concern associated with industrial, agricultural, and mining activities, as well as inadequate waste management. Cadmium (Cd) is a metal used in various industrial applications, including alloys, pigments, plastic stabilizers, dyes, and paints (Rasin et al., 2025). Nickel (Ni), meanwhile, may be present in hazardous and toxic waste, including discarded batteries and lamps (Nurcahyo et al., 2023). Both metals are toxic and can accumulate in the human body, potentially causing adverse health effects following prolonged exposure. Certain cadmium and nickel compounds are also classified as carcinogenic (Charkiewicz et al., 2023). Even at relatively low concentrations, exposure to these metals may pose health risks, with the severity of their effects depending on exposure levels and duration (Hanum et al., 2024; Mayaserli & Rahayu, 2018). Female workers at temporary waste collection sites (TPS) and final waste disposal sites (TPA) may be particularly vulnerable to exposure because of frequent and direct contact with mixed domestic and hazardous waste, especially where waste segregation is inadequate. This occupational vulnerability highlights the need to assess Cd and Ni exposure among female waste workers and evaluate its potential health implications. Women waste workers are at high risk of health problems due to exposure to various hazardous materials from solid waste. Waste containing heavy metals has the potential to cause adverse health effects.

Cadmium and nickel can enter the body through several exposure pathways, primarily via inhalation of contaminated dust and ingestion of particles transferred from contaminated hands, food, or other sources (Genchi et al., 2020; Wang et al., 2020; WHO, 2023). Once inside the body, cadmium and nickel accumulate in tissues and are excreted through urine, so urinary

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cadmium levels can be used as a biomarker of long-term exposure in the body (Qu & Zheng, 2024). Long-term exposure to cadmium and nickel is known to be associated with an increased risk of cardiovascular disorders, including coronary heart disease in both men and women (Rasin et al., 2025; Tellez-Plaza et al., 2014). Therefore, female waste workers are at risk of chronic exposure to heavy metals in the long term due to direct contact with contaminated waste. Exposure to cadmium and nickel can trigger a systemic inflammatory response, so monitoring cadmium and nickel levels in urine is necessary for early detection of cardiovascular disorders in populations vulnerable to exposure.

This relationship can be explained through the toxicity mechanism of cadmium and nickel. Exposure to cadmium and nickel has been linked to an increased risk of cardiovascular disease through oxidative stress and systemic inflammation (Badawi et al., 2024; Farrokhpour et al., 2019). These heavy metals can increase the production of free radicals and disrupt the body's antioxidant balance, thereby triggering an inflammatory response. Chronic inflammation due to heavy metal exposure can contribute to endothelial dysfunction and the development of atherosclerosis, thereby increasing the risk of hypertension, coronary heart disease, and other cardiovascular disorders (Muhammad Baharul Iman et al., 2025). Furthermore, Cd and Ni exposure may induce oxidative stress and inflammatory responses that affect the hematological system, potentially altering blood parameters such as procalcitonin (PCT), mean corpuscular volume (MCV), and red cell distribution width–standard deviation (RDW-SD). Therefore, these inflammatory and hematological biomarkers can be used as early indicators in assessing the impact of cadmium and nickel exposure on cardiovascular risk.

Herawati et al. (2025) reported that nickel exposure among mining workers and communities living near mining sites may contribute to oxidative stress and inflammation, potentially increasing the risk of adverse health outcomes, including respiratory and cardiovascular disorders. Research by Zhou et al. (2016) states that Cd exposure in battery manufacturing workers is associated with an increased risk of cardiovascular disease. Although previous studies have examined the association between heavy metal exposure and cardiovascular outcomes, evidence remains limited regarding Cd and Ni exposure among informal waste workers, particularly female workers at TPS. Furthermore, the potential associations between heavy metal exposure and hematological parameters, including PCT, MCV, and RDW-SD, remain insufficiently understood among this population. Therefore, this study aims to examine the association between urinary cadmium (Cd) concentrations and subclinical cardiovascular risk among female waste workers using selected hematological parameters as potential indicators. The findings are expected to clarify the potential cardiovascular risks associated with occupational Cd exposure and inform the development of preventive strategies to protect the health of female workers in the informal waste management sector.

RESEARCH METHOD

This study used a quantitative approach with a cross-sectional observational design to analyze the relationship between exposure to heavy metals cadmium and nickel in urine and blood biomarkers MCV, RDW-SD, and PCT as indicators of cardiovascular disease risk in female waste workers. Measurements of exposure and outcome variables were conducted on female waste sorting workers as the exposed population. Sampling was carried out from March to November 2025 at the landfill and 3R waste transfer station. Hematological examinations were conducted at a local health facility laboratory. This study was also conducted

through collaborative effort involving the Wonjin Institute for Occupational and Environmental Health (WIOEH), Seoul, South Korea, ECOTON, and Universitas Airlangga.

The study population consisted of women of productive age (15–49 years) who were actively working at temporary storage sites (TPS) and final processing sites (TPA) and had been working in the waste management sector. Participants were categorized based on length of employment, namely K1 (< 1 year), K2 (1 -≤ 5 years), K3 (> 5 - ≤10 years), K4 (>10 - ≤ 15 years), and K5 (> 15 years). The study sample consisted of 35 respondents selected using purposive sampling based on inclusion criteria of active employment status and work location close to waste sources. Respondent characteristic data were collected using a structured questionnaire covering age, length of employment, daily exposure duration, and use of personal protective equipment (PPE).

The independent variables in this study were cadmium and nickel exposure measured through urine, while the dependent variables were blood biomarkers MCV, RDW-SD, and PCT. Urine samples were collected at the workplace at the end of the workday using 50 mL PP containers with a minimum volume of 45 mL, stored in cold conditions, then homogenized, centrifuged at 3,000 rpm for 10 minutes, and stored at -20°C until laboratory analysis was performed. Blood biomarker samples were collected using a 20 cc syringe, then divided into one 3 mL EDTA tube and two 5 mL tubes without anticoagulant. Blood samples in EDTA tubes were used for complete blood count (including MCV and RDW-SD) and heavy metal analysis. Samples were homogenized using a rolling mixer for ±30 minutes. Next, 1.75 mL of blood is transferred to a polypropylene (PP) tube and stored in cold conditions until laboratory analysis is performed.

Descriptive analysis was used to describe the characteristics of respondents and data distribution. Normality testing was performed using the Shapiro-Wilk test, due to the small sample size (N=35). Because the data were not normally distributed, the relationship between cadmium levels and blood biomarkers MCV, RDW-SD, and PCT was analyzed using Spearman's correlation test with a significance level of $p < 0.05$.

This study has obtained ethical approval from the Health Research Ethics Committee of Muhammadiyah University Lamongan with number 133/EC/KEPK –S3/04/2025 dated April 15, 2025. The research was deemed ethically sound and conducted in accordance with the principles of health research ethics. All respondents were given an explanation of the purpose and procedures of the research and signed an informed consent form prior to sampling. The confidentiality of the respondents' identities was maintained, and the data obtained was used solely for research purposes.

RESULTS AND DISCUSSION

Based on the results of descriptive analysis, several types of heavy metals were identified in the urine of waste workers: cadmium, lead, chromium, and nickel. However, of these four heavy metals, only two showed a significant relationship with the blood biomarkers analyzed. The heavy metals that had a meaningful relationship with blood biomarkers were cadmium and nickel, both of which were associated with PCT, MCV, and RDW-SD levels. These findings indicate that not all heavy metal exposures have the same biological impact on the body's inflammatory response.

Before conducting the Spearman correlation test, the data underwent a normality test. The normality test was conducted to determine the distribution of the Cd, Ni, and PCT variables before further statistical analysis. The normality test used the Kolmogorov-Smirnov and Shapiro-Wilk tests with a sample size of 35 respondents.

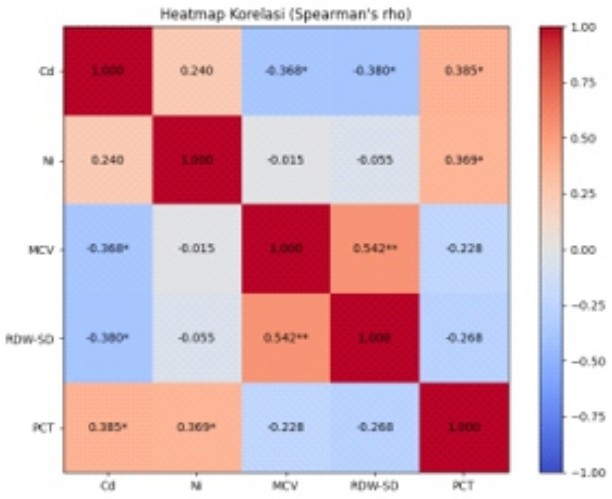
Table 1
Normality test of cadmium (Cd) levels in urine with MCV and RDW-SD biomarkers using Shapiro-Wilk

Biomarker Profiles	Kolmogorov - Smirnov (Sig.)	Shapiro -Wilk (Sig.)	Description
Cd	0.000	0.000	Not Normal
Ni	0.000	0.000	Not Normal
PCT	0.000	0.000	Not Normal
MCV	0.000	0.000	Not Normal
RDW-SD	0.200	0.017	Not Normal

Source: Processed Primary Data, 2026

Based on the results of Table 1, the two main variables of the study, namely cadmium and nickel levels in urine with PCT, MCV, and RDW-SD biomarkers, were also analyzed using the Shapiro-Wilk test. The normality test results showed that cadmium and nickel levels with blood biomarkers were not normally distributed, as indicated by the significance value ($p < 0.05$). The non-normal distribution of the data could also be influenced by the small number of data points, namely only 35 respondents. Because the distribution of the main variables was not normal, the correlation test was performed using the Spearman non-parametric method, which is suitable for non-parametric data and limited sample sizes.

The results of the Spearman correlation test showed a relationship between cadmium and nickel levels in urine and hematological biomarkers PCT, MCV, RDW-SD in female waste workers at waste disposal sites. Cadmium levels in urine were significantly positively correlated with PCT ($\rho = 0.385$, $p = 0.022$), indicating that an increase in Cd tends to be followed by an increase in PCT in the blood. Urine nickel levels also showed a significant positive correlation ($\rho = 0.369$, $p = 0.029$), indicating that higher Ni exposure is associated with higher PCT levels. Furthermore, urine cadmium levels were negatively correlated with MCV ($p = -0.368$; $p = 0.030$), indicating that increased cadmium exposure is followed by a



Note: the asterisk (*) indicates significance
Source: Processed Primary Data, 2026

Figure 1
Spearman's correlation heatmap between cadmium (Cd) and nickel (Ni) in urine with PCT, MCV, and RDW-SD biomarkers

decrease in MCV values. In addition, cadmium levels in urine also correlate negatively with RDW-SD (p = -0.380; p = 0.024), indicating that increased cadmium exposure is followed by a decrease in RDW-SD values. The existence of this correlation indicates that increased cadmium levels are associated with changes in erythrocyte size variation, reflecting the effect of cadmium exposure on red blood cell distribution parameters.

The findings of this study are consistent with previous research reporting heavy metal exposure among waste-related workers. Tahir et al. (2021) and Mansouri et al. (2025) identified heavy metal exposure among electronic waste workers in Pakistan and urban sanitation workers, respectively. Similarly, Abidin et al. (2025), Odewabi & Ekor (2016), and Tahir et al. (2021) reported greater heavy metal exposure among waste workers than among comparison groups, highlighting their potentially higher occupational exposure risks. These findings support the need to further investigate the association between heavy metal exposure and hematological alterations among female waste workers.

The Pathophysiological Mechanisms Linking Cadmium and Nickel Exposure to Cardiovascular Risk

Exposure to cadmium and nickel plays a role in triggering oxidative stress through increased production of reactive oxygen species (ROS) and decreased antioxidant capacity in the body. This condition causes cellular redox imbalance and can activate intracellular inflammatory pathways followed by increased release of pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β (Badawi et al., 2024; Farrokhpour et al., 2019; Guo et al., 2019). This systemic inflammatory activation was demonstrated in a study (Kumas et al., 2016), which showed that cadmium exposure in rats increased Total Oxidant Status (TOS), Oxidative Stress Index (OSI), and levels of IL-6 and Procalcitonin (PCT), accompanied by renal histopathological damage. This study shows that Cd and Ni not only increase oxidative stress but also cause systemic inflammation that can be detected through increased PCT.

In addition to affecting inflammatory biomarkers, oxidative stress and systemic inflammation caused by heavy metals also impact the erythrocyte hematological system. ROS causes erythrocyte membrane lipid peroxidation and disrupts the erythropoiesis process in the bone marrow, which can trigger changes in the size and heterogeneity of red blood cells (Genchi et al., 2020). This is reflected in changes in MCV and an increase in RDW-SD. MCV indicates the average red blood cell size, which, when abnormal, can disrupt blood flow and oxygen distribution, thereby increasing cardiovascular risk (Zhang et al., 2022). RDW-SD reflects the variation in red blood cell size, and elevated values may indicate abnormalities in erythrocyte production and maturation associated with inflammation and oxidative stress. Increased RDW-SD has also been associated with a higher risk of cardiovascular disease (Xanthopoulos et al., 2022). This inflammation and hematological changes contribute to endothelial dysfunction characterized by thickening of blood vessel walls. Endothelial dysfunction can accelerate the formation of atherosclerotic plaques (Muhammad Baharul Iman et al., 2025). The accumulation of endothelial damage and atherosclerotic plaque ultimately increases the risk of cardiovascular disease. Therefore, the combination of inflammatory (PCT) and hematological (MCV and RDW-SD) biomarkers can be used as early indicators to assess the biological impact of cadmium and nickel exposure, which has the potential to increase cardiovascular risk.

Hematological and Inflammatory Biomarkers in Cardiovascular Risk

Several studies have shown a positive correlation between MCV and cardiovascular disease risk. However, in

this study, the correlation coefficient between Cd and MCV was -0.368, indicating a weak to moderate negative correlation. This suggests that higher cadmium levels in the body tend to be associated with lower MCV values, although the correlation is not very strong. This finding is contrary to the report (Wu et al., 2018), which shows a positive correlation between MCV and cardiovascular risk, meaning that the higher the MCV value, the greater the risk of death from cardiovascular disease. The difference in the direction of this relationship indicates that changes in MCV values may reflect different pathophysiological mechanisms, depending on the causative factors.

Several studies have shown a positive correlation between cadmium and RDW-SD, indicating a link between RDW-SD and the risk of cardiovascular disease. However, the correlation value above is -0.380, which indicates a weak negative relationship. This suggests that an increase in cadmium levels tends to be followed by a decrease in RDW-SD values, although the correlation is not significant. Cadmium exposure to the RDW-SD produces a negative correlation, where high cadmium exposure results in a decrease in RDW-SD biomarker values. This is in contrast to the study (Peng et al., 2023) which shows a significant positive correlation between RDW-SD and Neuron-Specific Enolase (NSE) levels as a biomarker of nerve damage in patients with acute ischemic stroke ($r = 0.275$; $p < 0.001$). This study indicates that an increase in RDW-SD values is directly proportional to the level of neuronal damage experienced by patients. According to the study (Talarico et al., 2021) in the Journal of Cardiovascular Development and Disease in 700 patients with various cardiovascular diseases. The results showed that patients with the highest RDW values (≥ 14.1%) had a significantly higher risk of mortality and cardiovascular events compared to the lowest tertile, and RDW reflected systemic conditions such as chronic inflammation, oxidative stress, and endothelial dysfunction. From this overall study, it can be concluded that an increase in RDW-SD values is associated with the level of neuronal damage in stroke patients and also reflects a higher cardiovascular risk.

The correlation between cadmium and nickel with PCT shows a positive relationship with cardiovascular risk. The correlation value of cadmium with PCT is $p = 0.385$, which indicates a moderate positive relationship. This indicates that the higher the cadmium level in the body, the higher the detected PCT level. These findings suggest that cadmium exposure has the potential to trigger a systemic inflammatory response, as reflected in increased PCT. Meanwhile, the correlation between nickel and PCT is $p = 0.369$, indicating a moderate positive relationship. This suggests that an increase in nickel levels tends to be followed by an increase in PCT levels. The mechanism of this relationship is similar to that of cadmium, namely through the induction of oxidative stress and activation of the inflammatory pathway. Nickel exposure can trigger an immune response and increase the production of inflammatory mediators, which ultimately leads to increased PCT levels in the circulation.

This study is in line with several studies, including: 1) research by Sakarya et al. (2026) which shows that the median PCT level is significantly higher in the Acute Coronary Syndrome (ACS) and Chronic Coronary Syndrome (CCS) groups compared to the control group ($p < 0.001$). 2) Research by Katte et al. (2021) which examined the relationship between PCT levels and cardiovascular risk in patients with type 2 diabetes mellitus in Sub-Saharan Africa. This study showed that PCT levels were significantly higher in the group with high cardiovascular risk scores based on the ADVANCE model, with a moderate correlation ($r=0.58$; $p<0.001$). These results indicate that

increased PCT reflects systemic inflammation, which plays a role in increasing cardiovascular risk in diabetic populations. 3) Research by Kurtul & Elcik (2017) which evaluated the relationship between PCT levels and coronary atherosclerosis burden in 400 patients with stable coronary artery disease (CAD). PCT levels were found to be significantly associated with SYNTAX scores, which reflect the complexity and extent of atherosclerotic lesions. PCT was assessed as an independent predictor of atherosclerotic burden, meaning that high PCT levels are associated with more severe coronary disease and potentially increase the risk of subsequent cardiovascular events. 4) Research by (Yu et al., 2023) which assessed the role of PCT in the diagnosis and prognosis of coronary heart disease (CHD) in elderly patients. This study found that PCT levels were significantly higher in CHD patients than in the control group, and were also higher in the group with poor prognosis during the 12-month follow-up. This suggests that elevated PCT levels may be associated not only with coronary artery disease but also with an increased risk of cardiovascular complications and mortality.

The overall results of the study indicate that cadmium exposure is significantly negatively correlated with MCV and RDW-SD, suggesting changes in red blood cell size and distribution that are likely related to cell damage due to oxidative stress. Although the direction of this relationship is decreasing, these findings do not indicate an increased risk of cardiovascular disease directly, unlike the literature reporting that high MCV and RDW-SD are associated with cardiovascular risk. This confirms that the decrease in MCV and RDW-SD in this population is likely an adaptive response of erythrocytes to heavy metal exposure, rather than an indicator of cardiovascular vulnerability. However, this does not diminish the potential toxic effects of cadmium on the cardiovascular system, as cadmium is known to trigger oxidative stress and endothelial dysfunction, major pathways that increase cardiovascular risk. Cadmium-induced blood cell changes may also exacerbate endothelial dysfunction and vascular inflammation, making MCV and RDW-SD relevant as early indicators of cellular damage. The difference in the direction of the relationship between MCV and RDW-SD is likely due to the complexity of biological pathways, individual response variations, or differences in biomarker measurement methods, confirming that even though MCV and RDW-SD decrease, cardiovascular risk may still potentially increase through the mechanisms of oxidative stress and endothelial dysfunction.

On the other hand, cadmium and nickel exposure positively correlates with PCT, indicating activation of the systemic inflammatory pathway. Elevated PCT reflects persistent inflammation that may contribute to endothelial dysfunction and other mechanisms related to cardiovascular risk. Thus, although MCV and RDW-SD are decreased and do not indicate direct cardiovascular risk, elevated PCT still indicates the potential toxic effects of heavy metals on the cardiovascular system through inflammatory mechanisms and endothelial dysfunction. The combination of hematological and inflammatory biomarkers can be used as an early indicator to assess the biological impact of cadmium and nickel exposure, while also showing that not all changes in hematological biomarkers automatically increase cardiovascular risk.

In this study, the PCT biomarker referred to is procalcitonin, a biological marker (biomarker) protein in the blood used to detect bacteria. Procalcitonin in this study shows that a high inflammatory response can pose a risk of cardiovascular disorders. Meanwhile, the Plateletcrit (PCT) biomarker is used to measure the percentage of blood volume occupied by platelets (blood cells). High Plateletcrit can also pose a risk for cardiovascular disorders. According to a study (Gul et al.,

on patients with Non-ST Elevation Myocardial Infarction (NSTEMI), high plateletcrit (PCT) values (> 0.23) had a cardiovascular mortality rate of 20.4% compared to 4.5% in low PCT values. This study indicates that elevated PCT reflects a larger total platelet mass, which is associated with inflammation, platelet activation, and thrombus formation in acute coronary syndrome. A study by (Mushtaq et al., 2025) also showed that elevated PCT is associated with poor clinical outcomes during hospitalization in NSTEMI patients. The study noted that patients in the highest PCT tertile had significantly higher complication and mortality rates compared to the normal or low PCT groups.

CONCLUSION

This study demonstrates significant associations between urinary Cd and Ni concentrations and selected inflammatory and hematological biomarkers among female waste workers. Urinary Cd and Ni concentrations were positively correlated with PCT levels, suggesting a potential link between heavy metal exposure and systemic inflammation that may contribute to cardiovascular dysfunction. Conversely, urinary Cd concentrations were negatively correlated with MCV and RDW-SD, indicating potential alterations in erythrocyte indices associated with Cd exposure. Although elevated MCV and RDW-SD have been associated with cardiovascular risk in previous studies, the lower values observed in this study cannot be interpreted as evidence of reduced or increased cardiovascular risk without further clinical assessment. Overall, the findings suggest that Cd and Ni exposure may be associated with inflammatory and hematological alterations among female waste workers. However, the potential implications for cardiovascular health require further investigation, particularly through studies incorporating direct cardiovascular assessments and relevant confounding factors.

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