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Cadmium Exposure and Neutrophil Count as Indicators of Immunotoxicity Among Female Waste Workers

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Keywords

cadmium; neutrophils; immunotoxicity; female workers; waste sorters

Abstract

Cadmium exposure in female waste workers is an environmental health issue that has the potential to cause immune system disorders. This study aims to analyze the relationship between blood cadmium levels and neutrophil counts as an indicator of immunotoxicity. The study used a cross-sectional analytical observational design on female waste pickers working at waste collection sites (TPS) and final procesing sites (TPA). Cadmium levels were measured through blood samples, while neutrophil counts were obtained from routine hematology tests. Data analysis was performed using nonparametric correlation tests. The results showed a significant negative relationship between cadmium levels and neutrophil counts, indicating the potential for immunotoxic effects due to chronic cadmium exposure. It is recommended to conduct regular health monitoring, increase the use of personal protective equipment, and control cadmium exposure in the work environment.

INTRODUCTION

Heavy metal exposure remains a global environmental and occupational health concern, particularly in the waste management sector, where workers may be exposed to various potentially contaminated materials, including plastic waste and industrial residues. Cadmium (Cd) is a toxic heavy metal widely used in various industrial applications, including metal guide production (Mustikaningrum et al., 2025). Cd is commonly used in plastic stabilizers, batteries, pigments and dyes, surface coatings, electroplating, and metal alloys (Fadhilah & Fitria, 2020). Due to its toxic properties, cadmium exposure may pose adverse health effects even at relatively low levels. The toxic effects of cadmium are influenced by the duration and level of exposure, meaning that prolonged exposure to high levels can increase the toxic effects (Pulungan & Wahyuni, 2021). Cadmium inhalation is an important route of occupational exposure, as airborne cadmium-containing particles can enter the respiratory tract and be absorbed into the body (Andita & Wimpy 2023).

Female waste workers are at high risk of chronic exposure to cadmium due to often uncontrolled working conditions, increasing the risk of health disorders caused by environmental toxins that accumulate in the human body with a long biological half-life (Badawi et al., 2024; Wang et al., 2021). This chronic exposure can trigger oxidative stress and immune system disorders, including changes in the number and function of leukocytes such as neutrophils, which are the first line of defense against infection and toxins (Liu et al., 2025; Nie et al., 2024). Several studies have also shown that cadmium exposure can increase systemic inflammatory biomarkers, such as the neutrophil-lymphocyte ratio (NLR), which reflects the activation of the immune response to

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heavy metal toxins (Yang et al., 2025). This research is important because female waste workers are more vulnerable to heavy metal exposure due to differences in hormones, metabolism, and immune response, meaning that chronic exposure to cadmium can have a more pronounced effect on the immune system. Informal and poorly controlled working conditions also increase the risk of repeated exposure.

Biologically, Cd accumulated in the body can disrupt immune system homeostasis through the induction of oxidative stress and increased formation of reactive oxygen species (ROS), which affects the viability and function of immune cells (Jiaxin et al., 2020; Kumari et al., 2025). Oxidative stress caused by Cd has also been reported to induce apoptosis and leukocyte dysfunction, including neutrophils as a major component of innate immunity (Jiaxin et al., 2020). In addition, experimental studies show that chronic exposure to Cd can disrupt the balance of immune cells in lymphoid organs and affect the coordination of innate and adaptive immune responses (Kumari et al., 2025). Thus, alterations in peripheral neutrophil counts may serve as an early indicator of potential immunotoxic effects associated with chronic cadmium exposure.

Several international studies have investigated the association between cadmium exposure and white blood cell profiles. However, studies investigating the association between blood cadmium levels and neutrophil counts as potential indicators of immunotoxicity remain limited, particularly among female waste management workers. Epidemiological research by Xiong et al. (2022) shows that chronic cadmium exposure correlates with white blood cell and neutrophil counts in communities living in contaminated areas, indicating that neutrophils may serve as markers of the long-term immunosuppressive effects of Cd. However, similar studies have not been widely conducted on waste workers in Indonesia, particularly female informal workers who are repeatedly exposed to working conditions with minimal supervision and health protection.

Based on these gaps, this study aims to analyze the relationship between blood cadmium levels and neutrophil counts as indicators of immunotoxicity in female waste workers. Specifically, this study assesses the association between chronic blood cadmium exposure levels and changes in neutrophil counts, which represent innate immune system disorders resulting from heavy metal exposure. Thus, this study presents new findings by providing more comprehensive epidemiological evidence regarding the impact of blood cadmium levels on the immune system in female waste pickers.

RESEARCH METHODS

This study used a cross-sectional analytical observational design to analyze the relationship between cadmium exposure and neutrophil count as an indicator of immunotoxicity in female waste workers at waste collection sites (TPS) and final procesing sites (TPA) among female waste sorters as the exposed population. Sampling was conducted from March to November 2025. The study population consisted of women of productive age (15–49 years) who were actively working at TPS with a minimum exposure duration of 1 year. A sample of 35 respondents was selected using purposive sampling based on the inclusion criteria of active employment and proximity to the waste site.

Subjects were grouped based on length of occupational exposure into several categories, namely <1 year, 1–5 years, >5–10 years, >10–15 years, and >15 years. The sampling technique used purposive sampling with inclusion criteria of women aged 15–49 years, actively working as waste sorters, willing to participate, and signing informed consent. The independent variable in this study was the level of cadmium (Cd) exposure, which was measured through Cd levels in the blood, while the dependent variable

Table 1
Normality Test of Cadmium Levels in Blood with Neutrophils using Shapiro-Wilk

Variable	Shapiro-Wilk (Sig.)	Description
Cd	.000	Abnormal
NEUT	.320	Normal

Source: Primary Data Processed, 2026

was the number of neutrophils (Neut) as an indicator of immunotoxicity. Data on respondent characteristics, such as age, length of employment, duration of daily exposure, and use of personal protective equipment (PPE), were collected through a structured questionnaire.

Blood sampling is performed by trained health personnel using aseptic procedures. Blood samples are collected using a 20 cc syringe and placed in a 3 mL EDTA tube and a 5 mL non-anticoagulant tube, with a minimum total blood volume of 15 mL, consisting of 13 mL for cadmium level analysis and 2 mL for hematology testing. Approximately 3 mL of blood is homogenized in an EDTA tube using a rolling mixer for approximately 30 minutes or manually until evenly mixed, then 1.75 mL of blood is transferred to a polypropylene (PP) tube and stored in a cold chain until laboratory analysis in a standardized laboratory.

The data were analyzed using statistical software. Descriptive analysis was performed to describe the distribution of cadmium levels in the blood and the number of neutrophils (Neut). Normality testing was performed using the Shapiro–Wilk test. If not normal (as suspected from the Shapiro-Wilk test), because the data are not normally distributed, the analysis of the relationship between blood cadmium levels and neutrophil counts was performed 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. All respondents have provided written consent (informed consent) before participating in the study.

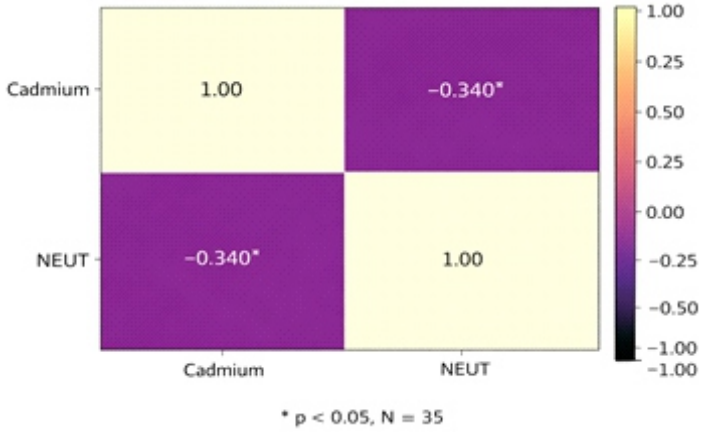
RESULTS AND DISCUSSION

Before analyzing the relationship between variables, a normality test is first conducted to determine whether the data is normally distributed or not. This normality test uses the Shapiro–Wilk and Kolmogorov–Smirnov methods as a basis for determining the appropriate statistical approach (parametric or nonparametric). The results of the normality test for cadmium (Cd) levels in the blood and neutrophil (NEUT) counts are presented in Table 1.

Based on the normality test results presented in Table 1, blood cadmium (Cd) levels showed a significance value of 0.000 in the Shapiro–Wilk test, indicating a non-normal distribution. In contrast, neutrophil counts (NEUT) indicating a normal distribution. Since the Cd data were not normally distributed, the association between blood Cd levels and neutrophil counts was analyzed using a nonparametric approach, specifically Spearman's rank correlation (Spearman's rho). This test evaluates the strength and direction of the association between two variables based on their ranked values, making it suitable for data that do not meet the assumption of normality.

The Spearman correlation coefficient (r_s) has a value between -1 and +1. A value close to +1 indicates a strong positive relationship, a value close to -1 indicates a strong negative relationship, while a value close to 0 indicates a weak or no relationship. A significance value (p-value) < 0.05 indicates that the relationship found is statistically significant. To facilitate the interpretation of correlation test results, Spearman correlation data is presented in the form of a heatmap visualization. Heatmaps are used to illustrate the strength and direction of correlations between variables through

color gradations, so that relationship patterns can be seen more clearly and intuitively than through tables of numbers alone. In the heatmap, differences in color intensity represent the magnitude of the correlation coefficient, while the direction of the color indicates a positive or negative relationship between variables.



Source: Processed Primary Data, (2026)

Figure 1
Heatmap of Spearman Correlation between Cadmium and Neutrophils

The heatmap in Figure 1 shows the pattern of relationships between variables. Specifically, this visualization shows the relationship between cadmium (Cd) levels in the blood and the number of neutrophils (NEUT). The dark color in the correlation cell indicates a negative relationship with a value of r = -0.340, which means that as Cd levels increase, the number of neutrophils tends to decrease. Although the strength of this correlation is classified as weak to moderate, this pattern shows a tendency for an inverse relationship between cadmium exposure and innate immune parameters.

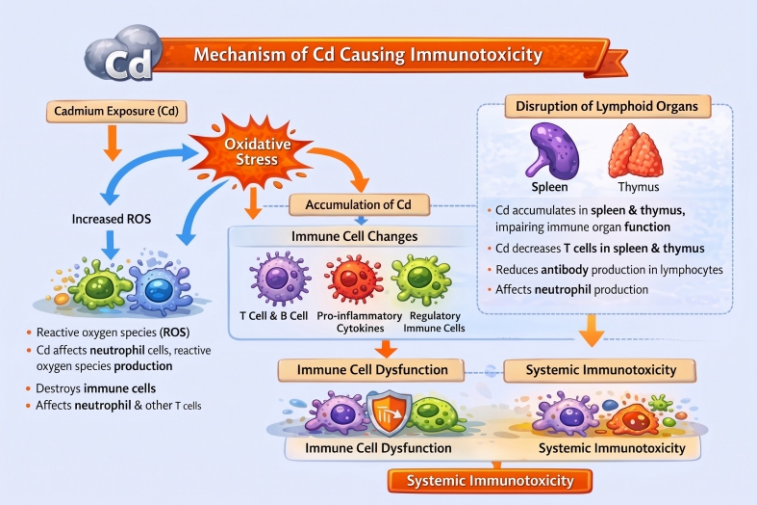
In the heatmap, colors closer to yellow indicate a stronger positive correlation, while darker colors indicate a negative correlation. It can be seen that the most prominent relationship is the negative correlation between Cd and NEUT, while the correlations between other variables are relatively weak. The Spearman test results reinforce these findings, with a value of r = -0.340 and p = 0.046, indicating that increased cadmium levels are significantly associated with a decrease in neutrophil counts in female waste workers.

Biologically, cadmium is known as a heavy metal that is immunotoxic and capable of disrupting the function of the innate immune system through various mechanisms, including the induction of oxidative stress, activation of inflammatory pathways, and modulation of cellular immune responses and inflammatory mediators (Badawi et al., 2024; Ma et al., 2025). The decrease in neutrophil count found in this study supports the hypothesis that cadmium exposure can cause immunotoxicity, especially in female waste workers who are at risk of chronic contact with waste. Immunotoxicity itself is the toxic effect of a substance on the immune system that can cause disruption to the regulation and function of the immune response, either through immunosuppression or uncontrolled inflammation (Wang et al., 2021). In addition, exposure to heavy metals such as cadmium is known to play a role in triggering oxidative stress and low-grade chronic inflammation, which contribute to immune system disorders (Qu & Zheng, 2024). These findings provide preliminary evidence of an inverse relationship between cadmium levels and immune parameters, while also emphasizing the importance of workplace monitoring and health interventions for workers in the waste management sector.

These findings are consistent with the results of studies on populations living in cadmium-contaminated areas, which reported a negative correlation between urinary cadmium levels and neutrophil counts, interpreted as an indication of immunotoxic effects and a tendency toward immunosuppression (Xiong et al., 2022). Thus, the negative correlation pattern observed in female waste pickers in this study further strengthens the assumption that chronic cadmium exposure has the potential to reduce important components of the innate immune system.

immunosuppression and impaired host defense against pathogens (Wang et al., 2021).

In the context of female waste workers, the significant negative correlation between Cd levels and NEUT indicates that exposure to heavy metals in the work environment has the potential to cause immunotoxicity, particularly through disruption of the innate immune system, characterized by a decrease in the number and function of neutrophils as the body's first line of defense against infection (Knoell & Wyatt, 2021). The weak to moderate correlation strength (r=-0.340)



Source: Processed Primary Data, (2026)

Figure 2
Mechanism of Cd in Causing Immunotoxicity

Mechanistically, Cd can trigger immune system disorders through the induction of oxidative stress, lymphoid organ dysfunction, and changes in immune cell regulation, leading to immunotoxicity. Cd accumulation in the spleen and thymus causes changes in the proportion of T and B lymphocytes, inhibits immune cell proliferation, and increases apoptosis, thereby disrupting both innate and adaptive immune responses (Kumari et al., 2025). In addition, increased ROS production and the activation of intracellular signaling pathways induced by Cd may reduce the viability and functional capacity of immune cells. Under chronic exposure, these effects may contribute to

may reflect that, in addition to Cd, other factors such as smoking habits, nutritional status, subclinical infections, and exposure to other heavy metals also influence the neutrophil profile. However, the significant association observed suggests that Cd may play an important role in influencing neutrophil counts (Mirkov et al., 2021). These findings reinforce the importance of monitoring hematological parameters, particularly neutrophils, in waste workers as an early indicator of immunotoxicity risk due to long-term Cd exposure.

Neutrophils in humans are influenced by many factors other than cadmium exposure, so the correlation results (r = -0.340) in this study should be

interpreted with consideration of possible confounding factors. Age, for example, is a factor closely related to changes in the quantity and function of neutrophils. Aging is known to affect chemotaxis, phagocytic activity, and the regulation of innate immune responses, potentially altering neutrophil profiles independently of exposure to specific metals (Simmons et al., 2021). In addition, demographic factors such as gender and race/ethnicity, as well as chronic conditions such as cardiovascular disease, diabetes mellitus, and hypertension, have also been reported to contribute to variations in leukocyte and neutrophil counts, which may ultimately affect the interpretation of an individual's immune status (Chen et al., 2025). In this context, although the negative correlation between Cd levels and neutrophil counts is statistically significant, its interpretation should consider biological variability and sociodemographic factors that may influence neutrophil levels. Therefore, controlling for potential confounders is essential to obtain a more valid estimate of the association between Cd exposure and immune function.

Other studies on workers exposed to multiple metals have also found changes in hematological parameters (including neutrophils and platelets) associated with levels of various metals in the body, not just one type of metal (Yasin & Salih, 2026). Therefore, the negative correlation between Cd and neutrophils found here likely reflects the combined effects of Cd and other metals. Work-related factors such as length of service and use of personal protective equipment (PPE) may also influence exposure levels and, indirectly, neutrophil profiles. Biomonitoring studies of waste workers and other high-risk sectors show that exposure to bioaerosols, dust, and heavy metals increases with duration of work and low compliance with the use of personal protective equipment, and is associated with increased leukocyte counts, neutrophils, and inflammatory biomarkers (Tehrani et al., 2024). These findings reflect the activation of innate immune responses due to occupational exposure. Chronic exposure may disrupt immune system regulation through persistent immune activation

Studies on informal waste workers in developing countries also report low use of PPE due to cost and discomfort, while workplace exposure remains high (Straumfors et al., 2025). In the context of this study, variability in working hours and PPE usage patterns among subjects may cause differences in actual Cd exposure levels, which are ultimately reflected in the variability of neutrophil counts, although not all of these factors are statistically measurable or controllable.

In practical terms, the research subjects, who were all female waste workers, had a particular vulnerability related to a decrease in neutrophils. Neutrophils are the first line of defense against pathogens; Van Avondt et al. (2023) reported that individuals with neutropenia or neutrophil dysfunction are more susceptible to respiratory tract infections and other severe infections. Waste management workers are known to be exposed to bioaerosols containing bacteria, fungi, endotoxins, and other biological particles in the work environment. Exposure to inhalable dust and bioaerosols has been linked to increased expression of immune cytokines such as IL-1Ra, IL-18, TNFα, and IL-8, reflecting activation of the innate immune response through stimulation of pattern recognition receptors to biological contaminants in the workplace air (Eriksen et al., 2023). Continuous immune activation due to chronic exposure has the potential to disrupt the balance of immune system regulation and alter the peripheral immune cell profile. If Cd exposure in the TPS environment is accompanied by a decrease in the number or function of neutrophils, the ability of female workers' bodies to respond to everyday biological agents may decrease, thereby increasing the risk of infection and worsening occupational health conditions.

In addition to potentially increasing susceptibility to acute infections, reduced neutrophil counts associated with Cd exposure may indicate long-term alterations in innate immune regulation. Studies of populations living in Cd-contaminated areas have reported a significant negative correlation between urinary Cd levels and peripheral neutrophil counts, suggesting a potential association between Cd exposure, mild immunosuppression, and alterations in circulating immune cell profiles (Feng et al., 2025). Among workers chronically exposed to bioaerosols and organic dust, alterations in cytokine profiles and leukocyte distribution have been reported, indicating persistent immune activation and potential immune dysregulation associated with prolonged exposure(Palomo et al., 2025). Within this framework, the negative correlation between Cd and neutrophils in female waste pickers can be interpreted as an early signal of an imbalance between environmental exposure and innate immune response capacity.

Given the multiple exposures present in TPS environments, including heavy metals and bioaerosols, as well as lifestyle-related factors and the social vulnerability of female waste workers, neutrophil counts may serve as an early indicator of potential immunotoxic effects associated with Cd exposure. This parameter can be obtained relatively easily and inexpensively through routine blood tests, making it a potential component of periodic occupational health monitoring. Such monitoring may help identify declining neutrophil counts or changes in neutrophil profiles as early indicators of altered innate immune function. Findings regarding changes in immune cell profiles in workers exposed to bioaerosols and organic dust (Palomo et al., 2025). Neutrophil-based parameters may also be sensitive to heavy metal exposure and lifestyle-related factors (Howard et al., 2019). Both findings support the use of neutrophils as an indicator of immunotoxic risk.

In reinforcing the interpretation of the negative relationship between cadmium exposure and neutrophil count in this study. A number of studies have shown that Cd can trigger oxidative stress through increased formation of reactive oxygen species (ROS), disrupting immune regulatory pathways, and affecting the viability and function of neutrophils as a major component of innate immunity. In short-term exposure, changes may take the form of fluctuations in the number or distribution of immune cells, while chronic exposure is more often associated with immune regulatory disorders and a tendency toward mild immuno-suppression.

In line with this mechanism, the results of this study indicate that increased Cd levels correlate with a decrease in neutrophil counts in female waste workers. In the context of multiple exposures in landfill and waste transfer station environments, this condition may indicate a disturbance in the innate immune response due to chronic exposure to heavy metals. Overall, this study confirms that neutrophils have the potential to be used as an early indicator of cadmium immunotoxicity in occupational health monitoring, while still considering the possibility of confounding factors.

CONCLUSION

This study demonstrates a significant association between urinary Cd levels and neutrophil counts among female waste sorting workers, highlighting the potential involvement of Cd exposure in alterations of the innate immune system. The negative correlation found indicates that an increase in blood cadmium levels tends to be followed by a decrease in the number of neutrophils, reflecting the potential for immune dysfunction due to chronic cadmium exposure in the workplace. These findings confirm that heavy metal exposure in the waste management sector can have biological effects on female workers who are exposed over the long term. Therefore, preventive measures are needed through

regular health monitoring, increased compliance with the use of personal protective equipment, and control of Cd exposure in the work environment to reduce the risk of health disorders in female waste sorting workers.

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