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Association between OPFR Levels and Metabolic Dysfunction Risk among Female Waste Workers

Aiskha Hasna Badriya[1]✉ , Lestari Sudaryanti[2], & Won Kim[3]
[1]Universitas Negeri Malang
[2]Universitas Airlangga
[3]Wonjin Institute for Occupational and Environmental Health

Keywords

DPHP; female waste workers; metabolic dysfunction; OPFR

Abstract

Exposure to organophosphate flame retardants (OPFRs) is positioned as an environmental determinant that potentially contributes to metabolic regulation disorders through endocrine disruption mechanisms. This study empirically examines the relationship between urinary OPFR levels, represented by diphenyl phosphate (DPHP), and the risk of metabolic dysfunction in female waste workers, a highly exposed occupational group. Using a cross-sectional design and a biomonitoring approach, the analysis shows that elevated DPHP levels significantly correlate with the accumulated risk of metabolic dysfunction, although not fully reflected in individual clinical indicators. These results indicate that the effects of environmental exposure are latent and more sensitive to detection through composite indicators than single parameters, while also emphasizing the urgency of integrating environmental biomarkers into occupational health monitoring in vulnerable populations.

INTRODUCTION

Organophosphate flame retardants (OPFR) are widely used as flame retardants and plasticizers in various consumer products, including electronics, textiles, paints, floor coatings, and furniture. These compounds are widely used as substitutes for polybrominated diphenyl ethers (PBDE), the use of which has been restricted globally, with OPFR consumption reaching hundreds of thousands of tons per year (Blum et al., 2020). Human exposure to OPFR occurs chronically through indoor environments, primarily through indoor air inhalation, ingestion of household dust, and dermal contact. Household dust is the primary source of exposure, with reported OPFR concentrations higher than those of PBDE during its peak period of use. Exposure patterns vary by age group and activity, with dust ingestion being more dominant in infants, while inhalation contributes more significantly in adults and workers with specific environmental exposures (Yang et al., 2019; Zhao et al., 2025).

Exposure to organophosphate flame retardants (OPFRs) is widespread in the general population, with bio-monitoring studies indicating near-universal human exposure. This pervasive exposure has raised concerns about the potential public health implications of OPFRs and underscores the need for further investigation into their potential adverse health effects. A biomonitoring study of pregnant women in Shanghai detected OPFR metabolites, particularly diphenyl phosphate (DPHP), in nearly all urine samples, indicating widespread exposure among pregnant women. in nearly all urine samples, highlighting the widespread exposure to these compounds among vulnerable populations (Feng et al., 2023). Preston et al. (2017) reported that urinary DPHP concentrations were relatively stable across repeated

✉ aiskha.hasna.2306126@students.um.ac.id, Blitar, East Java
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measurements, with geometric mean concentrations ranging from 1 to 3 ng/mL among adults in the United States, suggesting limited intra-individual variability over the study period. Furthermore, DPHP levels tend to be higher in women than in men, and increase significantly in occupational groups with specific environmental exposures, such as nail salon specialists, suggesting a role for chronic dermal exposure as a major route of exposure (Estill et al., 2021). In this context, female waste pickers are a particularly vulnerable group. The combination of intense environmental exposure, informal working conditions, and women's biological vulnerability to endocrine disruption places this group at risk for multiple metabolic health problems, yet to date, they have received minimal attention in environmental toxicology research. The widespread use and various exposure pathways increase the likelihood of widespread and sustained population exposure, raising concerns about long-term health effects, including potential metabolic disorders.

According to the endocrine disruption framework, OPFRs may act as endocrine-disrupting chemicals (EDCs) by interfering with hormonal regulation and energy metabolism. Recent studies show that OPFR, particularly aromatic compounds, can interact with adiponectin receptors (AdipoR1 and AdipoR2) and act as non-competitive antagonists, thereby inhibiting the activation of the AMP-activated protein kinase (AMPK) pathway, which plays an important role in glucose and lipid homeostasis (Liu et al., 2024). Disruption of the adiponectin –AMPK signaling pathway may contribute to the development of insulin resistance and metabolic dysfunction by impairing glucose and lipid homeostasis (Abdelhameed et al., 2025). In vivo studies have further linked OPFR exposure to insulin resistance, dyslipidemia, and increased oxidative stress, suggesting that these compounds may contribute to metabolic disturbances through multiple biological pathways (Ni et al., 2025). Within this conceptual framework, the use of a single biomarker such as adiponectin is considered insufficient to represent the complexity of metabolic disorders. Therefore, a composite indicator approach such as Metabolic Dysfunction (MXD), which integrates metabolic, inflammatory, and oxidative stress biomarkers, is more appropriate for describing the cumulative impact of exposure (Otvos et al., 2023; Srikanthan et al., 2016; Zhao et al., 2025).

Although OPFR exposure has been linked to metabolic disorders, most studies still focus on the general population based on surveillance data and use single biomarkers such as BMI, lipids, or HOMA-IR (Liu et al., 2024; Zhao et al., 2025). Studies on worker groups have been conducted more frequently in formal sectors such as salon workers, while vulnerable groups such as female waste pickers remain understudied (Estill et al., 2021). In addition, comprehensive approaches using composite indicators of metabolic dysfunction such as MXD have not been widely used in OPFR exposure studies (Otvos et al., 2023). Therefore, this study offers novelty by evaluating the relationship between urinary DPHP levels and the risk of metabolic dysfunction based on composite indicators in female waste pickers as a high-risk group.

Based on these gaps, this study aims to analyze the relationship between OPFR levels in urine as an indicator of internal exposure and the risk of metabolic dysfunction in female waste workers. Specifically, this study assesses the association between urinary OPFR metabolite levels, particularly diphenyl phosphate (DPHP), and the MXD composite indicator of metabolic dysfunction, which represents cumulative metabolic disorders. The results of this study are expected to provide more comprehensive epidemiological evidence regarding the impact of OPFR exposure on metabolic health in female waste workers with high levels of exposure vulnerability.

RESEARCH METHOD

This study is an analytical observational study with a cross-sectional approach that aims to analyze the relationship between organophosphate flame retardants (OPFR) levels in urine and the risk of metabolic dysfunction in female waste workers. Exposure and outcome variables were final processing sites (TPA) and waste collection sites (TPS) 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 in the study area who worked as waste sorters at TPS. The study sample consisted of 35 female waste worker respondents who met the inclusion criteria, namely aged 15-49 years and had worked in the waste management sector or TPS, categorized based on length of service: K1 (<1 year), K2 (1-≤5 years), K3 (>5–≤10 years), K4 (>10–≤15 years), K5 (>15 years). Hematological examinations were conducted at the local health facility laboratory, while urine phthalate metabolite analysis was performed at the ECOTON Laboratory in collaboration with the Wonjin Laboratory, South Korea, using standard human biomonitoring methods.

The variables studied in this research consisted of independent and dependent variables. The independent variable was the level of OPFR in urine measured as diphenyl phosphate (DPHP), while the dependent variable was metabolic dysfunction (MXD) expressed as a percentage (MXD%) as a composite indicator of metabolic dysfunction.

Data on independent and dependent variables were collected through urine laboratory tests to measure OPFR metabolite levels (DPHP, BuDP). A minimum of 45 mL of urine was collected at the end of the workday using polypropylene (PP) containers. Samples were centrifuged, transferred to storage tubes, and stored at -20°C until analysis. Complete blood count laboratory test results were obtained using ±15 mL of blood collected with a sterile syringe. Samples were centrifuged, separated according to analysis requirements, and stored at -70°C until testing was performed for MXD score assessment and calculation. All collected data were recorded in a pre-prepared research data collection sheet.

The collected research data were analyzed using statistical tests with SPSS. The analysis was conducted using a normality test and Spearman's correlation test. A normality test was performed on the DPHP and MXD variables using the Shapiro-Wilk test because the sample size was less than 50 respondents (N = 35). The data was declared normally distributed if the significance value (p) was > 0.05. Furthermore, based on the results of the normality test, a correlation analysis was performed between the DPHP level and the MXD score using the Spearman correlation test (rho). This test was used to determine the strength and direction of the relationship between independent and dependent variables that were not normally distributed. The correlation coefficient (ρ) ranged from -1 to 1 with a statistical significance level set at $p < 0.05$ using a two-tailed test.

The hypotheses proposed in this study were H0: There is no positive relationship between diphenyl phosphate (DPHP) levels in urine and metabolic dysfunction (MXD) scores in female waste workers, and H1: There is a positive relationship between diphenyl phosphate (DPHP) levels in urine and metabolic dysfunction (MXD) scores in female waste workers, where an increase in DPHP levels is followed by an increase in MXD scores.

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 respondents' identities was maintained, and the data obtained was used solely for research purposes.

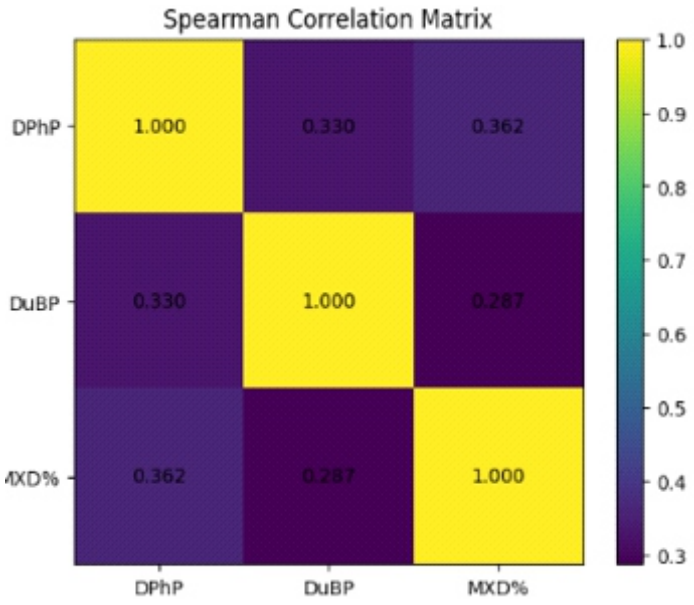
A normality test was performed on the main variables of the study, namely DPHP levels in urine and MXD scores, using the Shapiro–Wilk test because the sample size was less than 50 respondents. The test results showed that DPHP levels and several other OPFR metabolites, such as DuBP, were not normally distributed ($p < 0.05$). Therefore, the analysis of the relationship between variables was performed using a non-parametric statistical method, namely the Spearman correlation test, which is suitable for data with a non-normal distribution.

RESULTS AND DISCUSSION

Descriptive analysis showed variation in urinary OPFR metabolite concentrations among female waste workers. Of the nine OPFR metabolites examined, only two were detected, whereas the remaining seven were below the analytical detection limits. Among the two detected metabolites, DPHP was significantly associated with metabolic dysfunction (MXD), whereas the other detected metabolite showed no statistically significant association.

Based on Figure 1, there is a weak but significant positive correlation between DPHP levels in urine and MXD scores. The correlation coefficient value obtained is $\rho = 0.362$, with a significance value of $p = 0.033$ ($p < 0.05$). The positive correlation direction indicates that the higher the DPHP levels in urine, the higher the MXD score. Thus, increased OPFR exposure represented by DPHP levels shows a tendency toward an increased risk of metabolic dysfunction in female waste workers. Based on these results, the alternative hypothesis (H1) was accepted, while the null hypothesis (H0) was rejected. Conceptually, these results reinforce the biological framework that chronic OPFR exposure can affect metabolic regulation through endocrine and subclinical inflammatory mechanisms (Hsu, 2025; H. Li et al., 2024; X. Li et al., 2022).

Further analyses were performed to examine the associations of urinary DPHP concentrations and other OPFR metabolites with hematological parameters, including red blood cell (RBC) count, white blood cell (WBC) count, neutrophil count, and lymphocyte count.



Source: Processed Primary Data, (2026)

Figure 1

Spearman's correlation heatmap between urine OPFR metabolites and MXD%

The results of the Spearman correlation test showed that there was no statistically significant relationship between DPHP and DuBP levels and these hematological parameters (all p-values > 0.05). The correlation coefficients obtained were generally in the very weak to weak range, both positive and negative. These results indicate that at the level of OPFR exposure in this study, the effects were not yet clearly visible in each blood parameter separately, but were more apparent in combined metabolic indicators.

The results of this study show a significant positive correlation between DPHP levels in urine and MXD scores in female waste workers. These findings indicate that increased exposure to OPFR, represented by DPHP as the main metabolite of triphenyl phosphate (TPHP), is associated with an increased risk of cumulative metabolic dysfunction. Conceptually, these results reinforce the biological framework that chronic OPFR exposure can affect metabolic regulation through subclinical endocrine and inflammatory mechanisms.

The detection of DPHP in urine as an indicator of OPFR exposure in this study is consistent with previous biomonitoring findings. Feng et al. (2023) showed that DPHP was detected in almost all urine samples from pregnant women in Shanghai, confirming that TPHP exposure is widespread and chronic. Other bio-monitoring studies also show that OPFR metabolites are detected in more than 90% of urine samples from the general population, reflecting daily exposure through house dust, indoor air, and food (Blum et al., 2020; Chen et al., 2025; L. Li et al., 2023; Yang et al., 2019) . Thus, the measured DPHP levels in female waste workers in this study can be considered a representation of environmentally and biologically relevant internal exposure.

Mechanistically, the relationship between DPHP and MXD supports experimental evidence identifying OPFR as endocrine disrupting chemicals (EDCs). Research by Liu et al. (2024) shows that aryl-organophosphate flame retardants bind directly to adiponectin receptors (AdipoR1 and AdipoR2) and act as noncompetitive antagonists. This interaction inhibits the activation of the AMP-activated protein kinase (AMPK) pathway, which is a key regulator of cellular energy homeostasis (Newell & Patisaul, 2024; Xu et al., 2019). Decreased AMPK activation leads to impaired glucose uptake, increased lipid accumulation, and decreased fatty acid oxidation, which collectively contribute to insulin resistance and dyslipidemia.

The central role of the adiponectin–AMPK pathway in maintaining metabolic homeostasis has long been recognized (Ni et al., 2025) confirmed in their study that adiponectin and AMPK play important roles in regulating insulin sensitivity, lipid metabolism, and energy balance in various tissues. Disruption of this pathway has the potential to trigger systemic metabolic dysfunction. This finding is reinforced by Abdelhameed et al. (2025), who showed that pharmacological activation of the adiponectin receptor using the agonist AdipoRon improved insulin resistance, reduced obesity, and decreased mitochondrial oxidative stress in animal models.

The lack of a significant association between DPHP levels and individual hematological parameters in this study has important methodological implications. Single hematological parameters, such as leukocyte or erythrocyte counts, may not be sensitive enough to capture the early metabolic effects of OPFR exposure. This is consistent with the view that single biomarkers often fail to represent the complexity of metabolic disorders involving interactions between various biological pathways (Srikanthan et al., 2016; Zhang et al., 2025). Conversely, the use of MXD as a composite indicator allows for the detection of cumulative subclinical metabolic disorders, making it more relevant for assessing the impact of long-term environmental exposure.

These findings are also consistent with large-scale epidemiological evidence, Cheng et al. (2024) from the NHANES 2013–2014 dataset, which showed that urinary OPFR metabolite concentrations, including DPHP, were associated with alterations in serum lipid profiles and higher levels of systemic inflammatory markers. The study suggested that chronic OPFR exposure may be associated with dyslipidemia and alterations in immunometabolic pathways, both of which are implicated in the development of metabolic syndrome. The similarity in the direction of association between this study and the NHANES findings strengthens the external validity of the study results, even though the populations studied were different.

From an occupational and environmental health perspective, the results of this study have important implications for female waste workers as a vulnerable group. OPFR exposure in this group is potentially higher due to direct contact with plastic waste, dust, and uncontrolled working environments. Although hematological changes have not been detected significantly, the increase in MXD scores indicates that metabolic disorders may occur before the emergence of clear clinical manifestations. This condition underscores the importance of preventive approaches and metabolic health monitoring in groups of workers with high environmental exposure.

This study has limitations that need to be considered in interpreting the results. The cross-sectional design does not allow for causal conclusions, the sample size is relatively small, and limitations in covariate data such as dietary patterns and physical activity may affect the metabolic status of respondents. However, the strength of this study lies in the use of the diphenyl phosphate (DPHP) biomarker and the composite metabolic indicator (MXD), which are conceptually and biologically relevant for assessing the impact of chronic OPFR exposure. Therefore, the results of this study make an important contribution to understanding the relationship between OPFR exposure and the risk of metabolic dysfunction in vulnerable worker populations, and provide a basis for further research with longitudinal designs and larger sample sizes.

CONCLUSION

This study concludes that exposure to OPFR, represented by DPHP levels in urine, is associated with an increased risk of metabolic dysfunction in female waste workers. These findings indicate that the higher the exposure to OPFR, the greater the tendency for cumulative subclinical metabolic disorders, as reflected by an increase in indicators of metabolic dysfunction. This relationship reinforces the evidence that OPFRs act as endocrine disrupting chemicals that can interfere with energy metabolism regulation through complex biological pathways, so that their effects are not always apparent in single clinical or hematological parameters, but are more clearly detected through composite indicators. Therefore, monitoring OPFR exposure and metabolic status in groups of workers at high risk of exposure, such as female waste workers, is important as part of efforts to prevent long-term metabolic diseases. This study also emphasizes the need for improved occupational health protection, education on the risks of exposure to environmental chemicals, and further research with longitudinal designs and broader sample coverage to strengthen understanding of the impact of OPFR on human metabolic health.

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