



KL-6 Serum Elevation among Supit Urang Landfill Workers: Based on the Length of Work Duration and the Type of Work

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Abstract

Background: Waste workers at the Supit Urang Landfill, Malang, Indonesia, are exposed to occupational inhalation hazards, including bacterial bioaerosols, VOCs, CH₄, CO, and H₂S. Chronic exposure to these agents may induce alveolar epithelial injury and inflammatory responses, potentially leading to increased serum Krebs von den Lungen-6 (KL-6) levels. KL-6 itself is a glycoprotein biomarker associated with lung epithelial injury and inflammation. Therefore, this study was conducted to analyze serum KL-6 levels in relation to occupational exposure duration and type of work.

Methods: This analytical observational study used a cross-sectional design. A total of 79 workers were categorized based on exposure duration (<5 years, 5–10 years, >10 years) and type of work (scavengers, waste sorters, waste processors, laboratory technicians). Measurement of serum KL-6 levels used ELISA. Then, group differences were analyzed using the Kruskal–Wallis test.

Results: KL-6 serum levels were higher among workers with >10 years of exposure (1170.3±621.4 U/mL) compared to the other groups ($P=0.0001$). KL-6 levels differed significantly across job types ($P=0.402$), with higher levels observed among scavengers (1049.6±586.6 U/mL).

Conclusion: Serum KL-6 levels were associated with job type and showed a rising trend with longer exposure duration, particularly among workers with more than 10 years of occupational exposure.

Keywords: duration of exposure, KL-6 serum, Supit Urang Landfill, waste workers, work type

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INTRODUCTION

Projected estimates suggest global waste production will rise to approximately 3.40 billion tons by the year 2050—especially in developed nations—leading to increased risk of occupational diseases within low-income developing countries due to inadequate waste management practices.^{1,2} These waste management issues also include environmental contamination, social problems, and economic impacts. So, focus is needed on developing countries due to non-holistic waste management affected the health of waste workers.³

One of the focuses is on respiratory health that critically important for waste workers, due to their frequent exposure to various risks that can damage the respiratory system, besides frequently encountering substantial workloads. Various respiratory hazards that expose them, particularly bioaerosols and airborne pollutants, are classified into organic types, including bacteria and volatile organic

compounds (VOCs), as well as inorganic substances such as harmful inhalants like methane (CH₄), carbon monoxide (CO), hydrogen sulphide (H₂S), or microplastics.^{3,4} These substances can cause occupational lung illnesses, including chronic bronchitis, chronic obstructive pulmonary disease (COPD), asthma, respiratory tract infections, and parenchymal lung disorders like hypersensitivity pneumonitis (HP) and interstitial lung disease (ILD).^{5–7}

Chronic inhalation of waste-derived dust and bioaerosols can induce oxidative stress and inflammatory responses in the alveolar epithelium, leading to epithelial injury and regeneration of type II pneumocytes. This process results in increased release of Krebs von den Lungen-6 (KL-6) into the bloodstream as a biomarker of lung damage. KL-6 itself is a high-molecular-weight, mucin-like glycoprotein (human MUC1) expressed on type II alveolar pneumocytes and bronchiolar epithelial cells.^{8,9}

Previous studies have shown that occupational dust exposure is associated with altered KL-6 levels, even among exposed workers without clinically apparent disease, and increases progressively with disease severity.^{10,11} So, this study was conducted to evaluate serum KL-6 levels among landfill workers in relation to duration of exposure and type of work.

METHODS

This analytical observational study employed a cross-sectional design and was conducted at the Supit Urang Landfill in Malang City, Indonesia. This study was approved by the Institutional Ethics Committee of Medical Faculty Universitas Brawijaya Malang (Approval No. 293/EC/KEPK/10/2023) and was conducted in accordance with the Declaration of Helsinki.

Respondents were recruited using a consecutive sampling method among eligible landfill workers during the study period. Eligible participants, in accordance with the inclusion criteria, were aged 17–80 years and had at least 6 months of employment with daily working hours exceeding 8 hours, and exclusion criteria included individuals with pulmonary or extrapulmonary cancer and those with untreated pulmonary infections such as tuberculosis or pneumonia. The sample size was determined based on feasibility and the total number of eligible workers available, and obtained as many as 79 workers become respondents.

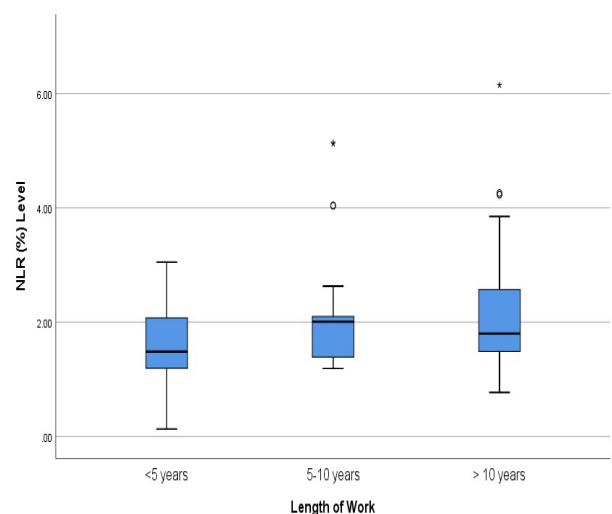
Then respondents were categorized based on length of work exposure, with the distribution of the number of samples in each group being: 1) <5 years: 24 respondents; 2) 5–10 years: 29 respondents; 3) >10 years: 26 respondents. Based on the type of work, the distribution of the number of samples in each group being 1) scavengers: 48 respondents; 2) waste sorters: 20 respondents; 3) waste processors: 9 respondents; 4) laboratory technicians: 2 respondents. All adult respondents provided written informed consent in accordance with applicable ethical guidelines.

Data on age, sex, smoking exposure, personal protective equipment (PPE) use, and clinical data,

including history of illness and treatment, were collected during the initial assessment. PPE use was categorized as complete (mask, gloves, and boots), partial (one or two items), or none (no PPE use). While serum KL-6 levels were measured using an enzyme-linked immunosorbent assay (ELISA). There are also additional parameters included, such as complete blood count analysis using flow cytometry, from which the neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, as well as exhaled carbon monoxide (eCO) levels measured using a Smokerlyzer (Bedfont Scientific Ltd., UK).

RESULTS

Demographic data show that the mean age was over 40 years found on 57% respondents. Males were more dominant (64.6%) compared to females (35.4%). The types of work among the respondents were divided into 4 groups: 48 scavengers, 20 waste sorters, 9 waste processors, and 2 laboratory technicians. Respondents who used complete personal protective equipment (PPE) at work were just 19%. Some others partially used PPE, only gloves or masks, or just boots, and others none, as shown in Table 1. Meanwhile, Figure 1 shows that the NLR value does not differ significantly in the waste worker group across exposure durations.



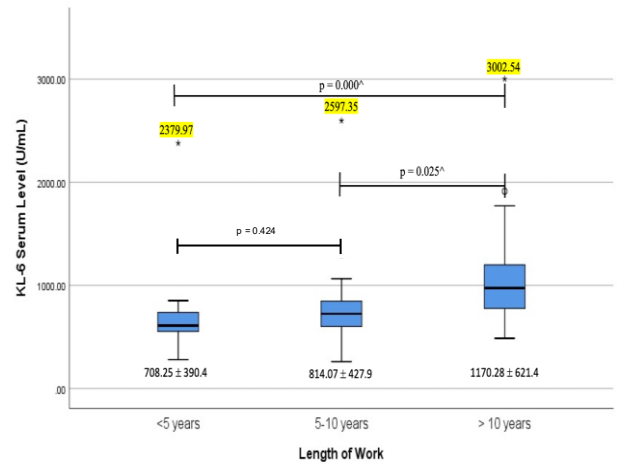
Note: *max value

Figure 1. NLR level according to the length of work exposure group in the Supit Urang Landfill

Table 1. Demographic characteristic data of waste workers at Supit Urang Landfill

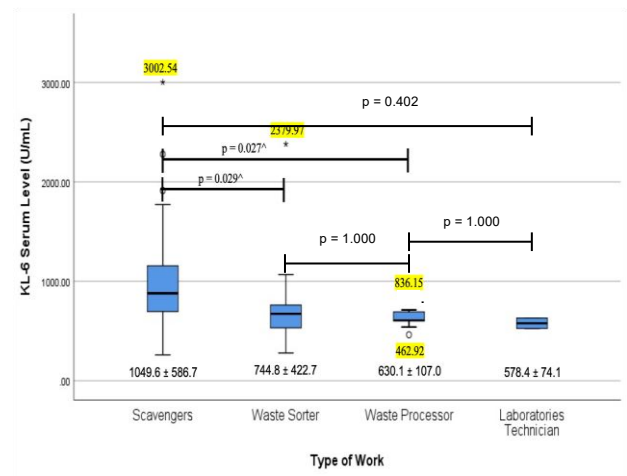
Characteristic	n (%)	Mean±SD
Age (years)		
<20	2 (2.5%)	17.5±0.7
20-40	32 (40.5%)	28.5±5.4
>40	45 (57.0%)	57.8±9.9
Gender		
Male	51 (64.6%)	---
Female	28 (35.4%)	---
Last Education		
Not school	24 (30.4%)	---
Elementary School	16 (20.2%)	---
Junior High School	6 (7.6%)	---
Senior High School	24 (30.4%)	---
Bachelor	9 (11.4%)	---
Body Mass Index (BMI)		
Underweight	13 (16.5%)	17.5±0.7
Normal	48 (60.8%)	21.6±2.0
Overweight	14 (17.7%)	27.2±1.1
Obesity	4 (5.0%)	34.9±0.9
Respiratory symptoms		
Shortness of breath	7 (8.5%)	---
Cough	6 (7.3%)	---
Personal Protective Equipment (PPE)		
Complete Used	15 (19.0%)	---
Partially used	35 (44.3%)	---
None	29 (36.7%)	---
Exhaled Carbon Monoxide (eCO)		
Normal (0-9 ppm)	56 (82.9%)	2.9±2.4
Mild (10-29 ppm)	13 (15.9%)	13.8±4.0
Moderate (30-69 ppm)	1 (1.2%)	31±0.0
High (70-149 ppm)	0 (0.0%)	0
Very High (150-249 ppm)	0 (0.0%)	0
Dangerous (>249 ppm)	0 (0.0%)	0
Blood Diff. Count Absolute Level		
Eosinophils	---	302.4±238.9
Basophil	---	53.29±26.6
Neutrophil	---	4409.6±1849.9
Lymphocyte	---	2836.8±4082.9
Monocyte	---	560.3±189.0
NLR	---	2.01±1.1

Based on the study results, the mean serum KL-6 levels with a length of work exposure <5 years were 708.25±390.4 U/mL, for the 5-10 years group were 814.07±427.91 U/mL, and for the >10 years group were 1170.28±621.37 U/mL. Serum KL-6 levels differed significantly across the length of work exposure ($P=0.0001$), with the highest levels observed among those with a length of work exposure >10 years. Post-hoc analysis indicated that this difference was primarily observed in the >10 years group and other groups ($P=0.025$), as shown in Figure 2.



Note: *max value; ^significant if $P<0.05$; yellow markers represent the highest KL-6 levels within each group

Figure 2. The mean of serum KL-6 level in the length of work exposure group, with Post-hoc multiple comparison by the Kruskal-Wallis test



Note: *max value; ^significant if $P<0.05$; yellow markers represent the highest KL-6 levels within each group

Figure 3. Mean of serum KL-6 levels in the type of work with Post-hoc multiple comparison by the Kruskal-Wallis test

Multiple linear regression analysis identified the length-of-work-exposure group and body mass index (BMI) as significant predictors of serum KL-6 levels. The length of work exposure group was positively associated with KL-6 levels (OR=216.302; $P=0.048$), indicating that individuals in the group with >10 years of work exposure had higher KL-6 concentrations compared to the reference group. Similarly, BMI showed a significant positive association (OR=32.319; $P=0.038$), suggesting that higher BMI is associated with increased KL-6 levels. Other variables, including age, gender, type of work, PPE, eCO, and NLR, were not significantly associated with KL-6 levels ($P>0.05$).

Table 2. Multiple Linear Regression Analysis of Factors Associated with Serum KL-6 Levels

Variable	OR	P	95% CI
Age	6.823	0.257	-5.080 to 18.726
Gender	-84.838	0.605	-410.814 to 241.139
Body Mass Index (BMI)	32.319	0.038*	1.869 to 62.768
Personal Protective Equipment (PPE)	-53.400	0.557	-233.777 to 126.977
Exhaled Carbon Monoxide (eCO)	30.404	0.206	-17.164 to 77.972
Neutrophil-to-Lymphocyte Ratio (NLR)	-56.181	0.327	-169.698 to 57.336
Length of Work Exposure	216.302	0.048*	2.118 to 430.486
Type of Work	33.899	0.720	-154.113 to 221.911

Note: OR=odds ratio; CI=confidence interval; BMI=body mass index; *if statistically significant $P<0.05$

DISCUSSIONS

Demographic factors, including age, sex, education level, and BMI, were significantly associated with exposure duration ($P<0.05$). Older workers and male scavengers tended to work longer hours per day (1–6 vs. >6 hours) and were more frequently engaged in high-exposure tasks, which may contribute to increased inhalation of hazardous substances. In addition, the low utilization of PPE observed in this population may further exacerbate exposure risks.¹⁰

Interestingly, eCO levels did not differ significantly across exposure groups and were not associated with KL-6 levels or NLR as an inflammatory marker. This finding is consistent with previous studies reporting that eCO may not adequately reflect chronic occupational exposure in landfill settings. Unlike eCO, which primarily reflects recent exposure, KL-6 may serve as a potentially useful biomarker of chronic alveolar epithelial injury. This suggests that KL-6 may provide additional value in detecting subclinical lung damage not captured by conventional exposure indicators.^{11–13}

The average result eCO among waste processors was modestly elevated at 8.1 ppm. In waste workers who are continuously exposed to dust, CO gas obtained from burning, plastic biodegradation, and infection sources such as parasites and fungi, may contribute to a decline in lung function, especially if they do not use adequate PPE.^{11–13}

Body mass index in waste workers is associated with respiratory health, with obesity increasing susceptibility to respiratory impairment. In this study, BMI remained significantly associated with

serum KL-6 levels after adjustment, while previously significant variables lost significance. This positive association is biologically plausible, reflecting low-grade inflammation and altered pulmonary mechanics. However, the modest effect size suggests a limited contribution to KL-6 variability.¹⁴

The observed increase in NLR with longer length of work exposure suggests the presence of low-grade systemic inflammation (value 2–3). NLR is widely recognized as a simple and accessible inflammatory marker, reflecting the balance between innate and adaptive immune responses. Although elevated NLR values in this study remained within a moderate range, the trend toward higher values in long-term workers may indicate early inflammatory processes associated with repeated exposure to dust, bioaerosols, and toxic gases.^{15,16}

In previous studies, sputum analysis demonstrated increased neutrophil and lymphocyte proportions, indicating airway inflammation.¹⁷ However, blood-based inflammatory markers, such as the NLR, have also been widely used as systemic indicators of inflammation. In occupational settings, increased NLR has been reported in workers exposed to airborne pollutants and particulate matter, suggesting its role as a practical biomarker for systemic inflammation due to chronic inhalation exposure.^{15,18} In line with this study, the observed increase in NLR with longer exposure duration supports the presence of low-grade systemic inflammation in landfill workers, consistent with findings from prior studies using blood-based inflammatory parameters.

The elevation of KL-6 levels (>500 U/mL) in workers with prolonged exposure, particularly those with more than 10 years of exposure in this study, is

biologically plausible. Chronic inhalation of particulate matter and microbial bioaerosols can induce oxidative stress and inflammatory responses in the alveolar epithelium, leading to injury and regeneration of type II pneumocytes. This process results in increased release of KL-6 into the circulation as part of epithelial repair mechanisms. Serum levels increase with pulmonary fibrosis, alveolitis, and other inflammatory lung diseases. In occupational settings, prolonged exposure to respirable particulates induces repetitive alveolar damage, triggering KL-6 overexpression as part of the repair process.^{19,20}

In the multivariable analysis, length of work exposure was associated with serum KL-6 levels, although this may reflect confounding rather than an independent effect. Post-hoc analysis showed that the significant difference was primarily observed in workers with >10 years of exposure. The association with the treatment group may indicate differences in exposure intensity, but its broad categorization limits interpretation.

These findings are consistent with previous occupational studies showing increased KL-6 levels with longer length of work exposure and disease severity. Research on workers in bird markets reveals that serum KL-6 concentrations were significantly elevated, averaging 1152.67 ± 583.92 U/ml, with exposure duration over 20 years.¹⁷ This difference may be explained by variations in exposure intensity, environmental conditions, and population characteristics, as well as the relatively shorter exposure duration in the present cohort.

Biomarkers such as KL-6, surfactant protein D (SP-D), and matrix metalloproteinase-2 (MMP-2) have been used to diagnose occupational lung diseases, including asbestosis and silicosis, with reported sensitivity of 83% and specificity of 62%.^{21,22} In experimental studies, bronchoalveolar lavage fluid (BALF) KL-6 levels have been shown to correlate with silicosis progression in mice exposed to silica, particularly by day 45.^{8,9} In human studies, serum KL-6 levels have also been reported to be higher in patients with pneumoconiosis compared to healthy controls.²³

Differences in KL-6 levels across job types further support the role of exposure intensity. Scavengers exhibited the highest KL-6 levels, likely due to direct and prolonged exposure to landfill-derived dust, gases, and bioaerosols.²⁴ In contrast, workers in more controlled environments, such as laboratory technicians, demonstrated lower levels.

These findings are consistent with previous studies showing that outdoor and high-contact occupations are associated with greater respiratory risk due to increased exposure to environmental contaminants, including methane (CH₄), carbon monoxide (CO), hydrogen sulfide (H₂S), and microbial agents.^{22,25,26} Organic particles may activate Toll-like receptor 4 (TLR4) on macrophages, leading to the release of interleukin-8 (IL-8) which recruits neutrophils to the airways.²⁷ Increased serum SP-D 81.39 ng/mL in scavengers is associated with endotoxin exposure >10 years due to damage to the alveolar-capillary barrier.²⁸

This study found that the relationship between length of work exposure and serum KL-6 levels among landfill workers, highlighting potential early lung injury associated with prolonged exposure, particularly those with more than 10 years of work, was negatively correlated with serum KL-6 levels, which may reflect cumulative exposure-related effects.¹⁷ Outdoor workers had high blood KL-6 levels, which were negatively correlated with occupation. The kind of profession and room environment impact blood KL-6 levels because they alter inhalation exposure quantity and duration.^{29,30}

LIMITATION

This study has several limitations. First, the cross-sectional design precludes causal inference between the length of work exposure and KL-6 levels. Second, chest radiographic examinations were not conducted as an initial screening tool to assess respiratory health status and detect possible lung abnormalities. Third, the relatively small sample size, particularly within certain subgroups, may have limited data homogeneity and reduced statistical power, thereby increasing the risk of bias.

Additionally, respiratory symptoms and clinical signs were recorded only once, as participant recruitment and follow-up were challenging. Therefore, the findings should be interpreted with caution. Future studies are recommended to adopt a longitudinal or stepwise design with periodic evaluations and larger sample sizes to provide a more comprehensive assessment of respiratory outcomes.

CONCLUSION

Serum KL-6 levels were associated with longer length of work exposure and type of work, with higher levels observed among workers with more than 10 years of exposure and among scavengers. These findings suggest a potential cumulative effect of occupational exposure, although causality cannot be inferred.

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CONFLICT OF INTEREST

The authors claimed no conflicts of interest.

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