The Indonesian Journal of Occupational Safety and Health
2023, 12 (2): 304-312
p ISSN: 2301 8046, e ISSN: 2540 7872
http://doi.org10.20473/ijosh.v12i2.2023.304-312

SYSTEMATIC REVIEW

Association Between Cadmium Exposure and Kidney Disorder Among Workers in the Battery Industry

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ABSTRACT

Introduction: Workers in the battery industry are at risk of being exposed to cadmium (Cd), which can cause various health problems, including kidney disorders. This study aims to investigate the association between biomarkers of Cd exposure and effect with kidney disorders among workers in the battery industry. **Methods:** A systematic review approach was used in this study, employing relevant keywords and inclusion criteria to search electronic databases, such as Google scholar, PubMed, Science Direct, and Research Gate. The selected articles included research articles published between 2010 and 2020, with cross-sectional, cohort, and case-control study designs. To ensure the quality of the articles reviewed, the Critical Appraisal Skill Programme (CASP) was used. **Results:** The CASP tools facilitated the exploration of trustworthy and relevant articles for the literature review. Previous studies revealed that individuals of various ages, ranging from teenagers to adults aged 12-60, both males and females, are commonly employed in the battery industry. Cadmium was detected in the hair, urine, and blood samples of these workers. Previous studies also identified kidney disorders among these workers by analyzing biomarkers such as creatinine, retinol-binding protein, blood urea nitrogen, and hemoglobin, which were all found to be above the normal range. Furthermore, increased Cd levels in the blood of workers caused glomerular disorder and tubular dysfunction, eventually resulting in kidney function disorders. **Conclusion:** Cd levels in the bodies of workers in the battery industry serves as a reliable biomarker of Cd exposure, and are closely related to the number of effect biomarkers that can contribute to kidney disorders. This study emphasizes the importance of monitoring Cd exposure levels among workers in the battery industry.

Keywords: battery industry, effect biomarkers, health risk, kidney disorder, workers' characteristics

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INTRODUCTION

Cadmium (Cd) is a highly toxic metal that can accumulate in the human body for 20-30 years, especially in the soft tissues located between the skin and organs. Exposure to cadmium can cause cancer, kidney disorders, hormone disorders, reproductive disorders, and cellular differentiation disorders. Industrial and environmental waste is a great source of cadmium, and workers in the industrial sector are particularly at risk of exposure to cadmium (Hassanin, El-Bassel and El-Razek, 2017). Cadmium enters their bodies by being inhaled through the air containing a high level of cadmium. In addition, exposure can occur through smoking and consuming foods contaminated by cadmium (Victoria State Gov., 2021).

Cd is highly toxic to humans, thus it is not necessary for normal body functioning and development. Cd exposure can lead to acute or

Cite this as: Choirunnisa', A., *et al*. (2023) 'Association Between Cadmium Exposure and Kidney Disorder Among Workers in the Battery Industry', *The Indonesian Journal of Occupational Safety and Health*, 12(2), pp. 304-312.

 doi:10.20473/ijosh.v12i2.2023.304-312
Received July 08, 2021; 1st revision August 09, 2021; 2nd revision August 13, 2021; Accepted August 17, 2021; Published: August 2023. Published by Universitas Airlangga.

chronic effects that can disrupt various organ functions, including the liver, lungs, testes, brain, bones, blood, and kidneys. Among these organs, the kidneys are particularly vulnerable to the toxic effects of Cd (Hernayanti *et al*., 2019). Chronic Cd exposure primarily affects the proximal tubules of the kidneys, which can result in increased excretion of protein in the urine. The first sign of Cd nephrotoxicity is tubular dysfunction, which is associated with increased excretion of low-molecular-weight proteins in the urine, such as β 2-microglobulin (β2M) and retinol-binding protein (RBP). In addition, Cd exposure can affect the glomerulus, which is characterized by increased excretion of high-molecular-weight proteins in the urine, including albumin, transferrin, and immunoglobulin G (Winata, 2017). These changes in protein excretion serve as biomarkers of Cd exposure and effects in the kidneys. Regular monitoring of Cd exposure levels is important to prevent the adverse health effects associated with Cd exposure, particularly in the kidney.

Workers employed in the battery industry are particularly susceptible to being exposed to harmful substances such as Cd. This is due to the fact that Cd is used in various aspects of the battery manufacturing process, including as a component of solder and alloys used in batteries. In addition, CdSO4 is used in the production of Winston cells for its stable potential of 1.0186 Volts. Moreover, Cd is used as the negative electrode in NiCad batteries, while nickel oxyhydroxide is used as the positive electrode. As a result, workers in this industry are at an increased risk of Cd exposure. A study conducted by Choi *et al*. (2020) found that workers in the nickel-cadmium battery recycling industry were exposed to relatively high levels of cadmium, which were 0.066 mg/m3 and 0.017 mg/m3. The study also found that the cadmium levels in the kidneys had a positive correlation with the damage to the body. Particularly, kidney damage caused by cadmium was identified in workers who had long working tenures.

The use of Cd as a raw material in the battery industry highlights the necessity for further investigation into the influence of workers' characteristics and Cd biomarkers on the prevalence of kidney disorders. In light of this, a comprehensive literature review on this topic is necessary. This study aims to investigate the association between Cd exposure and kidney disorders among workers employed in the battery industry.

METHODS

This study used a systematic review approach to gather scientific articles from electronic databases such as Google scholar, PubMed, Science Direct, and Research Gate. This study also used specific keywords according to the Population, Exposure, Comparator, and Outcome (PECO) framework. The population keyword was "battery workers", the exposure keywords was "cadmium", the comparator keyword was "no control", and the outcome keywords were "effects on kidney" and "renal injury". Five inclusion criteria were considered, namely (1) the articles should discuss kidney disorders in workers in the battery industry as a result of cadmium exposure; (2) the publication time frame should be within the past 10 years (2011-2020); (3) the articles should be available in full text and open access; (4) the articles should be original with cross-sectional, cohort, or case-control study designs; and (5) the articles should be written in English. The quality of the articles was assessed using the Critical Appraisal Skills Programme (CASP) tools. Furthermore, this study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to compile systematic reviews and meta-analyses, which facilitated the identification, screening, eligibility criteria, and selection of the articles.

This study investigates the influence of workers' characteristics in the battery industry on the prevalence of kidney disorders while examining the relationship between exposure biomarkers such as Cd levels in the body, effect biomarkers in the kidneys caused by Cd exposure, and kidney disorders as dependent variables. This study was conducted in 2021 and used published articles from 2011 to 2020. However, it should be noted that this study was not registered in Prospero. Six procedures were used to process the data in this study. First, the topic was defined as investigating the relationship between Cd exposure and kidney disorders among workers in the battery industry. Second, relevant articles were identified by organizing the findings of electronic database searches. Third, articles that met the inclusion criteria based on the keywords were chosen. Fourth, a table was compiled to summarize the literature for simplified display. Fifth, the data were reviewed to identify interesting issues related to the relationship between Cd exposure and kidney disorders among workers in the battery industry. Finally, the data were organized and analyzed to

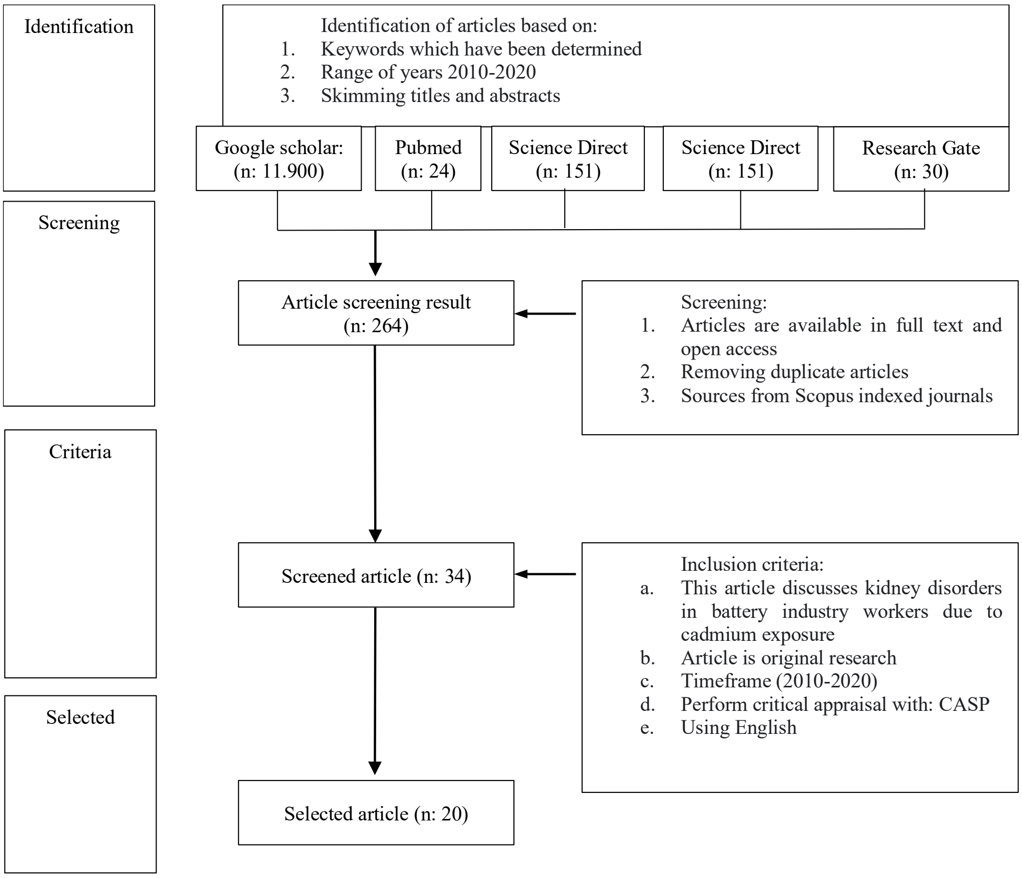

Figure 1. PRISMA Flow Diagram

provide useful insights. This method ensured that the data were thoroughly processed in order to produce accurate and reliable results (Verdejo *et al*., 2021).

RESULTS

This study used a systematic review approach, drawing upon data obtained from 20 scientific articles written in English (Appendix A). The majority of these articles were published in 2018, with 5 out of the 20 articles focusing on research conducted in Nigeria. This is interesting to note, considering Nigeria's significant consumption of both new and used battery-related products.

The majority of the original articles reviewed (80%) used a cross-sectional approach. The types of battery industry were battery manufacturers, battery repair industries, battery recycling industries, and battery charger industries. Figure 1 presents the PRISMA flow diagram, outlining the process of obtaining relevant and trustworthy articles for the literature review. This diagram can also serve as an efficient tool for further researchers focusing on health intervention topics. In the identification stage, 264 articles were selected for screening (n = 264). Among them, only 34 articles met the inclusion criteria and were included in this study (n = 34), while the remaining 230 articles were excluded from this study. Out of the 34 articles, 10 articles did not fall within the specified time frame (2010-2020) and four articles were not written in English. As a result, in the final stage, only 20 articles from the initial 34 articles that met the inclusion criteria and were selected for this study (n = 20).

Characteristics of Workers in the Battery Industry

Table 1 provides information on the demographic characteristics of workers in the battery industry, including age and sex. Out of the 20 reviewed articles, only 15 articles mentioned the workers' characteristics. The table demonstrates a wide range of ages among workers in the battery industry from different countries, ranging from teenagers (12 years) to the elderly (60 years). Additionally, out of the 13 articles that mentioned sex distribution, seven articles solely focused on male workers, while one article solely focused on female workers.

Table 1. Demographic Profile of Workers in the Battery Industry according to Age and Sex

Author(s)	Research Location	Type of Industry	n	Age group	Sex	
					M (%)	F (%)
(Lison *et al*., 2018)	Belgium	Battery factory	60	Average of 50	63.3	36.6
(Dartey *et al*., 2017)	Ghana	Battery reparation	64	18-50	-	-
(Sovičová *et al*., 2019)	Czech Republic	Battery factory	59	Average of 39.4	61	39
(Adejumo *et al*., 2018)	Nigeria	Accumulator recycling	18	18-60	100	-
(Li *et al*., 2020)	China	Battery factory	53	Average of 38	100	-
(Alli, 2015)	Nigeria	Battery charger	9	15-40	90.6	9.4
(Dix-Cooper and Kosatsky, 2018)	Canada	Battery factory	91	19-45	-	100
(Arain *et al*., 2015b)	Pakistan	Battery recycling	110	12-15	100	-
(Ishola *et al*., 2017)	Nigeria	Battery recycling	14	16-60	100	-
(Bot *et al*., 2020)	Nigeria	Battery reparation	80	18-60	100	-
(Freire. *et al*., 2015)	Brazil	Battery reparation	28	<30	75.2	24.8
				>30		
(Chaumont *et al*., 2011)	France, Sweden, United States	Battery factory	599	Average of 45.4	75.3	24.7
(Baloch *et al*., 2020)	Pakistan	Battery recycling	12	12-45	100	-
(Al-Rabia *et al*., 2018)	Saudi Arabia	Battery factory	40	20-42	-	-
(Arain *et al*., 2015b, P2)	Pakistan	Accumulator recycling	201	12-15	100	-

Table 2. Relationship between Workers' Characteristics and Cd Levels in the Body

Author(s)	Statistical analysis	Sig.	Note
	Sex		
Lison *et al*. (2018)	Chi-square or Mann-Whitney U	0.001	Women had higher Cd levels in blood and urine than men
Sovičová *et al*. (2019)	Wilcoxon signed-rank test	<0.05	Cd levels in women's urine was higher than in men's urine
Freire *et al*. (2015)	Linear regression	<0.001	Women had higher Cd levels in blood than men
Chaumont *et al*. (2011)	Pearson correlation	<0.05	The relationship between Cd levels and urine was influenced by sex
	Age		
Lison *et al*. (2018)	Chi-square or Mann-Whitney U	<0.001	Cd levels in blood and urine was influenced by age
Sovičová *et al*. (2019)	Wilcoxon signed-rank test	<0.05	Cd levels in blood and urine was influenced by age
Alli (2015)	t-test	<0.05	Cd levels in adults were higher than in adolescents
Dix-Cooper and Kosatsky (2018)	t-test	<0.05	Cd levels was positively associated with age
Freire *et al*. (2015)	Linear regression	<0.001	Age >30 had higher Cd levels than age <30
Chaumont *et al*. (2011)	Pearson correlation	<0.05	The relationship between Cd and urine was influenced by age

Relationship Between Workers' Characteristics and Cd Levels in the Body

Table 2 provides information on the relationship between workers' characteristics and Cd levels in the body in 10 articles. Out of these articles, four articles found that women have higher Cd levels than men. In addition, all articles that compared different age groups found that older people have higher Cd levels than teenagers.

Table 3. Empirical Findings on the Association between Biomarkers of Cadmium Exposure, Effect Biomarkers, and Cd Levels with Kidney Function Disorders among Workers in the Battery Industry

Author(s)	Cd level in the Body	Effect Biomarker(s)	Indication of Kidney Function Disorder (yes /no)*	Type of Kidney Disorder
Chaumont *et al*. (2011)	-	Creatinine: 13300 (mg/dl)	Yes	Tubular dysfunction
Gao *et al*. (2016)	Cd levels in the urine of workers at the battery factory: 6.19 (μg/g)	RBP: 157 (μ g/l)	Yes	-
		β2M: 79 (μg/l)	No	
		β2M: 105.38 (μg/l)	No	
		RBP: 71.84 (μg/l)	Yes	
Ishola *et al*. (2017)	-	Creatinine: 1.03 ± 0.26 (mg/dl)	No	-
		Uric acid: 5.87 ± 1.35 (mg/dl)	No	
		Blood urea nitrogen: 27.38 (mg/dl)	Yes	
		Bicarbonate: 23.66 ± 5.40 (mmol/l)	No	
		Chloride: 105.44 ± 3.22 (mmol/l)	No	
		Potassium: 3.67 ± 0.34 (meq/l)	No	
		Sodium: 137.0 ± 3.86 (meq/l)	No	
YS, Bot *et al*. (2020)	Cd levels of workers in the battery industry: 0.24 ± 0.03 (μg/g)	Creatinine: 0.05 ± 0.02 (mg/dl)	No	Glomerular disorder (GFR)
		Urea: 4.79 ± 1.89 (mmol/l)	No	
		Micro albumin: 12.58 ± 5.24 (mg/l)	No	
Arain, *et al*. (2015a)	-	Hb: 10.1 ± 0.34 (g/dl)	Yes	-
Arain, *et al*. (2015b)	Cd levels in the hair of workers at the battery recycling: 2.12 ± 0.29 (μg/g) or over the normal limit	Hb within the normal limit		-

*Yes = abnormal; no = normal

*The normal level of creatinine is 1.3 mg/dl, urine beta-2-microglobulin is <300, RBP is 40-60 μg/ml, adolescent Hb is 11 - 13 g/dl, urea nitrogen is 8-21 mg/dL, uric acid is 3.5-7.2, potassium is 3.5-5 meq/L, sodium is 136-146 meq/L, bicarbonate is 23-29 mmol/L, chloride is 96-106 meq/L, urea is 1.8-7.1 mmol/L, and micro albumin is <30 mg.

Relationship Between Cd Levels, Biomarkers of Exposure, and Effect Biomarkers with Kidney Disorders Among Workers in the Battery Industry

Out of the 20 articles selected for this study, five of them focused on investigating the effect biomarkers of Cd exposure and its association with the pathogenesis of kidney disorders among workers employed in the battery industry. Table 3 presents various effect biomarkers that can serve as indicators of kidney disorders among workers in the battery industry. The table shows that effect biomarkers can be characterized using several parameters, including creatinine, retinol-binding protein (RBP), β-2-microglobulin, uric acid, blood urea nitrogen, bicarbonate, chloride, potassium, sodium, urea, microalbumin, and hemoglobin. Five effect biomarkers were found to exceed normal limits, indicating potential kidney disorders. The table also demonstrates three scholarly publications that discuss the relationship between Cd levels and effect biomarkers associated with kidney disorders among workers in the battery industry. These publications include studies by Gao *et al*. (2016), Bot *et al*. (2020), and Arain *et al*. (2015b). Among these, Bot *et al*. (2020) reported that Cd levels in the body that exceed normal limits are associated with a subsequent increase in effect biomarkers beyond the usual range.

DISCUSSION

The sex characteristics shown in Table 1 suggest that historically, the battery industry has been dominated by men. However, it also acknowledges that the pattern of male dominance in the battery industry is changing as a result of modernization and increasing female participation in the workforce.

On the other hand, Table 2 shows that compared to men, women tend to have higher Cd levels in their bodies. This can be attributed to the increased gastrointestinal uptake of Cd among women, especially those with reduced iron levels due to menstruation (Kim *et al*., 2014). In other words, increased Cd uptake and accumulation in the body can result from reduced iron levels. To prevent high levels of Cd in women's blood, it is necessary to manage food intake and ensure that women do not experience Ca and Fe deficiencies, especially during menstruation (Safitri, 2015). These findings highlight the importance of taking sex into account when assessing the health risks associated with occupational exposure to Cd in the battery industry.

Furthermore, Table 2 shows that six articles have reported a positive correlation between age and Cd levels in the body, with older people having higher Cd levels than adolescents. Age is thought to be a factor that influences Cd levels in the body. This phenomenon is attributed to the increased sensitivity of the body to Cd as individuals age. This is due to a decrease in biotransformation enzymes and greater susceptibility to the effects of Cd with age(Friberg, 2018). As a result, it can be concluded that age plays an important role in determining Cd levels in the body, with older people being more vulnerable to the toxic effects of Cd (Mayaserli and Rahayu, 2018).

This study revealed that a proportion of the battery industry's employees consisted of teenagers. However, previous studies such as the National Health and Nutrition Survey (NHANES) suggested that children and adolescents in the US, especially those aged 6 to 15 years, may be vulnerable to low-level Cd exposure. The NHANES study established a correlation between Cd levels in urine and a number of developmental disorders, such as hyperactivity, learning disabilities, cognitive disorders, and neuropsychological impairments. This finding highlights the importance of protecting young employees in the battery industry from exposure to toxic substances like Cd, which can negatively affect their health and well-being. This finding also highlights the need for health and safety regulations as well as training programs in the industry in order to mitigate occupational hazards and ensure workers' safety (Chandravanshi, Shiv and Kumar, 2021).

In Table 3, out of 5 articles, 3 articles reported the use of creatinine as a biomarker to identify kidney damage caused by Cd exposure in people working in the battery industry. This indicates that in this occupational context, creatinine levels can serve as a reliable indicator of kidney disorders caused by Cd exposure. Creatinine is a nitrogenous non-protein substance produced by the metabolism of creatine in muscles. It is an endogenous substance that can be easily filtered by the kidneys. Although creatinine can be secreted by tubule cells, it is not significantly reabsorbed in the renal tubules. The clearance of creatinine, which is generally stable in the plasma, can be used to determine the glomerular filtration rate. Increased creatinine levels are a sign of impaired kidney function, especially in the glomeruli (Lousiana Department of Health, 2017).

Besides creatinine, β-2-microglobulin can serve as a useful biomarker for evaluating renal health. This is due to the fact that β-2-microglobulin is filtered by the glomeruli, the blood filtration organs in the kidneys, and reabsorbed by the proximal tubules. In healthy individuals, only minimal amounts of β-2-microglobulin are found in the urine due to efficient reabsorption by the proximal tubules. However, when the tubules are damaged, the capacity to reabsorb β-2-microglobulin is reduced, resulting in an increase in the concentration of protein in the urine. Therefore, assessing the levels of β-2-microglobulin in urine can reveal important details about kidney health and help detect early indications of kidney disease or damage caused by Cd toxicity (Lab Test Online UK, 2021).

Meanwhile, a study conducted by Gao *et al*. (2016) showed that workers in the battery industry had increased levels of retinol-binding protein (RBP) above the normal levels. RBP is a low-molecular-weight protein that is commonly found in urine after prolonged Cd exposure. Research shows that increased RBP levels in affected individuals are frequently associated with a decrease in tubular reabsorption (European Chemicals Agency (ECHA), 2020) As a result, RBP testing can serve as a confirmatory test in cases of suspected Cd exposure. These findings indicate that RBP testing could be a useful biomarker for detecting potential Cd exposure among workers in the battery industry.

Uric acid is a byproduct of purine metabolism that is relatively insoluble in water. Allantoin, a water-soluble molecule, is formed through enzymatic conversion by uricase or urate oxidase. Increased uric acid levels in blood can be attributed to kidney disease, which can lead to reduced filtration function, impaired renal excretion, and decreased uric acid secretion in urine. Kidney disease can also result in electrolyte imbalances, including potassium and sodium. While the lower nephrons are primarily responsible for potassium secretion, chronic kidney disease can result in a failure to boost NaCl excretion (Durgapal *et al*., 2022). The natrium regulation is crucial in the early stages of chronic kidney disease to End-Stage Kidney Disease (ESKD) (Borrelli *et al*., 2020).

Hemoglobin (Hb) is one of the biomarkers that can be used to assess the prognosis of acute kidney disorders. Decreased hemoglobin (Hb) occurs simultaneously with decreased renal erythropoietin, which is caused by tubulointerstitial disorders. Therefore, monitoring Hb levels can be an effective approach to identifying renal impairment caused by Cd exposure in this population (Hansson *et al*., 2022).

Workers in the battery industry may develop kidney problems as a result of exposure to Cd, including glomerular disorder and tubular dysfunction. The tubules play a role in reabsorbing beneficial substances and excreting waste materials, while the glomerulus is in charge of filtering blood and eliminating waste products. A number of kidney diseases can result from Cd exposure because it can dagame the glomerulus and tubules. Reduced glomerular filtration rate (GFR), proteinuria (the presence of proteins such as albumin in urine), and glomerulonephritis can all result from Cd accumulation in the kidneys, which interferes with their regular function. Additionally, exposure to Cd can result in tubular dysfunction, which may cause renal tubular acidosis, a condition where the kidneys are unable to regulate acid-base balance in the body (Bot *et al*., 2020).

CONCLUSION

The findings suggested that age and sex are significant risk factors for high levels of Cd in the bodies of workers employed in the battery industry. Furthermore, this study identified several biomarkers, including creatinine, β-2-microglobulin, RBP, Hb, urea nitrogen, uric acid, potassium, sodium, bicarbonate, chloride, urea, macroglobulin, and creatinine, which can be used to detect kidney disorders in these workers. To reduce Cd exposure, workers should use personal protective equipment (PPE) such as masks properly and consistently. Furthermore, future research should be conducted on-site to obtain more reliable findings that can address health concerns among employees in the battery industry.

ACKNOWLEDGEMENTS

The authors of this study would like to thank the authors of the previous studies for their contributions as references in writing this review article. Additionally, the authors would like to extend their gratitude to Ms. Intan Maulida Qorry'aina for assisting with the English translation of the article. Conflict Interest:All authors declare that they have no conflicts of interest.

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