ORIGINAL ARTICLE
Bali Medical Journal (*Bali MedJ)* 2022, Volume 11, Number 2: 1034-1040
P-ISSN.2089-1180, E-ISSN: 2302-2914

Effect of occupational aluminum exposure on cognitive function among informal aluminum foundry industry workers

Nelmi Silvia[1*], Adi Heru Sutomo[2], Indwiani Astuti[3]

[1]Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia;
[2]Department of Public Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia;
[3]Department of Pharmacology and Therapy, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

*Corresponding author:
Nelmi Silvia; Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia
nelmisilvia@med.unand.ac.id

Received: 2022-07-05
Accepted: 2022-08-02
Published: 2022-08-31

ABSTRACT

Background: Occupational exposure to aluminum can potentially cause health problems for workers in the aluminum foundry industry, which might associate with cognitive impairment. However, studies in the informal aluminum foundry industry are still very limited. This study aimed to determine the relationship between aluminum exposure and cognitive impairment in informal aluminum foundry workers.

Methods: This study used a cross sectional design with logistic regression analysis. Seventy-nine workers in the informal aluminum foundry industry participated in this study. Aluminum in urine was measured using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS). Cognitive function was measured using the Montreal Cognitive Assessment-Indonesian version (MoCA-Ina) instrument.

Results: A total of 69.6% of the subjects experienced cognitive impairment. There was a statistically significant relationship between urinary aluminum levels and cognitive impairment. Multivariate logistic regression analysis showed that urinary aluminum levels (adjusted odds ratio (aOR) = 6.550; 95% confidence interval (CI) = 1.281–33.499) and length of education (aOR = 16.885; 95% CI = 2.042–139.604) were associated with cognitive impairment, with cut-off value set at 45.985 µg/L. Other results showed that workers with less than 7 years of formal education have a 16.885 times higher risk of experiencing cognitive impairment.

Conclusion: Workers with urinary aluminum levels ≥ 45.985 µg/L and formal education fewer than 7 years have a higher risk of having cognitive impairment. Regular bio-monitoring of workers' urinary aluminum levels and adequate aluminum exposure control efforts are needed to prevent cognitive impairment in informal aluminum foundry workers.

Keywords: Aluminum, foundry, cognitive, occupational, informal.
Cite This Article: Silvia, N., Sutomo, A.H., Astuti, I. 2022. Effect of occupational aluminum exposure on cognitive function among informal aluminum foundry industry workers . *Bali Medical Journal* 11(2): 1034-1040. DOI: 10.15562/bmj.v11i2.3483

INTRODUCTION

Aluminum is the most abundant metal in the earth's crust. It has never been found as a free metal because it always binds with other elements, especially oxygen, silicon and fluorine.[1] It is also the most widely used non-ferrous metal.[2] Aluminum and its alloys are used in various fields, including canning, transportation, building and construction, and electrical equipment. They are also widely used in cooking utensils, decorations, and automotive parts.[3]

The aluminum foundry industry is an industry that produces aluminum castings. They are obtained through the process of melting aluminum alloy ingots and pouring the molten metal into a mold that gives the product's final or near-end shape.[4] Various hazards in the foundry industry, such as chemical, physical and mechanical hazards, can expose workers and pose a risk of health problems and injury to workers.[5] Aluminum workers may be exposed to aluminum fumes and particulates in the work environment.[6] Aluminum absorbed after inhalation exposure is excreted mainly in the urine.[1] A meta-analysis study found urinary aluminum levels in workers exposed to aluminum ranged from 13–133 µg/L.[7]

The impact of aluminum exposure in the workplace on workers' health has been studied for a long time. One of the effects of aluminum exposure is a decrease in performance in several tests that measure nervous system function.[1] Case of progressive neurological disorders has been reported in three potroom workers with 12 years of experience working in an aluminum smelter in the United States.[8] Still in the same aluminum smelter, of the 25 potroom workers with neurological symptoms, 84% had memory impairment, and 70–75% showed mild to moderate impairment on memory tests.[9] Concentration difficulty is one of the functional symptoms of the nervous system that is often complained about by aluminum production workers in Poland.[10] The prevalence rate of mild cognitive impairment was 18.2% in retired potroom workers at an aluminum smelting factory in China. This rate was significantly higher than the control group not exposed to aluminum.[11] Until now, the study of the neurological impact of aluminum exposure on workers, especially workers in the informal aluminum foundry industry, is still very limited. Meanwhile, the informal sector workplaces generally have a poor hazard control effort and working environment that can potentially increase the risk of occupational health and safety problems for workers. Therefore, this research is very important to do so that we can know the impact of aluminum exposure on cognitive impairment in informal aluminum foundry industry workers.

METHODS

Study design

This analytical, observational study used a cross sectional design and was conducted on workers in the informal aluminum foundry industry in Yogyakarta City. Inclusion criteria were: workers who have been working for at least 5 years, exposed to aluminum in their daily work, willing to participate in research and sign an informed consent form. Exclusion criteria were: having a history of diabetes mellitus, head trauma, depression/anxiety, hypertension, stroke, brain tumor, central nervous system infection, Parkinson's disease, epilepsy and kidney failure, having a history of using long-term sedatives, having a history of using long-term antacid drugs and received hemodialysis therapy. Seventy-nine informal aluminum foundry industry workers participated in this study as research subjects. All study subjects signed an informed consent form before participating in the study.

Measurement of urinary aluminum level

A total of 30 mL of respondent's post-shift urine was collected and brought to the Prodia Clinical Laboratory in Yogyakarta for handling and then stored at −20°C until all urine samples were collected. Furthermore, all the urine samples were sent to the Research and Esoteric Laboratory of Prodia Clinical Laboratory in Jakarta and stored at −70°C until analyzed. Urinary aluminum was analyzed using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) (Agilent 7700x ICP-MS, Agilent Technologies, Japan) by Prodia Industrial Toxicology Laboratory in Cikarang. With modifications, urinary aluminum was analyzed from a urine sample according to the Center for Disease Control (CDC) method No. 3018.3.[12] The level of accuracy of aluminum analysis is 89.88–100.18%. Urinary creatinine levels were analyzed using the enzymatic method on the Architect c8000 (Abbott, Abbott Park, Illinois, USA). Urinary aluminum levels were reported as uncorrected (μg/L) and corrected for creatinine concentration (μg/g creatinine).

Cognitive function measurement

A neurologist conducted cognitive function measurement using the Montreal Cognitive Assessment-Indonesian version (MoCA-Ina) instrument. MoCA-Ina is a global cognitive function measuring tool that includes cognitive domains in the form of visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall and orientation that have been validated for the Indonesian population. MoCA-Ina score < 26 is the cut-off point for cognitive impairment.[13]

Socio-demographic and occupational characteristics and nutritional status

Socio-demographic and occupational characteristics included age (< 45 years, ≥ 45 years), length of education (< 7 years, 7–12 years, > 12 years), smoking habits (never smoker, former smoker, current smoker), exercise habits (good, not good), years of service (5–10 years, > 10 years), habits of using personal protective equipment (good, moderate and poor), part of work (molding and casting, finishing) were obtained through interviews with questionnaires. Body weight and height were measured to determine body mass index. Body mass index was calculated by weight (kg) divided by height squared (m^2), and based on this body mass index, nutritional status was determined according to World Health Organization (WHO) Asia-Pacific criteria (underweight, normal, overweight, obese I, and obese II).[14]

Statistical Analysis

Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off point value for urinary aluminum level. To analyze the relationship between urinary aluminum levels, covariates (age, length of education, nutritional status, smoking habits, exercise habits, years of service, habits of using of personal protective equipment, part of work) and cognitive impairment, Chi-square tests were used. All independent variables with a *p*-value < 0.25 in bivariate analysis were then included in the multivariate logistic regression to control for confounding factors. In all statistical analyzes, *p* values < 0.05 in the two-tailed test indicated statistical significance. Statistical analysis was performed using SPSS Software version 22.0 (IBM Corp., Armonk, NY).

RESULTS

Socio-demographic and occupational characteristics, nutritional status, and cognitive function of the subject

Socio-demographic and occupational characteristics, nutritional status, and cognitive function of the subjects can be seen in **Table 1**. Most of the subjects were aged < 45 years (69.6%), length of education 7–12 years (68.4%), normal nutritional status (54.4%), current smokers (65.8%) and had poor exercise habits (91.1%). From the aspect of work, most of the subjects had a working period of > 10 years (68.4%), poor habits of using personal protective equipment (40.5%) and worked in the molding and casting department (57%).

Categorization of urinary aluminum level

The median urinary aluminum level was 21.30 μg/L (range 0.35–264.01 μg/L). After being corrected for creatinine, the level was 11.09 μg/g creatinine (range 0.11–109.33 μg/g creatinine). The ROC curve analysis was performed to determine the cut-off point for urinary aluminum levels in distinguishing between normal cognitive function and cognitive impairment. The cut-off point for the urinary aluminum level was 45.985 μg/L with an area under the curve (AUC) of 0.592 (**Figure 1**). Meanwhile, the cut-off point value for urinary aluminum levels that have been corrected for creatinine concentration was 15.495 μg/g creatinine with an AUC of 0.579 (**Figure 2**). Using this cut-off point, we further analyzed the relationship between urinary aluminum levels and cognitive impairment in bivariate and multivariate analyzes.

Bivariate analysis between urinary aluminum levels and covariates with cognitive impairment

Table 2 shows a bivariate analysis between urinary aluminum levels and covariates

Table 1. Socio-demographic and occupational characteristics, nutritional status, and cognitive function of the subject

Variables	Frequency	Percentage
Age		
< 45 years	55	69.6
≥ 45 years	24	30.4
Length of education		
< 7 years	24	30.4
7–12 years	54	68.4
> 12 years	1	1.3
Smoking habits		
Never smoker	22	27.8
Former smoker	5	6.3
Current smoker	52	65.8
Exercise habits		
Good	7	8.9
Not good	72	91.1
Years of service		
5–10 years	25	31.6
> 10 years	54	68.4
Habits of using personal protective equipment		
Good	18	22.8
Moderate	29	36.7
Poor	32	40.5
Part of work		
Finishing	34	43.0
Molding and casting	45	57.0
Nutritional status		
Underweight	16	20.3
Normal	43	54.4
Overweight	8	10.1
Obese I	10	12.7
Obese II	2	2.5
Cognitive function		
Impairment	55	69.6
Normal	24	30.4

with cognitive impairment. Bivariate analysis showed that urinary aluminum levels, age, education length, and service years were associated with cognitive impairment. Workers with urinary aluminum levels ≥ 45.985 μg/L had a higher 4.921 times risk of experiencing cognitive impairment compared to workers with urinary aluminum levels < 45.985 μg/L (OR = 4.921; 95% CI = 1.038–23.334). Workers under age ≥ 45 years have a 4.324 times higher risk of experiencing cognitive impairment compared to workers younger than 45 years (OR = 4.324; 95% CI = 1.148–16.289). Workers with less than 7 years of formal education have a 16.531 times higher risk of experiencing cognitive disorders than workers with formal education ≥ 7 years (OR = 16.531; 95% CI = 2.081–131.344). In addition, workers with years of service of > 10 years have a 3.231 times higher risk of experiencing cognitive impairment than workers with years of service of 5–10 years (OR = 3.231; 95% CI = 1.173–8.902).

Multivariate analysis

Table 3 shows the multivariate logistic regression analysis for factors associated with cognitive impairment after adjustment by controlling covariates. Urinary aluminum levels and length of education have a statistically significant relationship with cognitive impairment, as shown in Table 3. Workers with urinary aluminum levels ≥ 45.985 μg/L have a 6.550 times higher risk of having cognitive impairment compared to workers with urinary aluminum levels < 45.985 μg/L (adjusted odds ratio (aOR) = 6.550; 95% CI = 1.281–33.499). Workers with less than 7 years of formal education have a 16.885 times higher risk of experiencing cognitive impairment than workers with formal education ≥ 7 years (aOR = 16.885; 95% CI = 2.042–139.604).

DISCUSSION

The median urinary aluminum level was 21.30 μg/L; after being corrected for creatinine, the level was 11.09 μg/g creatinine. Bast-Pettersen et al.[15] reported average urinary aluminum levels of aluminum-exposed workers in primary aluminum mills of 12.6 μg/L (potroom workers) and 9.9 μg/L (foundry workers). Yang et al.[16] reported that the average urinary aluminum level of workers exposed to aluminum in a secondary aluminum smelter was 12.25 μg/L. Deschamps et al.[17] reported that the average urinary aluminum level of workers exposed to aluminum at an aluminum salvage plant was 11.59 μg/L. Meanwhile, Sinczuk-Walczak et al.[10] reported that the average urinary aluminum level of workers exposed to aluminum in the aluminum foundry was 42.9 μg/L. Guo et al.[18] reported that the average urinary aluminum level of workers exposed to aluminum at an aluminum production plant was 29.86 μg/L and 41.79 μg/g creatinine after being corrected for creatinine. From all these reports, urinary aluminum levels in informal aluminum foundry industry workers in this study fall in the range of urinary aluminum levels reported by other studies in workers exposed to aluminum in the aluminum smelting/foundry/production industry.

In this study, it was found that 69.6% of the subjects had cognitive impairment. This rate is much higher than the prevalence rate of mild cognitive impairment (MCI) for retired potroom workers at an aluminum smelting factory in China (18.2%).[11] Cognitive impairment in workers exposed to aluminum in the workplace has also been reported by several studies. Longstreth et al.[8] reported two out of three cases of potroom workers in an aluminum smelting plant with progressive neurological impairment experiencing cognitive deficits. White et

Table 2. Bivariate analysis between urinary aluminum levels and covariates with cognitive impairment

Variables	Cognitive Function				OR	95% CI	*p*
	Impairment		Normal				
	n	%	n	%			
Urinary aluminum level							
≥ 45.985 μg/L	17	89.5	2	10.5	4.921	1.038–23.334	0.031
< 45.985 μg/L	38	63.3	22	36.7	1.00	Ref.	
Corrected urinary aluminum level							
≥ 15.495 μg/g creatinine	24	82.8	5	17.2	2.942	0.960–9.017	0.053
< 15.495 μg/g creatinine	31	62.0	19	38.0	1.00	Ref.	
Age							
≥ 45 years	21	87.5	3	12.5	4.324	1.148–16.289	0.022
< 45 years	34	61.8	21	38.2	1.00	Ref.	
Length of education							
< 7 years	23	95.8	1	4.2	16.531	2.081–131.344	0.001
≥ 7 years	32	58.2	23	41.8	1.00	Ref.	
Smoking habits							
Current smoker	37	71.2	15	28.8	1.233	0.454–3.353	0.681
Never smoker and former smoker	18	66.7	9	33.3	1.00	Ref.	
Exercise habits							
Not good	52	72.2	20	27.8	3.467	0.712–16.886	0.191*
Good	3	42.9	4	57.1	1.00	Ref.	
Years of service							
> 10 years	42	77.8	12	22.2	3.231	1.173–8.902	0.020
5–10 years	13	52.0	12	48.0	1.00	Ref.	
Habits of using personal protective equipment							
Poor	23	71.9	9	28.1	1.198	0.447–3.207	0.719
Good and moderate	32	68.1	15	31.9	1.00	Ref.	
Part of work							
Finishing	24	70.6	10	29.4	1.084	0.411–2.862	0.871
Molding and casting	31	68.9	14	31.1	1.00	Ref.	
Nutritional Status							
Obese	9	75.0	3	25.0	1.370	0.336–5.581	0.747*
Non-obese	46	68.7	21	31.3	1.00	Ref.	

*) Fisher's test; CI, confidence interval; OR, odds ratio; Ref., reference.

Table 3. Multivariate logistic regression of factors associated with cognitive impairment

Variables	B	S.E	Sig	Exp (B)	95% CI
Age	1.237	0.739	0.094	3.446	0.810–14.658
Length of education	2.826	1.078	0.009	16.885	2.042–139.604
Urinary aluminum level	1.879	0.833	0.024	6.550	1.281–33.499
Constant	−0.313	0.351	0.372	0.731	

al.[9] reported of 25 symptomatic aluminum smelting potroom workers, 84% of patients had symptoms of memory impairment and 70–75% of patients showed mild to moderate impairment on memory tests with the Wechsler Memory Scale (WMS) and WMS-Revised. Meanwhile, Sinczuk-Walczak et al.[10] reported that concentration difficulty is one of the symptoms of functional disorders of the nervous system that is most frequently complained of by aluminum production workers who are chronically exposed to aluminum.

Cognitive impairment associated with aluminum exposure in the workplace has been investigated in various studies. Several studies have shown the significance of cognitive impairment in aluminum-exposed workers compared to controls using various measuring tools/instruments. A study on aluminum foundry workers by Polizzi et al.[19] reported a significant difference between the exposure and control groups when tested using cognitive measuring tools, the Mini Mental State Examination (MMSE) and Clock Drawing Test (CDT). Likewise, a study on aluminum recycling workers conducted by Kilburn et al.[20] concluded that aluminum has a role in cognitive impairment, as seen from its significantly lower score on the culture fair test and longer time in finishing Trail Making Test (TMT) and Grooved Pegboard Test among workers exposed to aluminum compared to controls. Similar results were reported in a study by Yang et al.[16] on aluminum smelting workers that showed the impact of aluminum exposure on cognitive impairment in the cognitive domain of memory. A study on retired aluminum smelting potroom workers by Lu et al.[11] also reported significantly lower total MMSE scores and higher MCI rates in the aluminum-exposed group of workers than in controls. Another study on aluminum factory workers by Zawilla et al.[21], using the Addenbrooke's Cognitive Examination-Revised (ACE-R) instrument as a measure of cognitive function, found scores were significantly lower in aluminum-exposed workers than controls on both the total score and the score on each subtest includes memory, verbal fluency, language and visuospatial & perceptual abilities.

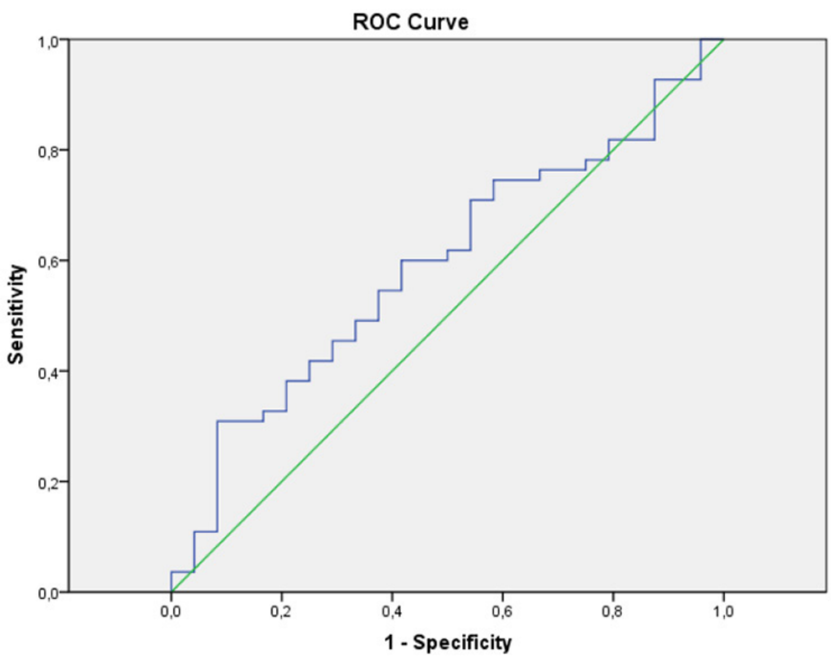

Figure 1. ROC curve for differentiating urinary aluminum levels in workers with cognitive impairment.

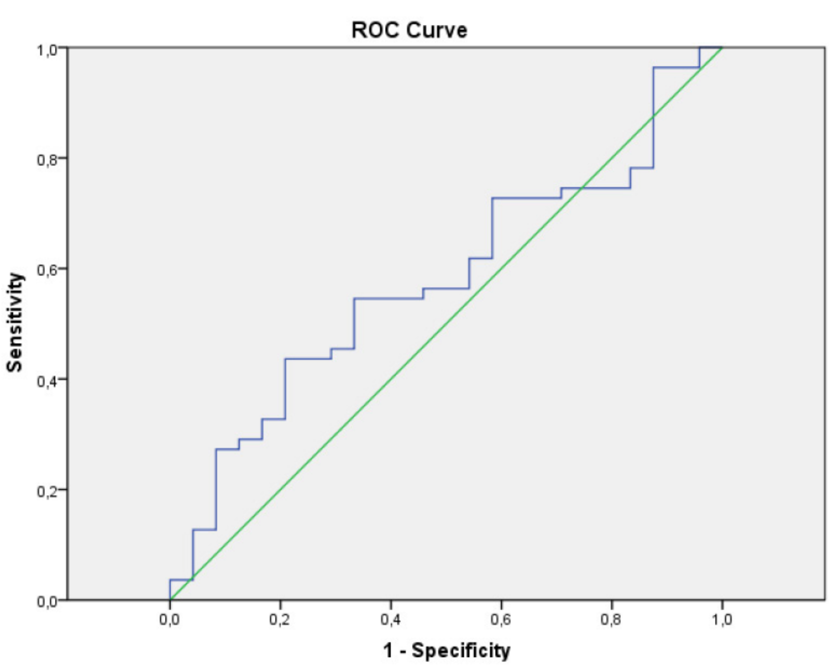

Figure 2. ROC curve for differentiating urinary aluminum level after corrected for creatinine concentration in workers with cognitive impairment.

The findings of this study are also in line with the results of another study on aluminum welders that demonstrated the impact of aluminum on specific cognitive domains. Sjogren et al.[22] reported an association between the symptoms of frequent problems with concentration and aluminum exposure (OR = 2.34; 95% CI = 1.15–4.76). Akila et al.[23] reported the effect of aluminum on cognitive function, especially on tasks that require working memory that have to do with processing visuospatial information. Meanwhile, the results of a study on aluminum welding workers reported by Riihimaki et al.[24] found the effect of aluminum, especially on tasks that require complex attention and information processing in the working memory system and in the analysis and recall of abstract visual patterns. Giorgianni et al.[25] also reported that decreased cognitive responses related to memory and attention were observed in the aluminum-exposed group.

Workers in the informal aluminum foundry industry can potentially be exposed to aluminum dust/fume in the work environment by inhalation. These aluminum particles can reach the brain via systemic pathways and through the nasal cavity via the olfactory nerves.[1,26–28] Furthermore, aluminum crosses the blood-brain barrier through the transferrin-receptor mediated endocytosis mechanism and the system Xc^{-}. It also tends to accumulate for a long time in the brain, potentially leading to a toxic level of aluminum deposit with repeated exposure. It is estimated that the elimination half-life of aluminum in the brain is about 7 years.[26–28]

The mechanism of aluminum neurotoxicity is still unclear. Several studies have tried to reveal the mechanism underlying the neurotoxicity of aluminum that can cause clinical neurological disorders. Oxidative stress, impaired calcium homeostasis, excitotoxicity,

Bali Medical Journal 2022; 11(2): 1034-1040 | doi: 10.15562/bmj.v11i2.3483

altered gene expression, and apoptosis may underlie neurotoxicity due to aluminum exposure.[29] Aluminum neurotoxicity may also occur through impaired neurotransmission[30] and its role as a cholinotoxic agent.[29] Likewise, the effect of aluminum on impaired mitochondrial function[31,32] and its role in causing inflammation have also been proposed as a mechanism that could underlie neurotoxicity due to aluminum exposure.[29,33–35] Another neurotoxicity mechanism is aluminum's role in protein aggregation and conformational changes.[29,36]

Although the mechanism of aluminum neurotoxicity that causes cognitive impairment is still unclear, the findings of this study and previous researchers have shown that aluminum exposure in the workplace can cause cognitive impairment in workers. Therefore, adequate control of aluminum exposure is necessary for preventing cognitive impairment in workers exposed to aluminum, either technically, administratively or with personal protective equipment.

CONCLUSIONS

Higher risk of having cognitive impairment was found in workers with urinary aluminum levels ≥ 45.985 µg/L and formal education of fewer than 7 years. Thus, bio-monitoring of the workers' urinary aluminum levels must be conducted regularly to prevent cognitive impairment due to long-term aluminum exposure in the workplace.

ACKNOWLEDGEMENTS

The researcher would like to thank the Faculty of Medicine, Universitas Andalas, which has funded this research.

DISCLOSURE

Conflict of interest

All authors declare that there is no conflict of interest regarding this article.

Funding

This research was funded by DIPA PNBP Faculty of Medicine, Universitas Andalas, Ministry of Research, Technology and Higher Education with Research Contract Number: 104/BBPT/PNP/FK-UNAND-2019.

Author contribution

All authors contributed equally in writing this article.

Ethics approval

This study has been approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia, with reference number KE/FK/0213/EC/2018.

REFERENCES

1. ATSDR. Toxicological Profile for Aluminum. Atlanta, Georgia: U.S. Department of Health and Human Services, Public Health Service; 2008.
2. Frank WB, Haupin WE, Vogt H, Bruno M, Thonstad J, Dawless RK, et al. Aluminum. In: Ullmann's Encyclopedia of Industrial Chemistry. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA; 2009. Available from: http://dx.doi.org/10.1002/14356007.a01_459.pub2
3. Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, et al. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. J Toxicol Environ Heal Part B. 2007;10(sup1):1–269. Available from: http://dx.doi.org/10.1080/10937400701597766
4. King JF. Aluminium products. In: The Aluminium Industry. Elsevier; 2001. p. 6–36. Available from: http://dx.doi.org/10.1016/B978-1-85573-151-6.50012-4
5. Mgonja CT. A review on effects of hazards in foundries to workers and environment. IJISET-International J Innov Sci Eng Technol. 2017;4(6):326–34.
6. Willhite CC, Karyakina NA, Yokel RA, Yenugadhati N, Wisniewski TM, Arnold IMF, et al. Systematic review of potential health risks posed by pharmaceutical, occupational and consumer exposures to metallic and nanoscale aluminum, aluminum oxides, aluminum hydroxide and its soluble salts. Crit Rev Toxicol. 2014;44(sup4):1–80. Available from: http://dx.doi.org/10.3109/10408444.2014.934439
7. Meyer-Baron M, Schäper M, Knapp G, van Thriel C. Occupational aluminum exposure: evidence in support of its neurobehavioral impact. Neurotoxicology. 2007;28(6):1068–78. Available from: http://dx.doi.org/10.1016/j.neuro.2007.07.001
8. Longstreth WT, Rosenstock L, Heyer NJ. Potroom palsy?: Neurologic disorder in three aluminum smelter workers. Arch Intern Med. 1985;145(11):1972–5. Available from: http://dx.doi.org/10.1001/archinte.1985.00360110042011
9. White DM, Longstreth WT, Rosenstock L, Claypoole KH, Brodkin CA, Townes BD. Neurologic syndrome in 25 workers from an aluminum smelting plant. Arch Intern Med. 1992;152(7):1443–8. Available from: http://dx.doi.org/10.1001/archinte.1992.00400190071014
10. Sińczuk-Walczak H, Szymczak M, Raźniewska G, Matczak W, Szymczak W. Effects of occupational exposure to aluminum on nervous system: clinical and electroencephalographic findings. Int J Occup Med Environ Health. 2003;16(4):301–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14964639
11. Lu X, Liang R, Jia Z, Wang H, Pan B, Zhang Q, et al. Cognitive disorders and tau-protein expression among retired aluminum smelting workers. J Occup Environ Med. 2014;56(2):155–60. Available from: http://dx.doi.org/10.1097/JOM.0000000000000100
12. CDC. Laboratory Procedure Manual. Multi-Element in urine. NHANES 2011–2012. 2012.
13. Husein N, Lumempouw S, Ramli Y, Herqutanto. Uji validitas dan reliabilitas Montreal Cognitive Assesment versi Indonesia (MoCA-Ina) untuk skrining gangguan fungsi kognitif. Neurona. 2010;27(4):15–22.
14. World Health Organization. Regional Office for the Western Pacific. The AsiaPacific perspective: Redefining obesity and its treatment. Sydney: Health Communications Australia; 2000.
15. Bast-Pettersen R, Drabløs PA, Goffeng LO, Thomassen Y, Torres CG. Neuropsychological deficit among elderly workers in aluminum production. Am J Ind Med. 1994;25(5):649–62. Available from: http://dx.doi.org/10.1002/ajim.4700250505
16. Yang HG, Lee BL, Liang YX, Zheng YX, Ong CN. The effects of exposure to aluminium on neurobehavioural function and dopaminergic metabolism. Int J Environ Health Res. 1998;8(2):101–10. Available from: http://dx.doi.org/10.1080/09603129873534
17. Deschamps FJ, Lesage FX, Chobriat J, Py N, Novella JL. Exposure Risk Assessment in an Aluminium Salvage Plant. J Occup Environ Med. 2009;51(11):1267–74. Available from: http://dx.doi.org/10.1097/JOM.0b013e3181bc2d35
18. Guo G, Ma H, Wang X, Liang Y. Age-dependent differences of neurobehavioural function among workers exposed to aluminium. J Environ Med. 1999;1(2):81–5. Available from: http://dx.doi.org/10.1002/(SICI)1099-1301(199904/06)1:2%3C81::AID-JEM17%3E3.0.CO;2-W
19. Polizzi S, Pira E, Ferrara M, Bugiani M, Papaleo A, Albera R, et al. Neurotoxic effects of aluminium among foundry workers and Alzheimer's disease. Neurotoxicology. 2002;23(6):761–74. Available from: http://dx.doi.org/10.1016/S0161-813X(02)00097-9
20. Kilburn KH. Neurobehavioral impairment and symptoms associated with aluminum remelting. Arch Environ Heal An Int J. 1998;53(5):329–35. Available from: http://dx.doi.org/10.1080/00039899809605717
21. Zawilla NH, Taha FM, Kishk NA, Farahat SA, Farghaly M, Hussein M. Occupational exposure to aluminum and its amyloidogenic link with cognitive functions. J Inorg Biochem. 2014;139:57–64. Available from: http://dx.doi.org/10.1016/j.jinorgbio.2014.06.003
22. Sjogren B, Gustavsson P, Hogstedt C. Neuropsychiatric symptoms among welders

exposed to neurotoxic metals. Occup Environ Med. 1990;47(10):704–7. Available from: http://dx.doi.org/10.1136/oem.47.10.704
23. Akila R, Stollery BT, Riihimaki V. Decrements in cognitive performance in metal inert gas welders exposed to aluminium. Occup Environ Med. 1999;56(9):632–9. Available from: http://dx.doi.org/10.1136/oem.56.9.632
24. Riihimäki V, Hänninen H, Akila R, Kovala T, Kuosma E, Paakkulainen H, et al. Body burden of aluminum in relation to central nervous system function among metal inert-gas welders. Scand J Work Environ Health. 2000;26(2):118–30. Available from: http://dx.doi.org/10.5271/sjweh.521
25. Giorgianni CM, D'Arrigo G, Brecciaroli R, Abbate A, Spatari G, Tringali MA, et al. Neurocognitive effects in welders exposed to aluminium. Toxicol Ind Health. 2014;30(4):347–56. Available from: http://dx.doi.org/10.1177/0748233712456062
26. Yokel RA. The toxicology of aluminum in the brain: a review. In: NeuroToxicology. 2000. p. 813–28. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11130287
27. Yokel RA, McNamara PJ. Aluminium toxicokinetics: an updated minireview. Pharmacol Toxicol. 2001;88(4):159–67. Available from: https://dx.doi.org/10.1111/j.1600-0773.2001.880401.x
28. Yokel RA. Blood-brain barrier flux of aluminum, manganese, iron and other metals suspected to contribute to metal-induced neurodegeneration. Miu AC, Benga O, editors. J Alzheimer's Dis. 2006;10(2–3):223–53. Available from: http://dx.doi.org/10.3233/JAD-2006-102-309
29. Maya S, Prakash T, Madhu K Das, Goli D. Multifaceted effects of aluminium in neurodegenerative diseases: a review. Biomed Pharmacother. 2016;83:746–54. Available from: http://dx.doi.org/10.1016/j.biopha.2016.07.035
30. Verstraeten S V., Aimo L, Oteiza PI. Aluminium and lead: molecular mechanisms of brain toxicity. Arch Toxicol. 2008;82(11):789–802. Available from: http://dx.doi.org/10.1007/s00204-008-0345-3
31. Kumar V, Gill KD. Aluminium neurotoxicity: neurobehavioural and oxidative aspects. Arch Toxicol. 2009;83(11):965–78. Available from: http://dx.doi.org/10.1007/s00204-009-0455-6
32. Kumar V, Gill KD. Oxidative stress and mitochondrial dysfunction in aluminum neurotoxicity and its amelioration: a review. Neurotoxicology. 2014;41:154–66. Available from: http://dx.doi.org/10.1016/j.neuro.2014.02.004
33. Bondy SC. The neurotoxicity of environmental aluminum is still an issue. Neurotoxicology. 2010;31(5):575–81. Available from: http://dx.doi.org/10.1016/j.neuro.2010.05.009
34. Bondy SC. Prolonged exposure to low levels of aluminum leads to changes associated with brain aging and neurodegeneration. Toxicology. 2014;315:1–7. Available from: http://dx.doi.org/10.1016/j.tox.2013.10.008
35. Bondy SC. Low levels of aluminum can lead to behavioral and morphological changes associated with Alzheimer's disease and age-related neurodegeneration. Neurotoxicology. 2016;52:222–9. Available from: http://dx.doi.org/10.1016/j.neuro.2015.12.002
36. Kawahara M. Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases. J Alzheimer's Dis. 2005;8(2):171–82. Available from: http://dx.doi.org/10.3233/JAD-2005-8210