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High Serum Lead Levels Increase the Incidence of Cognitive Impairment of Public Fueling Station Operators

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Abstract

BACKGROUND: Air pollution due to lead contained in motor vehicle fuel is inhaled for a long period causing cognitive impairment. Cognitive disorders in general fuel station operators are found in developing countries as a negative impact of environmental pollution.

AIM: This study aims to find out that high levels of lead in the blood increase the risk of cognitive impairment in operators of Public Fuel Filling Stations.

METHODS: This was a case-control study design to determine high lead levels in the blood increasing the risk of cognitive impairment in operators of General Fuel Filling Stations. There were 76 study subjects consisting of 38 case groups and 38 control groups.

RESULTS: Obtained lead levels of all research subjects in normal criteria (1.1-5.58 µg/dL). We used MoCA-Ina (a validated Indonesian version of MoCA questionnaire) to evaluate the cognitive function. High lead levels in the blood in the case group were 28 subjects (66.7%) and 14 subjects (33.7%) in the control group. Factors that significantly affected the occurrence of cognitive disorders are work periods of more than 3 years, which are 4 times higher risk of experiencing cognitive impairment (p = 0.021).

CONCLUSION: High lead levels in the blood have a 6 times greater risk of cognitive impairment than subjects with not high blood lead levels and work periods of more than 3 years have a risk of 6 times greater cognitive impairment.

Introduction

Some negative impacts on the environment and health are reported from the industrial sector. One effect of pollution is due to motorised vehicles. Cognitive impairment is a disorder of rational thought processes including the process of remembering, judging, orientation, perception and also paying attention. Disorders of cognitive function are often separated from our observations.

The Public Fuel Station is thought to be one of the places where air pollution occurs from vehicles using fuel which contains heavy metal components such as lead or Pb (plumbum) which are released as lead oxide, which is then inhaled by humans and causes the cognitive impairment. Symptoms of lead toxicity usually correlate with blood lead levels of 25–50 µg/dL in children and 40–60 µg/dL in adults [1]. The policy of standard quality specifications in the use of gasoline types does not fully eliminate the use of lead in 3 types of gasoline in developing countries. Gasoline type 88 (premium) consisting of 88 unleaded types of gasoline with a maximum lead level of 0.013 g/L and for 88 leaded gasoline types with a maximum lead level of 0.3 g/L. Gasoline type 92 (pertamax) with a maximum lead level of 0.013 g/L and gasoline type 95 (pertamax plus) with a maximum lead level of < 0.013 g/L [2].

This toxicity is a result of the ability of lead to replace Ca^{2+}, Mg^{2+}, Fe^{2+}, and Na^{+} which subsequently affects the basic biological processes of the body, replacing calcium ions, so that it can cross the blood-brain barrier. Lead accumulates and damages immature astroglia cells, interferes with sodium ion concentration and increases the action potential cause nerve cells damage and cognitive impairment [3], [4]. The lead that crosses the blood-brain barrier causes various neurological disorders such as behaviour changes, mental retardation, disorders in the prefrontal cortex, hippocampus and cerebellum [5], [6]. Cognitive impairment due to lead poisoning begins with a disruption of heme synthesis which inhibits the synthesis of aminolevulinic acid dehydratase (ALAD) in the cytoplasm and ferrochelatase (heme synthetase and protohemeferrolyase) in mitochondria. There is an increase in the initial aminolevulinic acid (ALA) urine, followed by an increase in erythrocyte protoporphyrin [7]. Inflammation results in disruption of the blood-brain barrier system and the nervous system as a whole. ALA enters and accumulates in the nerve tissue cause oxidative stress. The discovery of ALA in the nervous system is a neurotoxin and causes hydroelectrolyte changes and damage to nerve cells/apoptosis [8].

A cognitive function is an act of thinking, remembering, learning, and using language. Cognitive functions include attention, memory, consideration, and problem-solving abilities, and executive abilities such as planning, and evaluating [9]. There are several screening instruments for cognitive function disorders such as the Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT), Montreal Cognitive Assessment (MoCA). We used the MoCA-Ina questionnaire (Indonesian version of Montreal Cognitive Assesment questionnaire) which evaluate the visuospatial, naming, memory, attention, language, abstraction, delayed recall and orientation. The MoCA-Ina Kappa value is 0.820 which shows that this questionnaire has a very good inter-rater agreement value [10].

This study aims to find out that high levels of lead in the blood increase the risk of cognitive impairment in operators of Public Fuel Filling Stations.

Methods

The study was conducted at the South Denpasar regional gas station from December 2017 to January 2018. All research subjects were gas station operators in the city of South Denpasar who fulfilled the inclusion and exclusion criteria, then performed cognitive function assessment using the MoCA-Ina questionnaire and blood sampling for lead level for each study subjects

Observational, analytical research method using a case-control design to determine high lead levels in the blood increases the risk of cognitive impairment in gas station operators. Measurements were made using the AAS method (Atomic Absorption Spectrophotometry) at Prodia Laboratory. Values of blood lead levels are grouped into high and not high levels of lead which are distinguished by the results of Receiver Operating Characteristic (ROC) procedure statistics and Area Under Curve (AUC). Data were presented on a nominal categorical scale, high lead levels when ≥ 2.45 µg/dL and not high lead levels < 2.45 µg/dL. Multivariate analysis was performed to determine the risk factors for cognitive function disorders such as working period which is categorised into a work period of 1-3 years and a work period of more than 3 years, and the use of masks as protective devices while working.

The data were analysed statistically by the comparative hypothesis test of 2 unpaired groups, namely bivariate analysis using Chi-square because the independent variables and dependent variables were nominal. If the observed/expected value is < 5, the Fisher exact test is used, and the multivariate analysis uses logistic regression analysis because the dependent variable is the nominal categorical variable. The level of significance is expressed as $p < 0.05$ with a 95% confidence interval.

Results

The research subjects were gas station operators in the city of South Denpasar that met the inclusion and exclusion criteria, a total of 76 subjects. The study subjects were divided into cognitive impairment (cases) and did not experience cognitive impairment (control). The results of examination of blood lead levels in all samples included in the normal criteria range from 1.1 to 5.58 µg/dL, with a mean ± SD of 2.56 ± 0.86 with 95% CI 2.35-2.749 (normal value less than 10 µg/dl). The characteristics of the research subjects consist of several variables summarised in Table 1 below.

Table 1: Characteristics of Subjects

Variable		Cognitive Impairment n (%)	No Cognitive Impairment n (%)	p-value
Age	Adult	20 (58.8)	14 (41.2)	0.166
	Adolesence	18 (42.9)	24 (57.1)	
Sex	Men	10 (45.5)	12 (54.5)	0.613
	Women	28 (51.9)	26 (48.1)	
Working period	≥ 3 year	16 (72.7)	6 (27.3)	0.011
	1 - 3 year	22 (40.7)	32 (59.3)	
Gloves wearing	Without going	38 (50)	38 (50)	
Masker wearing	Wearing masker not routinely	29 (52.7)	26 (47.3)	0.442
	Wearing masker routinely	9 (42.9)	12 (57.1)	
Blood lead levels	High	28 (66.7)	14 (33.3)	0.001
	Not High	10 (29.4)	24 (70.6)	

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

The overall lead blood level of the research subjects in the normal range, then performed the statistical method of the ROC and AUC procedure to determine the ability to examine blood lead levels that cause cognitive impairment, AUC value was 83% with 95% CI ranging from 73.5-92.6%. Statistically, this

AUC value of 74.9% shows the strength of a relatively high diagnostic value. The results of the ROC coordinates indicate that the cut off level of the lead of 2.45 μg/dL used in this study had a sensitivity value of 73.7% and a specificity of 63.2%. Figure 1 below shows the results of the ROC and AUC.

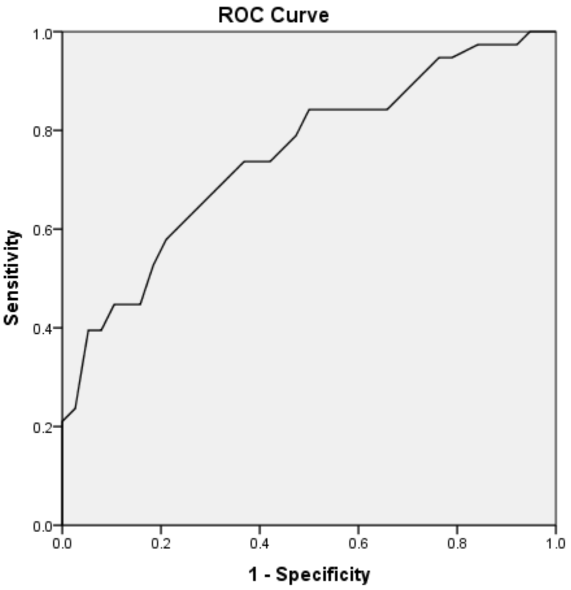

Figure 1: Results of the ROC procedure for lead levels against cognitive impairment

Research data on blood lead levels were grouped into two, namely high blood lead levels (≥ 2.45 μg/dL) and lead levels not high in the blood (< 2.45 μg/dL).

Bivariate analysis was performed to determine the relationship between high lead levels in the blood (independent variables) and cognitive function disorders (dependent variables), the hypothesis test used was risk estimate and Chi-square test. It was found that high blood lead levels had a higher risk of cognitive impairment than subjects with not high lead levels (OR 4.80; 95% CI 1.8-12.75; p < 0.001), shown in Table 2.

Table 2: Bivariate analysis of lead levels in the blood with cognitive impairment

Serum Lead Level	MoCA-Ina		Total n (%)	OR (95% CI)	p-value
	Cognitive Impairment n (%)	No Cognitive Impairment n (%)			
High	28 (66.7)	14 (33.3)	42 (100)	4,80	0,001
Not High	10 (29.4)	24 (70.6)	34 (100)	(1.80-12.75)	

*OR = odds ratio; CI = confidence interval; MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Bivariate analysis was performed to determine the relationship of age (independent variable) with cognitive impairment (dependent variable). Based on Pearson Chi-Square linear by linear data analysis for trends, p = 0,166, there is a significant relationship between age and cognitive impairment (OR 1,905; 95% CI 0,762-4,764), shown in Table 3 below.

Table 3: The relationship between adolescence and adulthood to cognitive impairment

Age	MoCA-Ina		Total n (%)	OR (95% CI)	p-value
	Cognitive Impairment n (%)	No Cognitive Impairment n (%)			
Adult	20 (58,8)	14 (41,2)	34 (100)	1,905	0,166
Adolesence	18 (42,9)	24 (57,1)	42 (100)	0,762-4,764	

*OR = odds ratio; CI = confidence interval; MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Gender did not affect the occurrence of cognitive impairment (p = 0.613), and cognitive impairment increased linearly with age (p = 0.011). The results of the analysis are shown in Table 4.

Table 4: Effect of sex and working period of gas station operators on the occurrence of cognitive disorders

Variable	MoCA-Ina		Total n (%)	OR (95% CI)	p-value
	Cognitive Impairment n (%)	No Cognitive Impairment n (%)			
Men	10 (45.5)	12 (54.4)	22 (100)	0.774	0.613
Women	28 (51.9)	26 (48.1)	54 (100)	(0.286-2.092)	
Working period > 3 years	16 (72.7)	6 (27.3)	22 (100)		
Working period 1-3 years	22 (40.7)	32 (59.3)	54 (100)	3,879 (1.312-11.467)	0.011

*OR = odds ratio; CI = confidence interval; MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

It was found that the use of masks when working did not have a statistically significant effect on the incidence of cognitive disorders. This indicates that the use of personal protective equipment, especially masks, does not play a protective role in the incidence of cognitive disorders (p = 0.442). The results of the analysis are shown in Table 5 below.

Table 5: Effects of mask use when working on cognitive impairments

Masker Wearing	MoCA-Ina		Total n (%)	OR (95% CI)	p-value
	Cognitive Impairment n (%)	No Cognitive Impairment n (%)			
Wearing masker not routinely	29 (52.7)	26 (47.3)	55 (100)	1.487 (0.540-4.097)	0.442
Wearing masker routinely	9 (42.9)	12 (57.1)	21 (100)		

*OR = odds ratio; CI = confidence interval; MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

The results of the bivariate analysis showed that the age, working period and blood lead levels were statistically significant for the incidence of cognitive impairment and the working period variable statistically with a value of < 0.25. The results of variable high blood lead levels (p = 0.001) and the working period (0.021) were statistically significant. Table 6 below shows the results of the analysis.

Table 6: Multinomial logistic regression on the variables of age, working period and lead levels in the blood with the incidence of cognitive disorders

	Coefficient	S.E.	Wald	DF	OR 95% CI	p-value
Constant	-1.962	0.632	9.639	1		
Adult	-0.151	0.645	0.055	1	0.860 (0.243–3.042)	0.814
Working period >3 years	1.742	0.756	5.309	1	5,707 (1.297-25.112)	0.021
High Lead Serum level	1.792	0.552	10.546	1	6.00 (2.035-17.695)	0.001

*OR = odds ratio; CI = confidence interval; S.E = standard error; DF = degree of freedom; MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Based on the equations above, high lead levels in the blood as a risk factor for cognitive impairment are 6 times greater than not high blood lead levels and work periods > 3 years as a risk factor for cognitive impairment 6 times greater than the working period of 1-3 year independently.

Discussion

The majority of the research subjects were in the teenage age category (55.3%), this was by the demographic characteristics of Indonesia, the majority of which were dominated by productive age. Female sex (71.1%) was obtained more than men because in this study many men were excluded because of active smoking. The working period is obtained for 1-3 years (71.1%) more than the other working period; this is due to several new gas stations standing around 1-5 years. In the case group (52.7%) and controls (47.3%) who were not routinely using masks while working for the past 1 month, the data shows that there is still a lack of discipline in the use of masks when working, caused by a lack of comfort when using masks.

This result is by previous studies which stated that the use of Personal Protective Equipment (PPE) was very influential and able to protect themselves from lead exposure ($p = 0.038$). The duration of working for 1-3 years was found to be the highest in the case group (71.1%); statistically, the duration of work affected the incidence of cognitive disorders.

The results of this study indicate that gender does not affect the occurrence of cognitive dysfunction, and there is a tendency for an increase in the incidence of cognitive impairment with age, so it was assumed that the incidence of cognitive impairment increases with age, regardless of factors in blood lead levels. This is probably because most of the age in this study sample tended to be in the age of adolescents so that statistically the apparent value was not significant with the opinions of previous studies. The results of this study found that the use of masks when working did not statistically affect the incidence of cognitive disorders, this indicates that the use of personal protective equipment, especially type 2 ply masks, does not play a protective role in the incidence of cognitive disorders.

Obtained subjects with high lead levels in the blood had a much greater risk of suffering cognitive impairment compared to subjects with not high blood lead levels. Lead can cause prominent abnormalities in the nervous system, in the form of slowness in action, decreased function of memory and concentration, depression, headaches, vertigo (dizziness), tremor (abnormal movement with rapid frequency), stupor (decreased consciousness), coma, convulsions, psychomotor disorders, mild intelligence disorders and personality changes. While the alkyl lead forms a special form of abnormalities in the central nervous system, with manifestations including insomnia, nightmares, and in severe cases can be schizophrenic. The strength of this study is that not many researchers have examined lead levels as a risk factor for cognitive impairment in gas station operators in Indonesia. This study cannot determine the length of exposure to lead that causes cognitive impairment and cannot determine the increase in minimum lead levels that cause cognitive impairment. Further studies are needed to determine these variables.

In conclusion, high lead levels in the blood have a 6 times greater risk of cognitive impairment compared to subjects with not high blood lead levels and work periods > 3 years have a6 times greater risk of experiencing cognitive disorders compared to 1-3 years of the work period. Blood lead levels and years of service are independent risk factors for the occurrence of cognitive impairments in oil refuelling station operators.

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