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## RESEARCH ARTICLE

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# Correlation of Carboxyhemoglobin Level with Alanine Aminotransferase Enzyme Level in Satay Traders

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## ABSTRACT

Carbon monoxide is a hazardous pollutant that results from incomplete combustion. Satay vendors are at risk because their daily activities interact with smoke from burning charcoal and other hazardous pollutants in the work environment. The more CO that is inhaled, it will form COHb in the body in large quantities which can cause hypoxia of liver tissue. This study aimed to determine the correlation of carboxyhemoglobin levels with alanin aminotransferase levels in satay traders. This was an analytic observational study with a cross-sectional approach. The population of this study were satay vendors who traded near the highway in the Gubeng Subdistrict area of Surabaya City with a total sample size of 20 which was determined by purposive sampling. Data collection used primary data by examining test materials at the Clinical Toxicology Laboratory of the Department of Medical Laboratory Technology of Poltekkes Kemenkes Surabaya and the Bakti Analysis Laboratory in April - May 2023. The results of the examination of carboxyhemoglobin levels and alanin aminotransferase levels showed that all samples were below the normal threshold with an average COHb of 0.91% and an average alanin aminotransferase level of 40.0 U/L. From the Spearman correlation test, the p-value = 0.015 and r = 0.536. It can be concluded that there is a high positive correlation between carboxyhemoglobin levels and alanin aminotransferase levels in satay traders.

**Keywords:** carboxyhemoglobin level; alanin aminotransferase level; satay vendors

## INTRODUCTION

Air pollution in Indonesia is 70% caused by motor vehicle emissions, then the rest comes from the industrial sector and household waste. According to research conducted by<sup>(1)</sup> entitled "Analysis of Environmental Health Risks of Carbon Monoxide (CO) Exposure to Satay Traders in Palembang" explains that one of the groups most at risk due to air pollution, especially exposure to carbon monoxide gas, is satay traders. Satay vendors usually use charcoal fuel to burn their satay on the grill. However, wood charcoal and other types of charcoal can cause harmful pollutants in the form of particulates, polyaromatic hydrocarbons (PAHs), volatile organic compounds, carbon monoxide (CO), heavy metals, and other toxic compounds.

Based on its source, CO gas is categorized into two: natural sources and artificial sources. Natural sources usually come from volcanic activity, electric shocks from lightning, iron oxidation in the atmosphere, and others. While many artificial sources come from human activities such as smoking, industry, transportation, combustion with fuel oil and charcoal burning.<sup>(2)</sup> Based on the Regulation of the Ministry of Health of the Republic of Indonesia No.70 of 2016 concerning Standards and Requirements for Industrial Work Environment Health states that the reference value for the concentration of carbon monoxide chemicals in the blood is 3.5% and the threshold value for air carbon monoxide in the workplace is 30 ppm. OSHA (Occupational Safety and Health Administration) states that the allowable CO exposure limit is 35 ppm for a working time of 8 hours/day.<sup>(3)</sup>

When a satay vendor inhales carbon monoxide (CO), the CO gas enters the respiratory tract into the alveoli of the lungs and then replaces oxygen (O<sub>2</sub>) to bind with hemoglobin (Hb) to form carboxyhemoglobin (COHb). This bond occurs because Hb has the ability to bind CO more strongly than O<sub>2</sub>. COHb will follow the bloodstream and interfere with the availability of oxygen needed by body tissues. The dangers of this toxic compound include causing health problems such as myocarditis, pancreatitis, pulmonary edema, bronchopneumonia, albuminuria, kidney damage, hepatomegaly, and liver damage.<sup>(4)</sup>

The main cause of death in many countries is carbon monoxide poisoning through tissue hypoxia which affects many organs.<sup>(5)</sup> This has been proven in<sup>(4)</sup> entitled "Duration of Carbon Monoxide Exposure to Alanine Aminotransferase Enzyme Profile in Tofu Factory Workers" says that if a person is exposed to carbon monoxide continuously, it will interfere with health, especially liver health because the liver organ has a high capacity to bind chemicals and toxicants so that chemicals are concentrated in the liver organ compared to other organs.

In the human body, the liver plays a role in digestion, glucose, protein and fat metabolism, bile secretion, and detoxification of toxins in the body. The detoxification process is done by neutralizing the toxin substances, which converts all toxic substances into materials that do not harm the body. One of the toxin substances that can trigger detoxification by the liver is carbon monoxide.<sup>(6)</sup> Prior research entitled "The Effect of Long Exposure to CO on alanin aminotransferase (ALT) levels" explains that long exposure to CO on ALT levels affects the occurrence of damage to liver organ function. Protection of liver cell damage by a toxic substance can be assessed based on its ability to affect various parameters, one of which is to suppress the increase in activity of aminotransaminase enzymes.<sup>(7)</sup>

One of the tests that can be used to determine the level of liver cell damage is the measurement of aspartate aminotransferase (AST) and ALT levels. ALT is localized in the liver in higher concentrations, while AST is localized in several tissues such as heart, skeletal muscle, kidney, brain and liver. In liver cell disorders, cytoplasmic enzymes especially ALT enzymes will circulate freely in the circulatory system and collect into the serum. Therefore, ALT enzyme activity is more specific to liver cell damage so that in mild degrees it can be used as a test to determine the presence of liver function disorders.<sup>(7)</sup>

In connection with the possible impact of carbon monoxide on the liver, research is needed regarding the correlation of carboxyhemoglobin levels with alanine aminotransferase enzyme levels in satay traders. The aim of this study was to determine the correlation between carboxyhemoglobin levels and alanine aminotransferase enzyme levels.

### METHODS

This type of research was analytical observational with a cross-sectional approach. The research was conducted in April - May 2023 with the measurement of carboxyhemoglobin levels carried out at the Clinical Toxicology Laboratory, Department of Medical Laboratory Technology, Poltekkes Kemenkes Surabaya, while the measurement of ALT levels was carried out at the Bakti Analisis Laboratory, Surabaya City.

The population in this study were satay traders who traded near the highway in Gubeng Subdistrict, Surabaya City as many as 20 samples were determined by purposive sampling technique with the following criteria: working period as a satay trader has been more than 10 years, not currently or not having a history of liver disease or infected with hepatitis virus, not consuming alcohol or drugs that induce liver damage.

Examination of carboxyhemoglobin levels using the conway diffusion cell method with a genesys 150 uv-vis spectrophotometer and examination of ALT levels using the enzymatic kinetic method according to IFCC with the BS-200 Chemistry Analyzer tool. The data collection technique used primary data which was first conducted interviews to obtain samples that fit the research criteria, then measured carboxyhemoglobin levels and ALT levels to obtain research data which were then statistically analyzed with the Spearman correlation test using the IBM SPSS 22.0 application program.

### RESULTS

The laboratory examination was successfully carried out according to previous planning, and the results are presented in the following tables, according to each type of examination.

Table 1. Distribution of COHb and ALT level examination results

Sample	COHb levels (%)		ALT levels (U/L)	
	Normal	Abormal	Normal	Abormal
R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20	100% (20 sample)	-	75% (15 sample)	25% (5 sample)

Table 2. Distribution of respondent characteristics based on age

No	Age	Frequency	Percentage
1	17 – 25	1	5
2	26 – 35	5	25
3	36 – 45	7	35
4	46 – 55	4	20
5	56 – 65	3	15

Based on table 1, the results of the examination of carboxyhemoglobin levels with 100% normal levels as many as 20 samples, while the results of the examination of ALT levels obtained 75% normal levels as many as 15 samples and 25% abnormal levels as many as 5 samples.

Based on table 2, most of the respondents in this study were from the age group 35-45 years (35%) with the youngest age of 23 years and the oldest age of 60 years.

Table 3. Distribution of respondent characteristics by working mass

No	Length of work per day	Frequency	Percentage
1	≤8 hours	17	85
2	>8 hours	3	15

Based on table 3, most respondents work ≤8 hours per day (85%). The results of the examination of COHb levels in satay traders who work for ≤8 hours per day have an average COHb level of 0.89% while satay traders who work for >8 hours per day have an average COHb level of 1.0%.

Based on table 4, it is known that most of the respondents' working period as satay traders is 10-15 years (40%). The results of the examination of COHb levels in satay traders with a working period of 10-15 years had an average COHb level of 0.89%, satay traders who worked for 16-20 years had an average COHb level of 0.92%, satay traders who worked for 21-25 years had an average COHb level of 0.92%, and satay traders who worked for 26-30 years had an average COHb level of 0.94%.

Table 4. Distribution of respondent characteristics by working mass

No	Tenure (years)	Frequency	Percentage
1	10 – 15	8	40
2	16 – 20	3	15
3	21 – 25	6	30
4	26 – 30	3	15

Table 5. Distribution of respondent characteristics by type of smoker

No	Type of Smoker	Frequency	Percentage
1	passive smokers	10	50
2	active smokers	10	50

Table 6. Distribution of respondent characteristics by smoker category

No	Smoker category	Frequency	Percentage
1	Light smokers	5	50
2	Moderate smokers	5	50
3	Heavy smokers	0	0
4	Very heavy smoker	0	0

Table 7. Distribution of respondent characteristics by mask use

No	Mask use	Frequency	Percentage
1	Not using a mask	14	50
2	using a mask	6	50

Based on tables 5 and 6, it was known that some of the respondents (50%) are active smokers with 50% categorized as moderate smokers. Based on table 7, it was known that 70% of respondents do not wear masks while working.

### DISCUSSION

All respondents were in the productive age category, as according to Law No. 13 of 2003 that productive age ranges from 15-64 years, while non-productive age is 0-14 years and >64 years. Someone who is at a productive age has the ability to work well when compared to non-productive age. This is supported by the results of the questionnaire which showed no symptoms of CO poisoning in respondents when working, such as feeling dizzy, nauseous, and shortness of breath.<sup>(8)</sup>

From the results of the examination of COHb levels, respondents aged 23 years had higher COHb levels. This research is not in line with the prior research<sup>(9)</sup> which states that with increasing age, COHb levels are getting higher. This can be caused by several factors, including nutritional status and lack of sleep. According to Mulia in (10) someone with good nutrition will have better capacity and endurance. One way to determine nutritional status in the adult age group >18 years is based on the body mass index (BMI) indicator.<sup>(11)</sup> Based on the results of the interview, it is known that the respondent has a BMI with an overweight classification. In addition,

respondents also have a habit of sleeping 3-4 hours per day, meaning that respondents miss the sleep time that adult humans should need, which is 7-8 hours per day. During sleep, body cells work more optimally to improve the immune system and repair damaged cells.<sup>(12)</sup> Lack of sleep can disrupt the body's metabolism by triggering oxidative stress, which is an imbalance in producing antioxidants and free radicals in the body.<sup>(13)</sup> There was no significant relationship between age and respondents' blood COHb, so it cannot be confirmed that someone who is getting older has higher COHb levels.<sup>(14)</sup>

Most respondents work  $\leq 8$  hours per day (85%). The results of the examination of COHb levels in satay traders who work for  $\leq 8$  hours per day have an average COHb level of 0.89% while satay traders who work for  $> 8$  hours per day have an average COHb level of 1.0%. These results are in line with prior research which shows that the longer workers in the basement who are daily exposed to CO gas from motor vehicle exhaust fumes, the higher the COHb levels in the blood.<sup>(15)</sup>

It is known that most of the respondents' working period as satay traders is 10-15 years (40%). The results of the examination of COHb levels in satay traders with a working period of 10-15 years had an average COHb level of 0.89%, satay traders who worked for 16-20 years had an average COHb level of 0.92%, satay traders who worked for 21-25 years had an average COHb level of 0.92%, and satay traders who worked for 26-30 years had an average COHb level of 0.94%. The concentration of COHb in the blood is directly proportional to the inhaled air CO. As the research he has done regarding the environmental health risk analysis (ARKL) of carbon monoxide exposure in the satay burning area that uses charcoal fuel in 58 samples, with the results of the analysis stating safe conditions, but it is predicted that it will cause health problems in traders after the 10th year of exposure which is influenced by the increase in exposure time. Repeated exposure to CO gas at certain levels can lead to an adaptation mechanism. CO gas inhaled every day will enter the body binds to hemoglobin and will accumulate with the length of exposure.<sup>(16)</sup>

It is known that some of the respondents (50%) are active smokers with 50% categorized as moderate smokers.<sup>(17)</sup> Smokers in general will suck as many as 4000 compounds in the form of volatile chemicals and some in the form of gas from cigarette smoke which is toxic to cells in the body, especially in the respiratory system because cigarette smoke can affect the mucociliary escalator system which makes it easier for nanoparticles to reach the lower airway. This study is in line prior research which shows that smokers are more vulnerable to exposure to ambient air pollutants. The results of the examination of COHb levels vary because the effect of smoking on each person varies depending on the age of first smoking, length of smoking, number of cigarettes smoked per day, and a person's susceptibility to chemicals in cigarette smoke.<sup>(18)</sup>

It is known that 70% of respondents do not wear masks while working. The use of masks that meet the standards is an important Personal Protective Equipment (PPE) to minimize the potential for exposure to carbon monoxide or dust particles that can enter the body.<sup>(19)</sup> The results of examining COHb levels in respondents who wear masks can give varying results because it depends on the mask material used and the frequency of changing masks. If the mask material used can filter nanoparticles, and the more often you change the mask or the mask used is new and sterile, it can reduce the possibility of high COHb levels.

Based on the results of the examination of carboxyhemoglobin levels and ALT levels in 20 satay vendors who trade near the highway in Gubeng District, Surabaya City, the average carboxyhemoglobin level was 0.91% and the average ALT level was 40.0 U/L. These results indicate that the overall levels of carboxyhemoglobin and ALT levels in satay traders are below the threshold, as determined by the Regulation of the Ministry of Health of the Republic of Indonesia No.70 of 2016 concerning Health Standards and Requirements for the Industrial Work Environment that the reference value of the concentration of carbon monoxide chemicals in the blood is  $< 3.5\%$  and the normal reference range set in the examination of ALT levels with the BS-200 Chemistry Analyzer IFCC kinetic method is  $< 40$  U/L. After statistical analysis using the Spearman Correlation test, the p value was 0.015, indicating a correlation between carboxyhemoglobin levels and ALT levels in satay traders. The correlation between carboxyhemoglobin levels and ALT levels has a high level of relationship strength. The correlation coefficient is positive, which means that the higher the carboxyhemoglobin level, the higher the ALT level. Conversely, the lower the carboxyhemoglobin level, the lower the ALT level.

Satay grilling is done by using charcoal to produce embers as fuel. This combustion process produces smoke containing harmful pollutants, one of which is carbon monoxide.<sup>(20)</sup> Generally the body is exposed to carbon monoxide gas through the inhalation route.<sup>(21)</sup> Inhaled carbon monoxide gas goes to the lung alveolus, then when it reaches the alveolar capillary membrane, carbon monoxide gas changes to liquid which then dissolves into plasma and then binds to hemoglobin in red blood cells. Carbon monoxide poisons blood hemoglobin by changing the conformation of hemoglobin. Hemoglobin from red blood cells that should bind oxygen to oxyhemoglobin ( $\text{HbO}_2$ ) to be transmitted to body tissues that need it becomes insufficient because hemoglobin switches to binding carbon monoxide to form a more stable carboxyhemoglobin ( $\text{HbCO}$ ) bond.<sup>(22)</sup> This mechanism and the slow decomposition of carboxyhemoglobin, the body experiences symptoms of aphasia so that the body's metabolism becomes less effective and disrupts the function of intra-cellular enzymes.<sup>(5)</sup> COHb potentiates vascular permeability and causes increased interstitial fluid accumulation with decreased circulating blood volume (hemoconcentration) affecting many organs, such as brain edema with neurological symptoms and impaired

consciousness; pulmonary edema with respiratory failure; decreased myocardial contractility, arrhythmias and heart failure; and renal failure.

Carbon monoxide along with the bloodstream is delivered to peripheral tissues.<sup>(23)</sup> In the liver, the acinar parenchyma cells are divided into three zones based on the blood flow system, namely, zone 1 (periportal or peripheral) which receives blood supply from the hepatic artery so that it gets the most oxygen and nutrients but few metabolites, and there are many enzymes that play a role in oxidative metabolism and gluconeogenesis; zone 2 (midzonal) receives blood containing less oxygen and nutrients than zone 1; and zone 3 (centrilobular) which is located closest to the central vein so that it receives blood that contains little oxygen and nutrients but is rich in metabolites, zone 3 also contains a lot of smooth reticulum rich in cytochrome P450 enzymes, and contains enzymes that play a role in glycolysis reactions, lipid metabolism, biotransformation of drugs and potentially toxic exogenous compounds so that in this zone more often experience necrosis.<sup>(24)</sup> The detoxification process in the liver is carried out by neutralizing toxin substances by enzymes and other chemical compounds in the liver, but when CO-Hb levels exceed the liver's tolerance limit, it will interfere with the work of biological enzymes and liver cells experience membrane permeability until cell damage occurs. When cells are damaged, cytoplasmic enzymes including the ALT enzyme which is an enzyme that plays a role in the process of gluconeogenesis with its soluble nature will be absorbed into the blood plasma and follow blood circulation, so that ALT levels increase when measurements are taken.<sup>(7)</sup>

The biological mechanisms underlying the harmful effects of ambient air pollution on the liver have not been clarified, but may be explained by several direct or indirect causes. One rational mechanism is the oxidative stress response as it is known to contribute to liver damage and disease pathogenesis.<sup>(25)</sup> An experimental study in the journal showed 3 hypothesized mechanisms of particulate air pollutants on liver toxicity, namely, 1) hydrophilic constituents of inhaled air pollutants can translocate directly into the extra-pulmonary circulation especially the liver, 2) nanoparticles with insoluble properties inhaled can directly cross the alveolar-capillary layer, circulate in the bloodstream and interact with kupffer cells, liver-resident macrophages to produce proinflammatory cytokines, 3) inhaled nanoparticles first interact with alveolar or bronchiolar macrophages which stimulate the innate immune response to release proinflammatory cytokines into the bloodstream.

This research is in line with prior research<sup>(4)</sup> which states that there is a long relationship between CO exposure and ALT levels in tofu factory workers with a p value = 0.001 and r = 0.783. The effect of ultrafine particle emissions from biomass burning of pine branches and rice straw on liver damage in mice found that the more ultrafine particle emissions given or entering the body through respiration, the more damage to mice liver cells. This is known from the results of microscopic examination obtained 3 types of liver cell damage including parenchymal degeneration, binuclear cells, and necrosis.<sup>(26)</sup> In addition to CO, there are other factors that affect ALT levels including consuming alcoholic beverages<sup>(28)</sup> taking drugs that induce liver damage,<sup>(29)</sup> and hepatitis virus infection.<sup>(30)</sup>

## CONCLUSION

Based on the results of the study, there is a high positive correlation between carboxyhemoglobin levels and alanine aminotransferase enzyme levels in satay vendors. Suggestions for satay traders should pay attention to health when trading by wearing masks to reduce exposure to carbon monoxide gas from charcoal smoke and pollutants in the work environment. Future researchers are expected to pay attention to other factors that are likely to affect the results of the study such as age and nutritional status, ensure that respondents answer questionnaires honestly to get appropriate research criteria, and use a representative sample so that accurate results and appropriate conclusions are obtained. For the community, they should maintain a healthy body from the dangers of carbon monoxide exposure around them by implementing a healthy lifestyle as a preventive effort against the emergence of health problems.

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