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Relationship of Carboxyhemoglobin (CoHb) and Hemoglobin (Hb) Levels in Active Smokers in Gresik Regency

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ABSTRACT Smoking is a prevalent habit known to have adverse health effects, primarily due to the inhalation of toxic chemicals such as carbon monoxide (CO), which can bind to hemoglobin forming carboxyhemoglobin (COHb). Despite extensive research, the relationship between elevated COHb levels resulting from cigarette smoke and overall hemoglobin (Hb) concentrations remains inconclusive, particularly within specific populations such as active smokers. This study aims to investigate the potential correlation between COHb and Hb levels among active smokers in Gresik Regency, Indonesia. An analytical observational cross-sectional design was employed, involving 30 male respondents who have a minimum of one year smoking history, consume at least three cigarettes daily, and are willing to participate. Whole blood samples were collected and analyzed to determine COHb levels using the Conway diffusion method, which involves incubation and spectrophotometric measurement at specific wavelengths. Simultaneously, hemoglobin concentrations were assessed using the cyanmethemoglobin method via the Mindray BC-5000 Hematology Analyzer. The collected data were statistically examined by Spearman's correlation test to evaluate the relationship between COHb and Hb levels. The results indicated that the average COHb level was 0.89%, all of which fell within normal limits (< 3.5%). The mean hemoglobin concentration was 14.6 g/dL, with only one respondent exhibiting below-normal levels. The statistical analysis revealed no significant correlation between COHb and Hb (p-value = 0.304), suggesting that, within this sample, cigarette-induced CO exposure does not directly influence hemoglobin levels. The findings suggest that in light to moderate smokers in Gresik Regency, COHb levels do not significantly affect hemoglobin concentrations. These results imply that factors other than carbon monoxide exposure may have a more substantial impact on hematological parameters in this population. Further studies with larger sample sizes and varied smoking intensities are recommended to elucidate the complex interactions between smoking-related toxins and hematologic health.

INDEX TERMS Level Carbon Monoxide, Carboxyhemoglobin, Hemoglobin, Smoking, Spectrophotometry

I. INTRODUCTION

Tobacco smoking remains a critical global public health challenge, contributing to numerous adverse health outcomes, including cardiovascular diseases, respiratory disorders, and malignancies [1]. In Indonesia, smoking prevalence is alarmingly high, with the 2023 Health Survey indicating that East Java ranks among the top regions for smoking rates, with approximately 30.2% of its population engaged in smoking [2]. In Gresik Regency, East Java, an estimated 360,000 residents aged 15 years and older are active smokers, according to 2022 regional health data [3]. The detrimental effects of smoking are primarily driven by toxic substances, such as carbon monoxide (CO), which binds to hemoglobin, forming carboxyhemoglobin (COHb). This binding reduces oxygen transport, potentially causing hypoxia, increased blood viscosity, and cardiovascular complications [4], [5]. Despite these known risks, the relationship between COHb and hemoglobin (Hb) levels in active smokers, particularly in localized populations like Gresik Regency, remains underexplored. Current methodologies for assessing COHb levels utilize the Conway diffusion method with UV-Vis spectrophotometry, valued for its precision in quantifying COHb in whole blood [6], [7]. Hemoglobin levels, on the other hand, are typically measured using automated hematology analyzers, such as the Mindray BC-5000, employing the cyanmethemoglobin method for high accuracy [8]. Prior studies have reported conflicting findings on the COHb-Hb relationship. For example, a 2021 study found a positive correlation between COHb and hematocrit levels in male smokers, suggesting compensatory erythropoiesis due to CO-induced hypoxia [9]. Conversely, a 2022 study reported no significant association between smoking habits and Hb levels, indicating variability influenced by factors such as smoking intensity and lifestyle [10]. These inconsistencies highlight the

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need for further investigation, particularly in specific demographic and geographic contexts.

The research gap lies in the lack of clarity regarding the COHb-Hb relationship in active smokers, modulated by factors such as cigarette consumption, smoking duration, and lifestyle variables (e.g., diet and physical activity) [11], [12]. Additionally, the applicability of the Conway diffusion method in regional settings and its correlation with hematological parameters requires validation [13]. This study aims to analyze the relationship between COHb and Hb levels in active male smokers in Gresik Regency, employing the Conway diffusion method for COHb measurement and the cyanmethemoglobin method for Hb assessment. This study contributes to the field by:

1. Providing localized data on COHb and Hb levels in Gresik Regency's active smokers, addressing a regional public health concern.
2. Evaluating the Conway diffusion method's effectiveness in a specific context, potentially informing laboratory practices.
3. Enhancing understanding of smoking's physiological impacts, guiding targeted health interventions.

The article is structured as follows: Section II details the methodology, including study design, sample selection, and analytical procedures. Section III presents the results, followed by Section IV, which discusses findings in the context of existing literature. Section V concludes with recommendations for future research and public health strategies.

II. METHODOLOGY

This study utilized an analytical observational design with a cross-sectional approach to examine the relationship between carboxyhemoglobin (COHb) and hemoglobin (Hb) levels in active smokers in Gresik Regency, Indonesia. Conducted from March to June 2023 at the Toxicology and Hematology Laboratory, Department of Medical Laboratory Technology, Poltekkes Kemenkes Surabaya, the methodology was designed to ensure reproducibility through standardized procedures, precise instrumentation, and clearly defined participant criteria. The study adhered to ethical guidelines, with participants providing informed consent.

A. STUDY POPULATION AND SAMPLING

The study population comprised active male smokers aged 18–50 years residing in Gresik Regency. Inclusion criteria required participants to have smoked for at least one year, consume a minimum of three cigarettes daily, and frequent coffee shops, which are common venues for smoking. Exclusion criteria included individuals with chronic illnesses affecting hematological parameters or those unwilling to participate. A purposive sampling method selected 30 participants, representing light to moderate smokers based on daily cigarette consumption [14]. The sample size was calculated to achieve 80% power with a 5% significance level, assuming a moderate correlation coefficient [15]. Participants were informed of the study's purpose and procedures, and their anonymity was maintained through coded identifiers.

B. MATERIALS AND EQUIPMENT

Whole blood samples were collected in EDTA anticoagulant tubes to preserve sample integrity for COHb and Hb analyses. For COHb measurement, reagents included CO-free distilled water (aquades), 5N sulfuric acid (H_2SO_4), 0.005N palladium chloride ($PdCl_2$), and 5% potassium iodide (KI), sourced from certified laboratory suppliers [16]. A UV-Vis spectrophotometer (Shimadzu UV-1800) was used for COHb quantification, with daily calibration to ensure precision. Hemoglobin levels were measured using the Mindray BC-5000 Hematology Analyzer, employing the cyanmethemoglobin method for automated Hb quantification [17]. All equipment was maintained and quality-checked according to manufacturer protocols [18].

C. COHb MEASUREMENT PROCEDURE

COHb levels were determined using the Conway diffusion method, a validated technique for quantifying COHb in blood [19]. The procedure involved adding 0.25 mL of whole blood to 1.5 mL of CO-free aquades in the outer compartment of a Conway dish to lyse erythrocytes. The inner compartment contained 1.0 mL of $PdCl_2$ solution, and 0.2 mL of 5N H_2SO_4 was placed in the middle compartment to facilitate CO release. The dish was sealed and incubated at room temperature for 1.5 hours to ensure complete reaction [16]. Post-incubation, 0.25 mL of $PdCl_2$ solution was transferred to a 25 mL flask containing 10 mL aquades and 1 mL 5% KI. Absorbance was measured at a maximum wavelength of 420 nm using the UV-Vis spectrophotometer, with a blank sample to minimize errors. A standard curve was established using six $PdCl_2$ concentrations (0.35–0.60 mL) to ensure accurate quantification [19]. Quality control measures included daily calibration and duplicate measurements to verify reproducibility.

D. HEMOGLOBIN MEASUREMENT PROCEDURE

Hemoglobin levels were quantified using the cyanmethemoglobin method on the Mindray BC-5000 Hematology Analyzer, a standard for automated hematological analysis [17]. Blood samples were homogenized by gentle inversion to ensure uniformity. The analyzer was pre-warmed for 30 minutes and calibrated with manufacturer-provided controls to verify reagent performance [18]. Sample details (name, age, address) were entered into the analyzer's interface. A 0.5 mL blood sample was aspirated, processed for one minute, and Hb results were automatically displayed on the screen. Results were reviewed for outliers, and equipment maintenance was performed post-analysis to ensure reliability [20].

E. STUDY DESIGN AND DATA ANALYSIS

This non-randomized, cross-sectional study collected data at a single time point to assess the correlation between COHb and Hb levels. The observational design was selected to evaluate naturalistic associations without intervention, aligning with the study's objectives [21]. Data were analyzed using SPSS version 26.0. The Spearman correlation test was applied due

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to the non-normal distribution of COHb and Hb data, with a significance threshold of $p < 0.05$ [22]. Descriptive statistics, including means and ranges, were computed to summarize COHb and Hb levels.

F. QUALITY CONTROL AND ETHICAL CONSIDERATION

Quality control procedures included daily equipment calibration, reagent validation, and duplicate sample testing to ensure accuracy [18]. Ethical considerations followed international guidelines, with participants informed of the study's purpose, procedures, and potential risks. Data confidentiality was maintained through anonymized coding, and biological samples were disposed of per laboratory biosafety protocols [23].

III. RESULTS

The study was conducted on 30 respondents of active smokers in Gresik Regency. Respondents are selected according to sample criteria, which include being male, having smoked for at least one year, consuming more than three tobacco cigarettes every day, and being willing to be a respondent (TABLE 1).

TABLE 1
CHOb and Hb Results

No	Sample Code	COHb levels (%)	Hb levels (mg/dL)
1	001	1,38	14,4
2	002	0,43	13,9
3	003	0,50	14,9
4	004	1,18	14,8
5	005	0,63	14,3
6	006	0,86	14,1
7	007	0,67	13,8
8	008	0,42	15,4
9	009	1,34	14,4
10	010	1,56	13,9
11	011	0,62	14,2
12	012	1,09	14,2
13	013	0,62	13,8
14	014	1,37	14,9
15	015	0,44	13,9
16	016	1,35	14,5
17	017	0,63	13,9
18	018	0,49	16,0
19	019	0,49	15,5
20	020	0,56	15,1
21	021	0,36	15,5
22	022	1,96	13,3
23	023	0,68	12,4
24	024	0,62	15,9
25	025	1,10	17,8
26	026	0,68	15,7
27	027	0,91	15,3
28	028	0,87	13,8
29	029	1,18	13,9
30	030	1,75	15,4
average		**0,89**	**12,4**

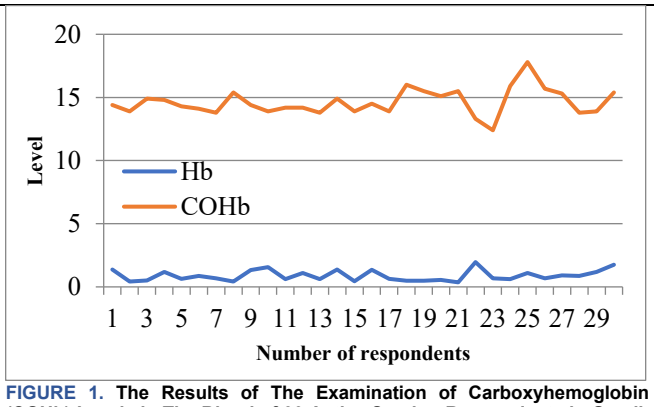

FIGURE 1. The Results of The Examination of Carboxyhemoglobin (COHb) Levels in The Blood of 30 Active Smoker Respondents in Gresik Regency.

The results of the examination of carboxyhemoglobin (COHb) levels in the blood of 30 active smoker respondents in Gresik Regency were below the normal value of carboxyhemoglobin (COHb) (COHb levels < 3.5%) (FIGURE 1). The highest COHb content result in sample 022 was 1.96%. The lowest COHb level was found in sample 021 at 0.36%. The results of checking blood hemoglobin (Hb) levels in 30 respondents of active smokers in Gresik Regency had an average of 14.6 g/dL. The highest hemoglobin (Hb) content resulted in sample 025, with a result of 17.8 g/dL. The lowest hemoglobin (Hb) level in sample 023 was of 12.4 g/dL. The results of the examination of COHb and Hb levels were analyzed using the SPSS program with the Spearman Test. After the data from the examination of carboxyhemoglobin and blood hemoglobin levels, the Spearman correlation test in the SPSS program version 16.0 obtained a Sig. (2-tailed) values of 0.304 > 0.05. Thus, it was concluded that there is no relationship between carboxyhemoglobin and hemoglobin in the blood of active smokers in Gresik Regency.

IV. DISCUSSION

This study investigated the relationship between carboxyhemoglobin (COHb) and hemoglobin (Hb) levels in active male smokers in Gresik Regency, Indonesia, revealing no significant correlation between the two variables, with a Spearman correlation coefficient of -0.194 and a significance value of 0.304 ($p > 0.05$). The findings provide insights into the physiological impacts of smoking in a specific regional population, contributing to the broader discourse on tobacco-related health effects. The absence of a significant correlation between COHb and Hb levels in this study suggests that, within the sampled population of light to moderate smokers, COHb levels do not substantially influence Hb concentrations. The mean COHb level was 0.89%, well below the normal threshold of 3.5%, indicating minimal CO exposure relative to clinical toxicity levels [24]. This low COHb level may be attributed to the participants' smoking habits, as most consumed 3–10 cigarettes daily, classifying them as light to moderate smokers [25]. Light smoking is associated with lower CO exposure, which may not sufficiently disrupt oxygen transport to trigger compensatory erythropoiesis, a process that could elevate Hb levels in response to hypoxia [26]. The average Hb level of 14.6 g/dL falls within the normal range (13–17 g/dL for males), with only one participant

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exhibiting a slightly subnormal value of 12.4 g/dL. This outlier could reflect individual factors such as nutritional deficiencies or underlying health conditions, which were not controlled in this study [27]. The Spearman correlation test, chosen for its suitability with non-normally distributed data, indicated a weak, non-significant negative correlation (-0.194), suggesting that COHb and Hb levels do not vary in a consistent, directional manner [28]. This finding aligns with the hypothesis that low COHb levels, as observed in light smokers, may not induce sufficient hypoxic stress to alter Hb production significantly. However, the variability in Hb levels among participants highlights the influence of external factors, such as diet, physical activity, or environmental exposures, which may modulate hematological responses to smoking [29]. The results underscore the complexity of physiological responses to CO exposure, where individual differences in smoking behavior and lifestyle may obscure direct correlations.

The findings of this study contrast with some prior research while aligning with others, reflecting the variability in the COHb-Hb relationship across different populations and methodologies. A 2021 study by Ischorina et al. reported a positive correlation between COHb and hematocrit levels in male smokers consuming at least 10 cigarettes daily, suggesting that higher CO exposure may stimulate erythropoiesis to compensate for reduced oxygen-carrying capacity [30]. The discrepancy with the current study may be attributed to differences in sample characteristics, as Ischorina et al.'s participants were heavier smokers, likely resulting in higher COHb levels that could trigger hematological adaptations [31]. In contrast, a 2022 study by Wibowo et al. found no significant association between smoking habits and Hb levels in adult smokers exposed to CO, consistent with the present findings [32]. This similarity suggests that, in populations with lower smoking intensity, COHb levels may remain below the threshold required to impact Hb production significantly. Further, a 2023 study on urban smokers in Indonesia using the Conway diffusion method reported COHb levels comparable to those in this study (0.5–2.0%), with no significant Hb correlation, supporting the notion that light to moderate smoking may not substantially alter hematological parameters [33]. However, a 2020 study on occupational CO exposure in traffic officers found elevated COHb levels associated with increased Hb, likely due to chronic, high-level CO exposure in their environment [34]. These contrasting findings highlight the role of smoking intensity and environmental factors in modulating COHb-Hb interactions. The current study's focus on light to moderate smokers in a semi-urban setting like Gresik Regency may explain the lack of correlation, as the CO exposure levels were insufficient to induce significant physiological changes compared to populations with heavier smoking or occupational exposures [35].

This study has several limitations that warrant consideration. First, the sample size of 30 participants, while statistically adequate for detecting moderate correlations, may limit the generalizability of the findings to broader populations [28]. A larger sample could enhance the statistical power to detect subtle correlations. Second, the study did not account for confounding variables such as nutritional status, physical activity, or exposure to environmental pollutants, which could influence Hb levels independently of COHb [29]. Third, the purposive sampling method, while practical for targeting active smokers, may introduce selection bias, as participants frequenting coffee shops may not represent the broader smoking population in Gresik Regency [14]. Fourth, the cross-sectional design captures data at a single time point, precluding the assessment of temporal changes in COHb and Hb levels in response to varying smoking patterns [21]. Finally, the study focused exclusively on male smokers, limiting its applicability to female smokers or passive smokers, who may exhibit different physiological responses [33]. The findings have several implications for public health and clinical practice. The absence of a significant COHb-Hb correlation in light to moderate smokers suggests that low-level CO exposure may not immediately impact Hb levels, but this does not negate the broader health risks of smoking, such as cardiovascular and respiratory diseases [24]. Public health campaigns in Gresik Regency should emphasize smoking cessation, particularly in social settings like coffee shops, to reduce both active and passive smoke exposure [25]. The use of the Conway diffusion method for COHb measurement proved reliable in this regional context, supporting its application in similar settings for monitoring CO exposure [19]. Clinically, the normal COHb and Hb levels observed suggest that routine screening for COHb in light smokers may not be necessary, but monitoring for other smoking-related biomarkers (e.g., inflammatory markers) could be prioritized [35]. Future research should explore longitudinal designs to assess the cumulative effects of smoking on hematological parameters and incorporate female smokers and passive smokers to broaden the understanding of CO's physiological impacts [33]. Additionally, interventions targeting lifestyle factors, such as improved nutrition, could mitigate potential hematological effects in smokers [27]. This study provides evidence that COHb and Hb levels are not significantly correlated in light to moderate smokers in Gresik Regency, consistent with some prior research but contrasting with studies involving heavier smokers. The findings highlight the influence of smoking intensity and individual factors on hematological outcomes, underscoring the need for targeted public health strategies to address smoking in regional contexts.

V. CONCLUSION

This study aimed to evaluate the relationship between carboxyhemoglobin (COHb) and hemoglobin (Hb) levels in active male smokers in Gresik Regency, Indonesia, using the Conway diffusion method for COHb measurement and the cyanmethemoglobin method for Hb quantification. The findings revealed no significant correlation between COHb and Hb levels, as evidenced by a Spearman correlation coefficient of -0.194 and a significance value of 0.304 ($p > 0.05$). The mean COHb level was 0.89%, ranging from 0.36% to 1.96%, well below the clinical threshold of 3.5%, indicating minimal carbon monoxide exposure among the participants,

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who were predominantly light to moderate smokers consuming 3–10 cigarettes daily. The average Hb level was 14.6 g/dL, within the normal range of 13–17 g/dL for males, with one participant exhibiting a slightly subnormal value of 12.4 g/dL, potentially influenced by factors such as nutritional status or individual health conditions. These results suggest that low-level CO exposure in this population does not significantly alter Hb concentrations, likely due to insufficient hypoxic stress to trigger compensatory erythropoiesis. The findings underscore the importance of considering smoking intensity and lifestyle factors in assessing hematological impacts. For future research, longitudinal studies are recommended to explore the cumulative effects of smoking on COHb and Hb levels over time, incorporating larger and more diverse samples, including female and passive smokers, to enhance generalizability. Additionally, investigating confounding variables such as diet, physical activity, and environmental exposures could provide a more comprehensive understanding of hematological responses to smoking. Public health interventions should focus on reducing smoking prevalence in social settings like coffee shops in Gresik Regency to mitigate both active and passive smoke exposure, thereby minimizing associated health risks. These efforts could be supported by integrating COHb monitoring into routine health screenings to identify at-risk individuals and promote smoking cessation programs tailored to regional populations.

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DATA AVAILABILITY

No datasets were generated or analyzed during the current study.

AUTHOR CONTRIBUTION

Roudhotin Nur Azizah conceptualized the study design and research objectives, developed the methodology for COHb measurement using the Conway diffusion method, conducted participant recruitment and data collection in Gresik Regency, performed laboratory analyses for carboxyhemoglobin levels, drafted the initial manuscript including the introduction, methodology, and results sections, and served as the corresponding author coordinating the research activities. Ayu Puspitasari supervised the overall research project, provided guidance on study design and methodology, conducted statistical analysis using SPSS software including the Spearman correlation test, performed data interpretation and validation, and critically reviewed and revised the manuscript for intellectual content. Indah Lestari contributed to the experimental design and methodology development, managed laboratory procedures and quality control protocols, assisted in hemoglobin measurement using the Mindray BC-5000 Hematology Analyzer, participated in data collection and sample processing, contributed to data interpretation, and reviewed the manuscript for technical accuracy. Ismath Mohammad provided expertise in hematological analysis and interpretation, validated the laboratory results and analytical methods, contributed to the discussion of findings in the context of existing literature, reviewed the manuscript for scientific accuracy and clinical relevance, and provided guidance on the clinical implications of the research findings. All authors participated in the final review and approval of the manuscript, contributed to the revision process, and are accountable for the integrity and accuracy of the work presented.

DECLARATIONS

ETHICAL APPROVAL

Ethical approval is not available.

CONSENT FOR PUBLICATION PARTICIPANTS.

Consent for publication was given by all participants.

COMPETING INTERESTS

The authors declare no competing interests.

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