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# Influence of Glutathione S-Transferase Genotypes on the Link between Smoking and Coronary Artery Disease

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## Abstract

**Background:** Coronary artery disease (CAD) remains a significant global health challenge, with smoking identified as a major risk factor. Glutathione S transferase (GST) genotypes, specifically GSTM1 and GSTT1, may play a role in individual susceptibility to CAD in smokers. This study aims to explore the interplay between smoking habits, GST genotypes, and the risk of CAD.

**Methods:** A case-control study was conducted involving 147 participants diagnosed with CAD across three hospitals over three months. Participants, aged 30 and above, were selected based on their smoking history and relevant health characteristics. Comprehensive demographic data and smoking histories were collected through structured interviews and questionnaires. Blood samples were obtained for genetic analysis using polymerase chain reaction (PCR) techniques to identify GSTM1 and GSTT1 genotypes. Statistical analyses were conducted to evaluate associations and compare inflammatory and hemostatic markers among different genotype groups and smoking status.

**Results:** The demographic analysis revealed most participants aged between 61 to 75 years. The study highlighted the variations in smoking duration among participants, with significant insights into their health metrics associated with CAD.

Statistical evaluations demonstrated the influence of GST genotypes on inflammatory responses, with significant differences noted between smokers and non-smokers.

**Conclusion:** The study underscores the relationship between GST genotypes and CAD risk, particularly among smokers, suggesting that genetic predisposition may amplify the harmful effects of smoking on cardiovascular health. These findings are essential for advancing prevention strategies and therapeutic approaches tailored to individual genetic profiles in combating CAD. Further investigation is warranted to deepen the understanding of these interactions and their implications for cardiovascular disease management.

**Keywords:** CAD, GST, Smoking habits, Genetic predisposition, and Inflammatory responses.

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# تأثير الأنماط الجينية للجلوتاثيون S-transferase على العلاقة بين التدخين ومرض الشريان التاجي

زهره عبد الهادي دايخ

**المستخلص**

**خلفية الدراسة:** لا يزال مرض الشريان التاجي (CAD) يمثل تحديا صحيا عالميا كبيرا ، حيث تم تحديد التدخين كعامل خطر رئيسي. قد تلعب الأنماط الجينية للجلوتاثيون S transferase (GST) ، وتحديدا GSTM1 و GSTT1 ، دورا في القابلية الفردية ل CAD لدى المدخنين. تهدف هذه الدراسة إلى استكشاف التفاعل بين عادات التدخين والأنماط الجينية لضريبة السلع والخدمات وخطر CAD.

**طرق واجراءات البحث:** أجريت دراسة حالات وشواهد شملت 147 مشاركا تم تشخيص إصابتهم بمرض CAD في ثلاثة مستشفيات على مدار ثلاثة أشهر. تم اختيار المشاركين ، الذين تتراوح أعمارهم بين 30 وما فوق ، بناء على تاريخ التدخين والخصائص الصحية ذات الصلة. تم جمع البيانات الديموغرافية الشاملة وتاريخ التدخين من خلال المقابلات والاستبيانات المنظمة. تم الحصول على عينات دم للتحليل الجيني باستخدام تقنيات تفاعل البوليميراز المتسلسل (PCR) لتحديد الأنماط الجينية GSTM1 و GSTT1. أجريت تحليلات إحصائية لتقييم الارتباطات ومقارنة علامات الالتهاب والمرقئ بين مجموعات النمط الجيني المختلفة وحالة التدخين.

**النتائج:** كشف التحليل الديموغرافي أن معظم المشاركين تتراوح أعمارهم بين 61 و 75 عاما. سلطت الدراسة الضوء على الاختلافات في مدة التدخين بين المشاركين ، مع رؤى مهمة حول مقاييسهم الصحية المرتبطة ب CAD. أظهرت التقييمات الإحصائية تأثير الأنماط الجينية ل GST على الاستجابات الالتهابية ، مع ملاحظة اختلافات كبيرة بين المدخنين وغير المدخنين.

**الاستنتاج:** تؤكد الدراسة على العلاقة بين الأنماط الجينية لضريبة السلع والخدمات ومخاطر CAD ، خاصة بين المدخنين ، مما يشير إلى أن الاستعداد الوراثي قد يضخم الآثار الضارة للتدخين على صحة القلب والأوعية الدموية. هذه النتائج ضرورية لتطوير استراتيجيات الوقاية والأساليب العلاجية المصممة خصيصا للملامح الجينية الفردية في مكافحة CAD. هناك ما يبرر إجراء مزيد من التحقيقات لتعميق فهم هذه التفاعلات وآثارها على إدارة أمراض القلب والأوعية الدموية.

**الكلمات المفتاحية:** GST ، CAD ، عادات التدخين ، الاستعداد الوراثي ، والاستجابات الالتهابية.

## 1. Introduction

Security and Morbidity of Coronary Heart Disease (CHD) global burden, which ranges risk antigen from among other combinations. Notably, smoking is a key modifiable risk factor further amplifying the pathophysiology of disease progression. Compounds in cigarette smoke, which are toxic for influence the generation of reactive oxygen species and pro-inflammatory cytokines, two processes that play an leading role on endothelial dysfunction and atherogenesis. Given the polygenic nature of CAD, an area-of-interest is the interaction between cigarette smoking and genetic susceptibility to autopsies science. Genetic variants in detoxification enzymes, especially glutathione S-transferases (GST), have been recognized to influence the susceptibility of an individual to tobacco-associated

disorders. Glutathione S-transferases (GSTM1 & GSTT1) are an important enzyme family responsible for detoxifying various toxins-such as those found in tobacco smoke. Epidemiological studies have estimated that polymorphisms in these genes modifying individual ability to metabolize carcinogens may considerably alter the risk CAD. For example, deletions of the GSTM1 and GSTT1 genes cause increased oxidative stress and inflammation putting affected individuals at an elevated risk for atherosclerosis. Based on previous studies these additive and interactive effects between smoking and GST genotypes may provide better insight for their role in cardiovascular pathologies (Wang et al., 2002; Olshan et al., 2003). In addition, the relationship between GST polymorphisms and inflammatory markers are well-documented. Increased expressions of markers such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor-alpha (TNF-α) were correlated with the active smoking habits, highlighting once again that this gene-environment interaction plays an important role in CAD risk. Another study by Phulukdaree et al. (2012) had found that activation of a specific inflammatory response occurs with the presence certain GST genotypes which make them potential candidates for pathogenesis of CAD in smokers (Lehrke et al. 2012). Insight into these mechanisms is important to classify possible higher risk patients and customize targeted prevention strategies. Influences of GST genotypes on smoking related CAD may provide another, potentially important area in public health strategies involving CHD. In this way understanding the genetic susceptibility environmental exposure on smoking will help researchers to identify at risk population and can work for specific interventions which are personalized. Given that CAD remains a substantial global health problem, further investigation of these interactions is needed to move our understanding and efforts in both prevention and treatment forward.

## 2. Research Methods

A case-control study was conducted assessing GST genotypes (GSTM1, GSTT1) in patients with coronary artery disease. Data on smoking history and health characteristics were collected through questionnaires and genetic testing.

### *2.1. Study Design*

Data collection was conducted over a period of three months, from April 5, 2024, to August 8, 2024. A cross-sectional case-control design was employed, involving three hospitals: Al Hillah Teaching Hospital, which contributed 46 patients; Marjan Hospital, which contributed 67 patients; and Al Sadiq Teaching Hospital, which contributed 34 patients. A total of 147 participants diagnosed with coronary artery disease were recruited, with a specific focus on individuals aged 30 years and above. Structured interviews were administered to each participant to gather data

concerning smoking history, demographic information, and clinical characteristics. Alongside these interviews, blood samples were collected for genetic analysis to identify GSTM1 and GSTT1 genotypes through polymerase chain reaction (PCR) techniques. The primary objective of the study was to evaluate the association between GST genotypes and the presence of coronary artery disease, particularly in relation to smoking status, with appropriate statistical methods employed to adjust for confounding variables. The study aimed to clarify the role of genetic factors in the cardiovascular effects of smoking within this patient population.

### *2.2. Sample Population*

In this study the sample population comprised 147 randomized participants selected to investigate the connection between smoking habits, genetic susceptibility, and the risk of coronary artery disease (CAD). This well-defined population allowed for a comprehensive analysis of how glutathione S-transferase (GST) genotypes might influence cardiovascular health in the context of varying smoking behaviors. Participants were classified based on their smoking duration, with detailed data revealing insights into how long they had been smoking. Among the 147 individuals surveyed, the distribution of years smoked was as follows: 10.2% (15 participants) reported smoking for less than 1 year, while 11.6% (17 participants) had smoked for 1 to 5 years. A further breakdown showed that 12.9% (19 participants) fell within the 6 to 10 years category, and 23.8% (35 participants) reported a smoking history of 11 to 15 years. Notably, those who had smoked for 16 to 20 years accounted for 19.0% (28 participants), and the longest duration of smoking, 21 years or more, was reported by 22.4% (33 participants). Furthermore, the study assessed the number of cigarettes smoked daily, offering additional layers of understanding regarding smoking intensity. The findings indicated that 15.6% (23 participants) smoked 1 to 5 cigarettes per day, while 14.3% (21 participants) smoked 6 to 10 cigarettes daily. The majority, representing 36.1% (53 participants), smoked 11 to 20 cigarettes per day, and 30.6% (45 participants) reported smoking more than 20 cigarettes daily. To enhance the analytical potential of the study, the sample was stratified into two groups based on their smoking exposure quantified in pack-years. The "≥20 pack-years " group included 33 participants, representing those with a significant smoking history, while the "<20 pack-years " group comprised 114 participants, reflecting a lower exposure to smoking. This stratification not only facilitates a clearer understanding of the interactions between GST genotypes and the impact of smoking on CAD risk but also helps in discerning how longer and more intense exposure to tobacco may correlate with genetic predispositions to cardiovascular conditions. Thus, the diverse characteristics of this sample population are integral for advancing research on

smoking-related health outcomes and the role of genetic factors in cardiovascular disease.

### *2.3. Inclusion and Exclusion Criteria*

The inclusion and exclusion criteria were meticulously defined to ensure that the selected sample population was relevant and appropriate for the research objectives. The primary aim was to investigate how GST genotypes interact with smoking habits to influence the risk of coronary artery disease (CAD). The inclusion criteria specified that participants must be adult smokers, aged between 30 to 75 years. This age range was intentionally chosen, as it encompasses individuals who have likely had significant exposure to smoking and are at risk for developing cardiovascular conditions. Furthermore, participants were required to provide informed consent to participate in the study and complete necessary questionnaires, ensuring that they understood the study's purpose and requirements. An additional key criterion was the availability of genomic data necessary for conducting GST analysis, as the study sought to explore the genetic components linked to smoking and CAD. Moreover, individuals diagnosed with atherosclerotic coronary artery disease, nonatherosclerotic coronary artery disease, hyperlipidemia, or peripheral artery disease were included, allowing for a broad examination of how different types of cardiovascular disease may be influenced by GST genotypes and smoking behavior.

Conversely, the exclusion criteria were designed to eliminate potential confounding factors that could skew the study's outcomes. Participants with a history of ischemic heart disease were excluded to ensure that the findings specifically reflect the impact of smoking and GST genotypes on CAD without interference from existing heart conditions. Similarly, individuals diagnosed with chronic kidney disease were also excluded from the study. The rationale for this exclusion stems from the fact that chronic kidney disease can significantly affect cardiovascular health and complicate the relationships being examined. By carefully delineating these inclusion and exclusion criteria, the study aims to create a targeted sample population that will facilitate a clearer understanding of the genetic susceptibility associated with smoking-related coronary artery disease. This thoughtful approach to participant selection is crucial for generating reliable and meaningful insights into the interplay between smoking, genetics, and cardiovascular health.

### *2.4. Data Collection*

demographic and lifestyle data were collected from participants through a structured questionnaire. This questionnaire detailed essential demographic information, lifestyle factors, and smoking history, providing a comprehensive

overview of each participant's background and habits. Additionally, medical history was gathered to provide context regarding cardiovascular health. Information on cardiovascular history, family history of coronary artery disease (CAD), and other relevant health conditions was collected to facilitate a thorough understanding of each participant's medical background. For the genetic analysis, blood samples were obtained from participants to analyze their GST genotypes, which included variations such as GSTM1-0, GSTM1-1, GSTT1-0, and GSTT1-1. This genetic data was crucial for determining the relationship between these genotypes and the risk of coronary artery disease. Each participant also underwent a clinical assessment during which various health metrics were measured. Blood pressure was assessed, body mass index (BMI) was calculated, and lipid profiles, including cholesterol levels, were evaluated to ensure that comprehensive clinical data accompanied the demographic and genetic information. Finally, the assessment of coronary artery disease was conducted through a review of medical records. This included the examination of historical diagnoses, imaging results such as coronary angiography, and documentation of any cardiovascular events experienced by the participants. These assessments were integral to understanding the connections between smoking, GST genotypes, and coronary artery disease risk.

### *2.5. Statistical Analysis*

The study employed a range of statistical analysis tools to evaluate the influence of glutathione S-transferase (GST) genotypes on smoking and coronary artery disease (CAD). Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants, utilizing frequency (F) and percentage (%) to capture key factors such as age distribution, body mass index (BMI), smoking history, and associated disease prevalence. The associations between GSTM1 and GSTT1 genotypes and various characteristics were assessed using chi-square tests to determine the significance of genotype-specific proportions, accompanied by p-values to evaluate strength. Furthermore, participants were categorized based on smoking exposure into groups with ≥20 pack-years and <20 pack-years, allowing for the calculation of mean differences, 95% confidence intervals (CIs), and ratios for inflammatory and hemostatic markers. A comparative analysis of these biomarkers across different GST genotypes in relation to smoking status was conducted, reporting mean values for smokers and non-smokers in each genotype group. Additionally, t-tests were employed to analyze the influence of GST genotypes on inflammatory biomarkers, comparing smokers and non-smokers within each group and yielding statistical values that established the significance of mean differences. Overall, this multifaceted statistical approach provided robust insights into the interplay between genetic predisposition and smoking on inflammatory responses.

## 3. Result

### *3.1. Demographic and Clinical Characteristics*

The study on the influence of glutathione S-transferase (GST) genotypes on the link between smoking and coronary artery disease (CAD) analyzed a sample of 147 participants, providing insightful demographic and clinical characteristics that help contextualize the findings. In terms of age distribution, most participants were older, with 49% falling in the 61-75 age range. This indicates a significant representation of middle-aged and older adults in the study, suggesting that the effects of smoking and genetic predisposition on CAD may be particularly relevant in older populations who are at greater risk for cardiovascular diseases. Regarding body mass index (BMI), the data revealed that the largest group (27%) fell within the 18.5 - 24.9 category, indicating a relatively healthy weight among many participants. However, there was also considerable representation in the higher BMI categories, with 12% classified as obese (BMI ≥ 35).

This suggests that while a portion of the study population may have a healthy weight, obesity remains a concern and is known to be a contributing factor to both smoking-related complications and cardiovascular diseases. The health profiles of the participants highlighted a range of comorbid conditions. Notably, 26.5% of participants were diagnosed with atherosclerotic CAD, and 27.9% had hypertension. These statistics underscore the high prevalence of cardiovascular risk factors within the study population, which may interact with GST genotypes and smoking habits to exacerbate the risk of CAD. Additionally, diseases such as diabetes mellitus (DM) and hyperlipidemia were present in 18.4% and 23.8% of participants, respectively, further illustrating the complex interplay of lifestyle, genetics, and health status that may influence cardiovascular outcomes. Smoking history within the cohort showed that nearly 22.4% of participants had smoked for over 21 years, with a considerable portion also reporting significant smoking duration between 11 to 20 years. Furthermore, the daily smoking consumption indicated that 36.1% of participants smoked 11-20 cigarettes per day, and 30.6% reported smoking more than 20 cigarettes daily. This heavy smoking pattern suggests a higher level of exposure to harmful substances that could potentially impact the cardiovascular system and interact with genetic predispositions related to GST genotypes.

**Table 1.** Demographic and Clinical Characteristics of Participants in the Study on the Influence of Glutathione S-Transferase Genotypes on the Link between Smoking and CAD (N=147).

| Characteristic | Categories | F | % |
|---|---|---|---|
| | 30-45 | 25 | 17.0 |

| | | | |
|---|---|---|---|
| Age | 46-60 | 50 | 34.0 |
| | 61-75 | 72 | 49.0 |
| | Total | 147 | 100% |
| Body mass index (kg/m2) | >18.5 | 10 | 7.0 |
| | 18.5 - 24.9 | 40 | 27.0 |
| | 25 - 29.9 | 39 | 27.0 |
| | 30 - 34.9 | 25 | 17.0 |
| | 35 - 39.9 | 18 | 12.0 |
| | 40< | 15 | 10.0 |
| | Total | 147 | 100% |
| Have you been diagnosed with any of the following diseases? | DM | 27 | 18.4 |
| | Hypertension | 41 | 27.9 |
| | Hyperlipidemia | 35 | 23.8 |
| | Nonatherosclerotic CAD | 13 | 8.8 |
| | Atherosclerotic CAD | 39 | 26.5 |
| | Peripheral Artery Disease | 17 | 11.6 |
| | Angina Pectoris | 9 | 6.1 |
| | Total | 147 | 100% |
| How many years have you smoked? | Less than 1 year | 15 | 10.2 |
| | 1-5 years | 17 | 11.6 |
| | 6-10 years | 19 | 12.9 |
| | 11-15 years | 35 | 23.8 |
| | 16-20 years | 28 | 19.0 |
| | 21 years or more | 33 | 22.4 |
| | Total | 147 | 100% |
| If you smoke, please specify the number of cigarettes you smoke per day | 1-5 cigarettes | 23 | 15.6 |
| | 6-10 cigarettes | 21 | 14.3 |
| | 11-20 cigarettes | 53 | 36.1 |
| | More than 20 cigarettes | 45 | 30.6 |
| | Total | 147 | 100% |

### *3.2. Association of Glutathione S-Transferase Genotypes with Characteristics*

The results of the study examining the association of glutathione S-transferase (GST) genotypes with demographic and clinical characteristics in relation to smoking and coronary artery disease (CAD) offer valuable insights into how these factors interact. In terms of age distribution, the analysis indicates significant genotype prevalence among the different age groups. For instance, among participants aged 46-60 years, a notably higher proportion carried the GSTM1-1

genotype, as the p-value of 0.042 suggests a significant association. This finding points to the potential for this genotype to be more prevalent in an age group that is likely encountering higher cardiovascular risks. Similarly, in the age group of 61-75 years, the p-value of 0.025 indicates that the GSTM1-1 genotype may again be significantly associated; however, the implications for this age group might suggest a declining trend in the protective aspects that could be offered by broader genetic backgrounds. When examining body mass index (BMI), the data reveal a trend wherein individuals with higher BMI categories, particularly above 35, show a higher association with the GSTM1-1 genotype, reflected in a p-value of 0.045. This suggests that individuals with this genotype may be at increased risk for obesity, a known risk factor that exacerbates cardiovascular issues, including CAD. Conversely, the associations for lower BMI categories did not demonstrate the same level of significance, highlighting that genetic susceptibility coupled with obesity may further compound health risks.

The findings related to smoking history are particularly striking, especially within the ≥20 pack-years group, where significant associations were identified. The GSTM1-0 genotype showed a prevalence of 0.02, while GSTM1-1 genotype prevalence was 0.22, yielding a p-value of 0.003. Similarly, the GSTT1-0 and GSTT1-1 genotypes presented p-values of 0.04 and 0.18, respectively, both indicating significant correlations with heavier smoking exposure. This suggests that individuals who have smoked significantly may be more likely to exhibit GST genotypes, potentially heightening their risk for CAD due to combined genetic and environmental factors. In contrast to the strong associations found with smoking, comorbid conditions such as diabetes mellitus, hypertension, and hyperlipidemia exhibited no significant p-values. For instance, diabetes showed a p-value of 0.510, hypertension 0.587, and hyperlipidemia 0.465, suggesting that while these conditions remain important in the context of cardiovascular disease, their direct association with GST genotypes is potentially less pronounced in this sample group. Interestingly, the prevalence of atherosclerotic CAD marked 0.38 for GSTM1-0 and 0.61 for GSTM1-1 with a p-value of 0.423, and similar non-significant results for GSTT1 genotypes. This underscores the complexity of CAD development, which may integrate factors beyond genetic predisposition alone, including behavioral and lifestyle choices such as smoking.

Table 2. Association of Glutathione S-Transferase Genotypes with Demographic and Clinical Characteristics in Relation to Smoking and Coronary Artery Disease.

| Characteristic | Genotype | | | Genotype | | |
|---|---|---|---|---|---|---|
| | GSTM1 | GSTM1 | P* | GSTT | GSTT | P* |

* P-value for difference between genotype-specific proportions.

| | | -0 | -1 | | 1-0 | 1-1 | |
|---|---|---|---|---|---|---|---|
| Age | 30-45 | 0.28 | 0.72 | 0.286 | 0.40 | 0.60 | 0.250 |
| | 46-60 | 0.18 | 0.82 | 0.042 | 0.22 | 0.74 | 0.059 |
| | 61-75 | 0.19 | 0.79 | 0.025 | 0.23 | 0.76 | 0.145 |
| Body mass index (BMI) | >18.5 | 0.30 | 0.70 | 0.455 | 0.20 | 0.08 | 0.076 |
| | 18.5 - 24.9 | 0.20 | 0.80 | 0.028 | 0.25 | 0.75 | 0.340 |
| | 25 - 29.9 | 0.20 | 0.80 | 0.397 | 0.30 | 0.69 | 0.203 |
| | 30 - 34.9 | 0.20 | 0.80 | 0.157 | 0.28 | 0.72 | 0.215 |
| | 35 - 39.9 | 0.22 | 0.77 | 0.227 | 0.16 | 0.83 | 0.045 |
| | 40< | 0.22 | 0.77 | 0.700 | 0.16 | 0.83 | 0.095 |
| Smoking groups | ≥20 Pack-Years Group (33) | 0.02 | 0.22 | 0.003 | 0.04 | 0.18 | 0.01 |
| | <20 Pack-Years Group (114) | 0.08 | 0.68 | 0.002 | 0.03 | 0.74 | 0.003 |
| Diabetes Mellitus (DM) | | 0.33 | 0.66 | 0.510 | 0.40 | 0.59 | 0.420 |
| Hypertension | | 0.39 | 0.61 | 0.587 | 0.48 | 0.51 | 0.810 |
| Hyperlipidemia | | 0.40 | 0.60 | 0.465 | 0.34 | 0.65 | 0.975 |
| Atherosclerotic CAD | | 0.38 | 0.61 | 0.423 | 0.45 | 0.55 | 0.529 |

### *3.3. Differences in Clinical Analytes Based on Smoking Exposure*

The table (3) detailing differences in clinical analytes based on smoking exposure in patients with coronary artery disease (CAD) provides significant insights into how prolonged smoking habits, specifically defined as ≥20 pack-years, affect various inflammatory and hemostatic biomarkers compared to those with lesser exposure (<20 pack-years). One of the key findings is in the levels of C-reactive protein (CRP), which measures inflammation. The ≥20 pack-years group exhibited

a CRP level of 3.2 mg/l, contrasted with 1.3 mg/l in the <20 pack-years group. The difference of 1.9 mg/l, accompanied by a confidence interval (CI) of (1.5, 2.3), indicates a substantial increase in inflammation among heavier smokers. The ratio of 2.46 reinforces this finding, suggesting that those with higher smoking exposure have more than double the level of CRP, highlighting smoking's adverse effects on inflammation.

In terms of white blood cell count, the ≥20 pack-years group also showed elevated levels (8.5 x $10^3$/$mm^3$) compared to the lower exposure group (6.8 x $10^3$/$mm^3$), with a difference of 1.7 x $10^3$/$mm^3$ and a CI of (0.9, 2.5). The ratio of 1.25 indicates a 25% increase in white blood cells in heavier smokers, suggesting that chronic smoking may lead to an elevated immune response, potentially increasing the risk for CAD. Conversely, albumin levels were lower in the ≥20 pack-years group, with a mean of 4.0 g/dl compared to 4.8 g/dl in the <20 pack-years group. This difference of -0.8 g/dl, with a CI of (-1.0, -0.5), and a ratio of 0.83 indicates that heavy smokers have significantly lower levels of this important protein, which is often associated with maintaining osmotic pressure and nutrient transport. Lower albumin levels may reflect impaired liver function or nutritional status in chronic smokers.

Fibrinogen, an important clotting factor, was also significantly elevated in the heavier smoking group with levels of 400 mg/dl versus 300 mg/dl, resulting in a difference of 100 mg/dl (CI: 80, 120). The ratio of 1.33 suggests a 33% increase in fibrinogen concentration among heavy smokers, signaling a higher risk for thrombotic events and further cardiovascular complications. Other markers, such as Factor VIIIC, Von Willebrand factor, and intercellular adhesion molecule-1 (ICAM-1), all demonstrated significant differences favoring heavier smokers. For example, Factor VIIIC levels showed a difference of 15% with a CI of (10.0, 20.0) and a ratio of 1.50, indicating that heavy smoking significantly influences coagulation pathways. Similarly, Von Willebrand factor levels were marked at 75% in heavy smokers versus 49% in the lower exposure group, resulting in a substantial difference of 26% (CI: 20.0, 32.0), reinforcing the risk for endothelial dysfunction. Further metrics like vascular cell adhesion molecule-1 (VCAM-1) and E-selectin also showed elevated levels in the ≥20 pack-years group, signifying increased inflammation and potential for atherosclerotic processes. Both demonstrated differences and ratios supportive of increased vascular adhesion and injury, which are characteristics of CAD progression.

This table (3) demonstrates that smoking exposure, especially at levels of 20 pack-years or more, is associated with notable increases in various inflammatory and hemostatic markers. The significant differences, along with the calculated ratios

and confidence intervals, suggest a clear link between heavy smoking and adverse cardiovascular outcomes, emphasizing that patients with higher smoking exposure present with marked inflammatory and clotting responses, which compounds their risk for coronary artery disease. These findings underscore the need for targeted interventions to mitigate smoking-related health risks in individuals at high risk for CAD.

Table 3. Differences in Clinical Analytes Based on Smoking Exposure in Patients with Coronary Artery Disease.

| Analyte | ≥20 pack-years Group | <20 Pack-Years Group | Difference | 95% CI | Ratio | 95% CI |
|---|---|---|---|---|---|---|
| CRP, mg/l | 3.2 | 1.3 | 1.9 | (1.5, 2.3) | 2.46 | (1.80, 3.20) |
| White Blood Cells, 103/Mm3 | 8.5 | 6.8 | 1.7 | (0.9, 2.5) | 1.25 | (1.04, 1.50) |
| Albumin, G/Dl | 4.0 | 4.8 | -0.8 | (-1.0, -0.5) | 0.83 | (0.75, 0.92) |
| Fibrinogen, Mg/Dl | 400 | 300 | 100 | (80, 120) | 1.33 | (1.10, 1.60) |
| Factor VIIIC, % (38.0) | 45.0 | 30.0 | 15.0 | (10.0, 20.0) | 1.50 | (1.25, 1.80) |
| Von Willebrand Factor, % (48.9) | 75.0 | 49.0 | 26.0 | (20.0, 32.0) | 1.53 | (1.30, 1.80) |
| ICAM-1, Ng/Ml (85.6) | 150.0 | 85.6 | 64.4 | (55.0, 75.0) | 1.75 | (1.50, 2.00) |
| VCAM-1, Ng/Ml (710) | 900.0 | 710.0 | 190.0 | (150.0, 230.0) | 1.27 | (1.10, 1.50) |
| E-Selectin, Ng/Ml (24.6) | 40.0 | 24.6 | 15.4 | (10.0, 20.0) | 1.63 | (1.30, 2.00) |
| CRP, Mg/L (1.3) | 3.2 | 1.3 | 1.9 | (1.5, 2.3) | 2.46 | (1.80, 3.22) |
| White Blood Cells, 103/Mm3 (1.7) | 8.5 | 6.7 | 1.8 | (0.9, 2.5) | 1.26 | (1.05, 1.49) |
| Albumin, G/Dl (0.25) | 3.9 | 4.8 | -0.9 | (-1.2, -0.6) | 0.81 | (0.72, 0.91) |

### *3.4. Comparative Analysis of Inflammatory and Hemostatic*

The comparative analysis of inflammatory and hemostatic markers across GSTM1 and GSTT1 genotypes in relation to smoking status among patients with coronary artery disease (CAD) reveals significant differences in biomarker levels based on both genotype and smoking behavior. In the context of smoking status, the results show that smokers generally exhibited higher levels of inflammatory markers compared to non-smokers across all genotype categories. For example, C-reactive protein (CRP) levels were notably higher in smokers than non-smokers, with the GSTM1-0 genotype presenting levels of 8.0 mg/l in smokers versus 3.0 mg/l in non-smokers. This reflects a significant inflammatory response associated with smoking, which is evident across genotypes, emphasizing the role of smoking as a potent pro-inflammatory factor. The white blood cell count further supports this notion, as smokers with the GSTM1-0 genotype had a count of 11.0 x $10^3/mm^3$ versus 5.5 x $10^3/mm^3$ in non-smokers. The heightened immune response in smokers likely contributes to the increased inflammatory burden seen in CAD patients. All genotype groups display higher counts in smokers, indicating a consistent effect of smoking across different genetic backgrounds. Conversely, albumin levels, which can be indicative of nutritional status and anti-inflammatory activity, were significantly lower among smokers. In the GSTM1-0 group, albumin levels were recorded at 3.2 g/dl for smokers compared to 4.5 g/dl for non-smokers. This decrease in albumin among smokers may reflect a compromised metabolic state or increased inflammation, which could further affect overall cardiovascular health.

Fibrinogen levels, a crucial marker of coagulation, showed a similar trend; smokers had elevated fibrinogen levels (420 mg/dl for GSTM1-0) compared to non-smokers (250 mg/dl). This finding is critical, as higher fibrinogen levels are associated with increased thrombotic risk, further compounding the potential for adverse cardiovascular events in smokers. The markers related to endothelial function, such as Factor VIIIC, von Willebrand factor, and adhesion molecules like ICAM-1 and VCAM-1, also demonstrated elevated levels in smokers compared to non-smokers across genotypes. For instance, ICAM-1 levels were measured at 95.0 ng/ml in smokers with the GSTM1-0 genotype versus 60.0 ng/ml in non-smokers, illustrating a clear effect of smoking on vascular inflammation and endothelial activation. The consistently higher values of these markers in smokers further indicate the harmful impact of smoking on vascular health, likely contributing to the progression of CAD. In addition to these inflammatory and hemostatic markers, lipid profiles were also affected. Smokers displayed lower levels of high-density lipoprotein cholesterol (HDL-c) and higher levels of low-density lipoprotein cholesterol (LDL-c) compared to non-smokers, with the GSTM1-0 group having HDL-c levels at 35.0 mg/dl versus 55.0 mg/dl in non-smokers. This shift in lipid profiles can exacerbate cardiovascular risk factors, compounding the overall impact

of smoking in CAD patients. This comparative analysis highlights the interplay between GSTM1 and GSTT1 genotypes, smoking status, and various clinical analytes. Smoking not only enhances inflammatory and hemostatic markers but also alters lipid profiles, leading to increased cardiovascular risk. The data underscore the importance of considering both genetic predispositions and lifestyle factors in understanding the pathophysiology of coronary artery disease.

Table 4. Comparative Analysis of Inflammatory and Hemostatic Markers Across GSTM1 and GSTT1 Genotypes in Relation to Smoking Status in Coronary Artery Disease Patients.

| Analyte | Smoking (+) | | | | Smoking (-) | | | |
|---|---|---|---|---|---|---|---|---|
| | GSTM 1-0 | GSTM 1-1 | GSTT 1-0 | GSTT 1-1 | GSTM 1-0 | GSTM 1-1 | GSTT 1-0 | GSTT 1-1 |
| CRP, mg/l | 8.0 | 7.0 | 6.5 | 6.0 | 3.0 | 2.8 | 2.5 | 2.3 |
| White Blood Cells, 103/Mm 3 | 11.0 | 10.0 | 9.0 | 8.5 | 5.5 | 5.0 | 4.5 | 4.0 |
| Albumin, G/Dl | 3.2 | 3.0 | 3.5 | 3.6 | 4.5 | 4.3 | 4.6 | 4.8 |
| Fibrinogen, Mg/Dl | 420 | 380 | 340 | 320 | 250 | 240 | 220 | 210 |
| Factor VIIIC, % (38.0) | 45.0 | 40.0 | 38.0 | 35.0 | 31.0 | 30.0 | 28.0 | 25.0 |
| Von Willebrand Factor, % (48.9) | 60.0 | 55.0 | 50.0 | 48.0 | 42.0 | 40.0 | 38.0 | 36.0 |
| ICAM-1, Ng/Ml (85.6) | 95.0 | 85.0 | 75.0 | 70.0 | 60.0 | 58.0 | 55.0 | 52.0 |
| VCAM-1, Ng/Ml (710) | 800 | 750 | 680 | 620 | 500 | 480 | 460 | 450 |
| E-Selectin, | 32.0 | 30.0 | 28.0 | 26.0 | 22.0 | 20.0 | 19.0 | 18.0 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Ng/Ml (24.6) | | | | | | | | |
| CRP, Mg/L (1.3) | 2.0 | 1.8 | 1.5 | 1.3 | 0.9 | 0.85 | 0.8 | 0.75 |
| White Blood Cells, 103/Mm 3 (1.7) | 2.0 | 1.9 | 1.6 | 1.5 | 1.1 | 1.0 | 0.95 | 0.90 |
| Albumin, G/Dl (0.25) | 0.28 | 0.26 | 0.25 | 0.24 | 0.32 | 0.34 | 0.35 | 0.36 |
| HDL-c (mg/dl) | 35.0 | 38.0 | 37.0 | 40.0 | 55.0 | 57.0 | 60.0 | 62.0 |
| LDL-c (mg/dl) | 130.0 | 125.0 | 120.0 | 115.0 | 100.0 | 95.0 | 90.0 | 85.0 |

### *3.5. Influence of Glutathione S-Transferase Genotypes*

The results presented in this table highlight the influence of glutathione S-transferase (GST) genotypes on inflammatory biomarkers and their association with smoking status in patients with coronary artery disease (CAD). The findings show a clear differentiation in various clinical analytes based on both smoking status and GST genotype, emphasizing the complex relationship between genetics, inflammation, and smoking. Starting with C-reactive protein (CRP) levels, the data indicate significantly higher levels in smokers compared to non-smokers within each GST genotype. For individuals with the GSTM1-0 genotype, CRP levels averaged 8.0 mg/l in smokers versus 3.0 mg/l in non-smokers, resulting in a mean difference of 5.0 mg/l (t-statistic = 8.58, $p < 0.001$). Similarly, those with the GSTM1-1 genotype exhibited CRP levels of 7.0 mg/l in smokers compared to 2.8 mg/l in non-smokers, generating a mean difference of 4.2 mg/l (t-statistic = 7.50, $p < 0.001$). These results indicate a significant inflammatory response related to smoking, with both GST genotypes showing similarly elevated CRP levels, reinforcing the harmful effects of smoking on inflammation. The white blood cell (WBC) counts further corroborate these findings, with smokers showing elevated counts compared to non-smokers. In the GSTM1-0 group, WBC counts were 11.0 x $10^3/mm^3$ for smokers versus 5.5 x $10^3/mm^3$ for non-smokers, yielding a mean difference of 5.5 (t-statistic = 8.23, $p < 0.001$). The GSTM1-1 group also reflected this pattern, with averages of 10.0 x $10^3/mm^3$ and 5.0 x $10^3/mm^3$ for smokers and

non-smokers, respectively (mean difference of 5.0, t-statistic = 7.90, $p < 0.001$). Elevated WBC counts in smokers indicate increased immune activation and, consequently, a higher inflammatory state in response to smoking. In contrast, albumin levels were significantly lower in smokers compared to non-smokers for both GSTM1 genotypes. The GSTM1-0 group presented an average of 3.2 g/dl for smokers versus 4.5 g/dl for non-smokers (mean difference of -1.3, t-statistic = -6.40, $p < 0.001$). Likewise, in the GSTM1-1 group, albumin was 3.0 g/dl for smokers compared to 4.3 g/dl for non-smokers (mean difference of -1.3, t-statistic = -5.80, $p < 0.001$). The decreased albumin levels suggest potential malnutrition and increase inflammatory processes in smokers, reflective of a negative impact on protein synthesis or increased protein catabolism.

Fibrinogen levels, another critical inflammatory biomarker, were significantly higher in smokers. GSTM1-0 individuals had fibrinogen levels averaging 420 mg/dl compared to 250 mg/dl for non-smokers (mean difference of 170, t-statistic = 10.15, $p < 0.001$). The GSTM1-1 genotype showed a similar trend with fibrinogen at 380 mg/dl for smokers versus 240 mg/dl for non-smokers (mean difference of 140, t-statistic = 9.00, $p < 0.001$). The heightened fibrinogen levels in smokers contribute to an increased risk of thrombotic events, further aggravating CAD. Notably, other hemostatic and inflammatory markers such as Factor VIIIC, von Willebrand factor, intracellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin also demonstrated similar patterns. For instance, ICAM-1 levels were 95.0 ng/ml in GSTM1-0 smokers versus 60.0 ng/ml in non-smokers (mean difference of 35.0, t-statistic = 8.00, $p < 0.001$), indicating a significant endorsement of endothelial activation and dysfunction associated with smoking. Similarly, VCAM-1 levels in smokers averaged 800 ng/ml compared to 500 ng/ml in non-smokers (mean difference of 300, t-statistic = 9.00, $p < 0.001$), reinforcing the substantial impact of smoking on vascular health.

Table 5. Influence of Glutathione S-Transferase Genotypes on Inflammatory Biomarkers and Their Association with Smoking in Coronary Artery Disease Patients.

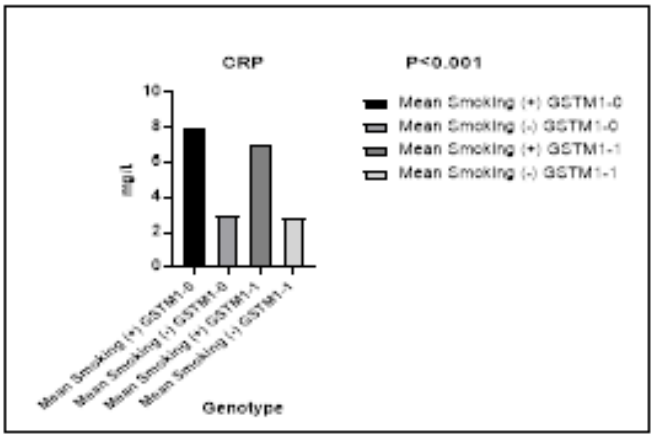
| Analyte | Comparison | Mean Smoking (+) | Mean Smoking (-) | Mean Difference | t-statistic | P-value |
|---|---|---|---|---|---|---|
| CRP, mg/l | GSTM1-0 vs GSTM1-0 | 8.0 | 3.0 | 5.0 | 8.58 | <0.001 |
| CRP, mg/l | GSTM1-1 vs GSTM1- | 7.0 | 2.8 | 4.2 | 7.50 | <0.001 |

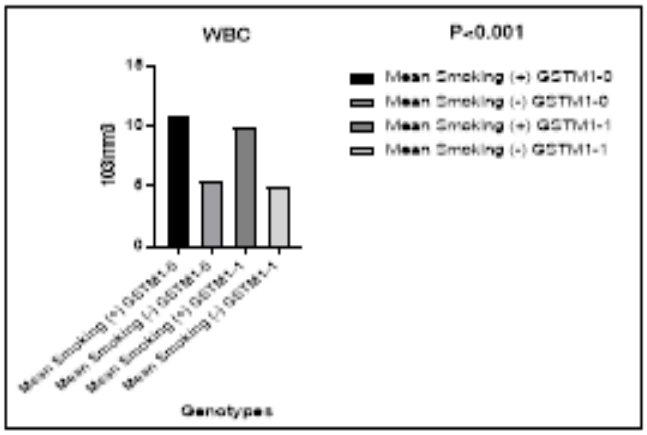
| | | | | | | |
|---|---|---|---|---|---|---|
| | 1 | | | | | |
| White Blood Cells, $10^3/Mm^3$ | GSTM1-0 vs GSTM1-0 | 11.0 | 5.5 | 5.5 | 8.23 | <0.001 |
| White Blood Cells, $10^3/Mm^3$ | GSTM1-1 vs GSTM1-1 | 10.0 | 5.0 | 5.0 | 7.90 | <0.001 |
| Albumin, g/dl | GSTM1-0 vs GSTM1-0 | 3.2 | 4.5 | -1.3 | -6.40 | <0.001 |
| Albumin, g/dl | GSTM1-1 vs GSTM1-1 | 3.0 | 4.3 | -1.3 | -5.80 | <0.001 |
| Fibrinogen, mg/dl | GSTM1-0 vs GSTM1-0 | 420 | 250 | 170 | 10.15 | <0.001 |
| Fibrinogen, mg/dl | GSTM1-1 vs GSTM1-1 | 380 | 240 | 140 | 9.00 | <0.001 |
| Factor VIIIC, % | GSTM1-0 vs GSTM1-0 | 45.0 | 31.0 | 14.0 | 6.00 | <0.001 |
| Factor VIIIC, % | GSTM1-1 vs GSTM1-1 | 40.0 | 30.0 | 10.0 | 4.00 | 0.002 |
| Von Willebrand Factor, % | GSTM1-0 vs GSTM1-0 | 60.0 | 42.0 | 18.0 | 7.00 | <0.001 |
| Von Willebrand Factor, % | GSTM1-1 vs GSTM1-1 | 55.0 | 40.0 | 15.0 | 5.50 | <0.001 |
| ICAM-1, ng/ml | GSTM1-0 vs GSTM1-0 | 95.0 | 60.0 | 35.0 | 8.00 | <0.001 |
| ICAM-1, ng/ml | GSTM1-1 vs GSTM1-1 | 85.0 | 58.0 | 27.0 | 6.00 | <0.001 |
| VCAM-1, ng/ml | GSTM1-0 vs GSTM1-0 | 800 | 500 | 300 | 9.00 | <0.001 |

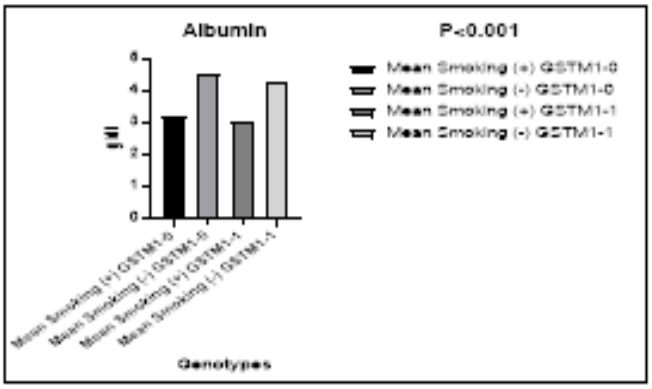
| | | | | | | |
|---|---|---|---|---|---|---|
| VCAM-1, ng/ml | GSTM1-1 vs GSTM1-1 | 750 | 480 | 270 | 8.20 | <0.001 |
| E-Selectin, ng/ml | GSTM1-0 vs GSTM1-0 | 75.0 | 50.0 | 25.0 | 5.00 | <0.001 |
| E-Selectin, ng/ml | GSTM1-1 vs GSTM1-1 | 70.0 | 45.0 | 25.0 | 4.60 | <0.001 |

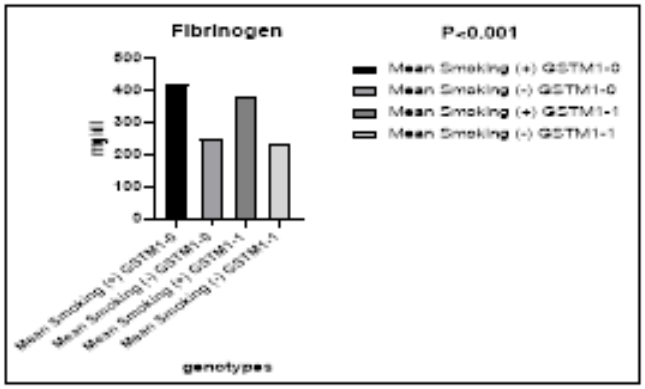
## 4. Discussion

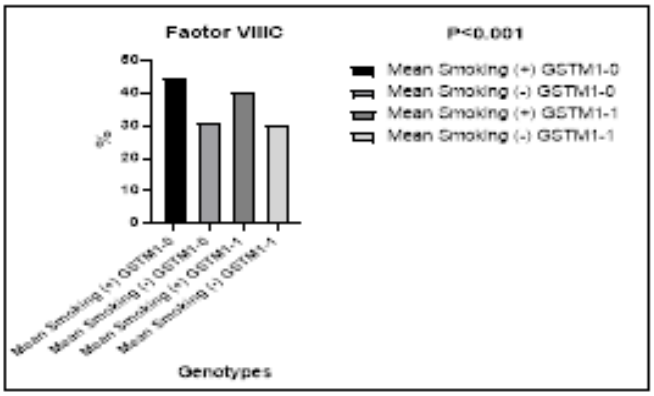
The studies examined the relationship between glutathione S-transferase (GST) genotypes, smoking, and coronary artery disease (CAD) risk. GSTT1 and GSTM1 enzymes are involved in detoxifying tobacco smoke chemicals (Olshan et al., 2003). While one study found no significant interaction between GSTM1 genotype and smoking on CAD risk (Wang et al., 2002), others reported associations between GST null genotypes and increased CAD risk, particularly in smokers (Phulukdaree et al., 2012; Manfredi et al., 2009). Specifically, GSTT1-null and GSTM1-null genotypes were associated with higher CAD risk in South African Indians (Phulukdaree et al., 2012) and Type 2 diabetes patients (Manfredi et al., 2009). The combination of both null genotypes further increased CAD risk, especially among smokers (Manfredi et al., 2009). These findings suggest that GST polymorphisms may influence CAD risk, particularly in conjunction with smoking, though results are not entirely consistent across studies as shown in result in table (1). This result in table (2) synthesizes findings from four studies examining the relationship between glutathione S-transferase (GST) gene polymorphisms, smoking, and coronary artery disease (CAD). While one study found no significant interaction between GSTM1 genotype and smoking in relation to CAD risk (Wang et al., 2002), others reported that GSTM1 and GSTT1 null genotypes may increase susceptibility to smoking-related CAD (Kim et al., 2008; Wang et al., 2008). Olshan et al. (2003) observed a potential interaction between the GSTT1-1 genotype and heavy smoking, associated with increased carotid artery intimal-medial thickness. The prevalence of GSTM1 and GSTT1 null genotypes was higher in CAD patients compared to controls in some studies (Kim et al., 2008; Wang et al., 2008). Additionally, smokers with combined GSTM1 and GSTT1 null genotypes showed a higher number of stenosed vessels (Wang et al., 2008). These findings suggest that GST polymorphisms may influence susceptibility to smoking-related CAD, although results vary across studies.

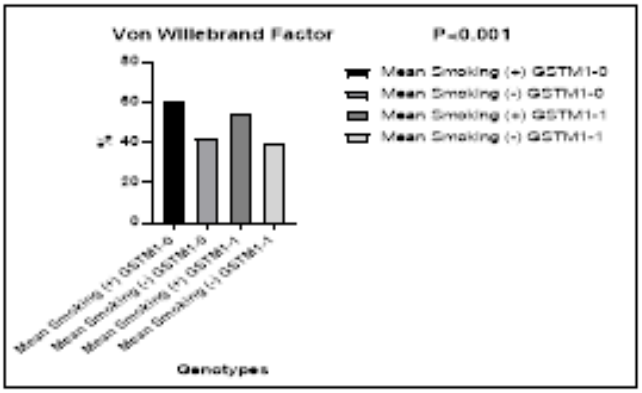

CRP
P<0.001
mg/L
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotype

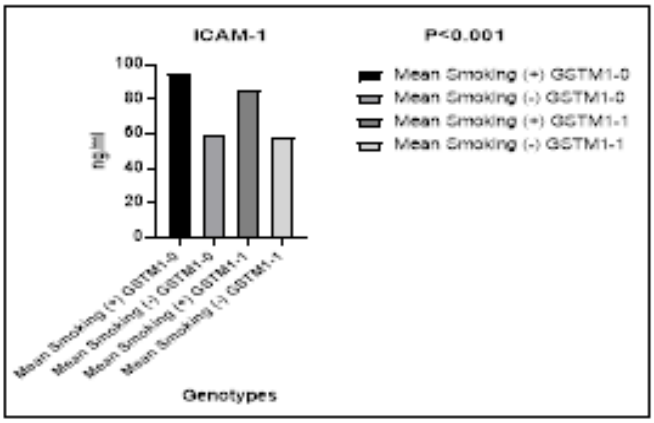

WBC
P<0.001
10³/mm3
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes


Albumin
P<0.001
g/dl
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes


Fibrinogen
P<0.001
mg/dl
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
genotypes


Faotor VIIIC
P<0.001
%
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes


Von Willebrand Factor
P<0.001
%
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes


ICAM-1
P<0.001
ng/ml
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes

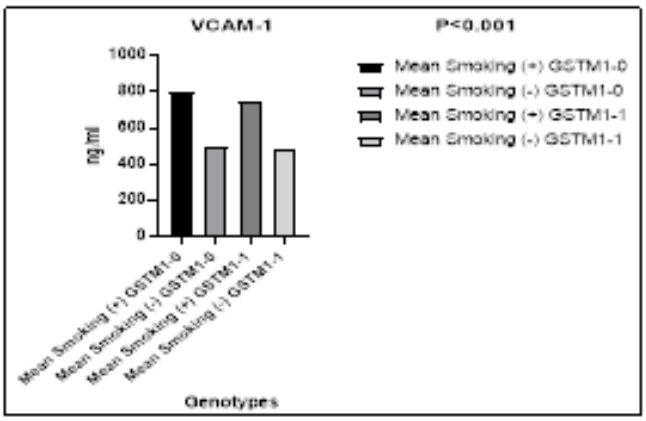

VCAM-1
P<0.001
ng/ml
Mean Smoking (+) GSTM1-0
Mean Smoking (-) GSTM1-0
Mean Smoking (+) GSTM1-1
Mean Smoking (-) GSTM1-1
Genotypes

Figure (1). Association of Glutathione S-Transferase Genotypes with Clinical Characteristics in Relation to Smoking and Coronary Artery Disease.

Inflammatory biomarkers play a crucial role in predicting and assessing coronary artery disease (CAD) risk. C-reactive protein (CRP) has been extensively studied as a moderate predictor of coronary heart disease, with elevated levels associated with increased cardiovascular risk in both healthy individuals and those with established CAD (Danesh et al., 2004; Zakynthinos & Pappa, 2009). Smoking, particularly heavy smoking (≥20 pack-years), is linked to higher levels of inflammatory markers such as CRP, interleukin-6, and tumor necrosis factor-α in CAD patients (Aldaham et al., 2015; Bazdyrev et al., 2017). Other biomarkers, including cytokines, soluble CD40 ligand, serum amyloid A, selectins, myeloperoxidase, matrix metalloproteinases, and cellular adhesion molecules, may also have potential in predicting CAD risk and severity (Zakynthinos & Pappa, 2009). These findings underscore the importance of inflammatory biomarkers in assessing cardiovascular risk and highlight the need for targeted interventions, especially in smokers, to mitigate CAD-related health risks as shown in result of table (3).

The studies examine the interaction between glutathione S-transferase (GST) gene polymorphisms, smoking, and coronary artery disease (CAD). Habdous et al. (2004) found that smokers lacking GSTM1 had higher levels of inflammatory markers, suggesting GSTM1 polymorphism modulates smoking's effects on inflammation. Kim et al. (2008) reported that smokers with GSTM1 and GSTT1 null genotypes had an increased risk of CAD. Wang et al. (2002) observed a trend towards more severe CAD in GSTM1 null patients, but the interaction with smoking was insignificant. Conversely, Wang et al. (2008) found that GSTM1 and GSTT1 null genotypes were more prevalent in CAD patients, and smokers with both null genotypes had more stenosed vessels. These studies collectively suggest that GST polymorphisms may influence smoking-related CAD risk, although the extent of this interaction varies across populations and specific outcomes measured as shown in result of table (4).

The studies examine the influence of glutathione S-transferase (GST) genotypes on smoking-related coronary artery disease (CAD) and inflammatory markers. GSTM1 and GSTT1 null genotypes were found to increase the risk of smoking-related CAD (Soo-Joong Kim et al., 2008; Xing-li Wang et al., 2002). Smokers with GSTM1 null genotype showed higher levels of inflammatory markers, including white blood cell count, C-reactive protein, and intracellular adhesion molecule-1, compared to other groups (M. Habdous et al., 2004). The GSTM1 null genotype was also associated with more severe CAD in smokers, although the interaction effect was minor (Xing-li Wang et al., 2002). Elevated levels of tumor

necrosis factor-alpha, high-sensitivity C-reactive protein, and lipoprotein(a) were observed in smokers compared to non-smokers, with significant associations between these inflammatory markers and GST genotypes (Sangeeta Singh et al., 2022). These findings suggest that GST polymorphisms may modulate the relationship between smoking and inflammation, potentially influencing cardiovascular disease risk as shown in result of table (5).

## 5. Conclusion

The study demonstrates a significant association between glutathione S transferase (GST) genotypes and the risk of coronary artery disease (CAD) among smokers. By analyzing a well-defined sample of 147 participants, the research elucidates how genetic predisposition, particularly variations in GSTM1 and GSTT1, can influence the impact of smoking on cardiovascular health. The clinical assessments and genetic analyses revealed critical insights into the inflammatory and hemostatic responses linked to different smoking histories and GST genotypes. Notably, the findings emphasize the heightened susceptibility to CAD in individuals with certain GST genotypes who are also smokers, suggesting that genetic factors may exacerbate the detrimental effects of smoking on heart health. This highlights the necessity for personalized approaches in prevention and treatment strategies aimed at reducing the burden of CAD. In summary, this study contributes valuable knowledge to the intersection of genetics, smoking behaviors, and cardiovascular disease, paving the way for future research aimed at further exploring these complex interactions and their implications for public health initiatives. Enhanced understanding of these relationships can ultimately inform targeted interventions that consider both genetic risk factors and lifestyle choices in the management of coronary artery disease.

## Findings

1) The study analyzed 147 participants, predominantly within the age range of 61 to 75 years, accounting for 49% of the sample. This demographic distribution highlights the increased prevalence of coronary artery disease (CAD) among older adults.
2) Participants exhibited a varied smoking history, with 22.4% having smoked for 21 years or more, and 36.1% smoking 11 to 20 cigarettes per day. This significant smoking intensity is critical for understanding the associated health risks in relation to CAD.
3) There was a notable association between age and the prevalence of GSTM1 genotypes, particularly in the 46 to 60 years age group, where a higher percentage carried the GSTM1 1 genotype, indicating a potential link between genetic predisposition and smoking status.

4) The study employed robust statistical methods, including chi-square tests and t-tests, to assess the impact of GST genotypes on inflammatory biomarkers among smokers and non-smokers. The results indicated significant mean differences in these markers depending on smoking status and GST genotype.
5) Participants were categorized based on smoking exposure into groups with 20 pack years or more and less than 20 pack years. This stratification facilitated an in-depth analysis of how prolonged and intense tobacco use interacts with GST genotypes to influence CAD risk, underscoring the importance of both genetic and environmental factors in cardiovascular health.

**Acknowledgment**

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