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RESEARCH ARTICLE

Study the association between myeloperoxidase gene single-nucleotide polymorphism G463A (rs2333227) and coronary artery disease in Iraqi patients

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Abstract

Acute coronary syndrome (ACS) is a major cause of morbidity and death globally, which is caused by the multifaceted interaction between oxidative stress and inflammatory processes. The enzyme myeloperoxidase (MPO) is secreted by activated leukocytes and is a determinant of vascular dysfunction and unstable plaque. The genetic variation within the MPO gene, especially G463A (rs2333227), may increase enzyme expression and contribute to disease occurrence. The aim of the study was to examine the relationship between the MPO G463A polymorphism, circulating MPO levels, and the risk of ACS. The case-control study included 129 patients with ACS and 66 apparently healthy controls. Immunoassay techniques were used to measure serum MPO and high-sensitivity troponin I levels, and PCR-based methods were used to assess the MPO G463A polymorphism. The MPO level in serum was significantly higher in ACS patients than in controls ($p < 0.001$). The ROC analysis revealed an average diagnostic ability for MPO (AUC = 0.686, sensitivity for70.7%). There was a significant association between the MPO G463A polymorphism and ACS susceptibility ($p > 0.05$). Nonetheless, some genotypes were correlated with changes in MPO levels, and they may contribute to the severity of the diseases. An elevated serum MPO level is strongly correlated with ACS and can serve as a useful biomarker for its detection. Conversely, the MPO G463A polymorphism does not appear to have a significant impact on disease susceptibility but may affect individual differences in the inflammatory response.

1. INTRODUCTION

Acute coronary syndrome (ACS) is a continuum of clinical syndromes that is related to the abrupt decrease of coronary blood flow, such as unstable angina and myocardial infarction. It is one of the chief causes of morbidity and mortality in the world and is mainly caused by instability of atherosclerotic plaque, inflammation, and oxidative stress. Knowledge of the molecular and genetic processes underlaying ACS is key to improving early diagnosis and risk classification. Myeloperoxidase (MPO) is a heme-based enzyme secreted by neutrophils and monocytes, which are activated and play a major role in oxidative and inflammatory reactions. MPO is also associated with the development of atherosclerosis through the formation of reactive oxygen species, lipid peroxidation, and endothelial disfunction. Higher levels of MPO have been correlated with disease activity, plaque instability and poor cardiovascular outcomes, which may demonstrate its potential as a of disease activity biomarker (1).

By 2030, over 23 million people worldwide are expected to die from heart disease. Myocardial infarction (MI) is one of the leading causes contributing to global mortality and disability (2). The MPO gene contains a functional promoter polymorphism, G463A (rs2333227), which has been shown to influence transcriptional activity and enzyme expression.

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The A allele is associated with reduced MPO expression compared to the G allele, suggesting a potential modulatory role in oxidative stress and inflammatory responses. Therefore, this polymorphism has been widely investigated in relation to cardiovascular diseases, although findings remain inconsistent across different populations. This disease begins as a sustained inflammatory, oxidative, and degenerative process in arterial tissue and within the lumen of atherosclerotic plaques in the coronary arteries (3).

Atherosclerosis is a chronic inflammatory disorder of the arteries characterized by the accumulation of lipids within the arterial wall. Oxidative stress may contribute to lipid and protein modifications and subsequent vascular wall responses, recruiting innate immune cells to atheromatous plaque (4). Atherosclerotic plaque formation is a complex process, from the initiation of endothelial dysfunction through the maturation, rupture, and inflammatory processes of mature atheroma, necessitating a detailed understanding of the contributing factors (5). Myeloperoxidase (MPO) has previously been associated with the development and progression of atherosclerosis, suggesting its role in enhancing plaque instability and function, thereby contributing to a pathogenetic role in atherogenesis and exacerbated oxidative stress (6). Also, MPO can use nitric oxide as a substrate, leading to endothelial dysfunction (7). Genetic variations influencing inflammation-related biomarkers are relatively fixed across a lifetime, are unaffected by external environmental and medical factors, and may thus produce lasting impacts once exposure to chronic inflammation occurs (8). Myeloperoxidase is a part of the peroxidase-cyclooxygenase subgroup in the heme peroxidase enzyme family. It is produced and secreted by neutrophils and monocytes and plays an important role in the innate immune response.

MPO serves as a critical mediator of the intracellular microbicidal pathway in phagocytes and the host's innate immune response (9). MPO promotes the production of hypochlorous acid, one of the strongest oxidant species formed in the human body by phagocytes during their microbicidal mechanism. MPO is necessary for immunological protection against pathogens, but MPO and its oxidative byproducts react with a wide variety of lipids, proteins, and nucleic acids, causing damaging events in host tissues generally associated with inflammatory diseases, including atherosclerosis (10). Polymorphisms in genes involved in inflammatory processes may modulate susceptibility to oxidative stress and cardiovascular injury. Unlike environmental risk factors, genetic polymorphisms remain stable throughout life and, once expressed, may exert long-term effects on inflammatory pathways and disease progression (11). The MPO gene, located on chromosome 17q, harbors a functional promoter polymorphism (−463G/A, rs2333227) that modulates transcriptional activity and enzyme expression (12).

Several studies have reported associations between this polymorphism, circulating MPO levels, and CAD risk. However, findings remain inconsistent, ranging from increased to reduced risk. Most studies have focused on European and East Asian populations, with limited data from Middle Eastern groups. Moreover, the relationship between MPO genetic variation, circulating MPO, and biochemical markers of myocardial injury and lipid metabolism remains poorly understood (13-16). The MPO-463G/A SNP may affect disease severity through oxidative and inflammatory pathways, although its impact on susceptibility remains unclear. Despite increasing evidence of the interrelation between MPO and cardiovascular pathology, the relationship between MPO gene polymorphisms, MPO plasma levels, and the risk of ACS remains unclear, especially in Middle Eastern populations. The majority of the past studies have been based on European and Asian cohorts, with little information on the Iraqi patients. Thus, the study was conducted to determine how the MPO G463A (rs2333227) polymorphism and circulating MPO are related to the acute coronary syndrome risk in one of the Iraqi populations. Our hypothesis was that high levels of MPO and genetic differences within the MPO gene can contribute to disease susceptibility and severity via oxidative and inflammatory pathways.

2. MATERIALS AND METHODS

2.1. Study Design and Ethical Approval

This case-control study, conducted from November 2023 to August 2024, aimed to evaluate the association between the myeloperoxidase gene polymorphism and coronary artery disease. The research plan received approval from the Institute's Committee and the Trenching Hospital and Al-Basra Specialized Heart Diseases and Surgery Teaching Hospital (Approval No. 49, January 18, 2024). Every working activity was carried out in line with the principles of the Declaration of Helsinki. All participants who had given informed consent were provided with it in written form before enrolment.

2.2. Study Population

It was an observational study setting of 129 patients with acute coronary syndrome: 47 females and 82 males, aged 45 to 75 years. Patients were recruited from Al-Sadr Teaching Hospital, Al-Basra Specialized Heart Diseases and Surgery Teaching Hospital, and Al-Faihaa Teaching Hospital. Cardiologists confirmed the diagnosis based on clinical history, physical examination, electrocardiographic findings, and biochemical tests, especially high-sensitivity troponin I. The control population consisted of apparently healthy individuals recruited from regular health check-up hospitals. Controls were frequency-matched to patients by age and sex to reduce confounding. They had no history of cardiovascular disease. Patient inclusion followed acute coronary syndrome criteria as determined by clinical, electrocardiographic, and biochemical results. Exclusion criteria included patients with an oncologic or autoimmune inflammatory malignancy,

severe hepatic or renal impairment, or a recent infection. To reduce potential confounding, medical records were used to gather demographic and clinical data, including for those on anti-inflammatory medications, corticosteroids, lipid-lowering medications, or immunosuppressive agents within 4 weeks prior to sampling. Smoking status, hypertension, diabetes mellitus, medication use, and family history of cardiovascular diseases were also considered as potential confounding factors in data interpretation.

2.3. Data Collection and Biochemical Analysis

Five milliliters of venous blood samples were collected from participants. MPO and high-sensitivity troponin I levels were determined using commercial enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. An automated clinical chemistry analyzer was used to measure biochemical parameters, including lipid profile, fasting glucose, urea, and creatinine (Roche Cobas Integra 400 Plus, Germany). Each assay was done twice, and internal quality control samples were incorporated in each run to enhance accuracy and reproducibility. The intra- and inter-assay coefficients of variation were kept within reasonable limits (less than 10 %).

All lab testing was performed by staff unaware of the clinical condition of the study subjects to reduce measurement bias. Serum myeloperoxidase (MPO) levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. In a nutshell, serum samples were placed in microplate wells pre-coated with MPO-specific antibodies, incubated, and washed. The second step was to add an enzyme-linked secondary antibody, then develop the reaction with a chromogenic substrate. Absorbance was measured at 450 nm using a microplate reader, and a standard calibration curve was used to determine MPO concentration. Each sample was analyzed twice to enhance precision, and quality control samples were included in each assay. The intra- and inter-assay coefficient of variation was kept below 10%.

2.4. Genotyping of MPO G463A (rs2333227)

Genomic DNA was cloned from whole blood samples using the Geneaid DNA extraction mini kit (version 06.22.16) according to the protocol. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis was used to genotype the myeloperoxidase G463A (rs2333227) polymorphism.

The primers were as follows: forward 5'-CGGTATAGGCACACAATGGTGAG-3 'and reverse 5'-GCAATGGTTCAAGCGATTCTTC-3'. The PCR amplification yielded a 350 bp fragment, which was later digested with 1 µL of AciI restriction enzyme (New England Biolabs, USA). The products of digestion were observed on a 2% agarose gel (Promega, USA), stained with ethidium bromide, and examined under UV transillumination (Vilber Lourmat, France). A number of quality control measures were used to ensure that genotyping was accurate and reliable. Positive and negative controls were included for all assays. About 10 percent of the random samples were re-genotyped, and 100 percent were concordant. Also, duplicate analyses were performed to reduce genotyping errors, and unclear results were re-examined. These protocols ensured high reproducibility and reduced genotyping error rates.

The specificity of the primers was confirmed by BLAST analysis against the human reference genome, which aligned to the promoter region of the MPO gene (chromosome 17) and included the polymorphic site at position 2333227. The size of the predicted PCR product (350 bp) and the formation of the restriction fragment patterns also corroborated the accuracy of the target amplification, Figure 1.

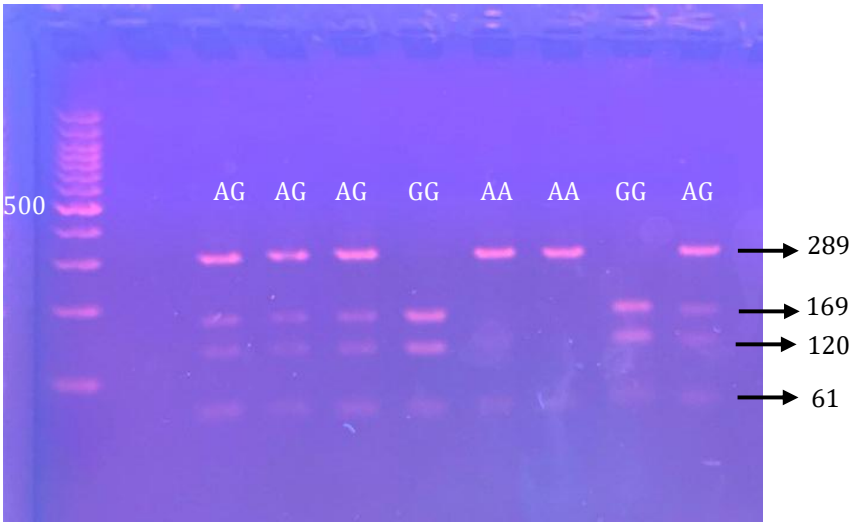

Figure 1: Electrophoretic pattern of the G463A SNP (rs2333227) polymorphism of the MPO gene. The GG allele yielded the uncut 350-bp PCR product; AA: 289- and 61-bp fragments; AG: 289-, 169-, 120-, and 61-bp fragments; and GG: 169-, 120-, and 61-bp fragments.

2.5. Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 26, USA, ANOVA, chi-square (χ^2), and logistic regression tests were used for all statistical analyses of the study. The distribution of genotypic frequencies followed the Hardy-Weinberg equilibrium. The significant p-value was <0.05. A multivariate logistic regression analysis was conducted to determine the independent association between MPO levels, MPO gene polymorphism, and the risk of acute coronary syndrome, with potential confounding factors, such as age, sex, smoking status, hypertension, diabetes mellitus, and medication use, adjusted. To assess the independent association between the MPO gene polymorphism and acute coronary syndrome, multivariate logistic regression was conducted while controlling for potential confounders, including age, sex, smoking status, hypertension, diabetes mellitus, and medication use.

3. RESULTS AND DISCUSSION

3.1. RNA Extraction and Purity Level

In Table 1, ages, BMI, fasting blood glucose, urea, creatinine, and HDL showed no significant differences between the two study groups (P values > 0.05). Lipid profile (except HDL), hs-troponin I, and MPO concentrations showed significant differences between patients and controls (P values <0.05). This study provides important insights into patients with confirmed coronary artery disease. The study's findings are allign to previous research revealing an increasing prevalence of genetic risk factors among individuals under 59 years of age who experienced their first acute myocardial infarction over time (13). The results of this study may support the prevailing understanding that males are more susceptible to coronary artery disease than females (12,14-16). Data from cardiology studies indicated that 11.5% of men and 4.2% of women were diagnosed with myocardial infarction between the ages of 60 and 79. The risk was higher in male patients compared to females (17). The sex distribution in patients and controls showed statistically significant difference (p = 0.011) that might be assumed as a possible confounding factor and should be taken into account when interpreting the results.

3.2. Lipid Profile and Metabolic Risk Factors

In Table 2, there were significant differences in MPO and HDL concentrations between males and females (P values <0.05). Otherwise, no significant differences were observed among patients with CAD in the study variables. Elevated total cholesterol and low-density lipoprotein cholesterol (LDL) are all risk factors for cardiovascular disease (18). Results suggests that these factors are confounding variables, making their role in cardiovascular disease uncertain (19). Also, the results from this study showed high triglyceride-level differences between the CAD patients and controls, confirming previous study associating high blood triglyceride levels with increased cardiovascular disease risk. Gu et al. (20) created a beneficial background for elevated blood triglyceride levels and the danger of ischemic stroke. Thus, it could be amenable to either drug or lifestyle intervention. A higher incidence of heart disease was associated with lower HDL cholesterol levels The association between HDL cholesterol and mortality due to cardiovascular disease was markedly inverse (21).

3.3. Cardiac Injury and Oxidative-Inflammatory Markers

The diagnostic performance of the tested biomarkers was assessed using the receiver operating characteristic (ROC) analysis. The high-sensitivity troponin I had an excellent diagnostic accuracy with an AUC of 1.0. On the contrary, myeloperoxidase (MPO) demonstrated moderate diagnostic performance, with an AUC of 0.686, sensitivity of 80.6, and specificity of 51.5. These results suggest that MPO is discriminatively weak and can be a supportive biomarker rather than an independent diagnostic marker (Table 3). High-sensitivity troponin (hs-cTnI) can serve as a biomarker of cardiac injury and may reflect long-term exposure to cardiovascular risk factors (22-24). In this study, high-sensitivity troponin I demonstrated high diagnostic performance (AUC = 1.0). This result must,, however, be viewed with caution, as apparent perfection may be due to the obvious distinction between patients with clinically diagnosed acute coronary syndrome and healthy controls in the study population. Even though high-sensitivity troponin I showed good diagnostic properties in this study, the 100% accuracy should be interpreted with caution.

The study design, especially the inclusion of clear-cut ACS cases and healthy controls, may have led to this result, as diagnostic performance may have been exaggerated. The diagnostic accuracy of troponin is generally lower in practice, particularly in conditions in which patients often present with overlapping conditions. Thus, the current results will not be entirely applicable to wider clinical groups (25). Causal factors of atherosclerotic plaque development include oxidative stress and inflammation at the early stage of atherosclerosis and its progression, which have a substantial impact on the development of IHD (26,27). MPO has a heme group, has peroxidase activity in inflammatory pathways, and is involved in the actions mediated by oxidative stress. High plasma MPO levels have been observed in coronary artery disease in many studies (28). Although MPO levels rose significantly in patients with acute coronary syndrome, the ROC analysis showed moderate diagnostic performance (AUC = 0.686). This implies that MPO is not a good diagnostic biomarker when used alone. Alternatively, MPO may be more appropriate as a complementary marker in combination with known biomarkers,

such as high-sensitivity troponin I. Such results are in line with the earlier research that has suggested that MPO is an indicator of oxidative and inflammatory processes, but is not a good diagnostic specificity of acute coronary events (29). MPO changes should be identified and studied to understand their biological significance to gain insight into pathways affecting risk for coronary artery disease (7).

3.4. MPO G463A Polymorphism and Disease Modulation

The logistic regression model was used to identify the risk of CAD in patients. The P values were not statistically significant for hs-troponin I and MPO (Table 4). A previous study indicated that an AG genotype may be an indicator of developing NSTEMI and STEMI (12). The study found that patients with the AA genotype had worse health markers, including higher triglycerides, higher high-sensitivity troponin levels, and increased myeloperoxidase activity. This profile indicates that the effects of having two copies of the A allele on inflammation and oxidative processes are stronger than having one of each allele.

In people with the AA genotype, higher MPO production or activity may alter lipoproteins and ultimately lead to greater heart damage, as evidenced by higher levels of high-sensitivity troponin. Notably, the effect of the significant confounding factors, such as age, sex, smoking, hypertension, and diabetes, were adjusted without any significant change in the observed correlations. This implies that the lack of association between the MPO gene polymorphism and disease susceptibility is not dependent on these known cardiovascular risk factors. However, the findings of this study did not align with another study that found that an A allele of the MPO-463G/A gene provides protection against coronary artery disease in the Chinese population (30).

In addtion, the G carriers showed more favorable coronary risk factors than the A carriers (7,31). This indicates that having an AG genotype is a middle-ground trait because the G allele can help reduce some of the overactivity of the MPO enzyme. Importantly, the excess of the AG genotype does not confer greater disease severity, as symptom severity was higher among individuals with the AA genotype, supporting the genotype-phenotype gradient for MPO enzyme activity (AA > AG > GG).

A study reported an association between the recessive allele A and the risk of coronary artery disease (32). These findings suggest that MPO polymorphisms mainly modify the course of disease through oxidative/inflammatory stress but do not act as genetic determinant of coronary artery disease. Therefore, MPO genetic variants may be important determinants of atherosclerotic disease and related risk factors. Despite the potential clinical significance of MPO-related pathways, the existing evidence does not provide sufficient grounds for their use in individual treatment plans. More extensive, mechanized studies are necessary to apply it in clinical settings. The statistically non-significant association between the MPO G463A polymorphism and the risk of acute coronary syndrome was also observed after the potential confounders, including age, sex, smoking status, hypertension, and diabetes were taken into consideration ($p > 0.05$) (33).

Table 5 shows significant differences in the triglycerides, LDL, HDL, high-sensitivity troponin I, and MPO levels across the three categories of genotypes (GG, AG, and AA). Interestingly, patients with the AA genotype tended to exhibit higher triglycerides, troponin I, and MPO levels, along with lower LDL and reduced HDL levels. Nevertheless, the findings are subject to interpretation as the AA genotype subgroup of (n = 11) is relatively small and may limit the ability to conduct statistically sound comparisons between genotypes and phenotypes. The risk association of CAD with MPO genotypes across different inheritance models is shown in Table 6. Odds ratios did not indicate a significant association between certain genotypes (P values > 0.05; Table 6).

Table 1. Basic and biochemical characteristics of the study population

Variables		CAD Patients (N=129) Mean ± SD	Control (N=66) Mean ± SD	P. Value
Age (Years)		56.42±8.11	54.62±7.73	0.638
BMI (Kg/M^2)		27.98±4.22	26.98±3.28	0.096
Sex	Males	83 (64.3%)	30 (45.5%)	0.011
	Females	46 (35.7%)	36 (54.5%)	
FBS (mg/dL)		94.866±3.336	94.013±3.975	0.143
Urea (mg/dL)		33.927±6.880	33.722±5.279	0.481
Creatinine (mg/dL)		0.825±0.213	0.776±0.230	0.159
Cholesterol (mg/dL)		199.457±36.263	184.472±40.283	0.003
Triglyceride (mg/dL)		190.613±67.399	165.867±65.687	0.049
HDL (mg/dL)		40.09±7.165	43.652±6.394	0.001
LDL (mg/dL)		122.545±35.997	109.928±33.970	0.026
VLDL (mg/dL)		38.580±14.867	33.069±13.174	0.035
Troponin I hs (pg/ mL)		535.108±486.247	2.799±3.495	0.001
MPO (pg/mL)		9.523±5.422	6.163±6.816	0.001

CAD: Coronary artery disease, SD: Standard deviation

Table 2. Differences in biomarker levels between patients according to sex

Variables	Male patients (N=82) Mean ± SD	Female patients (N=47) Mean ± SD	P. Value
BMI (Kg/m²)	28.116±4.111	27.747±4.450	0.636
FBS (mg/dL)	95.108±3.394	94.429±3.221	0.270
Urea (mg/dL)	33.887±7.397	33.997±5.910	0.931
Creatinine (mg/dL)	0.862±0.198	0.757±0.223	0.105
Cholesterol (mg/dL)	203.34±35.853	192.45±36.333	0.103
Triglyceride (mg/dL)	190.09±70.854	191.55±61.414	0.906
HDL (mg/dL)	40.822±7.517	44.511±6.54	0.002
LDL (mg/dL)	125.269±32.328	117.630±41.750	0.250
VLDL (mg/dL)	38.402±16.484	38.901±11.549	0.856
Troponin I hs (pg/L	526.035±502.598	551.478±460.221	0.777
MPO (pg/mL)	10.310±5.374	8.104±5.273	0.019

Table 3. Receiver-operating characteristic (ROC) curve and area under the curve (AUC) analyses for the values of serum biomarkers for the diagnosis of CAD.

Variables	Area under the ROC curve (AUC)	p-value (AUC=0.5)	Cut off	Sensitivity (%)	Specificity (%)	Efficacy
Troponin hs	1.0	0.0001	36.8	100	100	100
MPO	0.686	0.0001	4.69	80.6	51.5	70.7

Table 4: Logistic regression model of the risk of CAD in patients

Variables	Regression coefficient	Standard error	Wald	P Vale.	Odds ratio	95% confidence Limits
hs Troponin I	0.518	11.922	0.002	0.965	1.678	0.0-34.0
MPO	0.154	38.040	0.000	0.997	1.166	0.0-3.0

Table 5. Relationship between MPO genotypes and parameters in the patient group

Parameters	MPO SNP genotypes			P. Value
	GG (N=53) Mean ± SD	AG (N=65) Mean ± SD	AA (N=11) Mean ± SD	
FBS	94.95±3.40	94.21± 3.74	94.88± 3.38	0.36
Urea	34.30± 5.51	33.92± 6.18	31.34± 10.12	0.21
Creatinine	0.82± 0.20	0.79± 0.23	0.83± 0.17	0.59
Cholesterol	190.40± 36.39	193.74± 40.22	217.01± 27.64	0.03
Triglyceride	190.14± 56.74	164.46± 68.27	245.99± 70.14	0.001
HDL	41.112± 8.142	40.104± 6.375	35.081± 4.390	0.031
LDL	116.49± 35.79	115.83± 36.60	140.67± 21.41	0.02
VLDL	38.60±10.89	34.44±16.30	40.66±17.39	0.082
Troponin I hs	310.62±258.15	440.93±331.17	951.70±765.87	0.001
MPO	6.99± 5.33	8.14± 5.81	16.40± 5.579	0.001

Table 6. Risk of CAD associated with MPO genotype according to different models of inheritance

Genetic Model	Genotype	Patients (N=129)	Controls (N=66)	Unadjusted OR (95% CI)	P-value	Age-adjusted OR (95% CI)	P-value
Codominant	**GG (Reference)**	53 (41.1%)	28 (42.4%)	1.00 (Reference)	—	1.00 (Reference)	—
	GA vs GG	65 (50.4%)	32 (48.5%)	1.07 (0.57–2.00)	0.83	1.11 (0.36–3.39)	0.85
	AA vs GG	11 (8.5%)	6 (9.1%)	0.97 (0.32–2.96)	0.96	1.06 (0.35–3.20)	0.92
Dominant Model	**(GA + AA) vs GG**	76 (58.9%)	38 (57.6%)	1.06 (0.58–1.92)	0.85	1.09 (0.40–3.00)	0.88
Recessive Model	**AA vs (GG + GA)**	11 vs 118	6 vs 60	0.94 (0.32–2.80)	0.92	1.05 (0.34–3.20)	0.91
Allelic Model	**G allele**	70.70%	66.70%	Reference	—	—	—
	A allele	29.30%	33.30%	0.84 (0.53–1.33)	0.46	0.95 (0.60–1.52)	0.82

This study is limited in several ways. Selection bias due to unequal sex ratios between groups can arise, and the case-control design is limited in its ability to establish causation. This could lower statistical power and precision due to the comparatively small sample size, the underrepresentation of the AA genotype, and the broad confidence intervals. As many confounder adjustments as possible had been conducted, residual confounding cannot be eliminated. Also, the single-population environment can impair the generalizability. Thus, the results must be viewed with caution, and further study is needed to confirm them. The sample size may limit the study's statistical power, especially in subgroup analyses. This could have influenced the ability to identify small genetic effects, particularly for less common genotypes.

4. CONCLUSIONS

The study has shown that the levels of myeloperoxidase (MPO) circulating, as well as the high-sensitivity troponin I, are significantly linked to acute coronary syndrome among the Iraqi population. Conversely, no significant association was observed between the MPO -463G/A polymorphism (rs2333227) and disease susceptibility. Even though the AA genotype tended to have a more pronounced inflammatory and oxidative profile, the results should be interpreted with caution because the sample size in this group is very small. On the whole, these findings indicate that MPO can be an indication of some underlying inflammatory and oxidative processes in heart attacks and not an absolute genetic risk factor. More extensive, study-based study is needed to validate these results and gain greater insight into the possible role of MPO in cardiovascular disease.

Author contributions: WSA, DAS: Conceptualization, Software, Formal analysis, Data curation. HJA: Methodology, Validation, Investigation, Resources. WSA, DAS, HJA: Writing—original draft preparation, Writing—review and editing. DAS, HJA: Visualization. DAS: Supervision, Project administration. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest: The authors declare there is no conflict of interest.

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