Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2014; 2(4D):1402-1407 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sjams.2014.v02i04.052

Research Article

Role of-463 G/A Genetic Polymorphism & Myeloperoxidase Activity in Prediction of Cardiovascular Disease

D. Mandsorwale[1], S. Nagtilak[2]*, A. Lalchandani[3], A. K. Srivastava[4]
[1]Research Scholar, Department of Biochemistry, Subharti Medical College, Meerut (UP)-250005, India
[2]Professor, Department of Biochemistry, Subharti Medical College, Meerut (UP)-250005, India
[3]Professor & Head, Department of Medicine, GSVM Medical College, Kanpur (UP)-208024, India
[4]Ex-Professor & Head, Department of Biochemistry, GSVM Medical College, Kanpur (UP)-208024, India

***Corresponding author**
Dr S. Nagtilak
Email: nagtilak@yahoo.com

Abstract: Myeloperoxidase (MPO), a hemoprotein abundantly expressed by polymorphonuclear neutrophills (PMNs) secreted during activation, possess potent proinflammatory properties and contribute directly to tissue injury. Family history plays an important role in the genetic predisposition of cardiovascular disease (CVD). The influence of MPO -463 G/A genetic polymorphism on plasma levels and oxidative stress after neutrophill activation was studied. The case control study enrolled 54 control and 161 patients which further divided in three subgroups i.e SAP = 52, UAP = 53 and AMI = 56 respectively. Lipid profile, MDA, Catalase and Plasma MPO were analyzed by established techniques. Genotypic analysis of -463 G/A MPO was undertaken by PCR. Data suggest that the GG genotype occurs frequently in patient subgroups (SAP = 57.69%, UAP = 66.04% & AMI = 64.2%) compared with controls (51.85%). The plasma MPO levels in GG, GA and AA genotype of control with UAP and AMI subgroup have shown significant correlation ($p < 0.05$) whereas a non-significant ($p > 0.05$) association was observed in SAP subgroup. Study concluded that there is significant indirect association of GG genotype (with respect to AA genotype) in -463 G/A MPO genetic polymorphism in SAP, UAP and AMI subgroups respectively.
Keywords: Cardiovascular Disease, Myeloperoxidase, Genetic Polymorphism, Angina Pectoris, Acute Myocardial Infarction

INTRODUCTION

Coronary artery disease (CAD) is leading cause of cardiovascular mortality worldwide, with > 4.5 million deaths occurring in the developing countries [1]. Both CAD mortality and the prevalence of CAD risk factors continue to rise rapidly in developing countries [2]. According to World Health Report 2002, cardiovascular disease (CVD) will be the largest cause of death in India by 2020. It is predicted that 2.6 million Indians will die due to Coronary heart disease (CHD). This number will represent 54.1% of all CVD deaths in the age group of 30–69 years [3]. As a consequence, CVD has emerged as leading cause of death all over India, with CHD affecting Indians at least 5-6 years earlier than their western counterparts [4]. Current estimates from disparate cross-sectional studies indicate the prevalence of CHD to be between 7-13 % in urban and 2-7 % in rural India [5].

The mortality and morbidity of CVD are promoted by major risk factors, such as hyperlipidemia, hypertension, and smoking. Oxidative stress itself is a major step in CVD development. Several studies illustrate the association of Myeloperoxidase (MPO) with inflammation and oxidative stress. Moreover, family history along with multiple environmental factors contributes a major role in the genetic predisposition of CVD [6]. Existing literature reveals that several single nucleotide polymorphisms (SNPs) are found located in the promoter region of the *MPO* gene i.e -463G/A, -129G/A, -V53F, -A332V, -638C/A, I642L, and IVS11-2A/C. A functional MPO promoter polymorphism −463G/A alters MPO expression levels [7] and was found associated with increased incidence and severity of CVD [8].

The MPO gene itself in particular the promoter region with its sequences implicated in the transcriptional control is a prime factor for such investigation. Mutation in promoter region could affect transcription rates and alters the synthesis of MPO which may affect the progression and severity of CVD. There is paucity of reports dealing with association between -463 G/A MPO gene and CVD in Indian context. The present hospital based study was planned to investigate the association of Myeloperoxidase -463

G/A genetic polymorphism frequency distribution along with the levels of plasma MPO in various patient sub-groups i.e stable angina pectoris (SAP), unstable angina pectoris (UAP), and acute myocardial infarction (AMI) suffering from CVD.

MATERIAL AND METHODS

The study cohort comprises 215 subjects, divided into four groups i.e., healthy control (n=54), established patients with SAP (n=52), UAP (n=53), and AMI (n=56) respectively. All recruited subjects were selected from a series of consecutive outdoor patient department attending coronary clinic and indoor patient department of Laajpat Singhania Institute of Cardiology, GSVM, Medical College, Kanpur. Overnight fasting venous blood (5 ml) was drawn from subjects with 0.1% EDTA and the samples were transported immediately to the department of Biochemistry, GSVM, Medical College, Kanpur for further analysis.

One sample from each subject was used to analyze Total Cholesterol (TC), Triglycerides (TG), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), VLDL-cholesterol (VLDL-C), Malondialdehyde (MDA), Catalase and Plasma MPO, further sample was centrifuged (3,000 rpm for 15 min), the blood cells then being separated and stored in micro-tubes -80 °C for genomic DNA extraction. Plasma concentrations of TC, TG, HDL-C, LDL-C and VLDL-C were determined by commercially available kit method. Plasma MDA was estimated by TBARS method [9], Catalase was estimated by colorimetric assay [10] and Plasma levels of MPO were determined by kit method (AbFrontier) based on ELISA technique. DNA was extracted from blood cells by Phenol/chloroform method [11].

Established CVD patients with deranged lipid profile were selected for the study. Evaluation of the cardiovascular disease was performed by experienced investigators blinded for study aim. The study was approved by an institutional ethical committee, and informed consent was obtained from each subject in accordance with principles of the declaration of Helsinki. Family history of coronary artery disease, diabetes, hypertension and other major illness in the past, personnel history of smoking, alcohol, diet and drug history was recorded for each subject on a computerized working proforma. None of the control subjects had clinical or laboratory evidence of any disease that might have affected the parameters to be measured. Patients with diabetes mellitus, renal diseases, respiratory diseases, thyroid disorders, acute infection or any other systemic illness and on lipid lowering drugs for the past three months were excluded.

Myeloperoxidase-463 G/A Genetic Polymorphism Analysis

Genomic DNA was isolated from peripheral blood as per standard procedures. The -463 G/A polymorphism in the promoter region of MPO gene was determined by digesting PCR products with *restriction enzyme AciI* (Fermantas Inc., USA)[12] **.** A 350-bp DNA fragment was amplified using forward primer *MPOF (5'-CGG TAT AGG CAC ACA ATG GTG AG-3')* and reverse primer *MPOR (5'-GCA ATG GTT CAA GCGATT CTT C-3').*

Quality Control

Quality control and assessment was undertaken at every step of the study. The amount of isolated DNA was of good quality (absorbance 260 nm/280 nm, ratio>1.75). One sample with known genotype and a reagent blank were included after every 10 samples in the PCR. A 50 base‑ pairs' marker was included during electrophoresis.

Statistical Analysis

All statistical analysis was conducted by software package SPSS version 17.0 (IBM Corporation). Continuous variables of demographical and baseline characteristics were compared using Students t-test for two groups or analysis of variance by using one way ANOVA for multiple comparisons. Univariate comparisons of categorical variables were performed with chi-square test for analyzing allele frequencies and genotypic distribution. $p < 0.05$ considered significant.

RESULTS

The present study deals with total of 215 subjects for analyzing various risk factors i.e MPO, lipid profile, genetic polymorphism etc. Total 54 healthy controls (31 male, 23 female) and other three subgroup patients with stable angina pectoris (SAP), 52 (28 male, 24 female), unstable angina pectoris (UAP), 53 (33 male, 20 female) and patients with acute myocardial infarction (AMI), 56 (34 male, 22 female) respectively (Table 1A). It has been reported that diet rich in plant food is associated with lower risk of CVD. A large scale systemic review of association between diet and CVD concludes that beneficial substances in a vegetarian diet have a prominent role in reducing risk of CVD [13].

The baseline characteristics in control and patient sub-groups as age, BMI, Systolic and diastolic blood pressure (expressed as Mean ± SD). Results highlight that in subgroups SAP, UAP and AMI baseline characteristics were highly significant ($p < 0.001$) except for age in SAP subgroup where it is moderately significant($p < 0.01$) (Table 1B).

Table 1A: Demographical characteristics in control and patient subgroups

Sl. No.	Demographical Characters	Control (n=54)	Patient Subgroups (n=161)		
			SAP (n=52)	UAP (n=53)	AMI (n=56)
1.	Sex, male, n (%)	31 (57.4%)	28 (53.84%)	33 (62.26%)	34 (60.7%)
3.	Diet, (Non-veg) n (%)	28 (51.8%)	29 (55.76%)	31 (58.49%)	30 (53.57%)
4.	Smoking, n (%)	18 (33.3%)	21 (40.38%)	20 (37.73%)	24 (42.85%)
5.	Alcohol n (%)	3 (5.55%)	6 (11.53%)	5 (9.43%)	8 (14.28%)
6.	Family history n (%)	21 (38.8%)	25 (48.07%)	32 (60.37%)	30 (53.57%)

Table 1B: Baseline characteristics in control and patient subgroups

S. No.	Baseline Characters	Control (n=54)	Patient Subgroups (n=161)		
			SAP (n=52)	UAP (n=53)	AMI (n=56)
1.	Age (yrs)	41.31 ± 8.13	46.88 ± 8.96*	49.81 ± 8.06**	50.01 ± 7.25**
2.	BMI (kg/m²)	23.54 ± 1.29	25.63 ± 1.70**	26.07 ± 1.45**	25.02 ± 1.40**
4.	SBP (mmHg)	112.66 ± 9.06	139.78 ± 10.67**	135.05 ± 7.67**	129.28 ± 10.42**
5.	DBP (mmHg)	79.88 ± 6.58	89.5 ± 5.80**	89.52 ± 5.68**	85.69 ± 7.36**

Values expressed as mean ± SD, *p value: <0.01 moderately significant, **p value : <0.001 highly significant.

The clinical and laboratory characteristics such as Total Cholesterol, LDL-C, VLDL-C, and Triglycerides found highly elevated ($p < 0.001$) in patient subgroups than in healthy controls. On the contrary HDL-C was higher ($p < 0.001$) in controls with respect to patient sub-groups. Comparison of oxidative stress markers (MDA & Catalase) in control with patient subgroups indicates highly significant ($p < 0.001$) association (Table 2).

Table 2: Biochemical parameters in control and patient subgroups

Sl. No.	Biochemical Parameters	Control (n=54)	Patient Subgroups (n=161)		
			SAP (n=52)	UAP (n=53)	AMI (n=56)
1.	Total Cholesterol (TC) (mg/dl)	185.20 ± 10.28	215.69 ± 16.04***	212.03 ± 12.85***	213.69 ± 15.5***
2.	HDL-C (mg/dl)	42.47 ± 4.68	35.42 ± 3.52***	39.17 ± 3.38***	37.56 ± 3.53***
3.	VLDL-C (mg/dl)	30.14 ± 2.82	37.34 ± 4.33***	36.17 ± 3.16***	36.51 ± 2.98***
4.	LDL-C (mg/dl)	112.58 ± 8.61	142.92 ± 14.94***	136.68 ± 14.10***	139.61 ± 15.38***
5.	Triglycerides (TG) (mg/dl)	150.72 ± 14.10	186.74 ± 21.69***	180.87 ± 15.8***	182.56 ± 14.93***
6.	Lipid peroxidation (MDA) (µ mol /L)	2.15 ± 0.51	6.35 ± 0.76***	4.50 ± 0.722***	4.87 ± 0.77***
7.	Catalase (CAT) (µmol / min / gmHb.)	129.59 ±6.01	67.26 ± 7.33***	61.97 ± 8.60***	64.36 ± 8.62***
8.	Plasma MPO (ng/ml)	60.17 ± 7.69	62.96 ± 8.21*	85.24 ± 12.04***	91.01 ± 11.74***

Values expressed as mean ± SD, *p value: >0.05 non significant, **p value: <0.01 moderatly significant, ***p value : <0.001 highly significant.

Plasma MPO levels were highly significant in patients with UAP ($p < 0.001$) and AMI ($p < 0.001$) compared with controls. There is no significant difference in plasma MPO levels in patients with SAP ($p > 0.05$) and controls. Furthermore, plasma MPO levels were significantly higher in AMI and UAP compared with SAP ($p < 0.001$), but there is no significant difference between AMI and UAP ($p > 0.05$) as shown in Table 2.

Association of MPO -463 G/A gene polymorphism with CVD

The polymorphism was in Hardy–Weinberg equilibrium. The frequency distribution of allele G, 70.37% in control group versus 74.03% in SAP, 80.19% in UAP & 78.57% in AMI subjects; and allele A, 29.63% in control group versus 25.96% in SAP, 19.81% in UAP & 21.42% in AMI subjects respectively. The frequencies of GG, GA and AA genotype does not differ significantly in control and all

the other three patient sub-groups. Similarly frequency of allele A was not significantly different in patient subgroups with reference to control as mentioned in Table 3.

Table 3: MPO -463 G/A gene polymorphism frequency distribution in healthy control and patients with Angina subgroups and AMI

MPO -463G/A	Control (n=54)	Patient Subgroups (n=161)			χ^2 Test	p-value
		SAP (n=52)	UAP (n=53)	AMI (n=56)		
	Genotypic frequency distribution					
GG	28 (51.85%)	30(57.69%)	35 (66.04%)	36 (64.29%)		
GA	20 (37.04%)	17(32.69%)	15 (28.30%)	16 (28.57%)	3.15	0.789*
AA	06 (11.11%)	05(9.62%)	03 (5.66%)	04 (7.14%)		
	Relative allele frequency distribution					
G	76 (70.37%)	77(74.035%)	85 (80.19%)	88 (78.575%)	4.09	0.251*
A	32 (29.63%)	27(25.965%)	21 (19.81%)	22 (21.425%)		

*p value >0.05 non significant, ** p value <0.05 significant.

Association of MPO gene polymorphism with Plasma Levels of MPO

The comparison between plasma MPO levels in control and SAP subgroup as per GG, GA & AA genotypes, the Mean ± SD levels of plasma MPO in SAP were slightly higher and relatively non-significant ($p > 0.05$) whereas comparison of UAP and AMI with control showed significant association ($p < 0.05$) (Table 4).

Table 4: **Plasma MPO levels and MPO -463 G/A gene polymorphism frequency distribution between control and patient sub-groups**

Study Groups	Levels of Plasma MPO (ng/ml)					
	n	GG Genotype	n	GA Genotype	n	AA Genotype
Control (n=54)	28	61.37 ± 7.97	20	60.09 ± 7.51	06	54.82 ± 5.30
SAP (n=52)	30	66.29 ± 8.81*	17	65.41 ± 9.57*	05	58.3 ± 7.45*
UAP (n=53)	35	86.35 ± 12.30***	15	84.41 ± 11.76***	03	76.37 ± 9.42***
AMI(n=56)	36	92.07 ± 12.32***	16	90.35 ± 11.18***	04	84.18 ± 7.17***

*p value: >0.05 non significant, **p value: <0.01 moderatly significant, ***p value : <0.001 highly significant.

DISCUSSION

Myeloperoxidase (MPO), hemoprotein is a peroxidase enzyme produced by white blood cells mainly neutrophill, granulocytes and mononuclear cells. Various single nucleotide polymorphisms (SNPs) are present at sp1 binding sites in the promoter region of the MPO gene, including variants -463G/A, -129G/A, -V53F, -A332V, -638C/A, I642L, and IVS11-2A/C. Reports have shown that the -463G/A, -129G/A, -V53F, -A332V, and -638C/A SNPs and MPO levels are risk factors in coronary artery disease (CAD) [14]. Therefore it is in public interest to investigate the environmental as well as genetic factors determining the levels of plasma MPO and its association with MPO genetic polymorphism.

Present study suggests that the allele A of MPO gene was less frequent in comparison to allele G in different patient subgroups; this is similar to that of study conducted by Zhong *et al*. [15]. There is no significant association found between the MPO -463 G/A polymorphism and cardiovascular disease but indirectly this gene was found to regulate the synthesis of MPO affecting at transcriptional level signifies its indirect association with CVD (Table 4). Furthermore study showed that genotypes AA and GA were significantly associated with reduced risk of CVD whereas individuals with GG genotype found most probably suffering from CVD.

In a meta-analysis performed by Tang et. al [16] strong evidences were found regarding an association between the *MPO* -463G/A polymorphism and CAD. Furthermore, genotypes AA and GA were significantly associated with reduced risk of CAD (AA *vs.* GG: OR = 0.37, 95% CI = 0.17–0.78; GA *vs.* GG: OR = 0.73, 95% CI = 0.57–0.92). In subgroup analysis, statistically significant results were observed in the Chinese population (AA *vs.* GG: OR = 0.21, 95% CI = 0.10–0.43; GA *vs.* GG: OR = 0.57, 95%

CI =0.44–0.74) and in hospital-based control studies (AA *vs.* GG: OR = 0.20, 95% CI = 0.10–0.39; GA *vs.* GG: OR = 0.61, 95% CI = 0.48–0.77). This meta-analysis suggests that the *MPO* -463 G/A variant genotypes is associated with decreased risk of CAD.

Comparison between plasma MPO levels of control and SAP subjects according to the GG, GA and AA genotypes shows that the Mean ± SD levels of plasma MPO in SAP were slightly higher in comparison to control group which was found relatively non-significant ($p > 0.05$) which correlates with study conducted by Kubala *et al*. [17]. Comparisons of control with that of UAP and AMI have shown significant association ($p < 0.05$) between the plasma MPO levels of GG, GA and AA genotypes of both the sub-groups (Table 4). Furthermore, the Mean ± SD levels of Plasma MPO of GG genotype in all patient sub-groups in comparison with controls were found highly elevated suggested significant association of MPO genetic polymorphism and its levels with CVD (Table 4).

In agreement to our study, Ll Aihua *et al*. [18] explored the relationship between myeloperoxidase (MPO) and coronary heart disease to predict the risk of CHD and found that the plasma levels of MPO were higher in Acute coronary syndrome (ACS) group than that in SAP and control group ($P < 0.01$). The mean levels of plasma MPO in SAP group were not significantly different, compared with that of control group ($P > 0.05$). According to them the risk of CHD in the GA genotype, 3.1 times and in GG genotype was 2.7 times that of AA respectively. They concluded that MPO, a maker of the unstability of the plaque in coronary artery, is correlated with CHD and -463G/A polymorphism of the MPO gene influences the risk of CHD.

In present study comparison between plasma MPO levels in GG, GA and AA genotypes of SAP, UAP and AMI subgroup showed slightly higher, relatively non-significant ($p > 0.05$) elevation of plasma MPO in AMI subgroup compared to UAP subgroup whereas highly significant elevations ($p < 0.001$) were found in UAP and AMI subgroups when compared to SAP suggested plasma MPO levels along with -463 G/A genetic polymorphism found associated with the progression and severity of CVD (Table 4).

Literature review highlights that *MPO* gene -463G/A polymorphism related to changes in lipid levels, may be involved in the oxidation of low-density lipoprotein, the high levels of MPO increasing the brittleness of artery plaque, thereby converting the plaque from the stable to unstable state, thus increasing the risk of acute coronary syndrome [19]. The *MPO* -463A allele could interfere with the binding sites of sp1 transcription factor, by reducing the level of *MPO* gene expression and its role in atherosclerotic plaque formation, having a definite impact on risk of CAD. Meanwhile, MPO may promote the oxidation of HDL-C and affect the reverse cholesterol transport, thereby interfering in the development of atherosclerosis.

Study highlights indirect association of -463 G/A MPO genetic polymorphism expressed in the form of elevated plasma MPO levels in GG genotype with different forms of CVD in all the cases suffered with SAP, UAP and AMI respectively. It may be possible that the variation of genetic polymorphism regulates synthesis of MPO that modulates lipid profile by increasing oxidative stress thereby contributing generation of oxidized LDL and dys-functional HDL leading to the occurrence and progression of CVD.

CONCLUSION

Study demonstrates that MPO and its reactive oxidant species play an important role in the promotion of pathophysiological involvement in all stages of atherosclerotic CVD. The GG is the most predominant genotype in study patient subgroups compared with GA and AA genotype indicating its positive correlation with CVD. Individuals with GG genotype in UAP and AMI subgroups were found to have subsequently higher levels of plasma MPO with respect to GA and AA genotype indicating the indirect association of MPO gene with CVD. Thus associations between GG genotype of -463 G/A genetic polymorphism and systemic MPO levels with cardiovascular risks in study subjects suggest that MPO testing play a diagnostic role in prediction of clinical risk.

REFERENCES

1. Fox CS, Coady S, Sorlie PD, Levy D, Meigs JB, D'Agostino RB Sr *et al*.; Trends in cardiovascular complications of diabetes. JAMA,. 2004; 292(20): 2495-2429.
2. Okrainec K, Banerjee DK and Eisenberg MJ; Coronary artery disease in the developing world. Am Heart J., 2004; 148(1): 7-15.
3. National Cardiovascular Disease Database (Sticker No: SE / 04/ 233208), Supported by Ministry of Health & Family Welfare, Government of India and World Health Organization, 2011. Available from http://www.whoindia.org/
4. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy. KS, Gupta R *et al*.; Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet, 2008; 371 (9622):: 1435-1442.
5. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S; Epidemiology and causation of coronary heart disease and stroke in India. Heart, 2008; 94(1): 16-26.
6. Anbuselvan V, Padmavathi R, Velmurugendran CU, Ramnath S, Paulswamy J; Comparative study of lipid profile among stroke patients with

gender variations. Sch J App Med Sci., 2014; 2(1B):162-165.
7. Nikpoor B, Turecki G, Fournier C, Théroux P, Rouleau GA; A functional myeloperoxidase polymorphic variant is associated with coronary artery disease in French-Canadians. Am Heart J., 2001; 142(2): 336–339.
8. Asselbergs FW, Reynolds WF, Cohen-Tervaert JW, Jessurun GA, Tio RA; Myeloperoxidase polymorphism related to cardiovascular events in coronary artery disease. Am J Med., 2004; 116(6): 429–430.
9. Satho K; Serum lipid peroxidation in cerebrovascular disorders determined by a new colorimetric method. Clin. Chem Acta., 1978; 90(1): 37-43.
10. Sinha AK; Colorimetric assay of Catalase. Analytical Biochemistry, 1972; 47(2): 389-394.
11. Sambrook J, Fritsch EF, Maniatis T; In Nolan C editor; Molecular Cloning. A laboratory manual. 2nd edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor (NY), 1989: 9–17.
12. London SJ, Lehman TA, Taylor JA; Myeloperoxidase genetic polymorphism and lung cancer risk. Cancer Res., 1997; 57(22): 5001-5003.
13. Aggarwal J, Reddy S, Nagtilak S, Verma PK; Non-high density lipoprotein cholesterol-risk predictor for coronary heart disease in Indian population. International Journal of Advanced Research, 2014; 2(1): 810-817.
14. Stefanescu A, Braun S, Ndrepepa G, Koppara T, Pavaci H, Mehilli J *et al*.; Prognostic value of plasma myeloperoxidase concentration in patients with stable coronary artery disease. Am Heart J., 2008; 155(2): 356–360.
15. Zhong C, Quanzhong Y, Genshan M, Hua Z, Ruolong Z, Jiahong W *et al*.; Myeloperoxidase gene-463G > A polymorphism and premature coronary artery disease. Genetics and Molecular Biology, 2009; 32(2): 260-263.
16. Tang N, Wang Y, Mie Q; Myeloperoxidase G-463A polymorphism and susceptibility to Coronary artery disease : A meta-analysis. Gene, 2013; 523(2): 152-157.
17. Kubala L, Lu G, Baldus S, Berglund L, Eiserich JP; Plasma levels of myeloperoxidase are not elevated in patients with stable coronary artery disease. Clin Chim Acta., 2008; 394(1-2): 59–62.
18. Aihua L, Juan C, Xiaochen Y, Zhengang Z, Yulong L; Correlation between the myeloperoxidase genetic polymorphism and coronary artery disease. Journal of Clinical Cardiology, 2010-01.
19. Ndrepepa G, Braun S, Mehilli J, von Beckerath N, Schomig A, Kastrati A. Myeloperoxidase level in patients with stable coronary artery disease and acute coronary syndromes. Eur J Clin Invest., 2008; 38(2): 90–96.