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A comparison of macrophage migration inhibitory factor with C reactive protein in diabetic hypertensive patients with myocardial infarction that underwent primary percutaneous coronary intervention.

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Key words: diabetes mellitus; hypertension; macrophage migration inhibitory factor; high sensitivity C-reactive protein; myocardial infarction.

Abstract. The inflammatory response is one of the complications of diabetic hypertensive patients with myocardial infarction (MI). The purpose of this study was to determine the diagnostic value of macrophage migration inhibitory factor (MIF) compared with high sensitivity C reactive protein (hs-CRP) in diabetic hypertensive patients presented with MI; and to determine the concomitant association between these factors in MI patients. For this purpose, 100 patients with MI were categorized into four groups, according to the existence of diabetes mellitus (DM) and/or hypertension (HTN), with 38 subjects with normal angiography considered as the control group. The levels of MIF and hs-CRP were estimated quantitatively using a sandwich enzyme-linked immunosorbent assay and a particle-enhanced immune turbidimetric assay, respectively. In addition, lipid profiles, hematological indicators, and certain clinical features were compared among the studied groups. The levels of MIF and hs-CRP increased significantly in MI patients compared to the controls ($p<0.05$). Additionally, the levels of MIF differed significantly between all MI groups and the control group ($p<0.05$). Although the group DM-HTN showed the highest MIF level within the MI groups, the difference was not significant ($p>0.05$). However, the hs-CRP level showed a significant difference ($p<0.05$). In addition, the MIF level correlated positively with hs-CRP, leukocytes, and neutrophils ($p<0.05$). Both MIF and hs-CRP levels correlated positively with age, body mass index (BMI), total cholesterol, triglyceride, low-density lipoprotein-cholesterol (LDL-C) and non-high density lipoprotein (HDL), but they correlated negatively with HDL-C. According to the results, although MIF was a valuable diagnostic marker for MI, the hs-CRP showed to be a better prognostic indicator than MIF in diabetic hypertensive patients that presented MI.

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Comparación entre el factor inhibitorio de la migración de macrófagos con la proteína C reactiva en pacientes diabéticos hipertensos con infarto del miocardio, sometidos a una intervención coronaria percutánea primaria.

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Palabras clave: diabetes mellitus; hipertensión; factor inhibidor de la migración de macrófagos; proteína C- reactiva de alta sensibilidad; infarto de miocardio.

Resumen. La respuesta inflamatoria es una complicación del infarto de miocardio (IM) en pacientes diabéticos hipertensos. Este estudio se realizó para determinar el valor diagnóstico del factor inhibitorio de la migración de macrófagos (MIF) en comparación con la proteína C reactiva de alta sensibilidad (hs-PCR), en pacientes diabéticos hipertensos con IM; y también para precisar la asociación concomitante entre estos factores en pacientes con IM. Con este propósito, 100 pacientes con IM se clasificaron en cuatro grupos, de acuerdo con la existencia de diabetes mellitus (DM) y/o hipertensión (HTN) y 38 sujetos con angiografía normal se consideraron como el grupo control. Los niveles de hs-PCR y MIF se estimaron cuantitativamente utilizando un ensayo inmunoabsorbente ligado a enzimas y un ensayo inmunoturbidimétrico mejorado con partículas, respectivamente. Además, se compararon entre los grupos del estudio, los perfiles lipídicos, parámetros hematológicos y algunas características clínicas específicas. Los niveles de MIF y hs-PCR aumentaron significativamente en pacientes con IM en comparación con los controles ($p<0,05$). Así mismo, los niveles de MIF fueron significativamente diferentes entre todos los grupos con IM y el grupo control ($p<0,05$). Aunque el grupo DM-HTN mostró el nivel más alto de MIF dentro de los grupos IM, la diferencia no fue estadísticamente significativa ($p>0,05$). Sin embargo, los niveles de hs-PCR sí mostraron una diferencia significativa ($p<0,05$). Adicionalmente, los niveles de MIF se correlacionaron positivamente con la hs-PCR, leucocitos y neutrófilos ($p<0,05$). Tanto los niveles de hs-PCR como los de MIF se correlacionaron positivamente con la edad, índice de masa corporal, colesterol total, triglicéridos, LDL-C, y no HDL, pero mostraron una correlación negativa con HDL-C. Según los resultados, aunque el MIF representó un valioso marcador de diagnóstico para el infarto de miocardio, la hs-PCR mostró ser un mejor indicador pronóstico que el MIF para pacientes diabéticos hipertensos con IM.

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INTRODUCTION

Evidence shows that inflammation occurs at every stage of coronary atherosclerosis, which starts from fatty streaks as well as plaque development and ends in its rupture, causing acute coronary syndrome (ACS) (1), including myocardial infarction (MI) (2). The coexistence of both, diabetes mellitus (DM) and hypertension (HTN), appears to be related to mortality more frequently in patients with ACS than in those with either DM or HTN (3). Macrophage migration inhibitory factor (MIF) is a proinflammatory and pro-

atherosclerotic factor involved in the induction of foam cell production, atheroprogression, and plaque vulnerability (4). Reports indicate that deficiencies in MIF prevent the heart from suffering ischemia reperfusion damage in mice by overcoming the inflammatory response (5). In addition, reports indicate that MI results in the fast release of MIF from myocardium to the circulatory system. As a result, MIF makes peripheral blood mononuclear cells produce proinflammatory mediators and facilitates myocardial inflammatory responses. The weakening of these events and the post-MI cardiac rupture by the anti MIF anti-body suggests that MIF could be a possible therapeutic target after MI (6).

It has been reported that high sensitivity C-reactive protein (hs-CRP) levels are elevated in patients with coronary artery atherosclerosis, which is associated with its severity and complications (7); however, the principal mechanisms of hs-CRP as a catalyst of ACS, for instance MI, are not fully known. Research has revealed that hs-CRP presumably activates complements and leads to the persistence of the inflammatory process of plaque or causes plaque rupture and its bleeding, yet it has not been determined whether the level of hs-CRP is associated with the severity of the damage (8). This study aims to compare the diagnostic significance of MIF with that of hs-CRP in MI diabetic hypertensive patients and to determine the correlation between both factors in MI patients.

MATERIALS AND METHODS

A total of 100 patients with MI was enrolled consecutively in this case control study, who attended the emergency department of the surgical specialty hospital-cardiac center in Erbil City, Iraq, for primary percutaneous coronary intervention (PCI) during the period from January 2017 to December 2017. MI was diagnosed based on the World Health Organization (WHO) criteria, including clinical history, abnormal electrocardiogram (ECG) findings, and raised cardiac markers (troponin and creatine kinase-MB) (9). An angiography was performed for all patients with positive troponin, and patients with no arterial occlusion were excluded from the study.

In addition, stroke and post-MI patients, those with heart failure, congenital heart disease, cardiomyopathy, myocarditis, pericarditis, severe valvular heart disease, the ones with the history of recent surgeries or traumas, malignancies, active inflammatory or autoimmune diseases, as well as those with bleeding and clotting disorders were excluded from the study. Patients were categorized into the following groups, based on the patients' history of DM and/or HTN:

i. Those with neither DM nor HTN
ii. Those with only DM but no HTN
iii. Those with only HTN but no DM
iv. Those with both DM and HTN

The study excluded certain groups such as DM without MI or HTN, as the main point of the study was focusing on MI and the mentioned group was not engaged within the study aim.

The control group included 38 subjects who were confirmed angiographically to have normal coronary arteries and found out to have chest pain not related to cardiac source and showed no any apparent meaningful manifestations of lung alteration. The serum concentrations of high-sensitive cardiac troponin T and CKMB were within the allowed ranges. Subjects in this group did not suffer from DM and obesity.

The study protocol was approved by the medical ethics committee at the College of Medicine, Hawler Medical University. Information on the medical history was obtained during personal interviews using especially formatted questionnaires. Diabetic patients were diagnosed on the basis of the past history of DM in case they were treated with or without anti-diabetic therapies and

were confirmed to have haemoglobin A1c (HbA1c) level >6.5% (10). In the same vein, hypertension (≥140/90 mmHg) was confirmed based on one of the factors of past diagnosis, the receiving of antihypertensive drugs at present, and repetitive blood pressure measurements minimally 2-3 times under stable conditions. Weight (kg)/height m^2 was the standard method for calculating the body mass index (BMI).

Coronary angiography (COA) was performed for all study groups, i.e. patients and controls, on the right femoral artery as a standard method for the decision of having either normal or diseased artery, which achieved only to those who admitted for different reasons (for example atherosclerotic coronary artery disease, MI, and chest pain. The control group comprised individuals who complained from chest pain but were confirmed by angiography to have normal coronary arteries (no lesions). Many other reasons could be the source for the chest pain, for example psychological causes like severe depression and severe stress, but actually we were just concerned if the patient was free from chest pain related with cardiac origin but no other causes. All patients received the loading doses of aspirin (300 mg) and clopidogrel 300-600 mg; or were reloaded with ticagrelor 180 mg before the angiography procedure and with heparin prior to PCI for patients confirmed to have had a new arterial occlusion. Diagnostic and guiding catheters were used through a 6 French femoral sheath to engage the coronary sinuses. All patients with new arterial occlusion underwent PCI for culprit lesions. The location of the culprit lesions and the number (one, two, or three) of the affected vessel(s) were determined using COA findings.

Blood samples were drawn from all participants immediately after admission and prior to COA using the venipuncture technique. Serum and plasma were obtained from the collected blood and stored at -80°C for further analysis. Baseline laboratory investigations of biochemical and hematological tests were carried out for all participants. The plasma MIF level was measured quantitatively using the human MIF ELISA kit (Mybiosource, USA). Cobas c111 was used to determine hs-CRP (Roche Diagnostics GmbH) concentrations based on the particle enhanced immunoturbidimetric assay. HbA1c and lipid profiles were analyzed using cobas c111 (Roche Diagnostics GmbH), and the total blood count was determined using Swelab Alpha Coulter Analyzer (Swelab, Sweden).

Data were analyzed statistically using SPSS Statistics 23.0. The continuous variables of the studied groups were determined as mean ± SE. The one-way analysis of variance (ANOVA) was used for multiple comparisons. Student's *t*-test was performed to compare the two continuous parameters. In addition, categorical variables were evaluated using a chi-squared test or Fisher's exact test. The correlation between MIF and hs-CRP as well as the correlation between the two markers and other study parameters were determined using Pearson's correlation coefficient. P-value was considered significant at $P<0.05$.

RESULTS

As Table I shows, the levels of MIF and hs-CRP increased significantly in MI patients compared to the controls ($P<0.05$). In addition, the increased levels of leukocytes, neutrophils, platelets, low density lipoprotein–cholesterol (LDL-C), non-high density lipoprotein-cholesterol (HDL-C), total cholesterol/HDL, LDL/HDL, BMI, and HbA1c differed significantly between the two groups ($P<0.05$). No statistically significant differences were observed between the patients and the controls in systolic blood pressure (SBP), diastolic blood pressure (DBP), cholesterols, and triglycerides ($P>0.05$). According to the COA results, the majority of MI patients had three diseased vessels, and the most frequently affected artery was the left anterior descending artery (LAD), followed by the right coronary artery (RCA) and the left circumflex (LCX).

TABLE I
BASELINE CHARACTERISTICS OF MYOCARDIAL INFARCTION PATIENTS AND CONTROLS

Variables	MI	Controls	p
Age (years)	59.28±1.62	52.42±1.99	0.021
Male	76(76)	22(57.89)	0.036
Diabetes	46(46)	-	
Hypertension	52(52)	12(31.58)	0.032
Smokers	72(72)	16(42.11)	0.001
SBP(mmHg)	131.38±3.82	128.87±9.17	0.767
DBP (mmHg)	80.04±2.42	79.37±2.06	0.879
BMI (kg/m^2)	28.99±0.65	25.87±0.44	0.006
HbA1c%	7.31±0.32	5.56±0.06	0.001
Lipid profiles and lipid ratios			
Total cholesterol (mg/dL)	184.56±5.82	164.10±11.39	0.086
Triglyceride (mg/dL)	161.11±16.77	121.15±10.88	0.160
HDL-C (mg/dL)	37.22±1.39	49.70±2.46	0.000
LDL-C (mg/dL)	120.23±4.23	93.05±7.79	0.001
Non-HDL (mg/dL)	147.33±5.42	114.40±11.90	0.005
Total cholesterol/HDL ratio	5.18±0.21	3.48±0.29	0.000
LDL/HDL ratio	3.48±0.16	1.98±0.18	0.000
Inflammatory biomarkers			
MIF(ng/mL)	41.60±3.09	20.94±3.43	0.000
hs-CRP(mg/L)	10.45±1.80	1.98±0.31	0.005
Hematological indices			
Leukocyte count (103/μL)	12.44±0.43	6.71±0.35	0.000
Neutrophil count(103/μL)	9.64±0.45	4.08±0.55	0.000
Platelet(103/μL)	240.08±7.14	202.73±12.03	0.008
Angiographic findings			
1 vessel	15(15)	-	
2 vessels	20(20)	-	
3 vessels	65(65)	-	
Location of culprit lesion			
LAD	50(50)	-	
RCA	39(39)	-	
LCX	11(11)	-	
Medications			
Aspirin	92(92)	-	
Ticagrelor	72(72)	-	
Clopidogrel	27(27)	-	
Tablets or insulin injection	42(42)	-	
Betablocker	75(75)	8(21.05)	0.000
Statin	82(82)	-	

Values are presented as mean± SE and n (%) for continuous variables (t-test) and categorical variables, respectively.
MI: myocardial infarction.

Non-DM, Non-HTN represented 30% of the MI groups, followed by DM-HTN, HTN only, and DM only (28%, 24%, and 18% respectively). The mean values of age, BMI, total cholesterol, triglycerides, LDL-C, non-HDL, total cholesterol/HDL, and LDL /HDL were higher in the group DM-HTN. Increased levels of inflammatory markers were observed in all MI groups compared to the control group. Although the group of diabetic hypertensive patients showed an increase in MIF, hs-CRP, and platelet count, a significant difference was observed only in hs-CRP compared with other MI groups ($p<0.05$). The details are illustrated in Table II.

Patients aged ≥55 were found more in the DM-HTN group (78.57%) than in other groups. A higher rate of smokers was found in the group HTN only (83.33%), followed by group DM-HTN (82.14%). The mean duration of DM and HTN was higher in the group DM-HTN than in the groups DM only and HTN only, respectively ($p>0.05$). A lower percentage of patients with the ≥6-hour duration of MI onset and a higher percentage of those treated by statin were found in the group DM only (55.56% and 88.89%, respectively). LCX was the least frequently affected artery among all MI groups, while among all MI groups, the group non-DM-non-HTH was the least affected by three diseased vessels (Table III).

The results of the Pearson's correlation coefficient proved the significant positive correlation of MIF and hs-CRP ($r=0.356$, $p=0.011$) with leukocytes ($r=0.493$, $p=0.001$) and neutrophils ($r=0.411$, $p=0.003$). Both MIF and hs-CRP showed an no significant positive correlation with age, BMI, total cholesterol, triglyceride, LDL-C, non-HDL, and platelets. However, HDL-C correlated negatively with MIF, hs-CRP ($r=-0.043$, $P=0.769$), and ($r=-0.038$, $P=0.791$) respectively (Table IV).

DISCUSSION

According to the findings of this study, the levels of MIF, and hs-CRP increased significantly in all MI patients compared to the control group, with this finding being in agreement with past research (11–13). Although the MIF is formed by numerous cell types in the human atherosclerotic plaque (14), myocardium is the main source of circulating MIF because of its high MIF content (15). Unlike many cytokines, MIF could be released rapidly with no need for de novo synthesis due to the constitutive expression of MIF and its storage in intracellular pools (16). In addition, hs-CRP increases rapidly following tissue damage, including MI. High cytokine production and inflammatory cell distribution occur in the ischemic and necrotic areas, with the elevated levels of hs-CRP being in part associated with the infarct size (17,18).

This study showed a non-significant increase in MIF but a significant increase in hs-CRP in the DM-HTN group, when compared to other MI groups. To the best of our knowledge, few studies have been done on comparing MIF with hs-CRP in diabetic hypertensive patients with MI. MIF and hs-CRP levels were found out to increase more in hypertensive hyperlipidemic patients than in the healthy controls (19). Recent studies show an insignificant increase in MIF levels in coronary artery disease (CAD) patients with DM compared to those with non-DM (20). Similar results were obtained concerning hs-CRP (21). In addition, MIF increased significantly in diabetic ACS patients compared to diabetic stable CAD and stable angina pectoris (20). The aforementioned findings elucidate the impact of both DM and HTN on MIF levels and verify the significance of MIF as a diagnostic inflammatory marker for ACS. This is indicative of the fact that the major rea-son for the increase in MIF in the present study could be the severity of the MI itself, and the minor reason could be the effects of DM and HTN. According to past research, a high percentage of MI patients showed an increase in MIF in the first samples obtained, with this predicting the final infarct intensity and the degree of cardiac remodeling (22).

TABLE II

MEAN CONCENTRATION OF INFLAMMATORY MARKERS AND OTHER VARIABLES IN MYOCARDIAL INFARCTION GROUPS COMPARED WITH CONTROLS

Variables	MI				Control	P value
	Non-DM- Non-HTN n 30 (30%)	DM only n 18 (18%)	HTN only n 24 (24%)	DM- HTN n 28 (28%)	Non-DM- Non-HTN N 26 (68.42%)	
Age (yr)	56.73±2.96^{ab}	56.55±3.05^{ab}	61.16±3.98^{a}	62.14±2.86^{a}	53.46±2.57^{b}	0.258
SBP (mmHg)	122.13±4.42^{a}	123.37±6.7^{a}	140.27±10.85^{a}	139.46±7.36^{a}	120.72±11.95^{a}	0.257
DBP (mmHg)	74.66±3.75^{a}	76.12±7.06^{ab}	85.09±5.46^{b}	84.38±4.1^{ab}	78.27±2.80^{ab}	0.334
BMI (kg/m^2)	28.76±1.10^{ab}	29.18±1.70^{ab}	28.30±1.29^{ab}	29.56±1.43^{b}	26.06±0.58^{a}	0.292
HbA1c%	5.50±0.06^{a}	9.85±0.52^{b}	5.39±0.06^{a}	9.28±0.40^{b}	5.55±0.05^{a}	0.000
Lipid profile and lipid ratios						
Total cholesterol (mg/dL)	176.82±11.45^{a}	172.63±9.48^{a}	191.97±11.78^{a}	194.16±12.08^{a}	169.47±15.49^{a}	0.526
Triglyceride (mg/dL)	125.06±18.17^{a}	137.63±19.38^{a}	161.52±40.52^{ab}	214.50±41.39^{b}	118.02±13.57^{a}	0.131
HDL-C (mg/dL)	34.94±1.97^{a}	34.69±1.52^{a}	42.80±4.03^{bc}	36.50±2.50^{ac}	49.01±2.83^{b}	0.001
LDL-C (mg/dL)	121.20±8.42^{a}	117.04±8.61^{ab}	124.99±9.14^{a}	128.88±7.99^{a}	94.93±11.14^{b}	0.084
Non-HDL (mg/dL)	141.87±10.56^{ac}	137.94±9.29^{abc}	149.17±11.21^{ac}	157.65±11.27^{a}	120.46±15.58^{bc}	0.251
Total cholesterol /HDL ratio	5.16±0.31^{a}	5.03±0.32^{a}	4.80±0.45^{a}	5.61±0.52^{a}	3.59±0.34^{b}	0.011
LDL /HDL ratio	3.56±0.27^{a}	3.42±0.29^{a}	3.09±0.26^{a}	3.76±0.39^{a}	2.01±0.23^{b}	0.001
Inflammatory biomarkers						
MIF(ng/mL)	41.81±5.21^{a}	35.61±6.22^{a}	43.41±7.21^{a}	43.69±6.50^{a}	19.01±3.05^{b}	0.015
hs-CRP(mg/L)	7.94±2.22^{a}	7.02±2.45^{a}	7.61±3.23^{a}	17.79±4.71^{b}	1.92±0.37^{a}	0.009
Heamatological indices						
Leucocyte count (103/μL)	12.49±0.67^{a}	11.58±1.15^{a}	13.53±1.10^{a}	12.00±0.66^{a}	6.22±0.40^{b}	0.000
Neutrophil count (103/μL)	9.68±0.63^{a}	9.18±1.42^{a}	10.27±1.23^{a}	9.36±0.65^{a}	3.75±0.56^{b}	0.019
Platelet (103/μL)	239.66±14.16^{a}	239.22±22.83^{a}	239.41±13.73^{a}	241.64±10.63^{a}	184.38±14.37^{b}	0.027

Values are presented as mean ± SE, tests between groups (ANOVA), different letters mean significant differences between the groups ($p<0.05$), and similar letters mean insignificant differences ($p>0.05$).

MI, myocardial infarction; Non-DM- Non-HTN, non-diabetic non-hypertensive; DM only, diabetes only; HTN only, hypertensive only; DM-HTN, diabetic hypertensive.

TABLE III
COMPARISION OF SOME RISK FACTORS AND OTHER VARIABLES IN MYOCARDIAL INFARCTION AND CONTROL GROUPS

Variables	MI				Control	P value
	Non-DM-Non-HTN n: 30 (30%)	DM only n: 18(18%)	HTN only n: 24 (24%)	DM-HTN n: 28 (28%)	Non-DM-Non-HTN n: 26 (68.42%)	
			No (%)			
Age (years) ≥55	14(46.67)	8(44.44)	14(58.33)	22(78.57)	12(46.15)	0.064
Male	28(93.33)	12(66.67)	20(83.33)	16(57.14)	16(61.54)	0.006
Smoker	21(70)	8(44.44)	20(83.33)	23(82.14)	10(38.46)	0.001
Duration of diabetes mellitus (years)*	-	6.79 ±2.00	-	7.74±2.28	-	0.758
Duration of hypertension (years)*	-	-	8.88 ±2.4	9.25±2.32	-	0.910
Duration of MI onset: ≥6 hours	19(63.33)	10(55.56)	18(75)	17(60.71)	-	0.582
Numbers of affected vessels						
1 vessel	4(13.33)	3(16.67)	4(16.67)	4(14.29)	-	0.978
2 vessels	8(26.67)	3(16.67)	4(16.67)	5(17.85)		
3 vessels	18(60)	12(66.66)	16(66.66)	19(67.86)		
Location of culprit lesion						
LAD	12(40)	16(88.89)	9(37.5)	12(42.86)	-	0.003
RCA	11(36.67)	2(11.11)	14(58.33)	12(42.86)		
LCX	7(23.33)	0(0)	1(4.17)	4(14.28)		
Medications						
Statin	24(80)	16(88.89)	20(83.33)	22(78.57)	-	0.874

Tests of significance between groups (chi-square test, Fisher exact test), * mean+- SE, t-test analysis.
MI, myocardial infarction; Non-DM-Non-HTN, non-diabetic-non-hypertensive; DM only, diabetic only; HTN only, hypertensive only; DM-HTN, diabetic hypertensive.

In the present study, although the DM group experienced an increase in MIF, hs-CRP, leukocytes, and neutrophils compared to the controls, it had the lowest values compared to other MI groups. Several considerations may explain this finding; the DM only group was comprised of the lowest percentage of smokers and had the lowest duration of MI onset (≤6 hours), but it had the highest percentage of receiving statin among the other groups (23–26). Although all parameters were high in the DM-HTN group, levels of SBP, DBP, HbA1c, leukocytes, and neutrophils were found out to be slightly lower than those of a particular MI group. In addition, all risk factors and other disease severity indicators were higher in DM-HTN, but they showed non-significant variations compared to other MI groups, with this indicating that MI patients associated with both DM and HTN experienced more complicated states.

Past research shows that MIF is positively correlated with BMI, total cholesterol, triglycerides, hs-CRP, and leukocytes, but it is correlated negatively with HDL-C (27).

TABLE IV
CORRELATION BETWEEN MIF AND DIFFERENT RISK FACTORS IN MYOCARDIAL INFARCTION PATIENTS

Parameters	MIF		hs-CRP	
	r	P value	r	P value
Age	0.018	0.904	0.038	0.795
BMI	0.022	0.878	0.017	0.908
MIF	-	-	0.356	0.011
Total Cholesterol	0.135	0.351	0.246	0.084
Triglyceride	0.043	0.765	0.113	0.434
HDL-C	-0.043	0.769	-0.038	0.791
LDL-C	0.120	0.407	0.194	0.176
Non-HDL	0.155	0.281	0.274	0.054
Leukocytes	0.493	0.001	0.246	0.085
Neutrophils	0.411	0.003	0.274	0.054
Platelets	0.218	0.128	0.130	0.367

Similar results were obtained in the present study; moreover, a significant positive correlation was found between MIF and hs-CRP with leukocytes and neutrophils in MI patients, indicating acute systemic inflammation.

The current study had some limitations, namely the level of MIF was measured only within 24 hours in a relatively small sample size in MI patients; thus, repeated measurements for longer times in larger sample sizes could be required to estimate MIF levels at different intervals starting from time of admission and is recommended. In addition, the estimation of MIF in recurrent MI and heart failure with higher MIF levels, compared to those with lower MIF levels could be useful in determining the predictive value of this parameter.

In conclusion, the MIF could be used as a new valuable diagnostic inflammatory biomarker for MI, but the hs-CRP proved to be significantly a better prognostic inflammatory parameter than MIF for MI intensity associated with DM and HTN.

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