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Early Diagnosis of Brain Natriuretic Peptide (Pro-BNP) and Ischemia Modified Albumin (IMA) Levels in Acute Coronary Syndrome Patients with ST Segment Elevation Myocardial Infarction (STEMI) and Non ST Segment Elevation Myocardial Infarction (NSTEMI)

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ABSTRACT

Background: Acute coronary syndrome (ACS) can be classified to ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina. The challenging in acute coronary syndrome remains, as it does not detect the myocardial ischemia by cardiac troponin and creatine kinase-MB. Pro brain-type natriuretic peptide (pro-BNP) was released when the heart need to hard works, which leads of retention fluid and expansion of veins and arteries. Therefore, this hormone release in the response of the changes of pressure in the heart especially for patients with ACS, which be benefit to use as an indicator to evaluate health problem that related with heart. Ischemia modified albumin (IMA) is a form of human serum albumin in which the N-terminal amino acids have been modified by ischemia as the result of acidosis, damaging occurs by free radicals, fatty acids releasing, exposures to free copper and iron, and disturbance of calcium pump. The aim of this study was to estimate the brain natriuretic peptide (Pro-BNP) and Ischemia Modified Albumin (IMA) Levels as early diagnostic markers and correlated with conventional cardiac markers at admission to the emergency department in Acute Coronary Syndrome Patients with ST segment elevation myocardial infarction (STEMI) and Non ST segment elevation myocardial infarction (NSTEMI).

Methods: Eighty ACS patients who arrived at the emergency department ED within 6h of clinical symptoms divided to STEMI and NSTEMI, and another 40 of noncardiac chest pain patients (NCCP) as control were enrolled in this study. pro-BNP was measured using a Cobas e 411 Roche, Germany, and IMA was measured using enzyme-linked immunosorbent assay (ELISA) kits. Tukey HSD Post hoc ANONA test and One-way ANOVA were used to compare differences of mean between groups. Pearson Correlation was calculated to assess the relation between the biomarkers of this study. Receiver Operating Characteristics (ROC) curve was calculated to estimate the sensitivity and specificity for the use of pro-BNP and IMA as biomarker in the diagnosis and discriminatory ability of ACS.

Results: pro-BNP and Ischemia modified albumin were significantly higher in acute coronary syndrome patients (STEMI & NSTEMI) compared to NCCP as controls (1359.82± 995.00 and 2698.22±1604.69 vs 180.07±90.24) ($p<0.01$) for pro-BNP and (96.79±16.03 and 86.00±15.14 vs. 69.42±10.65) for IMA. There were a significant differences in mean of each pr0-BNP and IMA values between two categories of acute coronary syndrome were seen ($p<0.01$). The correlation of IMA with CK-MB in NSTEMI patients was peak negative ($r=-0.41$, $p<0.01$). Receiver operator characteristics (ROC) curve was calculated to define the optimal cut-off values for the use of each pro-BNP and IMA as biomarkers in early diagnostic and distinguish of patients with STEMI and NSTEMI at admission to ED within 6h of clinical signs. ROC curve revealed to the optimal cutoff value for pro-BNP in STEMI was 231 pg/ml and NSTEMI was 400 pg/ml with sensitivity of 85% and 87.5% and specificity of 82.5% and 87.5% with area under curve AUC of 91.9% and 95.7%. The optimal cutoff value for IMA in STEMI was 89 U/ml and NSTEMI was 80.9 U/ml with sensitivity of 85% and 82.5% and specificity of 90.0% and 75.0% with AUC of 88% and 87.5%.

Conclusions: We conclude pro-BNP together with IMA assay as promising biochemical markers for the early diagnosis of ACS, and complement together as a good discriminator between STEMI patients and NSTEMI patients.

Keywords: Acute coronary syndrome, pro-brain natriuretic peptide, Ischemia modified albumin, conventional cardiac markers

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INTRODUCTION

Acute coronary syndrome is a term used to describe a range of medicals cases that associated with decrease the blood flow to the heart [1]. Inflammation plays a major role in atherosclerotic plaque destabilization. Acute myocardial infarction (AMI) is mainly due to atherosclerotic plaque rupture. Plaque rupture does not always cause an acute event; instead, healing of the plaque rupture results in stenosis progression [2,3]. ACS can be classified to ST elevation myocardial infarction (STEMI, 30%), non-ST elevation myocardial infarction (NSTEMI, 25%) and unstable angina (38%) [4]. Despite a similar pathophysiology of unstable angina (UA) and NSTEMI, the differentiation is based on the severity of symptoms and the presence of certain biomarker, chest pain is more severe in MI. ST segment refers to the pattern that appears on an electrocardiogram, which is a display of patient heartbeat [5]. The ACS is often associate with atherosclerosis, so the specialists recommends staying away about the causes factors of this condition, such as: unhealthy eating, lack of exercises, lack control of hypertension and diabetes, smoking and lack control of cholesterol levels [6]. The purpose of identifying and early diagnosis of ACS is to limit myocardial injury which can only be done by rapid initiation of therapy. This is the key point in the management of ACS patients which can be achieved by rapid, sensitive and specific biomarkers [7]. In the practice, ACS is diagnosed depending on typical patient's clinical history of chest pain, confirmed by laboratory tests of raised blood cardiac troponin T or I (TnT or TnI) levels and in addition to changes in electrocardiography. Cardiac CK-MB released from damaged cardiac muscle was classical marker in the past [8].

Pro brain-type natriuretic peptide (pro-BNP) was released when the heart need to hard works, which leads of retention fluid and expansion of veins and arteries. Therefore, this hormone release in the response of the changes of pressure in the heart especially for patients with ACS [9], which be benefit to use as an indicator to evaluate health problem that related with heart [10]. Means, when the symptom of ACS occur, it necessary to measure the level of this hormone and make medical decision to save the patients [11]. Estimation the level of BNP in human blood was contributed to

diagnosis the suspected left ventricular dysfunction of patients [12].

Ischemia Modified Albumin (IMA) is a human serum albumin with altered N-terminal amino acids due to ischemia [13]. IMA is a promising marker for early detection of myocardial ischemia [14], elevated within few minutes and remain elevated up to 12–24 hours after ischemia before returning to its normal [15]. IMA ability to detect ischemia before myocyte destruction would allow for earlier and accurate management decisions as well as its role in a definitive biochemical ruling out strategy [16]. However, studies have shown that the level of serum IMA increases within minutes of the onset of ischemia, remains elevated for 6–12 hours, and then returns to a normal level within 24 hours [17, 18]. IMA assay may be used as promising biochemical marker for the early diagnosis of ACS [19].

Diagnosis of acute coronary syndrome (ACS) is important, due to the associated very high mortality. Failure to diagnose ACS is a problem both for the patients and the clinicians [20]. Early diagnosis ACS patients are important for suitable treatment and management [21]. The troponins and ECG considered as conventional tests for diagnosis of ACS in the emergency department [22]. The troponins considered as a good and even better diagnostic markers than ECG that may be not diagnostic about half of ACS patients admitted to emergency department [24,25].

The objective of the study was therefore to compare pro-BNP and IMA as early diagnostic markers together with CK-MB, and TnT between patients admitted to an ED with symptoms suggestive of ACS and noncardiac chest pain patients (NCCP) as control group in our population. .

PATIENTS AND METHODS

The present study was executed during the term from February 2019 to August 2019, and the study was approved by the Institutional Ethics Committee. 80 patients who arrived at the emergency department ED with chest pain were diagnosed with acute coronary syndrome ACS, by electrocardiogram (ECG), echocardiogram, and biochemical test (serum Troponin T and CK-MB). These patients were divided into two groups; One group consist of 40 patients with ST segment elevation myocardial infarction (STEMI) and one group consist of 40 patients with Non ST segment elevation myocardial infarction (NSTEMI), and another group of 40 noncardiac chest pain patients (NCCP). All groups were collected from Al-Numan Hospital, Al-Kindy Teaching Hospital and Ibn Al-Nafis Hospital. Patients with a renal, liver, and chronic inflammatory disorders, brain ischemia, acute mesenteric ischemia, malignant tumor, and pregnant women were excluded from the study.

About seven milliliters of blood samples from all subjects were collected by venipuncture directly as they admission the ED within 6 hrs of clinical signs. Blood samples were left for 20 minutes at room temperature. After coagulation, sera were aspirated and divided into small aliquots for immediate measurements of serum lipid profile and CK-MB were done using appropriate enzymatic colorimetric method, and TnT by Cobas e 411 Roche, Germany . The rest will be stored at -20 until assayed for serum pro-BNP that measured using a Cobas e 411 Roche, Germany, and IMA that measured using enzyme-linked immunosorbent assay (ELISA) kits.

Statistical Analysis

Statistical analysis was carried out using Microsoft excel 2013 and SPSS version 20. The numerical data expressed as mean ±SD. For three groups, one-way ANOVA was performed. Furthermore, the Tukey HSD Post hoc ANONA test was used to compare between mean serum levels of pro-BNP and IMA together with CK-MB, and TnT for STEMI, NSTEMI and NCCP were performed. A $p \leq 0.05$ was considered statistically significant. Pearson correlation were calculated to assess the relation between each of pro-BNP and IMA with CK-MB and TnT. Receiver Operating Characteristics (ROC) curve was calculated to estimate the sensitivity and specificity of the used pro-BNP and IMA as biomarkers in the diagnosis and discriminatory ability of ACS.

RESULTS

Baseline and clinical characteristics of the patients and control groups are given in Table 1. The total number of ACS patients (STEMI & NSTEMI) and NCCP as control group were 40 for each group. There were no significant differences in age between all groups, whereas the body mass index (BMI) has a significantly elevated in patients group comparing with control (P<0.01). Duration from the onset of symptoms until admission and blood drawing was within 6h. Serum lipid profile between patients with ACS and control groups were studied, the results showed that the levels of the cholesterol and LDL were significantly (P<0.01) higher in the ACS patients (STEMI & NSTEMI) as compared to NCCP, whereas there was no significant differences in the level of triglyceride (TG) and HDL between all groups. The CK-MB, TnT, pro-BNP and IMA were significantly (P<0.01) higher in the ACS patients (STEMI & NSTEMI) as compared to NCCP.

Table 1: Baseline and clinical characteristics of the ACS patients and control groups

Tested value	Control (NCCP) (*n*=40)	Patients (STEMI) (*n*=40)	Patients (NSTEMI) (*n*=40)	p value
	Mean ±SD	Mean ±SD	Mean ±SD	
Age (year)	54.35±8.73	55.55±8.00	56.77±9.2	0.45
BMI (kg/m^2)	29.91±5.63	31.17±5.61	30.94±6.10	<0.01
Cholesterol (mg/dl)	167.05±25.35	197.07±33.30	201.25± 42.38	<0.01

T.G (mg/dl)	154.50±30.95	165.65±47.39	177.55±68.86	0.13
HDL (mg/dl)	53.87±7.33	52.95±9.29	49.47±8.60	0.053
LDL (mg/dl)	95± 34.12	111.65 ± 40.55	117± 39.46	<0.01
CK.MB (U/L)	20.04±5.44	65.62±58.10	58.97±73.25	<0.01
TnT (ng/ml)	0.11±0.07	5.27±8.00	4.63±8.75	<0.01
Pro-BNP (pg/ml)	180.07±90.24	1359.82± 995.00	2698.22±1604.69	<0.01
IMA (U/ml)	69.42±10.65	96.79±16.03	86.00±15.14	<0.01

One-way ANOVA was used to arrive at the p-value, NCCP non cardiac chest pain, STEMI ST-segment elevation myocardial infarction, NSTEMI non ST segment elevation myocardial infarction, CK-MB creatine kinase MB, TnT cardiac troponin T, pro-BNP pro-brain natriuretic peptide, IMA ischemia modified albumin.

Tukey HSD Post hoc ANOVA test results between ACS groups are given in Table 2. The results showed that the pro-BNP level has a significantly elevated in NSTEMI group comparing with STEMI group (P<0.01), whereas the IMA level has a significantly elevated in STEMI group comparing with NSTEMI group (P<0.01), but there were no significant differences for each CK-MB, and TnT levels between STEMI and NSTEMI groups.

Table 2: Comparison of the mean CK-MB, TnT, pro-BNP and IMA values between the ACS groups

Tested value	STEMI	NSTEMI	P value
	Mean ±SD	Mean ±SD	
CK.MB (U/L)	65.62±58.10	58.97±73.25	0.84
TnT (ng/ml)	5.27±8.00	4.63±8.75	0.90
Pro-BNP (pg/ml)	1359.82± 995.00	2698.22±1604.69	<0.01
IMA (U/ml)	96.79±16.03	86.00±15.14	<0.01

The correlation of each pro-BNP and IMA with CK-MB and TnT in STEMI and NSTEMI patients are given in table 3. The results revealed that there was a negative correlation between IMA with CK-MB in NSTEMI patients (r =-0.41, p<0.01).

Table 3: Correlation of each pro-BNP and IMA with CK-MB and TnT in ACS patients (STEMI & NSTEMI)

Tested value /patients		STEMI		NSTEMI	
		CK-MB	TnT	CK-MB	TnT
Pro-BNP	Pearson Correlation	0.12	0.04	0.03	0.01
	Sig. (2-tailed)	0.43	0.78	0.83	0.94
IMA	Pearson Correlation	-0.19	0.2	-0.41	0.01
	Sig. (2-tailed)	0.9	0.19	<0.01	0.94

The ROC curve of pro-BNP for diagnosis of ACS on admission is shown in Figure 1 and table 4.The AUC for pro-BNP in STEMI was 91.9% and 95.7% in NSTEMI. The cut-off value of the serum pro-BNP level in STEMI was (231 pg/ml) with sensitivity of 85% and specificity of 82.5%, whereas the cut-off value of the serum pro-BNP level in NSTEMI was (400 pg/ml) with sensitivity of 87.5% and specificity of 87.5%.

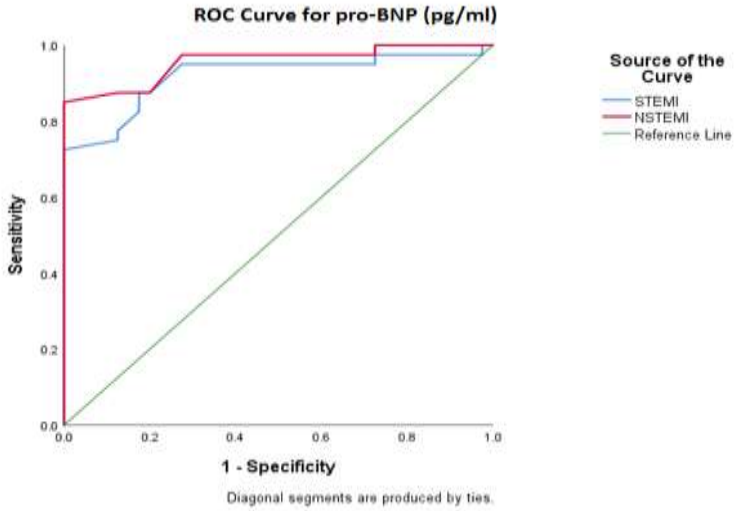

Figure 1: ROC curve of pro-BNP assay for comparing performance between STEMI and NSTEMI diagnosis.

Table 4: Cutoff, Sensitivity and Specificity of pro-BNP in patients with STEMI and NSTEMI

Test	Group	Sensitivity	Specificity	AUC	Cutoff
Pro-BNP (pg/ml)	STEMI	85%	82.5%	91.9%	231
	NSTEMI	87.5%	87.5%	95.7%	400

The ROC curve of IMA for diagnosis of ACS on admission was shown in figure 2 and table 5.The AUC for IMA in STEMI was 88% and 87.5% in NSTEMI. The cut-off value of the serum IMA level in STEMI was (89 U/ml) with sensitivity of 85% and specificity of 90%, whereas the cut-off value of the serum IMA level in NSTEMI was (80.9 U/ml) with sensitivity of 82.5% and specificity of 75%.

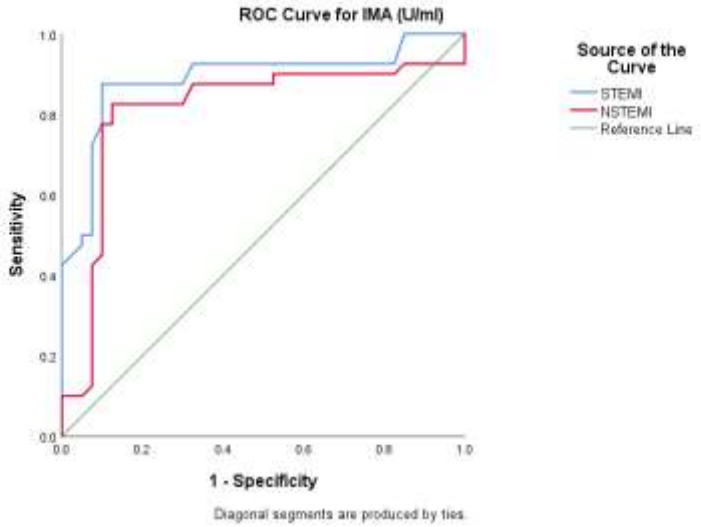

Figure 2: ROC curve of IMA assay for comparing performance between STEMI and NSTEMI diagnosis.

Table 5: Cutoff, Sensitivity and Specificity of IMA in patients with STEMI and NSTEMI

Test	Group	Sensitivity	Specificity	AUC	Cutoff
IMA (U/ml)	STEMI	85 %	90%	88%	89.0
	NSTEMI	82.5%	75%	87.5%	80.9

DISCUSSION

Baseline characteristics of the ACS patients and control groups

Age is one of the important factor of outcome of ACS by determine the normal level of biomarkers test [26]. The results in table (1) showed that the mean and standard deviation (Mean ± SD) of age for STEMI, NSTEMI and NCCP were 56.72±8.96, 58.10±10.16, and 52.10±10.28 respectively, and it has no significant difference between

ACS groups and control group (P=0.027). This result is agreed with the conclusion obtained from Haller et al [27].

Body mass index (BMI) refers to have a role factor to develop health problems [28]. Table (1) showed that the mean and standard deviation (Mean±SD) of BMI for STEMI, NSTEMI and NCCP were 31.17±5.61, 30.94±6.10, and 29.91±5.63 respectively, with significantly elevated in ACS groups comparing with the control group (P<0.01). These results agree with the conclusion obtained from Pan et al [29].

Clinical characteristics of the patients with ACS and control groups

The present study showed, the mean and standard deviation (Mean ± SD) of STEMI, NSTEMI and NCCP for cholesterol were 197.07±33.30, 201.25± 42.38, and 167.05±25.35 (mg/dl) respectively, and for LDL were 161.65 ± 40.55, 154± 39.46, and 145± 34.12 (mg/dl) respectively, whereas the mean and standard deviation (Mean ± SD) of STEMI, NSTEMI and NCCP for both triglyceride (TG) were 165.65±47.39, 177.55±68.86 and 123.30±37.11 (mg/dl) respectively, and HDL were 34.9±7.33 30.15±5.77 and 34.12±4.60 respectively, with no significance differences. These values showed that high levels of total cholesterol and LDL (p< 0.01), were associated with increased risk of acute coronary syndrome, this risk may modified to angina or heart failure or died, which agree with the finding of the significant association between the high levels of total cholesterol or LDL and acute coronary syndrome risk may be attributed to differences in fat metabolism among ACS patients and control. This results was agreed with a previous study that presented by Ahmad et al [26].

The present study showed the mean and standard deviation (Mean±SD) of the following markers for STEMI, NSTEMI and NCCP. For CK-MB were 65.62±58.10, 58.97±73.25, and 25.05±35.56 (U/L) respectively, and TnT were 5.27±8.00, 4.63±8.75, and 0.11±0.07 (ng/ml) respectively, and pro-BNP were 1359.82± 995.00, 2698.22±1604.69, and 180.07±90.24 (pg/ml) respectively and IMA were 86.79±16.03, 76.00±15.14, and 59.42±10.65 (U/ml) respectively, with significantly elevated in ACS groups comparing with the control group (P<0.01), as shown in table 1. These values showed that high levels of both CK-MB and TnT were associated with increased risk of acute coronary syndrome, this risk may be modified to heart failure or died, which agree with the previous study in Ndrepepa et al [30]. For this reasons, troponin used as an indicator to diagnosis of increasing of its levels in the human blood this study is deal with Scirica and David [31], on the other hand, this test may be used to evaluate other causes of heart problem, this is agreed with study of Levine et al [32]. As well as these results showed that the level of pro-BNP was significantly higher in ACS group as compared to the control group (P<0.01). The high level of Pro-BNP was associated with increased risk of acute coronary syndrome, this risk may be an indicated to evaluate health problem that related with heart, because this hormone release in the response of the changes of pressure in the heart especially for patients with ACS [33,34], also this study is deals with Giannitsis and Huge [11]. The results of present study showed that serum IMA level was significantly higher in ACS group as compared to the control group, thus in agreement with study of Bijaya et al [19]. Many mechanisms were proposed for production of IMA within minutes after the onset of acute myocardial ischemia like acidosis, damaging occurs by free radicals, fatty acids releasing, exposures to free copper and iron, and disturbance of calcium pump, all of which involves damage of the amino terminal of human serum albumin [20,35]. According to these results IMA is a useful biochemical marker to differentiate between NCCP patients and ACS patients [36]. In addition recent studies suggests the release of fatty acids in myocardial ischemia results in the binding of fatty acid to albumin, that may be caused a conformational changing in albumin, thus reducing its binding with Co(II) [37]. IMA results depend on the type of assay and instrument uses. The major strength of the present study is that used an ELISA for measuring serum IMA levels, which is faster, less expensive and comparably reliable with the albumin cobalt binding assay, which has been used in previous studies [38].

Comparison of CK-MB, TnT, pro-BNP and IMA values between the ACS groups

In the present study, CK-MB, TnT, pro-BNP, and IMA concentrations were compared between the patients with ACS who presented to the ED within 6hrs as shown in table 2. Although there were an increase in the mean and standard deviation (Mean±SD) of both CK-MB and TnT, the results revealed, that there were no significance differences in the concentrations of both CK-MB and TnT in STEMI patients as compared with the NSTEMI patients despite. These results are in agreement with other studies Tahir et al [39] and Loria et al [40]. Despite the fact that CK-MB acts as an indicator of cellular damage that reflects the vulnerable area and the resulting of infarction size, while TnT acts as an indicator of muscle myocardial damage and rises in proportion to the size of the infarction itself. The clinical spectrum of ACS consists of STEMI and NSTEMI elevation or UA, which are categorized by acute changes in ECG and expansion of myocardial necrosis [41], but this may be contributing to the lower sensitivity of these biomarkers in the first 6 hours after symptom onset. The present study disagreement with Ragaa et al [42], that showed the cardiac markers, such as CK-MB isozyme and TnT, detect the evolution of myocardial necrosis, and have appear as good predictors of risk in ACS patients, whereas the level of pro-BNP was significantly higher in NSTEMI patients as compared to the STEMI patients (P<0.01). These results agree with previous study of Ragaa et al [42], that pro-BNP rises in ACS patients with NSTEMI, not increased by myocardial necrosis, but ischemic insult in itself. This can be explained based on the releasing of cardiac markers, especially NT-proBNP, in ACS patients with NSTEMI differed from that in ACS patients with STEMI. These two groups showed different ischemic area spectrum. Furthermore, the cause of STEMI was complete occlusion in the coronary artery, while NSTEMI was related with susceptible plaque and subocclusive thrombosis [42]. The releasing of BNP and NT-proBNP were also tiggers by myocardial ischemia [43,44]. Our results disagreement with the finding of Mohamed and Babu Raj [45], that showed a higher value of NT- proBNP in STEMI patients as

compared with NSTEMI patients, this may be due to the increment of pro-BNP in NSTEMI patients are inversely proportional to the time course duration of admission and clinical signs [46]. Conversely the level of IMA was significantly higher in STEMI patients as compared to the NSTEMI patients (P<0.01). These results agree with previous study in Prema et al [16], and disagreement with other studies, that there was no significant difference between NSTEMI and MI [47,48].

Discrimination between ACS patient lacking myocardial necrosis and those having ischemia alone is of great value, the current cardiac markers such as CK-MB, and the cardiac specific troponin I although remain the most sensitive and specific for diagnosis of acute cardiac myonecrosis, still they cannot confirm absence of cardiac ischemia if they are negative at least initially. Therefore looking for new early marker in this regard is necessary for classifying ACS patients having ischemia or not [49,50]. Studies have shown that IMA rapidly rises following an ischemia when time frame comparison have been done the rise in IMA concentration was more rapid than TnT and CK-MB in diagnosis ACS [18]. IMA rises immediately after the onset of plaque rupture when compared to cardiac troponins and natriuretic peptides. It starts to fall at 6 hrs and returns to normal at 24 hrs. [51]

Correlation Coefficient of Parameters of Study by Pearson Correlation Coefficient Function

In the present study, each pro-BNP, and IMA levels were correlated with CK-MB and TnT in STEMI and NSTEMI patients are given in table 3. The results showed no relationship between Pro-BNP test and other parameter in serum of patient with ACS. Pro-BNP levels in patients with ACS in our study increased very early while the maximum levels were observed in the first 48 hours. These results agree with previous study of Baxter [52]. Together with these results, we provide evidence that cardiac marker pro-BNP is an independent marker for both diagnoses and also for prognosis in patients with the acute coronary syndrome [53]. This results disagreement with the finding of Stefan et al [54], that NT-proBNP showed a strong correlation with TnT, whereas Michael et al. [55], that showed a positive correlation of NT-proBNP with CK-MB and TnT, but they findings of time-dependent changes of BNP after acute myocardial infarction with peak values 20.6 hrs respectively 24 hrs after the onset of symptoms [56,57], wherease Ragaa et al [42], finding the negative correlation between NTBNP and CK-MB.

The present study showed no correlation of IMA with CK-MB and TnT in STEMI patients, and with TnT in NSTEMI patients, whereas there was a negative correlation with CK-MB in NSTEMI patients (Table 3). This results in agreement with another studies, that finding no correlation between IMA and troponin [58], and IMA with cTnI and CK-MB in unstable angina, NSTEMI and MI patients [47], this finding may be explained by the relative late appearance of most AMI markers being products of ischemic myocardial damage [59], and the negative correlation between IMA and CK-MB may be due to the increase of one variable, in a negative correlation, may represent the increase of a factor that is directly causing the decrease of another factor, this factor may be the time of admission the patients to the ED within 6 hrs of clinical signs. We think that this difference with the literature may be due to initial measurement of the patients at the time of our arrival [60]. Together with these results, we provide evidence that IMA may be act an independent marker for both early diagnoses in patients with the acute coronary syndrome.

Sensitivity and Specificity of Pro-BNP

Optimal cut-off values of receiver operator characteristics (ROC) curve were calculated for each pro-BNP (figure 1 & table 4) and IMA (figure 2 & table 5) as biomarkers in early diagnostic and distinguish of patients with STEMI and NSTEMI at admission to ED within 6hrs of clinical signs. The area under curve for pro-BNP in STEMI and NSTEMI were 91.9% and 95.7% respectively, this results may be indicated the diagnostic ability of this marker between patients with ACS groups and NCCP as control. The sensitivity of pro-BNP in STEMI and NSTEMI were 85% and 87.5% respectively, this mean that the positive detection rates were 85% and 87.5% respectively. The optimal cutoff values for pro-BNP in STEMI and NSTEMI were (231 pg/ml) and (400 pg/ml) respectively were derived from ROC curve analysis, this results may be indicated discriminatory ability of increased serum pro-BNP levels for STEMI patients as compared with NSTEMI patients. The results obtained were disagreement as reported by others [42, 54]. This may be attributed to differences in study population baseline characteristics, the time of sample collection, and the technique used.

The area under curve for IMA in STEMI and NSTEMI were 88% and 87.5% respectively, this results may be indicated the diagnostic ability of this marker between patients with ACS groups and NCCP as control. The sensitivity of IMA in STEMI and NSTEMI were 85% and 82.5% respectively, this mean that the positive detection rates were 85% and 82.5% respectively. The optimal cutoff values for IMA in STEMI and NSTEMI were (89 U/ml) and (80.9 U/ml) respectively were derived from ROC curve analysis, this results may be indicated discriminatory ability of increased serum IMA levels for STEMI patients as compared with NSTEMI patients, and were higher for STEMI and lower for NSTEMI as reported by others [61,62].

However, up to 90 U/mL [63] ,93.5 U/mL [64] and even >95U/ml [58] have been used in other studies which reflect different nature population in different studies.

CONCLUSIONS

Measurement of pro-BNP with IMA as a marker of myocardial ischemia in the absence or proceeding of myocardial necrosis can be a useful tools in the diagnosis of patients with STEMI and NSTEMI admitting to the emergency department. We conclude pro-BNP and IMA assay as promising biochemical markers for the early diagnosis of ACS, and use both of them as one complement to other as a good discriminator between STEMI patients and NSTEMI patients.

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