Relationship of Serum Copeptin Level with Traditional Risk Factors for Acute Coronary Syndrome in Early Diagnosis of this Syndrome in Iraqi Patients

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علاقة مستوى الكوببتين في المصل بعوامل الخطورة لمتلازمة الشريان التاجي الحادة في التشخيص المبكر لهذه المتلازمة لدى المرضى العراقيين

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Abstract

Background: Acute coronary syndrome (ACS) is still one of the main causes of morbidity and mortality worldwide and an early diagnosis of myocardial infarction (MI) aims to decrease mortality in MI patients. The ACS is manifested as one of three subtypes. These subtypes include MI with the electrocardiogram (ECG) is showing ST-segment elevation (STEMI), the other is MI with the ECG is showing no ST-segment elevation (NSTEMI) and the third type is unstable angina (UA). **Objectives**: To explore the Relationship of serum copeptin level with traditional risk factors for acute coronary syndrome in early diagnosis of this syndrome in Iraqi patients.

Methodology: 120 patients "72 males and 48 females", aged ≥ 30 years were consecutively selected from those who were admitted and diagnosed as ACS. The ACS patients were of three subtypes; STEMI, NSTEMI and UA and apparently healthy subjects were recruited as controls for this study. For each study subject, serum Copeptin, FBS, cholesterol and GOT levels were measured. **Results**: The copeptin level remained significant higher level in presence or absence of any of the studied risk factors .The CPP mean level showed an overall significant difference among study groups, copeptin mean level was significantly higher in each ACS subgroup than in controls group ($P < 0.001$).

Conclusion: Serum copeptin level remained significantly higher in ACS subgroups than in controls group in the first hurs. After onset of chest pain in presence or absence of any of the studied risk factors of ACS.

Keywords: Acute coronary syndrome, STEMI, Copeptin, Traditional risk factors, UA, NSTEMI.

المستخلص

الخلفية: لا تزال متلازمة الشريان التاجي الحادة (ACS) واحدة من الأسباب الرئيسية للمرض والوفيات في جميع أنحاء العالم، ويهدف التشخيص المبكر لاحتشاء عضلة القلب (MI) إلى تقليل الوفيات لدى مرضى احتشاء عضلة القلب. تتجلى متلازمة الشريان التاجي الحادة كواحد من ثلاثة أنواع فرعية. تشمل هذه الأنواع الفرعية احتشاء عضلة القلب مع تخطيط كهربية القلب (ECG) يظهر ارتفاع القطعة ST (STEMI)، والآخر احتشاء عضلة القلب مع تخطيط كهربية القلب لا يظهر ارتفاع القطعة ST (NSTEMI) والنوع الثالث هو الذبحة الصدرية غير المستقرة (UA).. **الأهداف:** استكشاف العلاقة بين مستوى الكوبتين في المصل وعوامل الخطر التقليدية لمتلازمة الشريان التاجي الحادة في التشخيص المبكر لهذه المتلازمة لدى المرضى العراقيين. **المنهجية:** تم اختيار 120 مريضًا "72 من الذكور و 48 من الإناث"، تتراوح أعمارهم بين 30 عامًا أو أكثر على التوالي من أولئك الذين تم إدخالهم وتشخيصهم على أنهم متلازمة الشريان التاجي الحادة. كان مرضى متلازمة الشريان التاجي الحادة من ثلاثة أنواع فرعية؛ تم تجنيد مرضى احتشاء عضلة القلب الحاد (STEMI) واحتشاء عضلة القلب الحاد (NSTEMI) واالذبحة الصدرية (UA) و أصحاء ظاهريًا كضوابط لهذه الدراسة. لكل مريض في الدراسة، تم قياس مستويات كوبتين في المصل، وFBS، والكوليسترول، وGOT.. **النتائج:** ظل مستوى كوبتين أعلى بشكل ملحوظ في وجود أو غياب أي من عوامل الخطر المدروسة. أظهر متوسط مستوى CPP فرقًا كبيرًا بشكل عام بين مجموعات الدراسة، وكان متوسط مستوى كوبتين أعلى بشكل ملحوظ في كل مجموعة فرعية من ACS مقارنة بمجموعة الضوابط ($P < 0.001$).

الاستنتاج: ظل مستوى كوبتين في المصل أعلى بشكل ملحوظ في المجموعات الفرعية من ACS مقارنة بمجموعة الضوابط في الساعات الأولى بعد ظهور ألم الصدر في وجود أو غياب أي من عوامل الخطر المدروسة لـ ACS.

الكلمات المفتاحية: متلازمة الشريان التاجي الحادة، احتشاء عضلة القلب الحاد مع ارتفاع المقطع اس تي (STEMI)، كوبتين، عوامل الخطر التقليدية، ال (UA)، الذبحة الصدرية , احتشاء عضلة القلب الحاد مع عدم ارتفاع المقطع اس تي (NSTEMI).

Introduction

Coronary heart disease (CHD) is caused by an poor myocardial oxygen supply because of narrowing or block of the coronary arteries and is the commonest reason of death worldwide(1). Clinically, the major acute clinical appearance of CHD is called Acute Coronary Syndrome (ACS ((2). The ACS could be manifested as one of three subtypes. These subtypes of ACS include myocardial infarction (MI) with the electrocardiogram (ECG) is showing ST-segment elevation (STEMI), the another is MI with the ECG is showing no ST-segment elevation (NSTEMI) and the third type is unstable angina (UA) (3).

Certain risk factors lead to increase occurrence of acute coronary syndrome like (Age , Being overweight or obese , Diabetes , Smoking , High blood pressure , High cholesterol , Family history of heart disease , chest pain, or stroke and Not being physically active may be altered by pharmacological treatment or behavioral adjustments, making them suitable goals for interventional efforts to reduce the risk of developing or slow down the development of CHD..(4)

A person with a high risk of developing CHD may still benefit from more aggressive and successful therapies for other risk factors, even while some risk variables are unmodifiable(5).

Copeptin (CPP) a polypeptide molecule that is derived from the precursor peptide prepro-vasopressin (164 amino acids) which consists of arginine vasopressin (AVP), neurophysinII, and copeptin(6) .

It has recently been stated that the level of copeptin, the “C-terminal part of AVP precursor” was **raised within 30 min after the onset of chest pain in patients with MI as an outcome of endogenous stress response** (7). The CPP level **did not required serial sampling** in contrast to troponin and so may signify an accurate anchor point to diagnose AMI in patients admitted to ED (8).

Hence, CPP level may confirm or rule-out ACS in patients admitted to emergency department an early time if it were of high sensitivity and specificity, a property that would reduce mortality rate and decrease the economic costs of ACS treatment. The aim of this study is to explore the relationship of serum copeptin level with traditional risk factors for acute coronary sydrome in Iraqi patients.

Materials and Methods

Study patients were recruited from the coronary care unit "CCU" at "Al-Yarmouk Teaching Hospital" during the period among the "1st of November 2022 to the 1st of Septemper 2023". 120 patients "72 males and 48 females", aged ≥ 30 years were consecutively selected from those who were admitted and diagnosed as "ACS" by specialist cardiologists. The diagnosis of ACS was based on the presence of two available of three criteria:

- Clinical presentation of the patients
- ECG changes
- A positive troponin test

Based on the same adopted criteria, ACS patients comprised three subgroups; namely, STEMI, NSTEMI and UA. The apparently healthy subjects as a controls group were recruited from those who had no current illness with consideration of age and sex matching with the ACS patients. They had no history of CHD or other systemic diseases and have had normal ECG recording.

Blood analysis

Blood samples were collected from patients and controls. Serum was separated, divided into aliquots, and used for measurement of CPP. The assays of CPP depended on use of enzyme linked immune sorbent assay kits that were supplied by MyBioSource Company, USA. Serum cholesterol, glutamate oxaloacetate transaminase (GOT), and fasting blood sugar (FBS) were measured by fully automated cobas c111 analyser.

Statistical analysis

Data were analyzed by the statistical package of SPSS-24. After assuring that the data was normally distributed, data presentation was done by mean, standard error or standard deviation of the mean, and percentage. LSD test was used for the difference between two means. A P-value of "< 0.05" was measured as statistically significant.

Results

The clinical characteristics of study subjects are shown in Table 1. The patients and the control subjects had a similar sex distribution (60 % males, 40% females). The study patients who were ≤ 50 years in age constituted 33.3% and persons were > 50 years constituted 66.66%. In regard to BMI, 20% normal weight of patients, "47.5%" overweight and "32.5% " were within the obese. The ACS patients included those with STEMI (40 patients), NSTEMI (40 patients) and UA (40 patients).

Table 1: Clinical characteristics of study subjects

Characteristic	Patients N= 120	Controls N=80
Age (years) ≤ 50 y > 50 y	 N= 40 (33.3%) N= 80 (66.66%)	 N = 27 (33.75%) N = 53 (66.2%)
BMI (kg/m2) Normal weight Over weight Obese	 N=24 (20%) N= 57 (47.5%) N= 39 (32.5%)	 N=16 (20%) N= 38 (47.5%) N= 26 (32.5%)
Sex Male Female	 N= 72 (60%) N= 48 (40%)	 N= 48 (60%) N= 32 (40%)
ACS subgroups STEMI NSTEMI UA	 N= 40 (33.3%) N= 40 (33.3%) N= 40 (33.3%)	 80 (100%)

"N: Number, BMI: Body mass index, STEMI: ST-elevation myocardial infarction, NSTEMI: non ST-elevation myocardial infarction, UA: Unstable angina".

The result of comparison of levels of study parameters among subgroups of ACS patients (STEMI, NSTEMI and UA) and controls is shown in Table 2. The comparison revealed significant differences among the study groups or subgroups in regard to the CPP mean level as well as to the mean levels of cholesterol, GOT, and FBS.

Table 2: Demographic, clinical Characteristics, baseline laboratory tests and copeptin level in subgroups of ACS patients and controls

Characteristic	STEMI N= 40	NSTEMI N = 40	UA N= 40	Controls N= 80	P-value
	Mean ± S.E.				
Age (years) Range Mean	45-75 years 59 ± 2	45-78 years 60 ± 3	47-80 years 61 ± 3	34-77 years 57 ± 2	0.065 NS
BMI (kg/m2)	28.53±0.57	28.17±0.53	27.53±0.57	23.37±0.46	0.032 Sig.
FBS (mg/dl)	194.27 ± 8.78	173.79 ± 11.32	152.77 ± 6.81	92.67 ± 2.37	0.001> Sig.
Cholesterol (mg/dl)	211.42 ± 5.2	173.87 ± 5.93	153.18 ± 4.58	141.64 ± 2.73	0.001> Sig.
GOT (IU/l)	146.1 ± 14.86	58.69 ± 3.17	15.74 ± 1.2	14.42 ± 0.56	0.001> Sig.
Copeptin (pg/ml)	341.41 ± 13.65	214.18 ± 8.02	185.82 ± 5.69	162.65 ± 3.19	0.001> Sig.

ANOVA test was performed, STEMI: ST-segment elevation myocardial infarction, NSTEMI: non ST-segment elevation myocardial infarction, UA: unstable angina, BMI: body mass index, FBS: fast blood sugar, GOT: glutamate oxaloacetate transaminase

The outcome of traditional CHD risk factors “age, hypertension, smoking and diabetes mellitus” on CPP in patients and compared with

controls is presented in tables (3-6). The changes in this study biomarker among patients and controls stayed significant in CPP above and below age of 50 years (Tables 3), with or without of systemic hypertension (Tables 4), in the presence or not of diabetes mellitus (Tables 5), and in smokers and non-smokers (Tables 6).

Table 3: Comparison of Copeptin between ACS patients and controls according to age

	Age (years)	Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	≤ 50 years	Patients	12	332.74 ± 23.51	<0.001
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	28	345.13 ± 16.92	<0.001
		Control	52	162.26 ± 3.55	
NSTEMI	≤ 50 years	Patients	8	195.01 ± 13.34	0.024
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	32	218.97 ± 9.35	<0.001
		Control	52	162.26 ± 3.55	
UA	≤ 50 years	Patients	8	182.55 ± 9.37	0.05
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	32	186.64 ± 6.77	0.001
		Control	52	162.26 ± 3.55	

Table 4: Comparison of copeptin level between ACS patients and controls according to hypertension

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	HT	Patients	20	366.59 ± 19.38	<0.001
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	20	316.23 ± 17.96	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	HT	Patients	30	212.6 ± 9.14	<0.001
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	10	218.9 ± 17.41	<0.001
		Control	80	162.65 ± 3.19	
UA	HT	Patients	20	187.16 ± 8.12	0.004
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	20	184.48 ± 8.17	0.004
		Control	80	162.65 ± 3.19	

Table 5: Comparison of Copeptin between STEMI patients and controls according to diabetic

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	DM	Patients	24	345.93 ± 18.37	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	16	334.64 ± 20.72	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	DM	Patients	16	216.88 ± 11.24	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	24	212.37 ± 11.25	<0.001
		Control	80	162.65 ± 3.19	
UA	DM	Patients	18	176.71 ± 8.61	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	22	193.28 ± 7.37	<0.001
		Control	80	162.65 ± 3.19	

Table 6: Comparison of copeptin levels between of STEMI patients and controls according to smoking status.

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	SMO	Patients	16	344.84 ± 24.55	<0.001
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	24	339.13 ± 16.24	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	SMO	Patients	20	219.28 ± 11.65	<0.001
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	20	209.07 ± 11.21	<0.001
		Control	80	162.65 ± 3.19	
UA	SMO	Patients	12	187.28 ± 11.03	0.294
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	28	185.2 ± 6.74	0.004
		Control	80	162.65 ± 3.19	

Discussion

Early identification of ACS patients among those presenting with chest pain to the emergency department in real-life daily clinical practice is important. Accelerated and intensive medical and interventional therapy can be beneficial for patients with ACS. Copeptin evaluation is therefore a useful diagnostic technique for AMI patients. Excluding healthy people who report having at least chest pain should improve the efficiency of emergency department operations. Nevertheless, when copeptin and hs-cTn-I are combined, the ACS patient exclusion rate is much higher than when those two markers are examined separately (9).

Traditional risk factor and their influence on core study biomarkers levels in ACS patients

When the major conventional risk variables were examined for their impact on the significant variations in CPP levels between ACS patients and controls, the results remained significant whether any of the risk factors under study was present or not. Nevertheless, this does not rule out the possibility that these risk variables have an impact on CPP levels. Then there are circumstances other than ACS presentation; these pertain to a predominance of alterations brought on by the existence of ACS and its underlying disease or effects.

In the present study, there was a significantly high level of copeptin in ACS patients with presence or absence of any of the studied risk factors when compared with controls in the first few hrs. after onset of chest pain (by LSD TEST) (10). Copeptin level may even be raised within 30 min after the onset of chest pain in patients with AMI as a result of endogenous stress response and so it does not need serial sampling like troponin and may signify an accurate anchor point to diagnose AMI in ACS patients on time of their admission emergency department (8). Hence, a diagnosis of AMI based on copeptin level may help to enable someone to approve or to rule-out ACS with higher sensitivity and specificity which could serve to decrease mortality rate and to reduction the economic costs of management of “ACS” patients and AMI patients in particular , this agree with (9) due to acute endogenous stress response (copeptin) seems to be real and effective .

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