Possible using of Obestatin as Diagnostic Marker in Iraqi Patient with Acute Coronary Syndrome

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Abstract

Background:Acute coronary syndrome (ACS) are brought on by coronary artery blockage. Consequences depend on degree and location of obstruction, is the major disease within world which is leading to death. Obestatin is a hormone produced via specialized epithelial cells of the stomach and small intestine, accumulating evidence supports positive actions on both metabolism and cardiovascular function. For example, obestatin has been shown to inhibit food and water intake, body weight gain, and gastrointestinal motility, as well as to mediate cell survival promotion and apoptosis prevention and improve lipid metabolism. Subjects and methods:Study design: case control study. These studies include 120 Iraqi participants (60 with Acute coronary syndromes (20 patients with ST elevation myocardial infarction, 20 with non-ST elevation myocardial infarction, 20 with unstable angina), 60 normal healthy control group) the age range (25-75) years. The following biochemical parameters have been studied, Obestatin by ELISA method, Troponin, CK-MB and Lipid profile by enzymatic method. also, body mass index (BMI) Measured. Blood samples were talked after fasting. ResultThe results of the study showed Obestatin was significant differences among the studied groups with ($p < .001$). And showed increase level of Obestatin in patients with STEMI as a compared with NSTEMI, Unstable angina and control group, the mean (35.27± 3.37, 53.56± 9.23, 71.87± 2.97, 89.26± 8.02) for the control, Unstable angina, NSTEMI and STEMI respectively. Conclusion: This study indicates that measuring of serum concentration of obestatin could be utilized for differentiate acute coronary syndrome patients from those without acute coronary syndrome. also serum FBS, serum CK-MB, serum h-s-Troponin I and serum lipid profile was measured, This coul provide clinical information's for disease.

Keywords: Diagnostic Marker; Acute Coronary; Iraqi Patient

1. Introduction

Acute coronary syndrome refers to a group of diseases in which the heart's blood flow is reduced. ST-elevation myocardial infarction, non-ST elevation myocardial infarction, and unstable angina are some examples. It's a form of coronary artery disease (CHD)و CHD can be asymptomatic in some cases, but ACS is always symptomatic (Singh and Jat.,2021).

Acute coronary syndrome refers to a group of diseases that are associated with acute myocardial ischemia and/or infarction due to varying degrees of reduced coronary blood flow caused by plaque rupture/erosion, thrombus development, or supply and demand mismatch (Dai et al .,2016).

Atherosclerotic plaque rapture causes ACS, which results in arterial blockage. Until the beginning of 20th century, it was believed that coronary thrombosis was always immediately fatal. Five individuals with acute myocardial infarction (MI) were described by two Ukrainian physicians in 1910, three of them had coronary thrombosis at postmortem. James Herrick provided the first comprehensive description of the clinical presentation of acute coronary syndrome in English in 1912 (Morrow, 2016) Obestatin is a 23-amino acid C-terminally amidated gastrointestinal peptide derived from preproghrelin and which forms an α helix. Obestatin has been shown to increase beta cell mass, improve adipogenesis, and improve lipid metabolism, as well as up-regulate genes involved in beta cell regeneration, insulin production, and adipogenesis. Furthermore, Obestatin appears to be involved in blood pressure regulation and to improve endothelial function, with experimental studies indicating that it may also promote cardioprotective actions against, for example, ischaemia–reperfusion injury. (Cowan et al., 2016) and (Alloatti et al., 2010).

II. Methods

The current study was case control study. The stud y

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was conducted during the period from November 2021 to August 2022. The study included 120 Iraqi participants, Sixty (60) patients and Sixty (60) control, in the University of Al-Naharin, College of Medicine, Department of Chemistry & Biochemistry, the patients admitted in (CCU) of Ibn Al-Bitar Hospital, Ibn Al-Nafes cardiac specialty teaching hospital and Al-Imamin Al-kadmeen city hospital, the patients divided into three groups: STEMI were their number (n=20), NSTEMI (n=20), and UA (n=20), number of control were (n=60). Participants were interviewed according to a well – structured questioner and examined by consultant physician. Physical examination was done and weight, height, BMI was measured. We calculated Body mass index (BMI) by the following formula (weight/height2) (kg/m2), The accepted ranges of BMI are as follows: (< 18.5) as considered as underweight, while (18.5 - 25) is considered as normal weight, and (25 - 30) is considered as overweight, lastly (> 30) is considered as obesity (WHO., 2019).

Preparation of blood samples

Seven milliliters (7 ml) blood of venous have be taken from aseptic area of patients and control. separate serum by centrifugation at 3000g for fifty minute and splatted into three parts:

1-Aliquot of serum was transferred into 1.5 ml Eppendorf tube, this part was use for assay (Total Cholesterol TC, Triglyceride TG, High Density Lipoprotein-Cholesterol HDL-C and blood sugar).

2- Aliquot of serum was transferred into1.5 ml Eppendorf tube, which is used to measure. the (CK-MB, High sensitive Troponin, were stored at -20 C° until analysis).

3-The remaining part was store in aliquots at -20 C° for subsequent assay of obestatin.

Statistical studies:

III. Results

The data were presented according to analysis of one hundred twenty (120) studied subjects that were assigned onto four (4) subgroups and as follows: twenty (20) apparently healthy individuals, twenty (20) patients that are STEMI, twenty (20) patients that are NSTEMI and twenty (20) patients that are UA. The respondents ages were grouped into 5 categories for analysis. The majority of patients within the NSTEMI were in age group between 61-70 (n = 6, 30.00%). The age groups (61-70), (41-50), and (25-40) were equally reported within the STEMI patients (n = 5, 25.00%) for each. While for Unstable group were (61-70), (41-50), and (51-60) (n = 5, 25.00%). The most frequently observed age group within the Control subjects was (61-70) (n = 22, 36.67%). Descriptive statistical studies shown that the minimum age of the patients was 25 years and maximum age was 75 years. Mean age of the cases was found to be 55.20 with a standard deviation of 13.29. While, for control the minimum age was 35 years and maximum age was 73 years. Mean age of the control was found to be 56.88 with a standard deviation of 8.75. There were no significant difference in Age among all the groups, F(3, 116) = 0.68, p = .566, Details of the demographic data ,The means and standard deviations are presented in (table 1) below.

(Table 1) descriptive statistics and comparisons of age in ACS and control and ACS subgroups.

Age	Min	Max	Mean± SD				SEM	t		df	P
ACS n= 60	25	75	55.20± 13.29				1.73	-0.813		102	.418
Control n = 60	35	73	56.88± 8.75				1.14				
Groups	Min	Max	1st Q	Median	3rd Q	Mean± SD	SEM	*F*		df	P
NSTEMI n=20	35	75	47.75	58	65.0	56.95± 11.70	2.68	0.680		3	.566
STEMI n = 20	25	75	41.25	52.5	68.0	52.85± 15.20	3.49				
Unstable n = 20	33	74	47.00	55.5	67.25	55.80± 12.37	2.84				
Control n = 60	35	73	49.75	57.5	63.25	56.88± 8.75	1.14				

Fisher's exact test was used to analyze the relationship between the 4 groups: (NSTEMI, STEMI, Unstable, and Control) and 5 levels of Age groups: [(71-80), (61-70), (51-60), (41-50) and (25-40)]. Fisher's exact test becomes computationally efficient for variables with a large number of categories or observations; consequently, Monte-Carlo simulations were employed to calculate the p-value instead of the exact p-value. The non-significance of the Fisher exact test, p =.391, suggests that the analyzed groups and Age categories may be independent of one another. This indicates that the observed frequencies did not differ significantly from the expected frequencies. Table 3-2 displays the outcomes of Fisher's exact test.

(Table 2) comparisons of age group distribution across the study groups

N= 120	Groups						
Age groups	NSTEMI	STEMI	Unstable	Control	χ^2	df	P
(71-80)	3 (15.00%)	3 (15.00%)	3 (15.00%)	3 (5.00%)	12.328	12	.420
(61-70)	6 (30.00%)	5 (25.00%)	5 (25.00%)	22 (36.67%)			
(41-50)	4 (20.00%)	5 (25.00%)	5 (25.00%)	15 (25.00%)			
(51-60)	5 (25.00%)	2 (10.00%)	5 (25.00%)	17 (28.33%)			
(25-40)	2 (10.00%)	5 (25.00%)	2 (10.00%)	3 (5.00%)			
Total	20	20	20	60			
	Group						
Age groups	NSTEMI	STEMI	Unstable	Control	*P**		

(Table 2) comparisons of age group distribution across the study groups					
(71-80)	3[2.00]	3[2.00]	3[2.00]	3[6.00]	.391
(61-70)	6[6.33]	5[6.33]	5[6.33]	22[19.00]	
(41-50)	4[4.83]	5[4.83]	5[4.83]	15[14.50]	
(51-60)	5[4.83]	2[4.83]	5[4.83]	17[14.50]	
(25-40)	2[2.00]	5[2.00]	2[2.00]	3[6.00]	
Note. Values formatted as Observed[Expected]. **Fisher's exact test, Monte-Carlo simulations were employed to calculate the p-value instead of the exact p-value*					

(Table 3) BMI and Lipid profile comparison between the study groups						
	Control 60	NSTEMI	STEMI	Unstable	F	p
	Mean± SD	Mean± SD	Mean± SD	Mean± SD		
BMI	25.93± 2.93	27.29± 2.20	26.78± 3.16	28.57± 3.76	4.10	.008
Cholesterol mg/dl	151.20± 12.78	161.95± 49.00	161.35± 38.14	148.40± 32.03	1.30	.279
TG mg/dl	105.75± 25.09	117.95± 47.02	153.15± 70.27	123.60± 49.73	6.03	< .001
HDL mg/dl	39.07± 6.68	35.67± 9.52	32.66± 9.11	33.79± 6.95	4.81	.003
LDL mg/dl	91.94± 7.22	154.28± 227.30	109.06± 38.64	88.64± 26.14	2.43	.069
VLDL mg/dl	21.15± 5.01	23.52± 9.45	30.49± 13.69	24.73± 9.95	5.98	< .001

There were significant differences in Obestatin among the studied groups , F(3, 116) = 549.59, p < .001. Means comparisons showed that the mean of Obestatin for NSTEMI (71.87± 2.97) was significantly smaller than for STEMI (89.26± 8.02), p < .001. but was significantly larger than for Unstable and control groups (53.56± 9.23), p < .001 and (35.27± 3.37), p < .001, respectively. On the other hand the mean of Obestatin for STEMI (89.26± 8.02) was significantly larger than for Unstable and control groups (53.56± 9.23), p < .001 and (35.27± 3.37), p < .001 respectively. , the mean of Obestatin for Unstable (53.56± 9.23) was significantly larger than for Control (35.27± 3.37), p < .001. The means and standard deviations are presented in (table 4).

(Table 4) Descriptive statistics of the Troponin, CKBM and Obestatin by groups with ANOVA results						
	Control 60	NSTEMI	STEMI	Unstable	F	p
	Mean± SD	Mean± SD	Mean± SD	Mean± SD		
Troponin pg/dl	3.91± 2.34	10130.4± 8889.83	17378.8± 8475.21	9.74± 3.97	75.09	< .001
CK MB ng/ml	3.34± 0.36	37.88± 2.97	46.47± 3.89	9.57± 1.54	2,922.20	< .001
Obestatin pg/ml	35.27± 3.37	71.87± 2.97	89.26± 8.02	53.56± 9.23	549.59	< .001

IV. Discussion

In this study there was significant for (TG and VLDL) but there was no significant for (Ch and LDL) in the ACS groups, see (table 3), Apart from serum HDL-C, which was found to be significantly lower in comparison to the control group, there was more clearly lipid disorder. The major cause of atherosclerosis is inflammation caused by fat buildup inside the arterial wall, these results are consistent with (Rallidis et al., 2018), (Al-Koofee et al., 2019) and (Al Tawil et al., 2007) A high level of lipoprotein is linked to an increased risk of acute coronary syndrome (ACS), Lp levels were found to be independently associated with ACS in younger (<45 years) and middle-aged (45-60 years) individuals, but not in individuals older than 60 years, And this is because of the over weight and Obesity in Iraqi people.

(Marchio et al., 2019) Atherosclerosis is a chronic inflammatory disease of the vascular system caused by endothelial dysfunction and oxidative stress, The oxidation of LDL-C is a crucial component in the development of atherosclerosis, while non-oxidized LDL has a low affinity for macrophages and it is not a risk factor, a common clinical practice to reduce oxidation and the risk of major events in patients with CVD is to lower LDL-C levels.

Data showed a increase in concentration of Obestatin in patient with ACS (STEMI, NSTEMI and UA), after admission in emergency department which is agreement with (Cowan et al., 2016) and(Alloatti et al., 2010) To date, clinical and experimental studies suggest that increased fasting obestatin levels in CVD patients and the obestatin play a rule in blood pressure regulation.

The study (Beberashvili et al., 2018) agreement with result of the present study that Serum obestatin acts as a biomarker in patients with cardiovascular disease. and agree with (Penna et al., 2017) and (Zhang et al., 2017) who appeared that Obestatin may play a role in human heart function, recent studies showed that obestatin may exert beneficial cardiovascular effects in humans, by producing vascular relaxation through activation of endothelium-dependent nitric oxide (NO) signaling through the PI3K/Akt/eNOS pathway, that show obestatin has a vasodilator effect on coronary arteries, which can counteract the strong vasoconstrictor impact of endothelin-1, The link between obestatin and NO has been confirmed in overweight and obese subjects, where obestatin induced vascular relaxation via specific activation of endothelium-dependent NO signaling, This peptide's effects could be proposed as a multiple target agent capable of counteracting maladaptive feed-back/responses in post-ischemic conditions

and obestatin suppresses excessive -adrenergic and endothelin-1 activity.

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