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ASSOCIATION BETWEEN FIBROBLAST GROWTH FACTOR- 23 AND APOLIPOPROTEIN A1 IN CORONARY ARTERY DISEASES OF IRAQI PATIENTS

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ABSTRACT

Background: Coronary artery disease is a clinical sign coming about because of a narrowing of epicardial coronary corridors that supply blood and oxygen to the heart. It is correspondingly called coronary heart disease (CHD).Coronary artery disease is greatest generally because of atherosclerotic obstruction of the coronary supply routes. Fibroblast growth factor 23 (FGF23) is a circulating peptide hormone emitted by bone cells, managing phosphate and vitamin D metabolism. A few late observational investigations detailed a free relationship of flowing FGF23 with a few cardiovascular malady hazard factors including left ventricular hypertrophy and vascular brokenness, CVD movement and occurrence clinical CVD occasions and mortality. Apolipoprotein A1 (ApoA1) is the essential protein related with high-density lipoprotein (HDL) particles, and assumes a focal part backward cholesterol transport. HDL-cholesterol (HDL-C) and Apo-A1 concentrations are contrarily relative to the hazard for coronary artery disease. **Aim**: To investigate the role of fibroblast growth factor-23 in coronary artery disease besides to its relationship with apolipoprotein-A levels. **Methods:** A case-control study included 42 elective patients attending the cardiology unit and the results of those patients were compared with (40) healthy control group. Blood samples were obtained for measurements of (FGF-23, troponin I, Apo-A1, total creatine kinase activity, urea, creatinine and lipid profile) for all participants. Serum urea, creatinine, creatine kinase and lipid profile were measured by Dimension Siemens. While serum FGF-23, troponin I and Apo-A1 were measured by ELISA technique. Statistical analyses were done by using statistical package for Social Sciences (SPSS). **Results:** The obtained results showed that there was a significant differences in serum FGF-23 and apoA1 in coronary artery disease (367.52±128.52 pg/ml), (2.03±0.90 mg/ml) as compared with the control (165.41±53.65 pg/ml) (1.49 ± 0.25 mg/ml) ($p< 0.005$, $P = 0.014$) respectively. There was a significant differences in age and TG level between CAD (58.66 ± 8.85 year, 99.50 ± 21.59 mg/dL) and control group (51.125 ± 11.71 year, 142.05 ± 66.24 mg/dL) ($P<0.005$, $P<0.0001$) respectively. **Conclusion:** According to the obtained results, it can be concluded that higher levels of FGF23 and Apo-A1 may be associated with complications and mortality of CAD in the Iraqi patients.

KEYWORDS: Fibroblast growth factor-23, Coronary artery disease and Apolipoprotein-A1.

INTRODUCTION

Coronary artery disease (CAD), also is the standard characterization of coronary illness. It is the fundamental wellspring of death in the United States in the two men and women. Coronary illness (CHD) is an infection in which a waxy substance rang plaque works inside the coronary courses. These veins supply oxygen-rich blood to the heart muscle.

Right when plaque creates in the supply courses, the condition is called atherosclerosis. The advancement of plaque occurs over various years. After some time, plaque can cement or split. Solidified plaque restrains the coronary conductors and lessens the flood of oxygen-rich blood to the heart. Coronary artery disease (CAD) is a standout amongst the most widely recognized sicknesses related with dyslipidemia and dyslipoprotenemia. Hoisted Apo-A1 levels are an autonomous hazard factor for untimely CAD. The component for atherogenic activity of Apo-A1 it meddles with fibrinolysis and advances smooth muscle multiplication and authoritative of proteoglycan to blood vessel divider. Apo-A1 level and Lp(a) isoforms are the vital markers for CAD (Jacobson, 2013).

(ApoA1) is the real protein part of high-density lipoprotein (HDL), blended basically in the liver (80%) and small digestive system (10%). It assumes a key part

backward cholesterol transport, advancing cholesterol efflux from tissues by going about as a cofactor for the lecithin cholesterol acyltransferase (LCAT). Low HDL-cholesterol fixation reflects expanded helplessness to cardiovascular maladies, and raising HDL pharmacologically remains a proposed procedure to lessen the event of cardiovascular illnesses (Huang *et al*., 2014).

Fibroblast growth factor 23 (FGF23) is the latest found individual from the fibroblast growth factors family (Chong et al., 2011). Fibroblast growth factor-23 (FGF-23) is a hormone engaged with phosphorous direction and vitamin D metabolism that might be related with cardiovascular hazard and it is a potential focus for intercession (Pamela et al., 2014). Fibroblast growth factor 23 (FGF23) has been accounted for to be associated with cardiovascular infection (Hu et al., 2015).

FGF-23 may influence cardiovascular hazard through the CKD or vitamin D pathways; CKD is a set up chance factor for cardiovascular disease (Go et al., 2004) and gathering proof recommends that low levels of vitamin D may increment cardiovascular hazard (Wang et al., 2012). Furthermore, late trial work in rat models proposes FGF-23 may have a direct pathophysiologic part in actuating left ventricular hypertrophy (LVH) (Faul et al., 2011). A marker of cardiovascular renovating related with expanded danger of sudden heart demise and movement to heart disappointment (Desai et al., 2012).

The presented work aimed to investigate the role of fibroblast growth factor-23 in coronary artery disease and then to its relationship with the levels of apolipoprotein-A and other biochemical markers.

MATERIALS AND METHODS

A case-control study including of 82 subjects, 42 patients of them were diagnosed as having coronary artery disease and another 40 healthy persons as control group, were conducted to assess the association of Fibroblast growth factor-23 and Apolipoprotein-A1 in coronary artery disease in Iraqi society.

The patient subjects were (24 males and 18 females) , whose ages ranged from 25 to 73 years and they diagnosed as having coronary artery disease and based on previous medical reports, laboratory tests and clinical examination by consultant cardiologist and attended from multi teaching centers in Baghdad (Ibn-Al bitar center for cardiac surgery, Baghdad teaching hospital and Ghazi Al Harriry teaching hospital).These centers are the biggest centers in Iraq for the period from December 2016 to Dec. 2017. Karbala Medical College Ethical Committee has approved the study protocol.

The inclusion criteria were

Patients those diagnosed as having coronary artery disease according to previous medical reports, laboratory tests and clinical examination by consultant cardiologist.

The exclusion criteria were

1. Patients were undergoing surgery more than 6 months
2. Patient with heart failure
3. Cardiomyopathy
4. Pregnant women
5. Refusal of participation of the study.

The control group included 40 persons(20 males,20 females) whose ages extended from (25 to 73) years were chosen arbitrarily as sound people without a past filled with coronary illness and not experiencing diabetes or hypertension and chose from the overall public who go to the healing center for checkup likewise from relatives and associates.

Data on statistic qualities, (for example, age, weight, stature, occupation, handedness, relationship and current smoking) were acquired through patient meeting at baseline. Causes and family history of Heart infection and the presence of coronary artery disease, hypertension and diabetes mellitus and also the medication history, drug history, were accounted for by the advisor cardiologist. Body mass index (BMI) was ascertained as weight in kilogram divided by height in meter square.

Statistical analyses were performed using SPSS statistical package for Social Sciences (type 17.0 for windows, SPSS, Chicago, IL, USA). Information are introduced as mean ± standard deviation for quantitative variables. Differences between groups were assessed with ANOVA (Analysis of Variance) test to look at between groups. Qualitative information relations were broke down by Chi square test. The connection between various parameters was tried by correlation test.

RESULTS

Age, Gender and BMI in coronary artery disease patients

Mean age of the subjects who enrolled in this study was 58.66 ± 8.85 years, as illustrated in the Table (1) which shown that there was a significant difference in age between CAD and control group ($P<0.005$). The count of male in CAD and control was (24, 20) respectively while the count of female in previous groups was (18,20) respectively. The percentage of male in CAD and control was (57.1%, 50%) respectively while the percentage of female in previous groups was (42.8% , 50%) respectively as shown in the Table (1) which mentioned that there was a non association between gender and the studied groups ($P>0.05$).

Table 1: Characterization of CAD and control groups according to their age, No., gender.

Groups		CAD	Control
No. (%)		42	40
Age (Year)	Mean	58.67	51.13
	SD	8.86	11.71
Gender No. (%)	Male	24 (57.1%)	20 (50%)
	Female	18 (42.8%)	20 (50%)

Table 2: Distribution of BMI among groups under study.

Groups		CAD	Control
No.(%) BMI value Kg/m^2	< 24	1	2
	24-30	20	25
	> 30	21	13

Lipid profile in coronary artery disease patients

The mean ± standard deviation (SD) of total serum cholesterol in coronary artery disease and control was (143.67 ± 47.64, 145.80 ± 22.90**)** mg/dl respectively**.** The mean ± SD of serum triglyceride in the previous groups was (142.05 ± 66.24, 99.50 ± 21.59) mg/dl respectively. The mean ± SD of HDL-C in the previous groups was (53.64 ± 25.13, 49.22 ± 2.73) mg/dl respectively. The mean ± standard deviation (SD) of LDL-C in the previous groups was (79.24 ± 42.13, 70.88 ± 16.07) mg/dl respectively. The mean ± SD of VLDL-C in the previous groups was (28.41 ± 13.25 ,19.90 ± 4. 32) mg/dl respectively as illustrated in the Table (3) which shown that there was a non-significant differences in total cholesterol, HDL-C, and LDL-C between groups (P>0.05); while there was a highly significant difference in TG where the control differ from CAD (P<0.0001)), and VLDL-C where control differ from CAD (P <0.0001).

Table 3: Lipid profile in coronary artery disease patients.

	Groups						
	CAD				Control		
	Mean±SD		SE	p-value	Mean±SD		SE
Cholesterol mg/dl	143.67	47.64	7.35	P>0.05	145.80	22.90	3.62
Triglyceride mg/dl	142.05	66.24	10.22	P<0.0001	99.50	21.59	3.41
HDL-C mg/dl	53.64	25.13	3.87	P>0.05	49.22	2.73	0.43
LDL-C mg/dl	79.24	42.13	6.50	P>0.05	70.88	16.07	2.54
VLDL-C mg/dl	28.41	13.25	2.04	P<0.0001	19.90	4.32	0.68

SSerum CK, FGF-23, Troponin I and Apo-A1 in coronary artery disease patients

The mean ± SD of serum total CK activity in coronary artery disease and controls was 187.45± 231.31, 126.70 ± 58.30) U/L respectively as illustrated in the Table (4) which shown that there was a non-significant difference in serum CK between the groups. The mean ± SD of serum FGF-23 in coronary artery disease, and controls was (367.52 ± 128.52, 165.41 ± 53.65) pg/ml respectively as illustrated in the Table (4) which shown that there was a significant difference in FGF-23 where control differ from CAD (P<0.005). The mean ± SD of serum Troponin I in coronary artery disease and controls was (34.81±7.74, 29.61 ± 9.75) ng/ml respectively as illustrated in the Table (4) which shown that there was a non-significant difference in troponin I between the groups.

The mean ± SD of serum ApoA1 in coronary artery disease and controls was (2.03±0.90, 1.49 ± 0.25) mg/ml respectively as shown in the Table (4) which showed that there was a significant difference in Apo-A1 where control differ from CAD (P = 0.014) .

*Test was done by Kruskal-Wallis test.

Table 4: Total CK activity, FGF-23,Troponin I and ApoA1in coronary artery disease patients.

	Groups						
	CAD				Control		
	Mean ± SD		SE	p-value	Mean ± SD		SE
Total CK activity, U/L	187.45	231.31	35.69	P >0.05	126.70	58.30	9.21
FGF-23 pg/ml	367.52	128.52	19.83	P<0.005	165.41	53.65	8.48
Troponin I ng/ml	34.81	7.74	1.19	P >0.05	29.61	9.75	1.54
ApoA1 mg/ml	2.03	0.90	0.13	P=0.014	1.49	0.25	0.04

DISSCUSION

Fibroblast growth factor-23 (FGF-23) has ascended as a fundamental hormone entangled in phosphorus and vitamin D homeostasis. Coronary artery Disease (CAD) is the most common clinical issue in which FGF-23 levels are emphatically and uniquely raised. Abnormal phosphate homeostasis and extraordinary circulating levels of FGF-23 are early complexities of CAD. Fibroblast growth factor 23 (FGF23) has been accounted

for to be associated with cardiovascular disease (Hu et al., 2015).

The potential role of FGF-23 in the advancement of cardiovascular infection, especially free of kidney work, is unclear. A few examinations have demonstrated FGF-23 to be related with cardiovascular occasions among patients with CKD (Nakano et al., 2012; Scialla et al., 2014) and in those with common coronary heart disease (CHD) (Parker et al., 2010).

FGF-23 seems to be a hazard factor of cardiovascular infection happenings in CAD, as has been set up in an investigation of 42 CVD patients, with 47 % in whom a raised gauge FGF-23 level anticipated subsequent myocardial infarction, coronary artery interventions, non-traumatic lesser extreme amputation, or death (Seiler, 2010). Essentially, another report of a settled case-control think about in the Health Professionals Continuation Study found no significant connection between baseline FGF-23 levels and future danger of nonfatal myocardial infarction and dangerous coronary heart disease (Taylor, 2011). Whether these divergent discoveries show specificity of FGF-23 impact needs assist examination. Be that as it may, the connection of FGF-23 with markers of myocardial damage mind natriuretic peptide, (Seiler, 2011) and Troponin (2011); Holden, 2011).

Various investigations have detailed a relationship amongst FGF23 and the dangers of mortality and CHD. Gutierrez et al. exhibited that the most elevated quartile of C-terminal FGF23 was related with a 5.7-overlay increment taking all things together reason mortality in the primary year following initiation of hemodialysis(Gutierrez et al., 2008).

A considerable measure of hazard variables of coronary artery disease (CAD) have been demonstrated by vast epidemiological examinations. Be that as it may, a few patients without the primary hazard factors still advance malady. Fundamental investigation of people specified for angiography, who had no principle chance components related with CAD, point to that ApolipoproteinA1 (ApoA1) was essentially lesser in patients with constructive angiograms. The hypothesis which ApoA1 was a free threat factor for CAD in okay populaces was put forward. Forty two progressive patients submit to angiography, lipid investigation, and completed a hazard factor survey.

The results of the present investigation are in concurrence with ponder led by Pischon et al. in Harvard University, establishing that serum Apo-A1 level isn't related with seriousness of coronary atherosclerosis disease. Sabino et al got comparable outcomes (Sabino et al., 2008). They found that subsequent to controlling the part of sexual orientation, age, smoking in addition to hypertension, ApoA1 level was freely related to fringe atherosclerosis and brain stroke. In a future report by Sweetnam et al., in the wake of managing the outcomes for cardiovascular hazard factors, independent of plasma lipids, a solid affiliation was found between the event of ischemic coronary disease in addition to low level of Apo lipoprotein A1 (Sweetnam et al., 2000). In current examination the mean age for CAD patients was (58.66) years in CAD, this gathering like Jabara R et al (2007) contemplate with a normal age in CAD patients multi year (Jabara et al., 2007).

Our study concurred with the result of Qazvin study. It was accounted for that the occurrence of CAD following 40 years old is 40% for males in addition to 32% for females (Assmann et al., 2002).

CONCLUSION

According to the results that were shown in the tables, we can be conclude that higher levels of FGF23 and Apo-A1 may be associated with complications and mortality of CAD in the Iraqi patients.

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