The association between lipid profile and severity of coronary artery disease as assessed by angiography

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ABSTRACT

Background: **Accumulation of cholesterol rich plaque in the arterial wall is the usual cause of coronary artery disease & cardiac events. These plaques are atheromatous narrowing in the arterial lumen that results in reduction of blood supply to myocardial cells, resulting in various presentations of coronary artery diseases according to the number and the degree of coronary vessels occlusion.**

Aim of the study: **To assess the relation of lipid profile and the severity of coronary artery disease as assessed by angiography.**

Patients and methods: **A prospective case-control study involved 223 individuals who underwent elective coronary angiography for angina in Basrah cardiac center from February till end of July 2015. Fasting lipid profile was tested for each patient, in addition to assessment of other coronary artery disease risk factors. The control group included 100 individuals with normal coronary artery angiography were tested for their lipid profile also.**

Results: **Patients were divided according to the number of affected vessel into 4 groups.**

Group 1: **includes those with normal coronary angiography, *Group 2:* those with single vessel disease**

Group 3: **patients with two vessel disease, *Group 4:* patient with three vessel disease. Smoking, DM, physical inactivity and hyperlipidemia are strongly related to the severity of CAD while triglyceride level and hypertension was not significantly related. Dyslipidemia was strongly associated with non-ST-elevation myocardial infarction and unstable angina. Total cholesterol, non-HDL cholesterol and raised total cholesterol / HDL ratio were found strongly associated with more severe form of coronary artery disease on coronary angiography.**

Conclusion: **Total cholesterol, non-HDL cholesterol and high TC / HDL ratio were found to be strongly associated with severity of coronary artery disease angiographically.**

Key words: lipid profile, coronary artery, angiography

الترافق بين مستوى الدهون وشدة الاصابة بأمراض شرايين القلب المقيم بفحص تلوين الشرايين.

الخلفية: مرض القلب التاجي هو النتيجة النهائية لتراكم اللويحات العصيدية على الجدران الداخلية للشرايين التي تغذي عضل القلب. ويعتبر السبب الرئيسي للموت في العالم.

هدف الدراسة: تهدف الدراسة الى تحري العلاقة بين مستوى الدهون في الدم مع مرض الشريان التاجي المشخص بواسطة تصوير الاوعية التاجية ودورها في التنبؤ بشدة تصلب الشرايين التاجية.

المرضى وطرق العمل: هذه الدراسة هي دراسة مقطعية ولقد ضمت ٢٢٣ شخص خضعوا لتصوير الاوعية التاجية، وذلك بسبب الألم شبيه بألم الذبحة الصدرية او لكون اختبار الجهد ايجابي او نتيجة الاشعة المقطعية بأستخدام الصبغة على الشرايين التاجية غير طبيعي. أجريت هذه الدراسة في وحدة قسطرة القلب في مستشفى الصدر التعليمي امتدت فترة الدراسة لمدة ستة اشهر من بداية شهر فبراير٢٠١٥ ولغاية نهاية شهر يوليو ٢٠١٥. تم تقييم مستوى الدهون في الدم وتشمل مستوى الكوليسترول الكلي ومستوى البروتينات الدهنية عالية الكثافة و مستوى البروتينات الدهنية منخفضة الكثافة ومستوى الدهون الثلاثية، بالإضافة الى ذلك تم تقييم عوامل الخطر الاخرى لمرض الشريان التاجي.

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النتائج: لقد ضمت هذه الدراسة ١٠٠ شخص يعانون من مرض الشريان التاجي الغير انسدادي و ١٢٣ شخص مصاب بمرض الشريان التاجي الانسدادي (اظهر تصوير الاوعية التاجية انسداد في اكثر من ٥٠% من الشريان التاجي الرئيسي الايسر مترافقا او بدون انسداد اكثر من ٧٠% في أي من الشرايين التاجية الاخرى).

تم تقييم المشاركين وفقا لعدد الشرايين التاجية المسدودة الى ٣ مجموعات:

المجموعة ١ (العدد = ١٠٠) وتشمل الاشخاص الذين يعانون من مرض الشريان التاجي الغير انسدادي. المجموعة ٢ (العدد = ٣٨): تشمل الذين يعانون من انسداد في شريان واحد. المجموعة ٣ (العدد = ٨٥) تشمل المرضى مع انسداد في شريانين او ثلاثة شرايين. التدخين و داء السكري قلة النشاط البدني و تاريخ عائلي بحدوث امراض الشريان التاجي و عسر شحيمات الدم كلها ترتبط بشدة مرض الشريان التاجي (عدد الشرايين المسدودة). مستوى الكوليسترول الكلي و بروتينات منخفضة الكثافة و الكوليسترول الذي ليس بروتينات عالي الكثافة ترتبط بشدة المرض (عند الشرايين المسدودة). تم تقسيم المرضى مرة اخرى اعتمادا" على اعراض مرض الشريان التاجي الى ثلاثة مجاميع: الذبحة الصدرية المستقرة (العدد = ١٤٥) و احتشاء القلب الحاد مع عدم ارتفاع مقطع اس تي او النتيجة الغير مستقرة (العدد ٥٠) و احتشاء القلب الحاد مع ارتفاع مقطع اس تي (العدد = ٢٨).

الاستنتاجات: اظهرت هذه الدراسة ان الاشخاص الذي يعانون من احتشاء القلب الحاد مع ارتفاع مقطع اس تي يكونون اقل عمرا" من بقية انواع مرض الشريان التاجي.

الكلمات المفتاحية: مستوى الدهون، الشرايين التاجية، تلوين الشرايين

INTRODUCTION

Atherosclerosis is a inflammatory disease known to be started since childhood, the changes in arterial wall often seen prominent among high risk groups as cigarette smokers, hypertensive patients or those with family history of hyperlipidemia but in most of cases gross picture of the disease is observed commonly on sixth, seventh or eight decades.[1] Framingham heart study in 1960 provided that the earliest descriptions that revealed the characteristic risk factors of coronary artery disease (CAD) followed by series of different studies concluded that the risk factors for CAD are either non modifiable factors included advanced age, male gender, family history of CAD or modifiable factors like hypertension, hyperlipidemia, diabetes mellitus (DM), smoking, sedentary lifestyle, obesity, heavy alcohol intake & metabolic syndrome.[2] CAD accounts for higher incidence of mortality & morbidity worldwide.[3] In between 1960-1980 & on attempt to be evaluation coronary disease prevention it had been shown that the preventive measures for CAD are more valuable in smoking reduction, HTN control & sedentary lifestyle change whilst for other risk factors like obesity & DM showed limited success.[4] In light of other studies hypertension was shown as the most preventable risk factor for CAD & being more prominent than cigarette smoking, dyslipidemia & DM.[5] In evaluation of dyslipidemia it was found that intensive reduction serum Low. Density Lipoprotein (LDL) had pivotal role in disease prevention and using statin therapy can reduce the CAD mortality by 12% in each reduction of 1mmol/L of serum LDL.[6] The effects of obesity as directly causes CAD or through the other risk factors is controversial[7] but still is important modifiable risk factor. The aim of this study is to assess the relationship between lipid profile & the angiographic severity and clinical stability of coronary artery disease.

METHODS

In this cross-sectional study on 223 individuals who underwent elective coronary angiography, due to angina-like chest pain and/or positive treadmill exercise test or positive coronary computed tomography angiography, in Basrah Cardiac Center in south of Iraq over a period of six months from beginning of February till end of July 2015. Participants were divided according to number of affected vessels into 3 groups; Group 1 (n = 100): includes those with non-obstructive coronary artery disease; Group 2 (n=38): includes those with single vessel disease; group 3 (n=85) includes patients with two and three vessel disease (multi-vessel coronary artery disease). The patients were then regrouped

into four groups according to coronary artery disease presentations into chronic stable angina (n =145), non ST segment elevation &/or unstable angina (n = 50) and those with ST segment elevation (n = 28). Blood samples were collected in the early morning before cardiac catheterization in the cath lab & send directly to the laboratory for fasting blood glucose & lipid profile measurements using an enzymatic, colorimetric method by using a COBAS Integra 400 plus analyzer and commercial kits from Roche Company to measure total cholesterol, LDL & HDL directly. Non-HDL cholesterol is calculated by subtraction of HDL from total cholesterol level & it is provide an estimate of cholesterol in the atherogenic particles including IDL,VLDL & LDL. The coronary angiography was performed for all patients by interventional cardiologists, using the Judkins technique. The lesion was considered significant if the luminal stenosis > 50% occlusion in the left main coronary artery and/or an occlusion greater than 70% in any of the other coronary arteries were diagnosed with obstructive CAD. The results were expressed as mean ± SD compared using one-way analysis of variance (ANOVA) performed by the Statistical Package for Social Science (SPSS) version. Results expressed as percentages were compared using Chi-Square test. Statistically significant differences were considered when $P < 0.05$.

RESULTS

(Table-1), shows that current smoking, diabetes mellitus, physical inactivity, family history of ischemic heart disease and dyslipidemia are strongly associated with severity of coronary artery disease in relation to number of affected vessels. While age, hypertension and obesity were not related to severity of coronary artery disease in relation to number of affected vessels.

Table 1. Population characteristics according to number of vessels occluded

	Variables	No obstruction (n=100)	One vessel disease (n=38)	Multi-vessel disease (n=85)	P value
1	Age (mean ±S D)	58.1 ± 7.6	55.5 ± 9.2	56.4 ± 10.4	≥ 0.05
2	**Sex (%)**				
3	Male	59 (59%)	26 (68.4%)	48 (56.5%)	≥ 0.05
4	Female	41 (41%)	12 (31.6%)	37 (43.5%)	
5	BMI (kg/m2) (mean ± SD)	28 ± 4.2	30.1 ± 4	30.1 ± 5.5	≥ 0.05
6	Normal weight (%)	11 (11%)	6 (15.7%)	21 (24.7%)	≥ 0.05
7	Overweight (%)	47 (47%)	12 (31.6%)	27 (31.8%) a	≥ 0.05
8	Obese (%)	42 (42%)	20 (52.6%)	37 (43.5%)	≥ 0.05
9	Ejection Fraction (mean ± SD)	55.7 ± 10.9	58.1 ± 8.7	54.9 ± 9.1	≥ 0.05
	Smoking History				
10	Current smoker	15 (15%)	12 (31.6%) a	40 (47.1%) ab	< 0.0001
11	Ex- smoker	23 (23%)	4 (10.5%)	24 (28.2%) b	≥ 0.05
12	Never Smoke	62 (62%)	22 (57.9%) a	21 (24.7%) ab	< 0.0001
	Disease History				
13	Diabetes mellitus	29(29%)	18(47.4%) a	40 (47.1%) a	0.022
14	Hypertension	55 (55%)	19 (50%)	44 (51.8%)	≥ 0.05
15	Dyslipidemia	37 (37%)	24 (63.2%) a	57 (67.1%) ab	< 0.0001
16	Family history of IHD	24 (24%)	15 (39.5%)a	44 (51.8%) ab	0.0005
17	Sedentary life style	32 (32%)	16 (42.1%) a	53(62.4%) ab	0.0002

a. Significant at P< 0.05 as compared with mild obstruction values

b. Significant at P< 0.05 as compared with no obstruction values

(Table-2), shows total Cholesterol, low density lipoprotein and non- high density lipoprotein cholesterol where found to be strongly associated with the severity of coronary artery disease while triglycerides, total cholesterol / high density lipoprotein ratio and low density lipoprotein/ high density lipoprotein ratio were not significantly related with the severity of coronary artery disease in relation to number of vessels occluded.

Table 2. Association of lipid profile and number of vessels occluded

Lipid profile (mean ± SD)	Non obstruction (n=100)	One vessel disease (n=38)	Multi-vessel disease (n=85)	P value
Total serum Cholesterol (mg/dl)	175.2 ± 44.3	191.2 ± 40.8	201.7 ± 53. a	0.001
LDL Cholesterol (mg/dl)	110.1 ± 29.9	114 ± 34.3	127.1 ± 45.7 a	0.008
HDL Cholesterol (mg/dl)	44.4 ± 9.6	48.3 ± 13.1a	47.6 ± 15.7 a	≥ 0.05
Triglycerides (mg/dl)	152.2 ± 66.4	158.2 ± 82.8	66.3 ± 81.5	≥ 0.05
Non HDL (mg/dl)	132.9 ± 44.3	141.9 ± 38.2	153.1 ± 53.1 a	0.016
TC-HDL Ratio	4.4 ± 1.5	4.1 ± 1.2	4.7 ± 2.1	≥ 0.05
LDL-HDL Ratio	2.8 ± 1.1	2.4 ± 0.9	2.9 ± 1.4 b	≥ 0.05

a. significant at P < 0.05 as compared with Mild obstruction values

b. significant at P < 0.05 as compared with non-obstruction values

(Table-3), shows that the patients with ST segment elevation myocardial infarction were significantly younger than other presentation of coronary artery disease. Diabetes mellitus, dyslipidemia and physical inactivity were strongly associated with severe presentation of coronary artery disease like ST segment elevation and non ST segment elevation & / or unstable angina. Other risk factors including obesity, smoking, hypertension and family history of ischemic heart disease showed no significant difference among presentation of coronary artery disease. Dyslipidemia was strongly associated with non ST segment elevation myocardial infarction and/or unstable angina.

Table 3. Characteristics of population and the presentation of CAD

	Variables	Stable angina (n=145)	Acs-nstemi (n=50)	Stemi (n=28)	P value
1	Age (mean ± SD)	58 ± 8.8	56 ± 9.9	53.4 ± 7.8 a	0.031
2	**Gender (%)**				
3	Male	85 (58.6%)	31 (62%)	17 (60.7%)	≥ 0.05
4	Female	60 (41.4%)	19 (38%)	11 (39.3%)	
5	BMI (kg/m2) (mean ± SD)	29.1 ± 4.9	28.7 ± 5.3	30.5 ± 4	≥ 0.05
6	Normal weight (%)	26 (17.9%)	10 (20%)	2(7.1%)	≥ 0.05
7	Overweight (%)	59 (40.7%)	17 (34%)	10 (35.7%)	≥ 0.05
8	Obese (%)	60 (41.4%)	23 (46%)	16 (57.1%)	≥ 0.05
9	Ejection Fraction (mean ± SD)	56.3 ± 10.2	56.1 ± 9.6	52.9 ± 8.9	≥ 0.05
	Smoking History				
10	Current smoker	38(26.2%)	17 (34%)	12 (42.9%)	≥ 0.05
11	Former smoker	29 (20%)	15 (30%)	7 (25%)	≥ 0.05
12	Never Smoke	78 (53.8%)	18 (36%) a	9 (32.1%) ab	0.0224
	Disease History				
13	Diabetes mellitus	51(35.2%)	21 (42%)	15 (53.6%)	0.0167
14	Hypertension	80 (55.2%)	25 (50%)	13 (46.4%)	0.625
15	Dyslipidemia	70 (48.3%)	33 (66%) a	15 (53.6%)	0.03
16	Family history of IHD	49 (33.8%)	20 (40%)	14 (50%)	≥ 0.05
17	Sedentary life style	55 (37.9%)	30 (60%) a	16 (57.1%) ab	0.0004

a. Significant at P < 0.05 as compared with Angina

b. Significant at P < 0.05 as compared with ACS value

(Table-4), shows that total Cholesterol, elevated triglycerides and non-HDL cholesterol where found strongly associated with more sever forms of CAD.

Table 4. Association between lipid profile and severity of CAD presentation.

Lipid profile (mean ± SD)	Stable angina (n = 145)	Nstemi &/or ua (n = 50)	Stemi (n = 28)	P value
Total serum Cholesterol (mg/dl)	183.7 ± 46.1	200.6 ± 53.1 a	188 ± 50.7	0.02
LDL Cholesterol (mg/dl)	110.5 ± 30.4	115.6 ± 44.9	121.5 ± 40.1	≥ 0.05
HDL Cholesterol (mg/dl)	45.4 ± 12.5	45.9 ± 14.9	48.7 ± 13.3	≥ 0.05
Triglycerides (mg/dl)	155.2 ± 72.3	148.9 ± 53.9	191.5 ± 109.5	0.042
Non HDL (mg/Dl)	138.38 ± 45.1	154.7 ± 50.1 a	139.3 ± 54.1	0.01
TC-HDL Ratio	4.4 ± 1.8	4.7 ±1.5	4.2 ± 1.8	≥ 0.05
LDL-HDL Ratio	2.8 ± 1.2	2.8 ±1.4	2.6 ± 1	≥ 0.05

a significant at P < 0.05 as compared with stable angina values

(Table-5), shows that the most common vessel involved in all subgroups was LAD (32.7%) followed by LCX (27.2%) then RCA (24.1%) and lastly LMS (16%).

Table 5. Type of coronary vessel involved

Type of coronary vessel involved	Over all ratio (n=275 records) No. (%)
LCMA	41 (16)
LAD	84 (32.7)
CFX	70 (27.2)
RCA	62 (24.1)

DISCUSSION

It is well known that dyslipidemia is a major risk factor for CAD.[8] However, studies on the role of lipoprotein levels as markers of severity of CAD are still scanty in the literature, but it can be presumed that if one of the lipid fractions is predictive of the degree of anatomical impairment on coronary angiography, it will potentially be able to affect the decision of involvement of invasive investigation in patients with CAD. Age, in this study; was not significantly affect the number of vessels occluded. This finding agree with Khashayar (2010),[9] but; disagree with the study of Alshehri (2014)[10] in which patients with multi-vessels disease were older .Regarding gender, number of vessels occluded were not significantly different between men and women. This finding disagree with study of Alshehi (2014).Obesity, in this study; was not significantly affect the number of vessels occluded which is in agreement with finding of Niraj A, et al (2007)[11] which stated that "obesity is not an independent predictor of severity of coronary artery disease". Even in overweight patients findings were same. This result could be explained by the greater likelihood that physicians would refer obese patients for coronary angiography at an earlier stage of CAD. Current smoking was strongly associated with severity of CAD (number of affected vessels), this result is consistent with the study of Mohammad et al (2013).[12] This may be mostly explained by the vascular endothelial dysfunction and activates the sympathetic nervous system induced by cigarette smoking, and these effects can result in inappropriate reduction in or failure to increase coronary blood flow in response to increases in myocardial demand.[13] Significantly (P < 0.05) higher percentage of multi-vessel CAD patients were diabetic (47.1%) and DM may associate

with severity of CAD, this result is in agreement with study of Mahadeva, et al (2014).[14] Patients with DM experienced more multi-vessel disease than nondiabetic patients and this findings are consistent with Wu, et al.[15] This may be mostly explained by coronary endothelial dysfunction and atherosclerotic process induced by glucose toxicity, inflammatory and immune mediated mechanisms.[16,17] Hypertension was not significantly associated with CAD severity and this comes in accordance with Masoumi, et al (2010).[18] Dyslipidemia was strongly associated with elevated occurrence of obstructive CAD and was associated with its severity, which is consistent with Khashayer (2010) who stated that "dyslipidemia was more prevalent among those with more severe coronary diseases". Family history of CAD was significantly associated with multi-vessel disease, similar results were revealed by Mohammad and Alshehri. Physical inactivity was associated with more severe CAD, which similar with that publish in AHA statement about the role of "Exercise and Physical Activity in the Prevention and Treatment of Atherosclerotic Cardiovascular Disease" published by Thompson PD, et al. (2003).[19] Average age of patients with STEMI were significantly lower than patients with other presentations of CAD like that published by Mohammad. Gender was unrelated to presentation of CAD while obesity was higher percentage in ACS patients but it was not significant and these were consistent with Ameen, et al study. Current smoking was not associated with presentation of CAD, this comes in accordance with Gehani, etal (2001).[20] Significantly high proportion of STEMI patients were diabetic (53.6%) which in contrast to finding of Gehani et al in which diabetes was a major risk factor for chronic stable angina. Hypertension was not significantly associated with IHD presentation. This finding was in contrast to Mohammad. Significantly high proportion of NSTEMI & / or UA patients were dyslipidemia (66%), this result unlike with Mohammad in which higher percentage of dyslipidemia was reported in chronic stable angina patients. High percentage of STEMI patients had +ve family history of IHD (50%), and this percentage was not significant ($P < 0.05$) difference among other presentation of CAD and this was revealed by Mohammad and Wagar, et al (1993).[21] Significant ($P < 0.05$) high percentage of STEMI and NSTEMI & / or UA patients showed Physical inactivity which is unlike finding of Mohammad that found there was no significant physical inactivity among CAD patients. Triglyceride, TC/HDL and LDL/HDL ratio not associated with number of vessel affected, this result agrees with study of Penalva, et al (2008).[22] In this study, 67.1% of patients with multi-vessels disease had dyslipidemia, Non-HDL cholesterol level was considered one of the most important lipid marker associated with CAD, it is more elevated in those with one vessel and multi-vessels disease (152.4±54.4,153.8±52.4 respectively), This result was similar to those published by Aggarwal et al (2014)[23] but this disagree with result of Penalva et al study. Total cholesterol was associated with the number of vessels affected, and was higher in the multi-vessel group when compared to the non-obstructive group. This result was similar to those offered by Alshehri. The mean values of LDL-C were higher in single vessel disease and multi-vessel disease while patients with nonobstructive CAD had lower LDL-C levels. Recent studies show that HDL are structurally and functionally diverse and consist of numerous, highly dynamic subpopulations of particles that do not all inhibit atherosclerosis to the same extent.[24] The analysis of LDL showed that this variable increased with the number of vessel occluded. Patients with one-vessel disease had LDL levels of 114 ± 34.3 mg/dl, whereas patients with multi-vessel disease had LDL levels of 127.1 ± 45.7 mg/dl. In agreement with Alsheri, The LDL-C levels were significantly correlated with the extent of CAD (number of affected vessels).

TC, non HDL and TG were higher in ACS patients as compared with stable angina patients. This is in agreement with Bhagwat, et al (2009).[25] The most common vessel involved in all subgroups was LAD (32.7%) followed by LCX (27.2%) then RCA (24.1%) and lastly LMS (16%) Similar results concerning common vessels involvement were revealed by other researchers like Ameen, et al and Satyendra, et al (2005).[26]

CONCLUSION

Total cholesterol, LDL-C and non-HDL cholesterol were a marker of severity of CAD in relation to the number of vessels involved. Dyslipidemia was strongly associated with NSTEMI &/or UA. Total cholesterol, triglycerides and non-HDL cholesterol were higher in ACS patients as compared with stable angina patients.

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