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Original Article

The relation between coronary angiographic findings and lipoprotein (a) in patients with chronic stable angina with and without xanthelasma

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Abstract

Introduction
Atherosclerosis develops in many patients in the absence of classical risk factors. The serum level of lipoprotein [Lp (a)] is of utmost importance in such cases. Many patients with elevated serum level of Lp (a) have xanthelasma with elevated total cholesterol and low-density Lp cholesterol levels.

Aim
To find the relation between the level of Lp (a) and the severity of coronary artery disease (CAD) in patients with chronic stable angina with and without xanthelasma.

Patients and methods
The study was carried out on 86 patients in the National Heart Institute. The patients were divided into two groups: group A (43 patients), with xanthelasma, and group B (43 patients), without xanthelasma. The patients were subjected to full clinical examination, echocardiographic examination and laboratory investigations, including the level of Lp (a) and coronary angiography.

Results
The age in patients with xanthelasma was significantly more than in those without xanthelasma but sex difference was not significant. Hypertension, diabetes mellitus, and dyslipidemia were significantly more common in patients with xanthelasma. Creatinine level, total cholesterol level, and low-density lipoprotein level were significantly higher in patients with xanthelasma. Lp (a) level is also significantly increased in patients with xanthelasma. The severity of CAD was significantly increased in patients with xanthelasma, and the level of Lp (a) was an independent predictor for left main disease.

Conclusion
There is a significant relation between xanthelasma palpebrarum (as a cutaneous marker of atherosclerosis) and Lp (a), and both of them are independent and causal risk factors for atherosclerotic CAD.

Keywords: LPa, LDL, TG, HDL

Introduction

Some patients may develop atherosclerosis without the presence of classical risk factors [1]. One of these nonclassic recently developed factors is lipoprotein (a) [Lp (a)] where it can accumulate in the intima of the arteries [2].

So, the level of Lp (a) should be screened in individuals at intermediate, high, or very high cardiovascular risk, with a desirable plasma concentration of less than 50 mg/dl [3].

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Although the risk of cardiovascular disease increases when Lp (a) level rises above 30 mg/dl, we must focus on individuals with the highest cardiovascular risk with concentrations above 50 mg/dl.

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Xanthelasma was found in some patients with elevated Lp (a) level with increased plasma total cholesterol and low-density lipoprotein (LDL) cholesterol levels [4].

Aim

The aim was to correlate between coronary angiographic findings and Lp (a) level in patients with chronic stable angina with and without xanthelasma.

Patients and methods

A written informed consent was taken from all included patients and approval of the CMREC (Cairo Medical Research Ethics Committee). This study was carried out in the National Heart Institute on 86 patients with chronic coronary syndrome scheduled for elective coronary angiography during the period from April 2017 till December 2019. Patients were divided into two groups: group A included 43 patients with xanthelasma, and group B included 43 patients without xanthelasma.

Exclusion criteria

The following were the exclusion criteria:

(1) Patients with elevated serum creatinine level above 2.0 mg/dl.
(2) Females receiving oral contraception.
(3) Patients on current medications causing secondary hyperlipidemia, for example, corticosteroid.

Laboratory investigation

A venous blood sample was collected from each patient to measure Lp (a), serum creatinine, and lipid profile [total cholesterol, triglyceride (TG), high-density lipoprotein (HDL), LDL, and very LDL after 12-h fasting].

Precatheterization assessment and preparation:

(1) The day before diagnostic coronary angiography, full medical history, including age and sex, history of risk factors (diabetes mellitus, dyslipidemia, and hypertension), history of special habits (smoking and alcohol), and drug history, was taken.
(2) Full clinical examination included general examination, especially for the presence of xanthelasma (unilateral or bilateral, single or multiple).
(3) Local cardiac examination was done.
(4) Laboratory investigations included Lp (a), serum creatinine, and lipid profile (total cholesterol, TG, HDL, LDL, and very LDL after 12 h fasting).
(5) 12-lead ECG was done.
(6) Trans-thoracic echocardiography was done.

Coronary angiography was done.

Results

The current study showed the following:

(1) Age was found to be significantly increased in patients with xanthelasma than in those without xanthelasma (49.3 ± 8.0 vs. 45.3 ± 4.2 years, $P = 0.005$).
(2) Sex difference was not significant in patients with and without xanthelasma (male/female = 17/26 vs. 21/22, $P = 0.515$) (Table 1).
(3) In patients with xanthelasma, hypertension was found to be significantly increased than in those without xanthelasma (51.2 vs. 16.3%, $P = 0.001$).
(4) Diabetes mellitus was significantly increased with xanthelasma compared with those without [$n = 12$ (27.9%) vs. three (7%), $P = 0.021$].
(5) Dyslipidemia was significantly increased with xanthelasma compared with those without [$n = 30$ (69.8%) vs. nine (20.9%), $P = 0.001$].
(6) Family history of coronary artery disease (CAD) was significantly increased with xanthelasma compared with those without [$n = 17$ (39.5%) vs. seven (16.3%), $P = 0.029$)].
(7) Smoking and family history of dyslipidemia were not significant in patients with and without xanthelasma [$n = 20$ (46.5%) vs. 19 (44.2%), $P = 1.000$, and $n = 24$ (55.8%) vs. 14 (32.6), $P = 0.050$, respectively] (Table 2).
(8) Creatinine was found to be significantly increased in patients with xanthelasma than in patients without xanthelasma ($P = 0.012$).

Table 1: Demographic characteristics of patients with or without xanthelasma

Variables	Xanthelasma ($n=43$)	Non-xanthelasma ($n=43$)	*P*
Age (years)	49.3±8.0	45.3±4.2	0.005
Sex (male/female)	17/26	21/22	0.515

Data are mean±SD or ratio.

Table 2: Prevalence of risk factors in patients with or without xanthelasma

Variables	Xanthelasma ($n=43$) [*n* (%)]	Non-xanthelasma ($n=43$) [*n* (%)]	*P*
Hypertension			
−	21 (48.8)	36 (83.7)	0.001
+	22 (51.2)	7 (16.3)	
DM			
−	31 (72.1)	40 (93.0)	0.021
+	12 (27.9)	3 (7.0)	
Dyslipidemia			
−	13 (30.2)	34 (79.1)	<0.001
+	30 (69.8)	9 (20.9)	
Smoking			
−	23 (53.5)	24 (55.8)	1.000
+	20 (46.5)	19 (44.2)	
Family history of CAD			
−	26 (60.5)	36 (83.7)	0.029
+	17 (39.5)	7 (16.3)	
Family history of dyslipidemia			
−	19 (44.2)	29 (67.4)	0.050
+	24 (55.8)	14 (32.6)	

CAD, coronary artery disease; DM, diabetes mellitus.

(9) LDL (mean 121.3 vs. 85.3, $P = 0.014$), TG (mean 191.6 vs. 161.7, $P = 0.042$), cholesterol (mean 233.4 vs. 191, $P = 0.015$), HDL (mean 41.6 vs. 12.9, $P = 0.039$) and Lp (a) (mean 33.6 vs. 18.2, $P = 0.001$) were found to be significantly increased in patients with xanthelasma than in patients without xanthelasma (Table 3).

Lp (a) was found to be significantly increased in patients with xanthelasma compared with those without (33.6 ± 21.6 vs. 18.2 ± 11.9, $P = 0.001$). The best cutoff criterion of Lp (a) was more than 25.8 mg/dl to discriminate between those with xanthelasma and those without (Fig. 1).

The correlation between xanthelasma and coronary angiographic findings:

The severity of CAD was found to be significantly increased in patients with xanthelasma than in those without [single-vessel disease nine (20.9%) vs. one (2.3%), $P = 0.001$); two-vessel disease seven (16.3%) vs. 0, $P = 0.001$; three-vessel disease 13 (30.2%) vs. 0, $P = 0.001$; and Left main artery (LMA) four (9.3%) vs. 0, $P = 0.001$]. The presence of Coronary artery disease (CAD) was found to be significantly increased in patients with xanthelasma than in those without [33 (76.7%) vs. one (2.3%), $P = 0.001$] (Table 4, Fig. 2).

Prevalence of CAD among patients with or without xanthelasma.

LMA disease was more significant in patients with xanthelasma compared with those without [LMA four (9.3%) vs. 0, $P = 0.001$].

Prevalence of LMA disease among patients with or without xanthelasma.

Discussion

Lp (a) is a macromolecule that was found to be associated with early atherosclerosis [5].

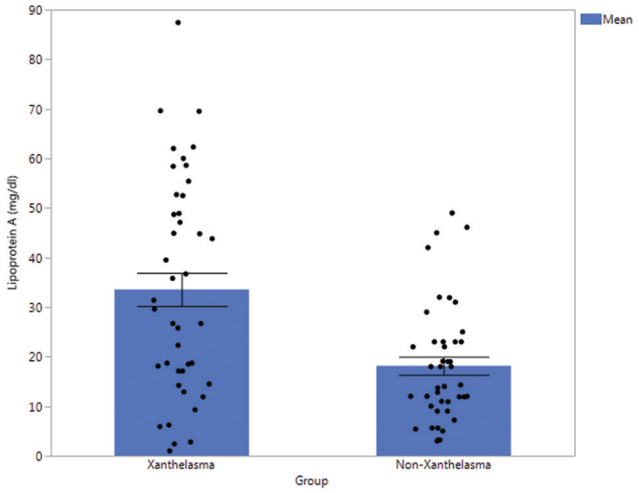

Figure 1: Mean lipoprotein (a) in patients with or without xanthelasma. Error bars represent the SE. Dots represent individual observations.

Most theories that tried to explain this association reported that Lp (a) can interact with macrophages to stimulate atherogenesis. Lp (a) has a significant homology with fibrinolytic enzyme plasminogen. So, Lp (a) may exert its effect in atherogenesis via the coagulation pathway as it competitively binds to plasminogen receptors thus inhibiting fibrinolysis [6].

In our study, there was no statistical difference between patients with and without xanthelasma regarding sex, smoking, and family history of dyslipidemia, but we found a significant difference between the two groups regarding age, diabetes mellitus, hypertension, dyslipidemia, family history of CAD, and the extent of CAD. These findings were concordant with the study done by Mia-Jeanne and Pretorius [7], which discussed the role of different risk factors including obesity, hypertension, and hypercholesterolemia in atherosclerosis and found that they may ultimately lead to either cardiovascular or cerebral complication.

Regarding coronary angiographic findings in our study, single-vessel, two-vessel, three-vessel disease, and LM disease were more prevalent in the xanthelasma group and the prevalence of CAD was significantly increased in the xanthelasma group, which ensures the relation between xanthelasma and atherosclerotic process. This was concordant with the results revealed by Christoffersen *et al*. [8], as

Table 3: Results of laboratory workup in patients with or without xanthelasma

Variables	Xanthelasma ($n = 43$) (mean ± SD)	Non-xanthelasma ($n = 43$) (mean ± SD)	*P*
Creatinine (mg/dl)	0.9±0.2	0.8±0.2	0.012
HDL (mg/dl)	41.6±9.7	46.7±12.9	0.039
LDL (mg/dl)	121.3±88.9	85.3±30.7	0.014
TG (mg/dl)	191.6±78.7	161.7±52.6	0.042
Cholesterol (mg/dl)	233.4±95.9	191.0±56.9	0.015
Lipoprotein (a) (mg/dl)	33.6±21.9	18.2±11.9	<0.001

HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

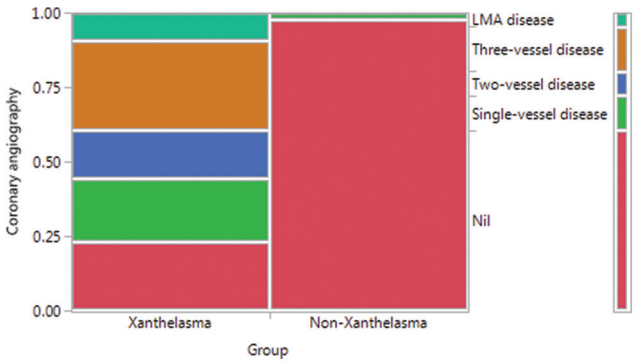

Figure 2: Coronary angiographic findings in patients with or without xanthelasma.

Table 4: Coronary angiographic findings in patients with or without xanthelasma

Variables	Xanthelasma ($n=43$) [n (%)]	Non-xanthelasma ($n=43$) [n (%)]	χ^2 (1)	P
Coronary angiography				
Nil	10 (23.3)	42 (97.7)	40.019	<0.001
Single-vessel disease	9 (20.9)	1 (2.3)		
Two-vessel disease	7 (16.3)	0		
Three-vessel disease	13 (30.2)	0		
LMA disease	4 (9.3)	0		
CAD				
−	10 (23.3)	42 (97.7)	-	<0.001
+	33 (76.7)	1 (2.3)		
LMA disease				
−	39 (90.7)	43 (100.0)	-	0.116
+	4 (9.3)	0		

CAD, coronary artery disease.

they tested the relation between the visible age-related signs (e.g., presence of fronto-parietal baldness, crown top baldness, earlobe crease, and xanthelasma) and the risk of ischemic heart disease, and their study was done on individuals free of Ischemic heart disease (IHD). They concluded that sex and xanthelasma are associated with increased risk of ischemic heart disease and myocardial infarction.

Fauzia *et al*. [9] studied the association between Lp (a) and CAD risk. Coronary angiography revealed CAD in 75% of patients, whereas 25% had no CAD. All clinical and laboratory factors were analyzed, and they detected that Lp (a) was considered an independent predictor for severity of CAD.

In the current study, there were statistical differences between the two groups regarding serum creatinine, LDL, HDL, cholesterol, TG, and Lp (a). This was in agreement with other reports by Sevil *et al*. [4], who investigated the relation between xanthelasma as a cutaneous sign and the other atherosclerotic risk factors and Lp (a) level. Their study was done on 100 patients with xanthelasma and other 100 patients without xanthelasma (controls). They reached to the conclusion that hyperlipidemia in the form of LDL level and total cholesterol level as well as Lp (a) value were significantly elevated in patients with xanthelasma.

This was also concordant with Kandula *et al*. [10], who studied the correlation between nonclinically evident atherosclerotic cardiovascular disease, which was assessed by coronary artery calcification and carotid intima thickness, and the level of Lp (a). They found that the presence and degree of coronary artery calcification were significant across higher Lp (a) levels.

This was also concordant with Anupam *et al*. [11], where their study was done to detect the relation between the presence of xanthelasma and the classic risk factors of CAD. The found that hypertension, diabetes mellitus, central obesity, smoking, and dyslipidemia were significantly prevalent in patients with xanthelasma than in those without.

Chieng *et al*. [12] studied the association between the presence of premature CAD in patients younger than 60 years and the severity and complexity of CAD. Both the levels of LDL and Lp (a) were measured, and the severity of CAD was assessed with both SYNTAX and Gensini scores. They reached to the conclusion that elevated Lp (a) and LDL cholesterol are independent predictors for the severity of CAD in patients younger than 60 years (premature CAD).

Summary

The study was conducted on 86 patients to investigate the association between xanthelasma palpebrarum, coronary angiographic findings, and Lp (a) in patients with chronic coronary syndromes scheduled for elective coronary angiography. The study population included group A (43) patients with clinical diagnosis of xanthelasma and group B (43) patients without xanthelasma.

In the current study, the results were obtained as follows: waist circumferences, hypertension, diabetes mellitus, family history of CAD, creatinine, LDL, TG, Lp (a), severity of CAD, and age were significantly increased in patients with xanthelasma than in those without xanthelasma. Sex, smoking, HDL, and family history of dyslipidemia were not significant comparing patients with and without xanthelasma.

Lp (a) was correlated to certain variables such as creatinine, LDL, TG, and cholesterol and there was a significant correlation between Lp (a) and CAD.

Conclusion and Recommendation

Conclusion

Our study revealed that there was a significant correlation between xanthelasma palpebrarum (as a cutaneous marker of atherosclerosis) and Lp (a), and both of them are an independent and causal risk factor for atherosclerotic CAD.

Recommendation

Patients with xanthelasma should be investigated for lipid profile and Lp (a) as predictors for CAD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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