

Serum lipid profile and clinical characteristics of patients with xanthelasma palpebrarum*

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Abstract: BACKGROUND: Although many factors are involved in the etiology of xanthelasma palpebrum, lipid disorder is strongly associated with its induction. Xanthelasma palpebrum, the most common type of xanthoma, usually presents in middle-aged females and results in aesthetic problems.

OBJECTIVE: To evaluate the lipid profile and important clinical aspects of xanthelasma palpebrum patients.

METHODS: In this descriptive study, we enrolled 42 xanthelasma palpebrum patients, and 42 cases of non-inflammatory skin disorders as the control group, matched for age and gender. The clinical characteristics of the patients and fasting serum lipid profile were recorded for both groups. The data obtained were analyzed using SPSS-16. RESULTS: Xanthelasma palpebrum was found more commonly in middle-aged females with disease onset of less than 1 year, and without significant familial history of xanthoma. Furthermore, xanthelasma lesions were most often seen in the upper lid with mild extension and was rarely associated with systemic disease. There was no statistically significant difference between two groups regarding hypertriglyceridemia ($p=0.231$) and hypercholesterolemia ($p=0.302$). The mean serum levels of cholesterol (221.51 ± 60.4 mg/dl), triglyceride (185.98 ± 71.1 mg/dl) and VLDL (37.7 ± 17.6 mg/dl) were significantly higher and the median HDL (36.2 (31, 41) mg/dl) level was lower in the patient group.

CONCLUSION: In our study, hypercholesterolemia and hypertriglyceridemia did not reveal a significant difference between the patient and control groups; however, mean serum values for cholesterol, triglyceride, VLDL and HDL showed a significant difference between the two groups. Therefore, in addition to lipid abnormality, other factors could be involved in the pathogenesis of xanthelasma palpebrum.

Keywords: Cholesterol; Cholesterol, HDL; Cholesterol, VLDL; Hypercholesterolemia; Hyperlipidemias; Hypertriglyceridemia; Triglycerides; Xanthomatosis

INTRODUCTION

Xanthoma are a common manifestation of lipid abnormality, the most common of which is xanthelasma palpebrum (XP), which usually appears in middle-aged females, with an incidence of 1.1%, and an incidence of only 0.3% in males. It manifests as symmetrical, soft, yellowish, velvety papules and plaques on the lower and upper eyelids.¹⁻⁴

The cause of XP is unclear, but some factors have been suggested in its pathogenesis, including: hormonal, local and macrophage factors. However, acetylated LDL and macrophages with their scavenger receptor were recently reported to be involved in the pathogenesis of XP.^{3,4}

Microscopically, XP is composed of foamy cells in the superficial dermis, where lipid-laden histiocytes exist. Esterified cholesterol is the predominant lipid in normo- and hyperlipidemic XP in xanthoma cells.⁵

XP most often results in cosmetic problems.⁶ It may also be a marker of the underlying coronary arterial disease, especially in patients with familial hypercholesterolemia.⁷

Numerous studies have investigated the correlation between XP and dyslipidemia.^{3,8-13} In our study, in addition to evaluating the lipid profile, we assessed the characteristics of xanthelasma lesions in patients.

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METHOD

This case-control study was performed over 3 years (2010-2013) at our dermatology clinic. We included 42 XP patients, as well as 42 cases as the control group, who presented for non-inflammatory skin disorders, all matched for age and gender. Careful medical histories were obtained for both groups and patients underwent precise clinical examination of xanthelasma lesions.

Firstly, a record was taken of demographic information such as age, gender, duration, location and extension of XP, history of other diseases and medication, and familial history of XP and hyperlipidemia.

Based on the percentage of eyelid area involvement with xanthematous lesions, the extension of XP lesions in eyelids was classified as mild, mild to moderate, moderate to extensive and very extensive, indicated by < 10%, 10%-20%, 20%-50% and > 50%, respectively.

Patients and controls were referred to one laboratory for the purposes of measuring the lipid profile, and fasted before the tests. Total cholesterol and triglyceride (TG) were enzymatically estimated, through colorimetry (photometric assay) by autoanalyser Erba XL600. HDL was calculated by precipitated method, and VLDL and LDL were calculated using the Friedwald formula.

Data analysis was carried out by SPSS (version 16) software. To compare serum lipid in both groups, firstly, one sample Kolmogorov-Smirnov test (KS) was performed to assess normality of serum lipid. Later it was used based on the results from Leven's test, and the independent T-test or Mann-Whitney test. Later based on the results of KS test, data were compared by Leven's and independent T-tests or Mann-Whitney test.

To compare the categorical data in both groups, we used the Chi-square or Fisher's exact tests. The significance level applied for test analyses was 0.05.

The patients and controls with diabetes mellitus and thyroid disorder, and who took hypoglycemic drugs, were excluded from the study. The lack of cardiovascular system assessment is a limitation of our study.

RESULTS

Our study recruited 42 patients, 36 (85.7%) females and 6 (14.3%) males; and 42 cases as the control group, 34 (81%) females and 8 (19%) males (Table 1).

The mean ages of the patient and control groups were 47.4±9.97 and 48.1±10.05 years, respectively. In the patient group, 19 (45.23%) samples were from individuals in the fifth decade of life.

There was no statistically significant difference between groups in terms of age (p= 0.610) or gender (p= 0.771).

In most patients (69%), duration of xanthelasma lesions was less than 1 year. There were 2 cases, acromegaly and rheumatoid arthritis, as the associated systemic disorder in the patient group (Table 2). We found in the patient group, 2 cases had associated systemic disorder, one of the patient suffered acromegaly and the other had rheumatoid arthritis (Table 2).

Moreover, there were 86 eyelid involvements entailing xanthoma lesions in 42 patients. Involvement of one upper lid and involvement of both upper lids, the most common form of distribution, were equally seen in 10 (23.8%) patients. Xanthoma lesions were located on one lower lid in 3 (7.1%) patients (Table 2).

The severity of xanthelasma lesions was mild in 24 (57.14%) patients and details on the extension are described in table 2.

Hypertriglyceridemia (over 200mg/dl) was seen in 13 (30.9%) cases in the patient group and in 8 (19.05%) cases in the control group. There was no statistically significant difference between two groups regarding hypertriglyceridemia (p= 0.231) (Table 1).

Hypercholesterolemia (over 220mg/dl) was seen in 19 (45.2%) cases in the patient group and in 14 (33.3%) cases in the control group. There was no statistically significant difference between two groups in terms of hypercholesterolemia (p= 0.302) (Table 1).

The mean levels of TG and cholesterol in the patient group were 185.98±71.1mg/dl and 221.51±60.4mg/dl; in the control group were 149.39±94.2mg/dl and 198.82±34.8mg/dl, respectively. There was a significant difference between groups regarding the mean levels of triglyceride (p=0.050) and cholesterol (p=0.041) (Table 1).

The median HDL levels were 36.2 (31,41) mg/dl and 50.5 (44.5, 56) mg/dl in the patient and control groups, respectively (p=0.001).

In the patient group, cholesterol: HDL ratio was 5.41± 1.76; while in the control group, this ratio was 4.24± 1.73. There was a statistically significant difference in cholesterol: HDL ratio between both groups (p= 0.001).

The characteristics of familial hyperlipidemia, familial xanthelasma, and mean serum levels of VLDL and LDL for both patients and controls are summarized in table 1.

TABLE 1: Clinical and lipid profile of patients and controls

	Patients	Controls	P-value
Female gender (N%)	36(85.7%)	34(81%)	0.771
Familial hyperlipidemia (N%)	11(26.2%)	3(7.1%)	0.022
Familial xanthelasma (N%)	2(4.8%)	0(0%)	0.494
Hypertriglyceridemia (N%)	13(30.9%)	8(19.05%)	0.231
Hypercholesterolemia (N%)	19(45.2%)	14(33.3%)	0.302
Mean level Cholesterol mg/dl	221.51±60.4	198.82±34.8	0.041
Mean level Triglyceride mg/dl	185.98±71.7	149.39±94.2	0.050
Mean level LDL mg/dl	120.3±43.6	110.6±26.7	0.233
Mean level VLDL mg/dl	37.7±17.6	30.1±12.46	0.050
Median level HDL mg/dl	36.2 (31,41)	50.5(44.5,56)	0.001

Hypertriglyceridemia above 200mg/dl; Hypercholesterolemia above 220mg/d

TABLE 2: Clinical characteristics of Xanthelasma palpebrarum patients

		Frequency (%)
Location	One upper lid	10(23.8%)
	Both upper lids	10(23.8%)
	One upper and one lower lids	7(16.7%)
	Both upper and both lower lids	6(14.3%)
	One lower lid	3(7.1%)
	Both lower lids	2(4.8%)
	Both upper and one lower lids	1(2.3%)
	One upper and both lower lids	3(7.1%)
	Extension	Mild
Mild to moderate		15(35.7)
Moderate to extensive		3(7.2%)
Veryextensive		0(0%)
Duration	Less than 1 year	29(69%)
	Between 1 and 2 years	12(28.6%)
	More than 2 years	1(2.4%)
Associated systemic disorder		2(4.8%)

There was no association between familial xanthoma and hypertriglyceridemia ($p=0.444$) and hypercholesterolemia ($p=0.155$). Due to numerous locations and the extension of xanthelasma lesions, the relation of location and extension to hypertriglyceridemia and hypercholesterolemia could not be established.

DISCUSSION

Our results showed that hypertriglyceridemia and hypercholesterolemia were not significantly different between groups. The mean serum levels of cholesterol ($p=0.041$), triglyceride ($p=0.050$), VLDL ($p=0.050$) and HDL ($p=0.001$) revealed a significant difference between both groups. But LDL ($p=0.233$) demonstrated no significant difference between the patients and controls.

Our findings indicated that the majority of XP patients were females in the fifth decade of life, consistent with the results of most of the previous studies.^{1-3,8-13} The predominance of females may be linked to the hormonal factor in the etiopathogenesis of XP and their higher sensitivity to cosmetic problems.^{3,8}

In line with the majority of previous studies, most of the patients (69%) who presented at our clinic with less than a 12-month duration. This may be related to the fact that the majority of XP cases are reported in females, who are more conscious about cosmetic issues.^{3,11,13}

According to Jain and Reddy, positive family histories of XP were noted in 9% and 10% of patients, respectively. But in our patients, there were 2 (4.8%) cases of family history of XP, which is lower than in previous studies.^{3,11} The importance of familial XP as a skin marker could be for the underlying lipid abnormality and accelerated atherosclerosis, especially in the early stages of life.^{14,15}

Familial XP variant could be an important skin marker for diagnosis of the underlying lipid abnormality and accelerated atherosclerosis, especially in the early stages of life.^{14,15}

Lee *et al.* showed that most of the patients who were seeking XP treatment had mild degrees of the disease.¹⁶ This finding is compatible with the results of our study in that more than half of the patients underwent a slight extension of xanthematous lesions.

Upper lid involvement was seen in 54 (62.8%) patients, sim-

ilarly to the results of most of the previous studies.^{1-3,8} Involvement of both the upper and lower eyelids was observed in 16 (38%) cases. But in other studies, involvement of two or more eyelids was noted in most patients.^{13,17} This difference may be related to the time of referral, diversity of lipid level and derangement of lipid metabolism of patients in different areas.

In our study, systemic diseases associated with XP were rarely observed, though Jain *et al.* reported XP-associated systemic disease in 42% of cases.³ This difference can be attributed to ruling out the diabetic patients and lack of cardiovascular system assessment in this study.

Moreover, familial hypercholesterolemia may present as XP, and we obtained familial hyperlipidemia in 26.2% of patients.¹⁸ Hence, familial hyperlipidemia could be an important underlying factor for XP induction.

We found that the mean serum levels of TG (185.98 ± 71.7 mg/dl) and cholesterol (221.51 ± 60.4 mg/dl) in the patient group were statistically higher than in the control group. Jain and Rubinstein observed significantly high mean serum values for TG and cholesterol in XP.^{3,12} Meanwhile, Sharma did not find any significant difference in mean TG level between the patient and normal groups.⁸

Similarly to findings in Urbano's study, there was a significant difference between our patient and control groups regarding the median level of HDL ($36.2 \pm (31, 41)$ mg/dl) and mean level of VLDL (37.7 ± 17.6 mg/dl).¹⁹ Unlike most studies, however, the mean LDL (120.3 ± 43.6 mg/dl) level in our patients was not statistically different compared to the mean LDL (110.6 ± 26.7 mg/dl) level in the control group.^{3,8,11,20-22}

Nearly 40-60% of the XP patients had normal lipid profiles (3, 8, 9). In our study, normal serum values for cholesterol and triglyceride were found in 54.8% and 69.1% of XP patients, respectively.

High ratios of cholesterol: HDL and low HDL levels have a direct effect on atherosclerosis.^{7,8,12,20} In our study, cholesterol: HDL ratios were significantly different between the patients and controls; XP lesions may therefore be a cutaneous sign for screening subclinical atherosclerosis.

CONCLUSION

According to the results of this study, there was no significant difference between patients and controls in terms of hypertriglyceridemia and hypercholesterolemia. However, a significant difference was observed in the mean serum values of some lipid profile parameters. In most studies, cholesterol and LDL are report-

ed to have an important pathogenic role in inducing XP. Yet, among our patients and controls, the mean serum levels for cholesterol and LDL revealed a significant difference and no significant difference, respectively.^{3,8,11,20-22} Thus, in addition to derangement of lipid metabolism, other factors including local, hormonal and macrophage abnormalities may be involved in the pathogenesis of XP. □

REFERENCES

- Sarkany RPE, Breathnach SM, Seymour CA, Weismann K, Burns DA. Metabolic and Nutritional Disorders. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's textbook of dermatology. vol. 3. 8th ed. Oxford: Wiley-Blackwell, 2010. p. 57: 60-75.
- James W, Berger TG, Elston DM. Andrew's disease of the skin clinical dermatology. 10TH ed. Philadelphia: Saunders & Elsevier, 2011 p.531-32.
- Jain A, Goyal P, Nigam PK, Gurbaksh H, Sharma RC. Xanthelasma palpebrarum-clinical and biochemical profile in a tertiary care hospital Delhi. Indian J ClinBiochem. 2007;22:151-3.
- Rohrich RJ, Janis JE, Pownell PH. Xanthelasma palpebrarum: a review and current management principles. Plast Reconstr Surg. 2002;110:1310-4.
- Bergman R, Kasif Y, Aviram M, Maor I, Ullman Y, Gdal-On M, et al. Normolipidemic xanthelasma palpebrarum: lipid composition, cholesterol metabolism in monocyte-derived macrophages, and plasma lipid peroxidation. Acta Derm Venereol. 1996;76:107-10.
- Borelli C, Kaudewitz P. Xanthelasma palpebrarum: treatment with the erbium:YAG laser. Lasers Surg Med. 2001;29:260-4.
- Korneva VA, Kyznetsova Tlu, Mandel'shtam Mlu, Konstantinov VO, Vasil'ev VB. The clinical manifestations of atherosclerosis in familial hypercholesterolemia. Ter Arkh. 2014;86:18-22.
- Sharma P, Patgiri D, Sharma G, Pathak MS. Serum lipid profile in Xanthelasma palpebrum. Indian J Basic Appl Med Res. 2013;7:732-737.
- Ozdöl S, Sahin S, Tokgözoğlu L. Xanthelasma palpebrarum and its relation to atherosclerotic risk factors and lipoprotein (a). Int J Dermatol. 2008;47:785-9.
- Zak A, Zeman M, Slaby A, Vecka M. Xanthomas: clinical and pathophysiological relations. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2014;158:181-8.
- Reddy SN, Singh G, Pandey SS, Tiwari D. Clinical and lipid profile studies in Xanthelasma Palpebrarum. Indian J Dermatol Venereol Leprol. 1983;49:127-31.
- Rubinstein TJ, Mehta MP, Schoenfield L, Perry JD. Orbital xanthogranuloma in an adult patient with xanthelasma palpebrarum and hypercholesterolemia. Ophthalmol Plast Reconstr Surg. 2014;30:e6-8.
- Bergman R. The pathogenesis and clinical significance of xanthelasma palpebrarum. J Am Acad Dermatol. 1994;30:236-42.
- Dwivedi S, Aggarwal A, Singh S, Sharma V. Familial Xanthelasma with Dyslipidemia: Just Another Family Trait? N Am J Med Sci. 2012;4:238-40.
- Dey A, Aggarwal R, Dwivedi S. Cardiovascular profile of xanthelasma palpebrarum. Biomed Res Int. 2013;2013:932863.
- Lee HY, Jin US, Minn KW, Park YO. Outcome of surgical management of xanthelasma palpebrarum. Arch Plast Surg. 2013;40:380-6.
- Ribera M, Pinto X, Argimon JM, Fiol C, Pujol R, Ferrandiz C. Lipid metabolism and apolipoprotein E phenotypes in patients with xanthelasma. Arch Plast Surg. 2013;40:380-6.
- Al-Rasadi K, Al-Waili K, Al-Sabti HA, Al-Hinai A, Al-Hashmi K, Al-Zakwani I, et al. Criteria for Diagnosis of Familial Hypercholesterolemia: A Comprehensive Analysis of the Different Guidelines, Appraising their Suitability in the Omani Arab Population. Oman Med J. 2014;29:85-91.
- Urbano FL. Ocular sign of hyperlipidemia. Hospital Physician. 2001;37:51-9.
- Pandhi D1, Gupta P, Singal A, Tondon A, Sharma S, Madhu SV. Xanthelasma palpebrarum: a marker of premature atherosclerosis (risk of atherosclerosis in xanthelasma). Postgrad Med J. 2012;88:198-204.
- Segal P, Insull W Jr, Chambless LE, Stinnett S, LaRosa JC, Weissfeld L, et al. The association of dyslipoproteinemia with corneal arcus and xanthelasma. The Lipid Research Clinics Program Prevalence Study. Circulation. 1986;73:1108-18.
- Gómez JA, González MJ, de Moragas JM, Serrat J, González-Sastre F, Pérez M. Apolipoprotein E phenotypes, lipoprotein composition, and xanthelasmas. Arch Dermatol. 1988;124:1230-4.

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