XANTHELASMA PALPEBRARUM-CLINICAL AND BIOCHEMICAL PROFILE IN A TERTIARY CARE HOSPITAL OF DELHI

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Abstract

Xanthelasma Palpebrarum is the most common of the xanthomas with asymptomatic, symmetrical, bilateral, soft, yellow, velvety, polygonal papules around the eyelids. Xanthelasmas may be associated with hyperlipidemia. This prospective study included 66 clinically diagnosed patients with Xanthelasma Palpebrarum and 50 controls with non-inflammatory skin disorders. Serum triglyceride, cholesterol, HDL, LDL and VLDL estimated in all cases indicated that patients with Xanthelasma Palpebrarum have underlying lipid abnormalities.

KEY WORDS

Xanthelasma Palpebrarum, Lipids, Hyperlipidemia

INTRODUCTION

Xanthelasma Palpebrarum is a disorder affecting eyelids with symmetrical soft, yellowish brown velvety papules on the inner canthi of upper and lower lids. These have a tendency to be multiple, progressive, permanent and coalescent. Though it is a benign lesion causing no functional disturbance, it is aesthetically annoying (1,2).

Xanthelasma Palpebrarum is one of the most common xanthomas seen in clinical practice. It is known to show a peak incidence at 30-50 years (3,4). The exact cause is not known but several factors like lipid abnormalities (1), hormonal factors (5,6), local factors (7-9) and macrophages (10) are attributed to play a role in its etiopathogenesis. Recently the role of acetylated LDL and macrophages with their scavenger receptors has been observed in the causation of Xanthelasma Palpebrarum. Xanthelasmas are composed of xanthoma cells which are foamy histiocytes laden with intracellular fat deposits primarily within the upper reticular dermis. The main lipid that is stored in both the hyperlipidemic and normolipidemic xanthelasmas is esterified cholesterol. The predominant lipid accumulated in normolipidemic Xanthelasmic lesions is

cholesteryl ester, but there is no evidence for intrinsic cellular cholesterol metabolism derangement in blood monocyte derived macrophages from patients which could account for this. Since macrophage cholesterol accumulation can also result from enhanced uptake of increased levels of oxidized LDL, the increased plasma lipid peroxidation (derived from oxidized LDL) might lead to accumulation of cholesterol in macrophages and formation of foam cells via this mechanism (10).

Xanthelasma Palpebrarum has been shown to have controversial association with plasma lipid abnormality. Its presence might suggest an underlying disorder of lipid metabolism. Patients with Xanthelasma Palpebrarum have lipid abnormalities ranging from 9.1% (2) – 67.9% (12). Since few studies are available in this regard in India, a prospective study was conducted to study the clinical profile and lipid abnormalities in diagnosed cases of Xanthelasma Palpebrarum in a tertiary care hospital in New Delhi.

MATERIALS AND METHODS

The study was conducted jointly in the Department of Dermatology and STD and Department of Biochemistry, Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital, New Delhi, India. Of the total 20089 cases that attended the dermatology OPD in one year, 66 clinically diagnosed cases of Xanthelasma Palpebrarum were selected after informed consent and these constituted the study group.

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Control Group consisted of 50 cases of non-inflammatory skin disorders, age and sex matched to the study group. Each patient was subjected to a detailed history and a thorough clinical examination. Venous samples were collected after overnight fasting of 12 hours and subjected to routine investigations like haemogram, blood sugar. A 12 lead ECG was done for every patient.

Serum total cholesterol was estimated by Enzymatic End Point (13). HDL Cholesterol was determined by precipitation method (14). Serum triglyceride was estimated enzymatically (14). VLDL and LDL were calculated by Friedwald formula. All biochemical tests were done on Beckman Synchron CX 5 Clinical Chemistry Analyzer using Randox kits.

RESULTS AND DISCUSSION

Xanthelasma Palpebrarum is the most common of the xanthomas characterized by asymptomatic usually symmetrical, soft, yellow, velvety polygonal papules around the eyelids. Xanthelasmas are rare in the general population. Variable incidence of 0.56%-1.5% has been reported from the western developed nations (6,15). The incidence in our study was 0.32% with 66 cases of Xanthelasma Palpebrarum of 20089 new cases attending the out patients department. Xanthomas can occur in people of any age. The age of onset of xanthelasmas ranges from 15-73 yrs with a peak in 4th and

5th decade. According to Marcelo (11), xanthelasmas usually occur in people older than 50 yrs. In our study also majority of patients were in the age group of 31-50 yrs. This is in agreement with observations of Chhetri (3) and Gangopadhya (4) from India and Ribera (16).

Sex preponderance in Xanthelasma Palpebrarum is debatable. Majority (81.9%) of patients in our study were females. Gangopadhya (4) and other authors (5,6,11,12,17) have also reported a higher prevalence in females. This may be due to the fact that females are more conscious from cosmetic point of view. However, Chhetri (3) reported a predominance of xanthelasmas in males because of more males attending the out patients department. Marcelo (11) reported equal prevalence in both sexes.

In our study majority of the patients had Xanthelasma of less than 12 months duration, with minimum duration being 6 months and the longest 72 months. Chhetri (3) and Reddy (2) had observed duration of 1-3 years in majority of their patients. Family history of Xanthelasma Palpebrarum was obtained in 12.1% of patients in our study. Chhetri (3) and Reddy (2) found a positive family history in 8.9% and 9.8% of patients respectively. They also observed a higher serum cholesterol levels in patients with a family history of Xanthelasma Palpebrarum. In our study majority of patients (91.0%) had multiple lesions. Two or more eyelids involvement was observed in 87.9% of the cases. Chhetri (3) and Ribera (16) also reported two or more eyelids involvement in majority of their patients. 42.4% of patients in this study had associated systemic diseases like hypertension, CAD, diabetes mellitus and cholelithiasis. According to Marcelo (11) prior history of MI and other forms of atherosclerosis and pancreatitis may be encountered in some patients. Chhetri (3) and Gangopadhya (4) reported CVD and hypertension in patients of xanthelasma palpebrarum in their studies. From western countries incidence of diabetes mellitus associated with Xanthelasma Palpebrarum was reported to be 6% (16) –34.2% (5).

The mean cholesterol level (216.8mg%) in Xanthelasma Palpebrarum cases was significantly ($p=0.001$) higher than in the control group (mean=173.6mg %). Likewise, the mean TG level (170.4mg%) in Xanthelasma Palpebrarum cases in our study was much higher than in controls (mean=106.7mg%). This difference too was statistically highly significantly ($p=0.001$). LDL (mean=134.4mg%) and VLDL (mean=34.0mg%) too were significantly higher in Xanthelasma Palpebrarum patients ($p=0.005$) and ($p=0.001$) respectively than in controls (mean LDL=112.8mg% and VLDL= 21.3mg%). Serum HDL levels were seen to be almost similar in

Table 1 Clinical Profile of Patients with Xanthelasma Palpebrarum

	N=66	Percentage (%)
Age (31-55 years)	25	37.9
Sex: M	12	18.1
F	54	81.9
Duration of Xanthelasma (<12 months)	34	51.5
Family history	8	12.1
Multiple lesions	60	91.0
Both lids involvement	48	72.7
Associated systemic disorders	28	42.4

Table 2 Mean Lipid Profile of patients with Xanthelasma Palpebrarum

	Study group (n=66)	Control group (n=50)	p value
TG (mg/dL)	170.4	106.7	0.001
Cholesterol (mg/dL)	216.8	173.6	0.001
HDL (mg/dL)	40.5	40.00	0.766
LDL (mg/dL)	134.4	112.8	0.005
VLDL (mg/dL)	34	21.3	0.001

Xanthelasma Palpebrarum patients (mean =40.5mg%) and in controls (mean=40.00mg%), this small difference being statistically non significant ($p=0.766$). Altered lipid levels were seen in 60.6% of patients with Xanthelasma Palpebrarum in our study. Reddy (2) from India also reported elevated lipid levels in 57.8% of patients. From western countries Pedace and Winkelmann (17) and Dean (18) reported higher lipid levels in 58.0% and 55.0% respectively. According to Tracey (19), 50% of patients with Xanthelasma Palpebrarum have associated lipid disorders.

The major risk factors for coronary heart disease include smoking, elevated blood pressure and elevated serum cholesterol. Risk reduction starts with identification of those at risk and then alteration of factors such as discontinuation of smoking, lowering of blood pressure and reduction of serum cholesterol. Patients who should have blood cholesterol testing include those with family history of premature coronary heart disease or hyperlipidemia, personal history of coronary heart disease or clinical evidence of elevated lipids with features of Xanthelasma, corneal arcus under age 50 years and cutaneous xanthomas at any age (20).

In the Lipids Research Clinics Program Prevalence Study, Xanthelasma and corneal arcus were associated with increased levels of serum cholesterol and low density lipoprotein cholesterol (LDL-C), especially in young males. People with either lesion had increased odds of having type IIa dyslipoproteinaemia. Adjusted odds ratios for ischaemic heart disease in participants with Xanthelasma and corneal arcus were generally increased. The study concluded that the clinical findings of Xanthelasma or corneal arcus, especially in young people, helped to identify those with plasma lipoprotein abnormalities (6).

We conclude that majority of patients with Xanthelasma Palpebrarum have abnormal lipid levels and its presence can be used to identify persons at greater risk of coronary artery disease due to dyslipidemia. The presence of Xanthelasma merits identification and treatment in order to prevent atherosclerosis which is gaining epidemic proportions in our country.

REFERENCES

1. Bergam R. The pathogenesis and clinical significance of Xanthelasma Palpebrarum. *J Am Acad Dermatol* 1994 Feb; 30(2 Pt 1): 236-42.
2. Reddy SN B, Singh G, Pandey SS, Tiwari D. Clinical and lipid profile studies in Xanthelasma Palpebrarum. *I J D V L* 1983; 49(3): 127-31.
3. Chhetri MK, Chowdhary ND, De B. Xanthelasma Palpebrarum. *J Asso Phy Ind* 1967; 15(9): 405-12.
4. Gangopadhyay BN, Dey SK, Mitra C, Pal D, Chaudhuri. Serum lipid profile in Xanthelasma Palpebrarum. *Ind J Dermatol* 1998; 43(2): 53-7.
5. Vacca JB, William AK, Broun GO. Clinical observations regarding xanthelasma. *Ann Int Med* 1959; 51: 1019-31.
6. 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* 1987; 73(1 Pt 2): 1108-18.
7. Wolff Eugene. Xanthelasma Palpebrarum. Tumor of sebaceous glands. *Br J Dermatol* 1951; 63: 296-302.
8. Thompson JA. Xanthelasma associated with throtoxicosis. *J Clin Endocr* 1965; 25: 758-60.
9. Scott J, Winterbourn CC. Low- density lipoprotein accumulation in actively growing xanthomas. *J Atheroscl Res* 1967; 7: 207-23.
10. Bergman R, Kasif Y, Aviram M, Maor I, Ullman Y, Gdal OM, et al. Normolipidemic xanthelasma palpebrarum: lipid composition, cholesterol metabolism in monocyte derived macrophages and plasma lipid peroxidation. *Acta Derm Venereol* 1996; 76(2): 107-10.
11. Marcelo GH, Janis PM. Xanthelasma. 2005 May 12. Available from: URL: eMedicine Specialties
12. Watanabe A, Yoshimura A, Wakasugi T, Tatami R, Ueda K, Ueda R, et al. Serum lipids, lipoprotein lipids and coronary heart disease in patients with xanthelasma palpebrarum. *Atherosclerosis* 1981; 38(3-4): 283-90.
13. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of serum cholesterol. *Clin Chem* 1974; 20: 470.
14. Buccolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. *Clin Chem* 1973; 19: 476-82.
15. Jonson A, Sigfusson N. Letter: Significance of xanthelasma palpebrarum in normal population. *Lancet* 1976; 1: 372.
16. Ribera M, Pinto X, Argimon JM, Fiol C, Pujol R, Ferrandiz C. Lipid metabolism and apolipoprotein E phenotypes in patients with xanthelasma. *Am J Med* 1995; 99(5): 485-90.
17. Pedace FJ, Winkelmann RK. Xanthelasma Palpebrarum. *J A M A* 1965; 13: 893-4.
18. Dean FD. Xanthelasma and hyperproteinemia. *Clinica Chimica Acta* 1976; 66(2): 189-93.
19. Tracey A Schmucker, Hampton Roy. Xanthelasma. 2006 May 17. Available from: URL: eMedicine Specialties
20. Farmer JA, Gotto AM Jr. The Heart Protection Study: expanding the boundaries for high-risk coronary disease prevention. *Am J Cardiol* 2003; 92(1A): 3i-9i.