CLINICAL STUDY

To Study the Prevalence of Metabolic Syndrome and Dyslipidemia in Patients of Xanthelasma Palpebrarum at a Tertiary Care Hospital

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ABSTRACT

Background: Xanthelasma palpebrarum (XP) are yellow plaques that occur most commonly near the inner canthus of the eyelid, more often on the upper lid than the lower lid, and are often associated with dyslipidemia, metabolic syndrome, cardiovascular disease, diabetes, obesity, etc. **Aim:** This study was planned to address the issue of prevalence of dyslipidemia and metabolic syndrome in xanthelasma patients attending dermatology clinic at a tertiary care hospital, Ajmer, Rajasthan. **Material and methods:** A total of 73 patients were detected to be having xanthelasma and constituted the study group. The control group constituted 73 apparently normal individuals. Each patient underwent detailed history and examination. Body mass index (BMI), waist circumference, arterial blood pressures, fasting plasma glucose (FPG), serum lipids, and liver enzyme levels were estimated in cases and controls. **Results:** The most prevalent age group was 40 to 50 years. Females outnumbered males. Dyslipidemia was present in 63% and metabolic syndrome in 45.2% of cases. The mean levels of FPG, BMI, waist circumference in XP patients were significantly higher in patients than those in controls. **Conclusions:** A significant number of cases of XP are found to be associated with metabolic syndrome, central obesity, hypertension, diabetes mellitus, and dyslipidemia which are the major risk factors for coronary artery diseases. Efforts should be made to rule out the same in xanthelasma subjects.

Keywords: Xanthelasma, dyslipidemia, metabolic syndrome

Xanthelasma palpebrarum (XP) (Greek; *xanthos*: yellow and *elasma*: beaten metal plate) are yellow plaques that occur commonly near the inner canthus of the eyelid, more often on the upper lid[1]. Xanthelasma can be soft, semi-solid or calcareous, and are frequently symmetrical with all four-eyelid involvement. They have a tendency to progress, coalesce and become permanent. Xanthelasma represent areas of macrophage containing lipids, primarily cholesterol esters, but the exact pathogenesis is not known[2]. Xanthelasma are composed of xanthoma cells which are foamy histiocytes laden with intracellular fat deposits primarily within the upper reticular dermis. Most studies have found increased concentrations of plasma total cholesterol or low-density lipoprotein (LDL) cholesterol in people with xanthelasma. It has been known to be associated with atherosclerosis, coronary artery disease (CAD), insulin resistance, diabetes mellitus (DM), hypertension, stroke, dyslipidemia, obesity, and hyperuricemia. However, it is still controversial whether such lesions are a marker for cardiovascular or metabolic disease or not. A study was planned to address the issue of prevalence of metabolic syndrome and dyslipidemia in xanthelasma patients attending dermatology clinic at our center.

MATERIAL AND METHODS

This study was conducted in the Dept. of Dermatology at JLN Medical College, Ajmer, Rajasthan. Seventy-three clinically diagnosed cases of XP were selected after informed consent and these constituted the study group. Control group was age- and gender-matched

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apparently healthy participants with no xanthelasma, randomly selected from the outpatient clinic.

Exclusion criteria were patients taking any drugs that could alter lipid level or blood glucose level, patient having concomitant disorder(s) that could affect the outcome of the study. Each patient underwent detailed history and physical examination including height, weight, waist and hip circumference. Body mass index (BMI) was calculated for the participants in both groups and obesity was defined by BMI 30 or greater.

All blood pressure (BP) measurements were taken with standard calibrated mercury manometers in the right arm of each individual in a sitting position after a rest of 5 minutes. Fasting blood samples were collected after 14-hour fasting. All cases underwent lipid profile study (total cholesterol [TC], LDL cholesterol, high-density lipoprotein [HDL] cholesterol, very-low-density lipoprotein [VLDL] cholesterol, triglycerides [TGs]) on empty stomach.

Dyslipidemia: Abnormal lipid levels were diagnosed according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines.

Metabolic syndrome: According to the third report of the NCEP-ATP III, adults to be diagnosed with metabolic syndrome must have three or more of the following:

- Waist circumference >102 cm (40.2 in) in men and >88 cm (35.6 in) in women
- Serum TGs ≥150 mg/dL
- BP ≥130/85 mmHg
- HDL cholesterol <40 mg/dL in men and <50 mg/dL in women
- Fasting plasma glucose (FPG) >6.1 mmol/L (≥100 mg/dL).

Data were statistically described in terms of mean (standard deviation), frequency (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was carried out using the Student's *t*-test and Chi-squared test, respectively. Statistical analysis was carried out using GraphPad software.

RESULTS

The total number of cases of xanthelasma and controls was 73. The youngest case with XP was 30 years of age, while the eldest was 73 years old, mean age of the cases being 51.18 and that of controls 52.01 with a 't' value of 0.4829 and p value of 0.6299 making the two groups statistically comparable. Prevalence was the highest in the age group of 40 to 50 years (33%). Prevalence was higher in females (82.2%) as compared to males (17.8%). Most of the cases (93.15%) were Hindus, while 6.85% were Muslims. While xanthelasma was found mostly bilaterally (56 cases; 76.72%), unilateral presentation was found in 17 cases (23.28%). In 9 cases (12.32%), it was present on all four eyelids. Family history of XP was obtained in 8 cases (10.95%) in our study.

TC levels were increased in 46 cases (63.01%) as compared to 20 controls (27.4%). Similarly, LDL cholesterol and TG levels were also increased in 52 cases (71.2%) as compared to 29 controls (39.72%) and in 29 cases (39.7%) as compared to 17 (23.3%) controls, respectively. HDL levels were decreased in 34 cases (46.6%) as compared to 22 controls (30.1%). VLDL cholesterol was increased in 15 cases (20.5%) and 11 controls (15%). Mean values of TC, LDL cholesterol, and TG levels were increased compared to control group with significant p value. Mean value of HDL cholesterol was found to be decreased compared to control group with significant p value; however, p value was not found to be significant in mean value of VLDL cholesterol compared to controls (Table 1).

Table 1. Relationship Between Various Cholesterol Fractions and XP in Cases and Controls

	Mean	SD	t value	P value*
TC				
Cases	212.6	(34.8)	4.9843	<0.0001 Highly significant
Control	181.8	(39.6)		
LDL				
Cases	137.3	(23.52)	3.4434	P = 0.0008 Highly significant
Control	124.3	(21.92)		
HDL				
Cases	41.33	(7.87)	2.288	P = 0.0236 Significant
Control	44.35	(8.09)		
TG				
Cases	152.29	(70.09)	2.1352	P = 0.0344 Significant
Control	132.27	(38.74)		
VLDL				
Cases	30.10	(15.89)	0.9445	P = 0.3465 Not significant
Control	27.8	(12.18)		

XP = Xanthelasma palpebrarum; TC = Total cholesterol; LDL = Low-density lipoprotein; HDL = High-density lipoprotein; TG = Triglyceride; VLDL = Very-low-density lipoprotein; SD = Standard deviation.

*P < 0.05 is considered to be statistically significant.

Table 2. Comparison Between Various Metabolic Syndrome Components in XP Patients and Controls

	No. of the patients		P value*
WC			
Cases	↑ 48 (65.8%)	N 25 (34.2%)	P = 0.0298 Significant
Control	↑ 35 (48%)	N 38 (52%)	
BP			
Cases	↑ 22 (30%)	N 51 (70%)	P = 1.245 Not significant
Control	↑ 14 (19.2%)	N 59 (80.8%)	
HDL			
Cases	↓44 (60.3%)	N 29 (39.7%)	P = 0.0314 Significant
Control	↓31 (42.5%)	N 42 (57.5%)	
TG			
Cases	↑29 (39.7%)	N 44 (60.3%)	P = 0.0325 Significant
Control	↑17 (23.3%)	N 56 (76.7%)	
MS			
Cases	P 33 (45.2%)	A 40 (54.8%)	P = 0.0002 Highly significant
Control	P 12 (16.4%)	A 61 (83.6%)	

XP = Xanthelasma palpebrarum; WC = Waist circumference; BP = Blood pressure; HDL = High-density lipoprotein; TG = Triglyceride; MS = Metabolic syndrome; ↑ = Increased; ↓ = Decreased; N = Normal; P = Disease present; A = Disease absent.

*P < 0.05 is considered to be statistically significant calculated from Chi-squared test.

Nearly, 18 (24.66%) patients and 8 (11%) controls were diagnosed with DM according to the American Diabetes Association (ADA) criteria and this difference was statistically significant (p = 0.0305).

Metabolic syndrome was present in 45.2% (33 cases) in XP patients as compared to 16.4% (12 cases) in control group with significant p value (p = 0.0002). Individual components of metabolic syndrome like hypertriglyceridemia, decreased HDL cholesterol, impaired FPG and waist circumference were also more prevalent in cases than in controls (Table 2).

However, systolic and diastolic BP were noted to be higher among cases (22 cases, 30%) as compared to controls (14 cases, 19.2%) but p value was not found to be statistically significant (p = 1.245). Mean value for BMI in case group (27.71) was higher than control group (26.50) with significant p value (p = 0.0268).

DISCUSSION

Xanthelasma is fairly prevalent in our population. However, people tend to complain only for esthetic reasons. Most of our cases were not aware of the significance of these deposits. Age distribution was wide ranging from 21 to 73 years. We found the peak incidence between 40 and 60 years. This was similar as that reported by Gangopadadhya et al[3] and Jain et al[2] in their studies from Delhi. They found the majority of patients in the age group of 31 to 50 years. XP was found more in females (82.2%) as compared to males (17.8%) in our study.

This was in concurrence with the study done by Jain et al, Gangopadadhya et al, Epstein et al, and Pedace et al[2-5]. But Chhetri et al[6] showed a male preponderance in his study. Jain et al, Chhetri et al, and Reddy et al found a positive family history in 12.1%, 8.9%, and 9.8% patients, respectively[2,6,7]. Family history of XP noted in our cases was 10.95%, similar to 10% cases with positive family history found by Vacca et al[8].

Jain et al reported that 91% of patients had multiple lesions and 72.7% had both lids involvement. Two or more eyelids involvement was observed in 87.9% of the cases[2]. Chhetri et al reported bilateral lesions in 39% cases, two eyelids involvement in 53.2% cases and one eyelid involvement in 7.8% cases[6]. Ribera et al reported that 11.3% patients had only one eyelid involvement, 42.6% in two eyelids, 12.2% in three eyelids and 33.9% in four eyelids[9].

In our study, 56 cases (76.72%) had bilateral lesions and 17 cases (23.28%) had unilateral lesions. Single lesions were present in 14 cases (19.18%) and multiple lesions were present in 59 cases (80.82%).

We found associations with hypertension, dyslipidemia, metabolic syndrome, and diabetes in a sizeable percentage of our patients. Increased TC value in xanthelasma patients have been observed by Gangopadadhya et al, Epstein et al, Pedace et al, and Kahán et al[3-5,10]. We also found similar results with TC levels increased in 46 cases (63%) as compared to 20 controls (27.4%) with p < 0.0001, making it highly significant. Increased LDL cholesterol levels have been observed by various authors[3,9,11-13].

The study done by Vermeer et al[14] found it to be normal. Our study showed increased LDL cholesterol levels in 52 cases (71.2%) as compared to 29 controls (39.72%), which was more significant in comparison to other studies and was statistically significant with p value of 0.001. Gangopadadhya et al[3], Bates et al[15], and Ribera et al[9] observed a significant decrease in HDL cholesterol levels. Similar results were shown in our study, which observed a decrease in HDL cholesterol in 34 cases (46.6%) as compared to 22 control (30.1%) with a significant p value of 0.0411.

We found TGs were increased in 29 cases (39.7%) and 17 controls (23.3%) with a significant p value of 0.0325

as observed by many authors[2,3,6,10,16], although there were no comparisons with controls by some authors. These findings were not similar to study done by Ribera et al in which 5.21% cases and 6.66% controls showed hypertriglyceridemia[9]. Watanabe et al reported that VLDL levels were significantly above the control levels ($p = 0.001$) in cases[11]. Sharma et al and Jain et al observed a significant increase in VLDL levels in patients with xanthelasma as compared to controls ($p < 0.01$, $p = 0.001$)[2,17]. In our study, VLDL cholesterol was increased in 15 cases (20.5%) and 11 controls (15%) but difference was not found to be statistically significant ($p = 0.3869$).

Jain et al[2] found that 42.4% of patients had associated systemic diseases like hypertension, CAD, DM, and cholelithiasis. Chhetri[6] and Gangopadadhya[3] reported cardiovascular disease (CVD) and hypertension in patients of XP in their studies. From western countries incidence of DM associated with XP was reported to be 6%-34.2%[8,9]. Clinical study done by Dey et al had observed prevalence of DM as 18.03% in XP[18]. In our study, 18 cases (24.66%) had DM as compared to 8 (11%) controls with significant p value ($p = 0.0305$). Various studies have observed that subjects with DM, hypertension, metabolic syndrome, and dyslipidemia have increased risk of CVDs[19-21].

We found metabolic syndrome was present in 45.2% (33 cases) in XP patients as compared to 16.4% (12 cases) in control group with significant p value ($p = 0.0002$). Individual components of metabolic syndrome like hypertriglyceridemia, decreased HDL cholesterol, impaired FPG, BMI, and waist circumference were also observed more prevalent in cases than in controls.

Whether or not xanthelasma alone can predict risk of CAD is still not clear, although studies have shown that it can. Christoffersen et al[22] reported that xanthelasma can predict the risk of myocardial infarction, ischemic heart disease, severe atherosclerosis and death in the general population, independently of the well-known cardiovascular risk factors[18].

At the end of this study, it was observed that there is a significant elevation in lipid profile in xanthelasma patients as compared to controls, thereby making lipid profile study mandatory for all patients. We also found significant association of DM and metabolic syndrome in xanthelasma patients as compared to controls. The presence of xanthelasma merits identification and treatment in order to prevent metabolic syndrome, which is gaining epidemic proportions in our country.

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