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Assessment and Predictors of Metabolic Syndrome in Patients of Xanthelasma Palpebrarum: An Observational Study

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ABSTRACT

Introduction: Xanthelasma palpebrarum is considered to be a cutaneous marker for cardiovascular diseases, and there is a known association with hypertension, insulin resistance, diabetes mellitus, obesity, and stroke.

Objectives: Our aim was to study the association and identify the predictors of metabolic syndrome in patients with xanthelasma palpebrarum.

Methods: An observational study was conducted on 55 patients in which patients of both sexes ages 20–70 years without any other skin condition were included after written informed consent. After history and examination, blood pressure and waist circumference were measured in all the subjects. Investigations were sent for fasting blood sugar levels and serum lipid profile. The 2006 IDF Definition of metabolic syndrome was used as assessment criteria.

Results: Among the 55 patients, metabolic syndrome was present in 23 patients (41.82%). There was a statistically significant ($P<0.05$) difference in the values of waist circumference (100% vs. 59.38%, $P=0.0003$), elevated blood pressure (82.61% vs. 9.38%, $P<.0001$), raised fasting blood sugar (47.83% vs. 18.75%, $P=0.021$), and raised triglyceride levels (56.52% vs. 25%, $P=0.018$) between

patients with metabolic syndrome and those without. However, HDL cholesterol levels (34.78% vs. 50%, *P*=0.262) were comparable between groups. Also, a patient aged 41 years or more with even a single xanthelasma of more than one year's duration has a 76.1% chance of developing metabolic syndrome.

Conclusions: Metabolic syndrome develops in a sizeable number of xanthelasma palpebrarum patients, and this therefore gives us an opportunity for early diagnosis and intervention to prevent the development of cardiovascular complications.

Introduction

Xanthelasma palpebrarum (XP) is a disorder of lipid metabolism which generally presents as asymptomatic single or multiple bilaterally symmetrical soft yellow velvety papules and plaques most frequently over the medial canthi of eyelids (upper > lower) [1,2]. The exact etiopathogenesis is not known, but it could be due to an underlying disorder of lipid metabolism and other factors like hormones, macrophages, and local factors [3]. It mainly presents in middle-aged individuals primarily as a cosmetic concern [4].

It is believed to have an association with diabetes mellitus (DM), coronary artery disease (CAD), atherosclerosis, insulin resistance, stroke, hypertension (HTN), hyperuricemia, dyslipidemia, and obesity. However, there is controversy regarding the lesions being a marker for metabolic syndrome (MS) [4].

Since both XP and MS are independently associated with cardiovascular disease (CVD), diabetes mellitus, and obesity, it is therefore possible for an association to exist between the two disorders. Therefore, this study was undertaken with the aim to assess the clinical features of xanthelasma palpebrarum along with the evaluation of the glycemic levels, body mass index (BMI), cholesterol and triglyceride (TG) levels, waist circumference (WC), and blood pressure (BP) recordings in the patients with xanthelasma palpebrarum. This would, therefore, help us to study the association between XP and MS. Through this study, we also aimed to identify the predictors of MS in XP patients.

Methods

Study Design and Setting

This hospital-based observational study was conducted in the Department of Dermatology of a tertiary care hospital in Northern India from January 2020 to June 2021 after approval from the Institutional Ethics Committee. A total of 55 clinically diagnosed cases of XP without other skin diseases between the ages of 20 and 70 years who consented to voluntary participation in the study were analyzed. Consecutive patients were selected after written informed consent. No patient refused participation, and there was no dropout.

Patient Assessment

A detailed clinical history was taken, and a detailed cutaneous examination of the lesions was done. Blood pressure, weight, height, and WC were measured in all the subjects during the first visit. Investigations in the form of fasting blood sugar (FBS), triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol, and VLDL cholesterol were done.

Assessment of the fulfilment of criteria for MS was done according to the 2006 IDF Definition of Metabolic Syndrome (with ethnic-specific WC for South and East Asian individuals). According to the criteria, MS is present if an individual has central obesity (WC ≥ 90 cm in females and ≥80 cm in males, assumed if BMI is >30 kg/m^2), plus any two of the following four factors, (1) raised triglycerides (≥150 mg/dL) or specific treatment for this lipid abnormality; (2) reduced HDL cholesterol (<40 mg/dL in males, <50 mg/dL in females) or specific treatment for this lipid abnormality; (3) raised blood pressure (≥ 130/85 mm Hg) or treatment of previously identified hypertension; and (4) raised fasting plasma glucose (≥100 mg/dL) or previously diagnosed T2DM.

Statistical Analysis

The presentation of the categorical variables is in the form of number and percentage (%); quantitative data are presented as the means ± standard deviation (SD) and as median with 25th and 75th percentiles (interquartile range). Multiple statistical tests were applied for the results. The association between the variables which were quantitative in nature were analyzed using independent t-test. The association between the variables which were qualitative in nature were analyzed using Chi-Square test. If any cell had an expected value of less than 5, then Fisher exact test was used. Receiver operating characteristic curve (ROC) was used to find the cutoff of various parameters for predicting metabolic syndrome.

The data entry was done in the Microsoft EXCEL spreadsheet, and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0. For statistical significance, a p-value of less than 0.05 was considered statistically significant.

Result

In the present study, among the 55 participants, 46 patients were females and 9 males. The average age was 39.16±10.4 years, with majority (36.36%) of patients between 41 and 50 years. The mean duration of onset of disease was 34.17 ± 29.09 months. Comorbidities were seen in the form of hyperlipidemia (45.45%), followed by hypertension (27.27%), DM (21.82%), and CVD (12.73%). Two patients (3.64%) had a known episode of stroke.

The maximum number of lesions in our patient was 12 and minimum was one. Mean number of total lesions was 3.05 ± 2.3. Upper eyelid involvement was seen in 82.22% of the patients and lower eyelid in 71.79% of patients. Bilateral involvement was seen in 47 (85.45%) patients and unilateral in eight (14.55%). Mean size of lesions over the upper eyelid and lower eyelid was 2.73 ± 1.55 and 2.99 ± 2.22 mm, respectively, with the majority of the lesions being yellow, well-defined, smooth, and soft in consistency and with papular morphology (Figures 1-4).

The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) (recorded in mmHg) in our study subjects was 126.73±15.16 and 81.67±11.01 mmHg, respectively. Elevated BP readings were present in 22 (40.00%) patients. The mean weight, height, and waist circumference were 64.88 ± 12.32 kg, 156.77 ± 7.49 cm, and 91.85 ± cm, respectively. Central obesity was present in 42 (76.36%) patients.

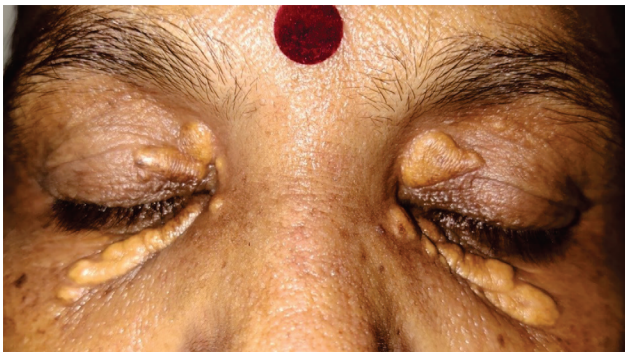

Figure 1. A 58-year-old female patient with xanthelasma palpebrarum with multiple papular soft lesions and a single semisolid lesion present over both upper and lower eyelids, with metabolic syndrome (BP 150/100 mmHg, waist circumference 93 cm, fasting blood sugar 104.1 mg/dL, triglycerides 189.9 mg/dL).

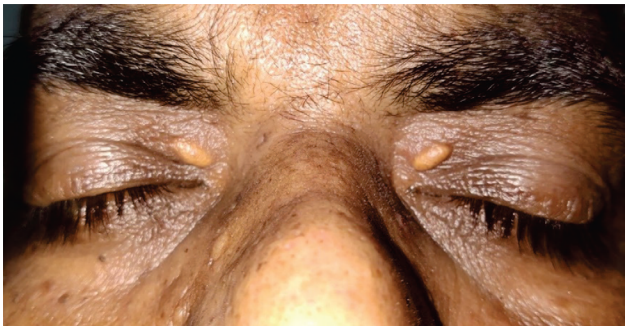

Figure 2. A 50-year-old female with two nodular lesions of xanthelasma palpebrarum, calcareous and semisolid, over the left upper and right upper eyelids, respectively, with metabolic syndrome (waist circumference 113 cm, fasting blood sugar 125 mg/dL, triglycerides 317.3 mg/dL).

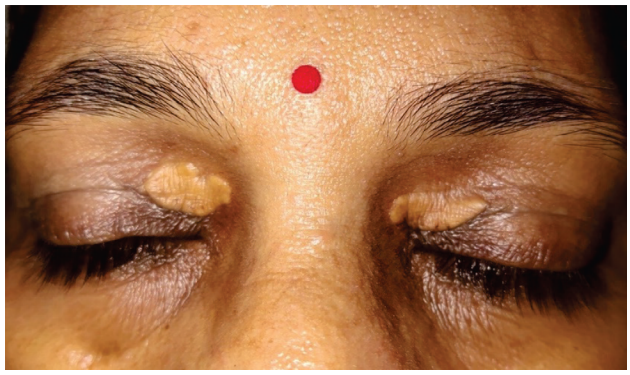

Figure 3. A 41-year-old female patient presenting with recurrence of xanthelasma palpebrarum with bilaterally symmetrical soft yellowish plaques over upper eyelids, without metabolic syndrome.

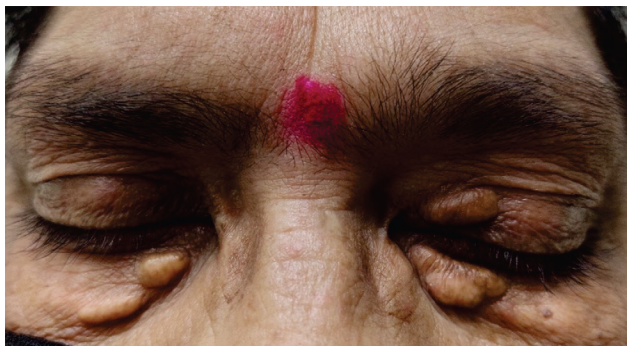

Figure 4. A 50-year-old female patient presenting with recurrence of xanthelasma palpebrarum lesions post prior treatment presented with multiple papulonodular lesions of varying consistency (soft, semi-solid, and calcareous), over both upper and lower eyelids, without metabolic syndrome.

Considering the laboratory parameters, the mean FBS levels were 105.1 ± 29.36 mg/dL, and elevated FBS levels were present in 17 (30.91%) patients. The mean value of TG levels, total cholesterol, LDL, VLDL, and HDL were 168.23 ± 98.9 mg/dL, 199.71 ± 53.51 mg/dL, 116.96 ± 42.34 mg/dL, 33.79 ± 19.77 mg/dL, and 49 ± 11.2 mg/dL, respectively. Reduced HDL was present in 24 (43.64%) and elevated TG levels in 21 (38.18%) patients. (Table 1). Metabolic syndrome was seen in 41.82% (23/55) of our patients (Table 2).

Comparison of Lipid Profile Between the Two Groups (Table 3)

As compared to those without MS, those with metabolic syndrome had significantly higher total cholesterol (217.77 ± 59.09 vs. 186.73 ± 45.75, *P*=0.032) but comparable TG (195.93 ± 109.83 vs. 148.33 ± 86.59, *P*=0.078), LDL

Table 1. Distribution of Components of Metabolic Syndrome of Study Subjects.

Components of Metabolic Syndrome	Frequency	Percentage
Central obesity	42	76.36%
Reduced HDL	24	43.64%
Elevated blood pressure	22	40.00%
Elevated fasting blood sugar levels	17	30.91%
Elevated triglyceride levels	21	38.18%

Table 2. Distribution of Metabolic Syndrome of Study Subjects.

Metabolic Syndrome	Frequency	Percentage
No	32	58.18%
Yes	23	41.82%
Total	55	100.00%

Table 3. Association of Lipid Profile with Metabolic Syndrome.

Lipid Profile	No Metabolic Syndrome	Metabolic Syndrome	Total	p- value
Triglyceride levels (mg/dL)				
Mean ± SD	148.33 ± 86.59	195.93 ± 109.83	168.23 ± 98.9	0.078
Median (25th-75th percentile)	129.05 (92.398-155.675)	164.41 (123.3-218)	137.1 (112.5-183.25)	
Range	68-419	101-516	68-516	
Cholesterol (mg/dL)				
Mean ± SD	186.73 ± 45.75	217.77 ± 59.09	199.71 ± 53.51	0.032*
Median (25th-75th percentile)	173.45 (158.5-201.775)	195 (180.13-246)	185.8 (167.5-222.7)	
Range	115.5-336	125-364	115.5-364	
LDL (mg/dL)				
Mean ± SD	108.9 ± 37.08	128.17 ± 47.29	116.96 ± 42.34	0.096
Median (25th-75th percentile)	101.6 (85-130.485)	119.2 (89.25-152.3)	110.6 (88.25-140.27)	
Range	41.7-202.6	54-225.72	41.7-225.72	
VLDL (mg/dL)				
Mean ± SD	29.91 ± 17.36	39.19 ± 21.97	33.79 ± 19.77	0.086
Median (25th-75th percentile)	25.7 (18.478-35.5)	32.88 (24.66-43.6)	27.42 (22.5-36.65)	
Range	13.6-83.8	20.2-103.2	13.6-103.2	
>50	10 (37.04%)	12 (63.16%)	22 (47.83%)	
HDL (mg/dL)				
Mean ± SD	48 ± 12.04	50.39 ± 9.99	49 ± 11.2	0.439
Median (25th-75th percentile)	47.4(41.615-51.15)	52(42-56.8)	47.8(42-54)	
Range	22-77	38-74.9	22-77	

Abbreviations: HDL: high-density lipoprotein; LDL: low-density lipoprotein; SD: standard deviation; VLDL: very low density lipoprotein.

(128.17 ± 47.29 vs. 108.9 ± 37.08, *P*=0.096), VLDL (39.19 ± 21.97 vs. 29.91 ± 17.36, *P*=0.086), and HDL levels (50.39 ± 9.99 vs. 48 ± 12.04, *P*=0.439) (Table 4).

Significance of Individual Components of Metabolic Syndrome (Table 4)

We adopted 2006 IDF criteria for estimating MS as per which blood pressure, lipid profile, blood sugar levels, and obesity were taken into account. When comparing the patients without MS, those with metabolic syndrome had significantly more central obesity (100% vs. 59.38%, *P*=0.0003), elevated blood pressure (82.61% vs. 9.38%, *P*<.0001), elevated FBS levels (47.83% vs. 18.75%, *P*=0.021), and elevated TG levels (56.52% vs. 25%, *P*=0.018) but comparable reduced HDL levels (34.78% vs. 50%, *P*=0.262) (Table 4). This showed that all the components of MS were deranged among the patients except for reduction in HDL.

Identification of Predictors of Metabolic Syndrome (Table 5)

Among the other laboratory parameters, we observed that compared to patients without MS, patients with MS had a higher mean age (44.74 ± 8.89 vs. 35.16 ± 9.55, *P*=0.0004), with ROC curve showing that age was the significant

Table 4. Significance of Individual Components of Metabolic Syndrome.

Components of MS	No MS (n=32)	MS (n=23)	Total	P-value
Central obesity	19 (59.38%)	23 (100%)	42 (76.36%)	0.0003*
Reduced HDL	16 (50%)	8 (34.78%)	24 (43.64%)	0.262
Elevated BP	3 (9.38%)	19 (82.61%)	22 (40%)	<.0001*
Elevated FBS	6 (18.75%)	11 (47.83%)	17 (30.91%)	0.021*
Elevated TG levels	8 (25%)	13 (56.52%)	21 (38.18%)	0.018*

Abbreviations: BP: blood pressure; FBS: fasting blood sugar; HDL: high-density lipoprotein; MS: metabolic syndrome; TG: triglyceride.

predictor of MS at cutoff of >41 years, with a 76.1% chance of correctly predicting MS in patients with XP (*P*=0.0001, sensitivity 69.57%, specificity 75%, positive predictive value (PPV) 66.7%, and negative predictive value (NPV) 77.4%). However, in terms of sex, there was no significant difference between the two groups (*P*=1). However, among the available literature, one of the studies observed that with the increase in age, the prevalence of MS increased five times in females and two times in males.

Also, the patients with MS had significantly longer duration of onset (44.61 ± 29.47 vs. 26.67 ± 26.81, *P*=0.023), with ROC curve showing that duration of onset was the significant predictor of MS at cutoff of >12 months, with diagnostic accuracy of 67.27% in predicting MS in patients with XP (*P*=0.0011, sensitivity 91.3%, specificity 50%, PPV 56.8%, NPV 88.9%). This might be because a longer duration of the disease may increase the chances of lipid abnormalities, thereby leading to increased chances of development of MS [5].This was also indirectly proven by the fact that the total number of XP lesions was significant but borderline predictor of MS at cutoff of >1, with diagnostic accuracy of 54.55% (*P*=0.0447, sensitivity 100%, specificity 21.87%, PPV 47.9%, NPV 100%).

Among the lipid levels, ROC curve showed that TG level was the significant predictor of MS at cutoff of >148.9, with diagnostic accuracy of 67.27% in predicting MS in patients with XP (*P*=0.0242, sensitivity 56.52%, specificity 75%, PPV 61.9%, NPV 70.6%). Total cholesterol was the significant predictor of MS at cutoff of >173.9 mg/dl, with diagnostic accuracy of 67.27% in predicting MS in patients with XP (*P*=0.0096, sensitivity 86.96%, specificity 53.13%, PPV 57.1%, NPV 85%). VLDL was the significant predictor of MS at cutoff of >29.78 mg/dl, with diagnostic accuracy of 65.45% in predicting MS in patients with XP (*P*=0.032, sensitivity 56.52%, specificity 71.87%, PPV 59.1%, NPV 69.7%). However, HDL and LDL were not found to be significant predictors of metabolic syndrome.

Discussion

XP, a disorder of lipid metabolism, generally presents as asymptomatic single or multiple bilaterally symmetrical soft yellow velvety papules and plaques most frequently over the medial canthi of eyelids (upper > lower) [1,2]. It is most common in the third to fifth decades of life[3,5]. It is seen more frequently in females as compared to males. XP may be soft to semisolid or calcareous in consistency, with a tendency to be progressive and coalescent [6].

Although the exact etiopathogenesis of XP is not known, it could be due to an underlying disorder of lipid metabolism. The predominant lipid present in the foam cells of normolipidemic and hyperlipidemic XP is esterified cholesterol [7]. Other factors like hormones, macrophages, and local factors are also believed to be involved in the etiopathogenesis [3].

XP is considered to be a cutaneous marker for CVDs (i.e., atherosclerosis and ischemic heart disease) along with disturbed lipid metabolism. It is also known to show an association with hypertension, insulin resistance, diabetes mellitus, obesity, and stroke [6]. Metabolic syndrome is also known as the "insulin resistance syndrome" or "Syndrome X". It represents a clustering of various abnormalities of metabolism that includes hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia [8].

There is an association between abdominal obesity and the resistance to actions of insulin on peripheral blood sugar levels and alteration in the fatty acid utilization, causing type 2 DM. Insulin resistance in addition to hyperinsulinemia and hyperglycemia and adipokines (adipocyte cytokines) may cause vascular endothelial dysfunction, hypertension, vascular inflammation, and deranged lipid profiles. All these factors lead to atherosclerotic CVD [9][10]. The simultaneous occurrence of metabolic risk factors in CVD as well as type 2 DM suggests the existence of a metabolic syndrome [11] [12]. Since both XP and MS are independently associated with cardiovascular disease, diabetes mellitus, and obesity, it is therefore possible for an association to exist between the two disorders.

It is important to diagnose metabolic syndrome to be able to identify the patients who need aggressive lifestyle modification focused on weight loss and enhanced physical activity, which are also the management options for XP.

In terms of blood pressure findings, previous studies have shown comparable results. Dey et al. reported that HTN was

Table 5. Receiver Operating Characteristic Curve (ROC) of Various Parameters for Predicting Metabolic Syndrome.

Parameters	Age (Years)	BMI (kg/m²)	Total lesions	TG levels (mg/dL)	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)	Duration of Onset (Months)
Area under ROC curve (AUC)	0.761	0.633	0.64	0.666	0.688	0.575	0.615	0.659	0.724
Standard Error	0.0656	0.0768	0.0697	0.0739	0.0727	0.0812	0.0803	0.0741	0.0683
95% CI	0.627 to 0.866	0.492 to 0.759	0.499 to 0.765	0.526 to 0.788	0.549 to 0.806	0.435 to 0.708	0.474 to 0.743	0.519 to 0.781	0.586 to 0.836
P-value	0.0001	0.0828	0.0447	0.0242	0.0096	0.3533	0.1525	0.032	0.0011
Cutoff	>41	>25.2	>1	>148.9	>173.9	>51.3	>141	>29.78	>12
Sensitivity (95% CI)	69.57% (47.1 - 86.8%)	69.57% (47.1 - 86.8%)	100% (85.2 - 100.0%)	56.52% (34.5 - 76.8%)	86.96% (66.4 - 97.2%)	52.17% (30.6 - 73.2%)	39.13% (19.7 - 61.5%)	56.52% (34.5 - 76.8%)	91.3% (72.0 - 98.9%)
Specificity (95% CI)	75% (56.6 - 88.5%)	56.25% (37.7 - 73.6%)	21.87% (9.3 - 40.0%)	75% (56.6 - 88.5%)	53.13% (34.7 - 70.9%)	78.12% (60.0 - 90.7%)	90.62% (75.0 - 98.0%)	71.87% (53.3 - 86.3%)	50% (31.9 - 68.1%)
PPV (95% CI)	66.7% (44.7 - 84.4%)	53.3% (34.3 - 71.7%)	47.9% (33.3 - 62.8%)	61.9% (38.4 - 81.9%)	57.1% (39.4 - 73.7%)	63.2% (38.4 - 83.7%)	75% (42.8 - 94.5%)	59.1% (36.4 - 79.3%)	56.8% (39.5 - 72.9%)
NPV (95% CI)	77.4% (58.9 - 90.4%)	72% (50.6 - 87.9%)	100% (59.0 - 100.0%)	70.6% (52.5 - 84.9%)	85% (62.1 - 96.8%)	69.4% (51.9 - 83.7%)	67.4% (51.5 - 80.9%)	69.7% (51.3 - 84.4%)	88.9% (65.3 - 98.6%)
Diagnostic accuracy	72.73%	61.82%	54.55%	67.27%	67.27%	67.27%	69.09%	65.45%	67.27%

Abbreviations: BMI: body mass index; CI: confidence interval; HDL: high-density lipoprotein; MS: metabolic syndrome; NPV: negative predictive value; PPV: positive predictive value; TG: triglyceride.

present in 37.7% and prehypertension in 8.77% of patients with XP [6]. Gondane et al. reported that hypertension was present in 30% (n=22) of patients with XP [4].

However, different studies have shown contrasting results when comparing the anthropometric parameters. Compared to our study, in which central obesity was seen in 42 (76.36%) patients, Gondane et al. reported similar results with waist circumference increased in 65.8% (n=48) of patients with XP [4]. However, Dey et al. reported that obesity was present only in seven out of 61 patients [6].

In the present study, the mean FBS level of study subjects were 105.1 ± 29.36 mg/dL. Elevated FBS levels were present in 17 (30.91%) patients.

Patients with XP are found to have lipid abnormalities in the range of 9.1% to 67.9% [8]. Serum lipids in patients with XP demonstrated increased LDL and VLDL levels and lower HDL cholesterol. This is an invaluable laboratory parameter for predicting CAD [5]. The mean value of TG levels, total cholesterol, LDL, VLDL, and HDL were comparable to the findings of Kavoussi et al. Reduced HDL was present in 24 (43.64%) and elevated TG levels in 21 (38.18%) patients. Kavoussi et al. found the mean serum cholesterol, triglyceride, and VLDL levels to be 221.51 mg/dl, 185.98 mg/dl, and 37.7 mg/dl, respectively, and the median value for HDL was 36.2 mg/dl. Hypertriglyceridemia (>200 mg/dl) was present in 30.9% of patients, and hypercholesterolemia (>220 mg/dl) was present in 45.2% of patients [13]. Almost comparable findings were seen by Gondane et al., who reported total cholesterol, LDL, VLDL, and TG levels to be increased in 63.01%, 71.2%, 20.5%, and 39.7% cases, respectively. HDL levels were decreased in 46.6%, which was similar to our study [4]. Gangopadadhya et al. reported increased cholesterol, TG, and LDL in 40% (of whom, 27.5% had cholesterol level >240 mg/dl), 22.5%, and >30% of patients, respectively. Reduced HDL was seen in 15% of patients [14]. A high ratio of cholesterol-to-HDL and low levels of HDL directly influence the atherosclerosis plaque formation. XP lesions are a dermatological sign for the screening of atherosclerosis at a subclinical stage [13].

Association With Metabolic Syndrome

XP is believed to be associated with dyslipidemia, MS, cardiovascular disease, diabetes, obesity, and insulin resistance [4].

We adopted 2006 IDF criteria for estimating MS as per which blood pressure, lipid profile, sugar levels, and obesity were taken into account. When compared to the patients without MS, those with metabolic syndrome had all the components of MS deranged except for a reduction in HDL. This holds importance since the presence of MS can have serious implications on the increase in CVD.

Overall, in the present study, MS was present in 23 out of 55 patients (41.82%). Similarly, Gondane et al. reported that MS was present in 45.2% of XP patients [4]. While comparing every component of MS, it was noted that other studies have also reported similar findings. Christoffersen et al. found that "Xanthelasma can predict the risk of ischemic heart disease, myocardial infarction, severe atherosclerosis and death, independently of the well-known cardiovascular risk factors" [15]. Mishra et al., Penalva et al., and Fallow et al. found that XP patients with DM, HTN, MS, and dyslipidemia have increased chances of developing CVDs [16-18]. However, while we found the association to be predominant in middle-aged individuals, possibly due to the higher prevalence of xanthelasma palpebrarum in this age group, it is worthwhile to note that metabolic syndrome is typically seen in older patients [19]. But a sex-based variation has been seen in the Asian population with advancing age. In males, the prevalence of metabolic syndrome has been reported to be highest during middle age as well as in older individuals, while in females, the prevalence has been found to increase with increasing age [19,20].

Limitations

The limitation of our study was that it was a single-center hospital-based study with a small sample size; therefore, the results might not be generalized to the population at a larger scale. Also, no control group was included in the present study, which might have reduced the statistical association for MS and its components.

Conclusion

Xanthelasma palpebrarum is a disease of middle-aged individuals with primarily a cosmetic concern. Therefore, the patient might not seek early treatment because of its asymptomatic nature and variable impact on the quality of life. Patients usually have accompanying deranged lipid profile, high BP recordings, high FBS levels, and obesity, making MS a significant association, as was seen in 41.82% of patients in the present study. Therefore, we recommend the monitoring for MS in all XP patients for early detection, prevention, and treatment of CVD and resulting mortality. The evaluation of metabolic syndrome should be especially undertaken in all middle-aged individuals who present even with a single lesion of XP of more than one year's duration.

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