Metabolic Profile in Xanthelasma Palpebrarum: An Observational Study

Dr. Darshini Gandhi[1*], Dr. Namrata Singh[2], Dr. Anushree Bangera[3], Dr. Sharmila Patil[4]

[1,2,3,4]Department of Dermatology, Venereology and Leprosy, Dr DY Patil Hospital, Navi Mumbai, Maharashtra.
[*]Corresponding Author: Dr. Darshini Gandhi, MBBS. Department of Dermatology, Venereology and Leprosy, Dr DY Patil Hospital, Ayyappa Temple Road, Sector 7, Nerul-400706, Navi Mumbai, Maharashtra.

ABSTRACT

Introduction: Xanthelasma Palpebrarum (XP) is a prevalent manifestation of cutaneous xanthoma, particularly affecting the eyelids. Its association with systemic conditions, including cardiovascular diseases, diabetes, and obesity, underscores its clinical significance. Despite its cosmetic impact, XP may indicate underlying systemic imbalances, necessitating comprehensive evaluation.

Aim and Objectives: To evaluate association between metabolic syndrome and Xanthelasma palpebrarum.

Materials and Methods: The study, conducted over 24 months, included 65 XP patients aged 25-80 years. Ethical approval was obtained, and participants provided written informed consent. Clinical examinations, anthropometric measurements, and laboratory investigations were conducted. Metabolic syndrome was assessed using NCEP ATP III criteria.

Results: The study revealed a skewed distribution towards females (82.5%) and middle-aged individuals (41–60 years). Higher BMI categories were prevalent, with a notable trend towards elevated BMI. Comorbid conditions included diabetes mellitus (34.5%) and hypertension (32.7%). XP duration varied, and bilateral, symmetric lesions were common (64%). Biochemical analysis showed significantly elevated total cholesterol and LDL cholesterol levels in XP patients.

Conclusion: XP, predominantly affecting middle-aged females, exhibited a strong association with lipid abnormalities, particularly elevated total cholesterol and LDL cholesterol.

Keywords: Metabolic Profile, Xanthelasma Palpebrarum (XP), Dermatology, Health Issues.

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INTRODUCTION

Xanthelasma Palpebrarum (XP) represents a specific manifestation of cutaneous xanthoma, primarily occurring on the eyelids and inner canthi. It stands out as the most prevalent form of cutaneous xanthoma and is known for its bilateral occurrence, with a tendency to be persistent, progressive, and symmetrical. The association of XP with systemic health issues such as cardiovascular diseases, diabetes, and obesity is well-documented, making it a condition of significant clinical interest [1]. The demographic distribution of XP shows a higher prevalence in middle-aged individuals, with a notable skew towards women. This gender disparity in XP incidence, combined with an age-related increase in occurrence, suggests the influence of hormonal and metabolic changes over time. [1,2].

Despite advances in dermatology, the exact etiology of XP remains elusive. However, various factors such as lipid abnormalities, hormonal influences, local factors, and macrophage activity is implicated in its development. Epidemiological data further illustrate the prevalence of XP, with a higher incidence reported in women (1.1%) compared to men (0.3%). [3]

The current study aims to explore the metabolic profile of individuals with XP, offering observational insights that could elucidate the systemic associations of this condition.

By establishing a clearer understanding of the metabolic profile associated with XP, healthcare providers can offer more holistic care.

AIMS AND OBJECTIVES

To evaluate association between metabolic syndrome and Xanthelasma palpebrarum.

MATERIALS AND METHODS

This study was initiated at the Department of Dermatology at a tertiary care centre after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from each patient prior to enrollment.

Our study is an observational cross-sectional study, aimed at examining the metabolic profile of patients diagnosed with Xanthelasma Palpebrarum (XP).

The study population comprised patients aged 25-80 years who were diagnosed with XP. The study spanned 24 months and included a total of 65 patients were selected from the Dermatology OPD, after assessing the inclusion and exclusion criteria. After explaining the purpose of the study, written informed consent was obtained from the patients followed by clinical examination and data collection.

Inclusion Criteria:

- Patients aged between 25-80 years.
- Patients of either gender (male/female).
- Patients diagnosed with Xanthelasma Palpebrarum.
- Patients willing to give informed consent and abide by the study procedure.

Exclusion Criteria:

- Patients outside the 25-80 age range.
- Patients not willing to give informed consent.

Sampling Method The sample size was calculated using the following formula:

n = Zα2 p q /L2,

This calculation resulted in a minimum sample size of 65 patient

Diagnostic and Data Collection Methods

Upon enrollment, each patient undergoes history taking and physical examination followed by clinical photography for documentation.

Anthropometric Measurements taken included Height (cm), Weight (kg), Body mass index (BMI) and Abdominal girth (cm) as well as blood pressure management.

- Laboratory Investigations: Fasting blood sugar and serum lipid profile.
- Metabolic Syndrome Assessment was done using the NCEP ATP III Criteria (three or more criteria confirm the diagnosis):

➢ Waist circumference of more than 102cm in men or more than 88cm in women
➢ Fasting triglyceride level of 150 mg/dL or higher
➢ Blood pressure level of 130/ 85 mm Hg or higher
➢ High density lipoprotein cholesterol (HDL- C) level of less than 40mg/dL in men or less than 50mg/dL in women
➢ Fasting glucose level of 100mg/dL or higher

Statistical Analysis: Descriptive statistics, including means, standard deviations, and percentage proportions, were used to describe baseline parameters of the study participants.

RESULTS

Our study's age-related findings in Xanthelasma Palpebrarum (XP) show that the most frequent occurrence of XP in our study was observed in the 41-50 and 51-60 age brackets, each capturing 32.31% of study subjects. However, there is a considerable frequency in the 31–40-year age range, accounting for 25% of study subjects. The incidence in the older age groups, 61- 70 and 71-80 years, comprised 6% and 4% in our study.

Table 1: Age distribution in cases

Range	Frequency (N=65)	Percentage (%)
31-40	16	24.61
41-50	21	32.31
51-60	21	32.31
61-70	4	6.15
71-80	3	4.62
Total	65	100

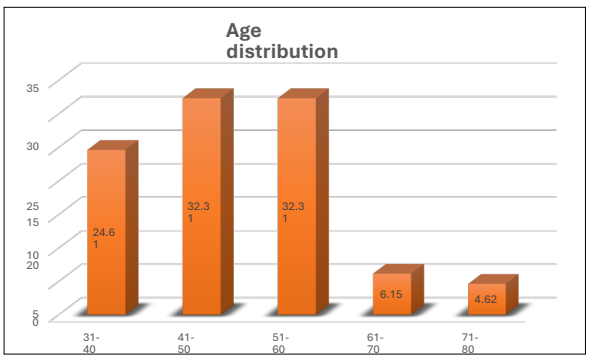

Figure 1: Age distribution in cases

In our study, the predominance of XP in females is notably high, with 82.5% of study subjects being

female.

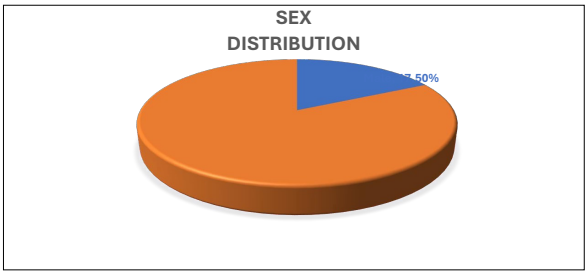

Figure 2: Sex distribution in cases

Bilateral lesions were present in 64% of patients. The frequency of unilateral lesions in our study was 36%, indicating an asymmetrical XP presentation. Thus, indicating variability in presentation.

None of the participants were underweight, and only a minor segment (12.31%) had a BMI within the normal range. The majority, 64.6%, were in the 'High Risk' category for BMI, and an additional 23.08% were classified as 'Higher High Risk', indicating a trend towards overweight and obesity.

Diabetes mellitus (DM) and hypertension (HTN) were the most prevalent comorbidities associated with XP, observed in 34.5% and 32.7% of study subjects respectively.

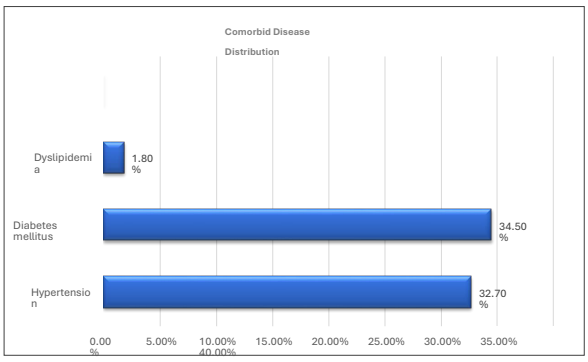

Figure 3: Distribution of Comorbid Disease

The occurrence of dyslipidemia in our study was significantly lower at 1.8%, suggesting it may be less commonly associated with XP. Additionally, the absence of hepatic disorders in our study group is notable.

There are higher cholesterol levels in XP study subjects in our study with mean value of 211.49 mg/dL. Our study reveals that 62% of XP study subjects had increased cholesterol levels with the mean cholesterol was notably higher in XP study subjects (211.49 mg/dL). The difference was statistically significant, with a p-value of 0.0036 underscoring a substantial link between elevated cholesterol levels and XP.

62% of XP study subjects had increased LDL levels. While our mean LDL range of 138 mg/dL, the significantly higher proportion of increased LDL levels in XP study subjects (p-value: 0.0085) indicated a strong association between elevated LDL cholesterol and XP.

Majority of both XP study subjects (70%) had normal HDL levels, with a smaller proportion having decreased levels. Interestingly, the mean HDL level was higher in XP study subjects (50.46 mg/dL) and this difference was not statistically significant.

Our data showed that 26% of XP study subjects had normal triglyceride levels. The mean triglyceride levels in our study were elevated in XP study subjects (190.02 mg/dL) However, this difference did not reach statistical significance, with a p-value of 0.3031 and a t-statistic of 1.0381.

We observed that 56% of XP study subjects had increased VLDL levels. The mean VLDL level in our XP study subjects was notably higher (33.31 mg/dL), with a p-value of 0.0015 and a t-statistic of 3.315, confirming the statistical significance of this difference.

Table 2: Lipid Profile in Individuals with Xanthelasma Palpebrarum.

Sr No.	Lipid Parameter		Frequency	Mean (mg/dl)	p-value	t-statistic
1.	Total Cholesterol (mg/dl)	Normal	25 (38%)	211.49	0.0036	10.25
		Raised	40 (62%)			
2.	LDL-Cholesterol (mg/dl)	Normal	25 (38%)	138.98	0.0085	2.72
		Raised	40 (62%)			
3.	HDL – Cholesterol (mg/dl)	Normal	45 (70%)	50.46	1	0.12
		Raised	20 (30%)			

4.	VLDL-Cholesterol (mg/dl)	Normal	30 (44%)	33.2	0.001509	3.3156
		Raised	35 (56%)			
5.	Triglycerides (mg/dl)	Normal	17 (26%)	190.02	0.3031	1.0381
		Raised	48 (74%)			

Among our patients, hypertension was prevalent in 21 individuals (32.70%), characterized by normal FBS levels (70-100 mg/dL) but significantly elevated BP (≥140/90 mmHg). In contrast, diabetes mellitus affected 22 patients (34.50%), who exhibited markedly high FBS levels (≥126 mg/dL) and moderately elevated BP (120/80 – 140/90 mmHg). The lone patient with dyslipidemia (1.80%) showed FBS levels within the range of 70-125 mg/dL and BP values between 120/80 and 140/90 mmHg. This distribution highlights that while hypertension and diabetes mellitus are common among these patients, they present distinct profiles in terms of FBS and BP. The total percentage of these conditions in the cohort was 67.69%, indicating a significant prevalence of metabolic and cardiovascular conditions. The range of FBS (70-250 mg/dL) and BP (120/80 to ≥140/90 mmHg) across the patients underscores the importance of monitoring these parameters for effective disease management and risk assessment.

Table no 3: Distribution of Comorbid conditions among cases

Condition	Frequency (n=44)	Percentage
Hypertension	21	32.70%
Diabetes mellitus	22	34.50%
Dyslipidemia	1	1.80%
Total	44	67.69%

DISCUSSION

Xanthelasma palpebrarum (XP) usually presents as asymptomatic single or multiple bilaterally symmetrical yellow plaques. Predominantly present over the medial canthus of eye, with upper eyelid more commonly involved as compared to lower eyelid with soft and velvety or calcareous in consistency with a tendency to coalesce. XP is considered to be a cutaneous marker for Cardiovascular diseases with disturbed lipid metabolism. It has shown association with hypertension, insulin resistance, diabetes mellitus, obesity and stroke. Metabolic syndrome represents a clustering of various abnormalities of metabolism that includes hypertension, central obesity, insulin resistance and atherogenic dyslipidemia.[4]

The recent focus on the role of acetylated LDL and macrophages with scavenger receptors highlights a complex interplay between systemic and local factors in the etiopathogenesis of XP [3,5]. XP's clinical presentation varies, ranging from soft to calcareous planar xanthomas on the eyelids. This variation in physical characteristics and the potential association with altered lipid profiles, particularly decreased levels of high-density lipoprotein cholesterol, underscore the importance of a comprehensive systemic evaluation in affected individuals. [6,7]

This study helps us conclude that there is a significant elevation in lipid profile in XP patients, therefore making lipid profile study mandatory for all patients.

The most frequent occurrence of XP in our study was observed in the 41-50 and 51-60 age brackets, each capturing 32.31% of study subjects, closely paralleling the observations by Chhetri et al., [8] who noted a peak incidence in the 40–50-year age group at 41.84%. This is slightly higher than the 30% prevalence reported by Gangopadadhya et al. [1] in the 31–40-year demographic, which Reddy et al. [9] also found to be the most affected age group. However, our study also underscores a considerable frequency in the 31–40-year age range, accounting for 25% of study subjects, which supports the notion that while XP is most prevalent in middle age, it can also affect younger adults.

In our study, XP in females is notably high, with 82.5% of study subjects being female, closely aligning with the findings of Nair et al., [10] who reported female affliction rates of 85.7% and 82%, respectively. While Sharma et al. [11] and Ozdol et al. [6] observed a slightly lower female predominance at 68% and 66%, there remains a clear gender disparity. The consistent observation of higher XP incidence among females across diverse studies suggests potential underlying factors such as hormonal influences, particularly estrogen, which is known to impact lipid metabolism and could contribute to gender-related susceptibility as well as possibility of a higher reporting frequency among females due to cosmetic concerns.

Bilateral lesions were present in 64% of our study subjects, which is comparatively lower than the 75.5% reported by Nair et al. [10] for upper eyelid involvement,

and it is marginally more aligned with the 62.8% upper lid involvement observed by Kavoussi et al. [12] The frequency of unilateral lesions in our study was 36%, which indicates that a considerable number of patients exhibit asymmetrical XP presentation. This is in contrast with Jain et al., [3] who found a high rate of multiple lesions and bilateral involvement in 72.7% of their subjects, suggesting that while bilateral presentation is common, unilateral involvement is not rare.

We found that none of the participants were underweight, and only a minor segment (12.31%) had a BMI within the normal range. The majority, 64.6%, were in the 'High Risk' category for BMI, and an additional 23.08% were classified as 'Higher High Risk', indicating a trend towards overweight and obesity. This finding is consistent with the observations of Epstein et al., [13] who reported a 51.4% obesity rate in XP patients, and Ribera et al., [14] who noted both a higher mean body weight and increased obesity frequency. Our results also show a more pronounced link with obesity compared to the 26.3% rate reported by Pedace et al. [15]

The comorbidities associated with XP, diabetes mellitus (DM) and hypertension (HTN) being the most prevalent, were observed in 34.5% and 32.7% of study subjects respectively. These findings echo those reported by Vacca et al., [16] who noted DM in 34.2% of patients and align closely with the incidence rates of HTN described by Gangopadadhya et al. [1] and Epstein et al., [13] who reported HTN in 32.5% and 28.6% of study subjects, respectively.

The occurrence of dyslipidemia in our study was significantly lower at 1.8%, suggesting it may be less commonly associated with XP than other systemic conditions. This contrasts with the broader spectrum of systemic diseases reported by Jain et al., where 42.4% of patients with XP had associated conditions like HTN, coronary artery disease (CAD), DM, and cholelithiasis, underscoring the potential diversity in comorbid profiles.

Additionally, the absence of hepatic disorders in our study group is notable, given Epstein et al.'s [13] report of cholelithiasis in 11.4% of study subjects, indicating variability in the manifestation of systemic diseases with XP. Other singular case associations like rheumatoid arthritis and acromegaly, as noted by Hossein Kavoussi et al., [12] were not seen in our study.

There is a notable trend indicating higher cholesterol levels in XP study subjects in our study with mean value of 211.49 mg/dL similarly the Sharma et al. [11] reported mean cholesterol levels of 201.2 mg/dL in his study, with a significant p-value, indicating a meaningful difference. Similarly, Dwivedi et al. [18] and Nair et al. [10] found significant differences, with 53.34% and 62.92% of XP study subjects. However, Kavoussi et al. [12] reported a lower difference with a non-significant p-value, suggesting a less pronounced relationship between XP and cholesterol in their study. Our study reveals that 62% of XP study subjects had increased cholesterol levels with the mean cholesterol was notably higher in XP study subjects (211.49 mg/dL). The difference was statistically significant, with a p-value of 0.0036 underscoring a substantial link between elevated cholesterol levels and XP.

Nair et al.[10] reported a significant difference, with 80.99% of XP study subjects showing elevated LDL levels compared to 35.16% in controls. Sharma et al. [17] and Akyuz et al. [19] both found significantly higher mean LDL cholesterol levels in XP study subjects (133.92 mg/dl and 142 mg/dl, respectively) compared to controls (91.68 mg/dl and 115 mg/dl). In our study, the distribution of LDL cholesterol levels also supported these findings, albeit with a different pattern. We observed that 62% of XP study subjects had increased LDL levels. While our mean LDL range of 138 mg/dL, the significantly higher proportion of increased LDL levels in XP study subjects (p-value: 0.0085) indicated a strong association between elevated LDL cholesterol and XP.

Majority of both XP study subjects (70%) had normal HDL levels, with a smaller proportion having decreased levels. Interestingly, the mean HDL level was higher in XP study subjects (50.46 mg/dL) and this difference was not statistically significant.

This pattern aligns with the results of studies by Dwivedi et al., [18] Sharma et al., [17] Nair et al., [10] and Akyuz et al.,[19] all of which reported no significant differences in HDL levels. On comparing of HDL cholesterol levels in XP, we observed a pattern largely consistent with other research in the field, which generally indicates no significant difference in HDL levels.

Our data showed that 26% of XP study subjects had normal triglyceride levels, in contrast with those of Dwivedi et al., [18] who reported a significant difference in triglyceride levels. In contrast, studies by Sharma et

al., [17] Kavoussi et al., [12] and Akyuz et al., [19] reported findings more in line with ours, where the differences in triglyceride levels between XP patients not statistically significant.

We observed that 56% of XP study subjects had increased VLDL levels. This finding is in concordance with Nair et al., [10] where the mean VLDL levels were significantly higher. Our results diverge from Dwivedi et al., [18] who reported that 16.67% of the subjects showed high VLDL, but this was not statistically significant.

CONCLUSION

Xanthelasma Palpebrarum (XP) predominantly affects females and is most commonly found in middle-aged individuals, particularly in the 41–60-year age group. A significant finding is the elevated levels of total cholesterol and LDL cholesterol in XP, highlighting a strong association between XP and lipid abnormalities. However, the study did not find a direct correlation between the severity or number of XP lesions and cholesterol levels. Additionally, the study notes a tendency towards higher body mass index in individuals with XP, underlining the importance of considering weight management in XP treatment. The prevalence of diabetes mellitus and hypertension as comorbid conditions was notable, while dyslipidemia was less common, suggesting variability in comorbid profiles. This study underscores the need for comprehensive clinical management of XP, taking into consideration its association with various metabolic risk.

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