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A Clinico-Demographic Study of Xanthelasma Palpebrarum at a Tertiary Care Centre with Special Reference to Its Association with Metabolic Syndrome

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ABSTRACT
Background - Xanthelasma palpebrarum (XP) is the most common type of xanthomamostly seen symmetrically near inner canthi of the eyelids.Metabolic Syndrome (MS) consists of a group of metabolic abnormalities that confer an increase of cardiovascular disease (CVD) and diabetes mellitus (DM). It consists of insulin resistance, central obesity, hypertension (HTN) &dyslipidemia.XP is often associated with hyperlipidemia, DM and low levels of high-density lipoprotein (HDL).We are conducting this study to document and analyse the clinico-demographic profile of XP and to find its association with MS.
Aims and objectives – To identify the clinico-demographic profile of xanthelasma palpebrarum and to find out its association with metabolic syndrome and its components.
Methods – This was a cross sectional study comprising of all consecutive patients of XP fulfilling inclusion and exclusion criteria over a period of one year. Demographic profile, history, clinical examination, fasting blood sugar levels and fasting lipid profile were noted. Metabolic syndrome was assessed in all patients using NCEP: ATPIII 2001 criteria.
Results – A total of70 patients were included in this period.The mean age of patients of XP was 39.18±11.0 years with female to male ratio - 2.68:1. The most prevalent age group was 31-40 years(41.4%).The mean age of onset was37.02 ± 11.01 years. XP was present bilaterally in 84.28% patients. The proportion of patients with MS among patients with XP was 52.8% and 90% patients were fulfilling atleast one criteria.
Conclusion - Xanthelasma palpebrarum was more commonly encountered between the age group of 31-40 years withfemale preponderance.The full-fledged metabolic syndrome was observed in more than half of patients.So, screening for the components of metabolic syndrome in patient with xanthelasma palpebrarum is very important to prevent the metabolic syndrome related complications.

KEYWORDS: Xanthelasma Palpebrarum, Metabolic Syndrome

I. INTRODUCTION

Xanthelasma palpebrarum (XP) is the most common type of xanthoma; characterized by soft, chamois-colored or yellowish-orange oblong plaques, mostly seen symmetrically near inner canthi of the eyelids about2 to 30 mm in length.[1]It is most commonly seen between the age of 30 and 55 years.[2]

Early childhood-onset of XP suggests hereditary lipid abnormality, especially familial hypercholesterolemia (FH) Type2.[1]The exact cause of XP is unknown but factors like lipid abnormalities, hormonal factors, local factors, and macrophages play a role in etiopathogenesis. Dyslipidemia is detected in 9.1% - 67.9% ofXP.[3]For every patient, a detailed history along

with the physical examination andbasic laboratory investigations like serum lipid profile, fasting bloodsugar (FBS) is necessary.[4]In normolipidemic XP lesions predominant lipid accumulation is cholesterylester. Since there is no evidence of intrinsic cellular cholesterol metabolism,its derangement might be due to enhanced uptake of increased levels ofoxidisedlow density lipoprotein cholesterol (LDLC), the increased plasmalipid peroxidation leading to accumulation of cholesterol in macrophages andformation of foam cells.[5]

Metabolic Syndrome (MS) consists of a group of metabolic abnormalities thatconfer an increase of cardiovascular disease (CVD) and diabetes mellitus(DM). It consists of insulin resistance, centralobesity, hypertension (HTN)&hyperlipidemia.[6]XP is often associated with components of MS like hyperlipidemia, DM and low levels of high density lipoprotein (HDL).[2]Since very few studies are conducted in India to find out the association of XP and MS, we conducted this study to document and analyse the clinico-demographic profile of XP and to find its association with MS. Hence, it will eventually help in making an early diagnosis of co-morbid conditions like coronary artery disease etc.

Criteria for metabolic syndrome[6]- NCEP: ATPIII 2001

Three or more of the following:

- Central obesity: waist circumference ≥102 cm (Male), ≥88 cm (Female)
- Hypertriglyceridemia: triglyceride (TG) level ≥150 mg/dL or on lipid loweringmedication.
- Low High density lipoprotein cholesterol (HDLC): <40 mg/dL and <50mg/dL for men and womenrespectively, or on lipid loweringmedication.
- Hypertension: blood pressure ≥130 mmHg systolic (SBP) or ≥85mmHg diastolic (DBP) or on antihypertensive medication.
- FBS level ≥100 mg/dL or on anti-diabetic medication or previously diagnosedtype 2 diabetesmellitus.

II. AIMS AND OBJECTIVES

1. To identify the clinico-demographic profile of xanthelasma palpebrarum.
2. To find out the association of metabolic syndrome and its components in patients with xanthelasma palpebrarum.

III. MATERIALS AND METHODS

Thiswas an Institution based cross-sectional study conducted at the out-patients Department (OPD) of Dermatology, Venereology & Leprosy (D.V.L.) at a tertiary care centre in Eastern India, with prior approval from the institutional ethics committee.Patients of all ages coming to the hospital on an out-patient basis with cardinal features of XP and executing written informed consent were included in the study.Duration of study was one year commencing from 1st April 2020 and concluding on 31st March 2021.A total 70 cases of XP were included in the study.

INCLUSION CRITERION

(i) All OPD patients presenting with XP.

(ii) Patient willing to execute informed written consent.

EXCLUSION CRITERION

(i) Patients who also have xanthomas at other sites of the body except XP.

(ii)Unwillingness to undergo investigation and comply follow up.

(iii)Patients who were on drugs that can cause dyslipidemia or hyperglycaemia or hypertension.

A proforma was filled for every patient comprising of personal details, clinical history, family history, examination findings and photographic records. Results were tabulated in a Grand Chart in Microsoft Excel Software [version Microsoft® Excel® 2019 MSO (Version 2109 Build 16.0.14430.20292) 64- bit and analysed. Data was presented by different tables, graphs, histograms, etc. Results of the clinical and investigation findings was analyzed to find out association of metabolic syndrome and its components in patients with XP.

IV. RESULT

A total of 70 patients presented with XP were recruited in the study. Prevalence of XP among total OPD patients in 1 year is 0.12%. The mean age of the patients was 39.18±11.0 years.The most prevalent age group was 31-40 years (n = 29, 41.43%), followed by 41-50 years (n = 15, 21.43%) then 21-30 years (n = 14, 20%). Majority of the patientshad an onset at the age of 31-40 years (40%)with the mean age of onset being 37.02 ± 11.01 years [Table 1]. Female to male ratio was 2.68:1. Majority of the study subjects belonged to sub-urban area (52.86%)followed by rural (37.14%) and urban area (10%).Majority of the study subjects belongs to lower class 56(80%).

Duration of XP was 1-5 years in 36(51.43%) and ≤1 year in 32(45.71%) patients.

While analysing the past history of significant illness, we found DM, HTN, thyroid dysfunction and dyslipidaemia in 8(11.43%), 5(7.14%), 3(4.28%) and 1(1.42%) patient respectively.

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In personal history of patients, high fat diet intake, high carbohydrate intake, nicotine addiction and alcohol addictionwas present in45(64.28%), 20(28.57%), 3(4.28%) patients and 1(1.42%) patient respectively. Among these patients, MS was found in 25, 7, 3 and 1 patient respectively.

In our study, the mean level of total cholesterol, serum TG, serum HDLC, serum LDLC and serum VLDL was 216.3 mg/dl, 177.01mg/dl, 58.75 mg/dl, 122.91 mg/dl and 37.81 mg/dl respectively. While the mean level of FBS level was 96.72 mg/dl.

The data regarding the number of XP patients with components of MS reveals that obesity was the commonest abnormality seen in 45 (64.28%)patients followed by hypertriglyceridemia in 37 (52.85%) patients, then low level of serum HDLC in 36 (51.42%) patients, then HTN in 34 (48.57%) patients and least common was high FBS level in 18(25.71%) patients [Table 2]

XP was present bilaterally in 59(84.28%) and unilateral in 11(15.72%) patients. Among these patients, 34 (57.63%) and 3 (27.27%) patients respectively were found to have MS.

The proportion of patients fulfilling the criteria of MS (NCEP: ATPIII 2001) among patients with XP in the present study was 52.86%.63(90%) patients in our study were fulfilling atleast one criteria of MS. [Table 3]

Age Group	Number	Percentage
≤10 years	0	0%
11-20 years	5	7.14%
21-30 years	15	21.43%
31-40 years	28	40%
41-50 years	13	18.57%
51-60 years	7	10%
61-70 years	2	2.86%
Total	70	100%
Mean age of onset	37.02 ± 11.01 years	

Table 1 : Age of onset of illness

Components		Total Patients	Number (n)	Percentage
WC (cm)	Male (≥102cm)	19	13	68.42%
	Female (≥88cm)	51	32	62.74%
	Total	70	45	64.28%
TG (mg/dl)	(≥150mg/dl)	70	37	52.85%
HDL (mg/dl)	Male (<50mg/dl)	19	10	52.63%
	Female (<40mg/dl)	51	26	50.98%
	Total	70	36	51.42%
BP (mmHg)	SBP (≥130mmHg)	70	33	47.14%
	DBP (≥85mmHg)	70	29	41.42%
	SBP or DBP	70	34	48.57%
FBS (mg/dl)	(≥100mg/dl)	70	18	25.71%

Table2 : Number of patients with each component of MS

[WC = Waist circumference, TG = Triglycerides, HDL = High density lipoprotein, BP = Blood pressure, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, FBS = Fasting blood sugar]

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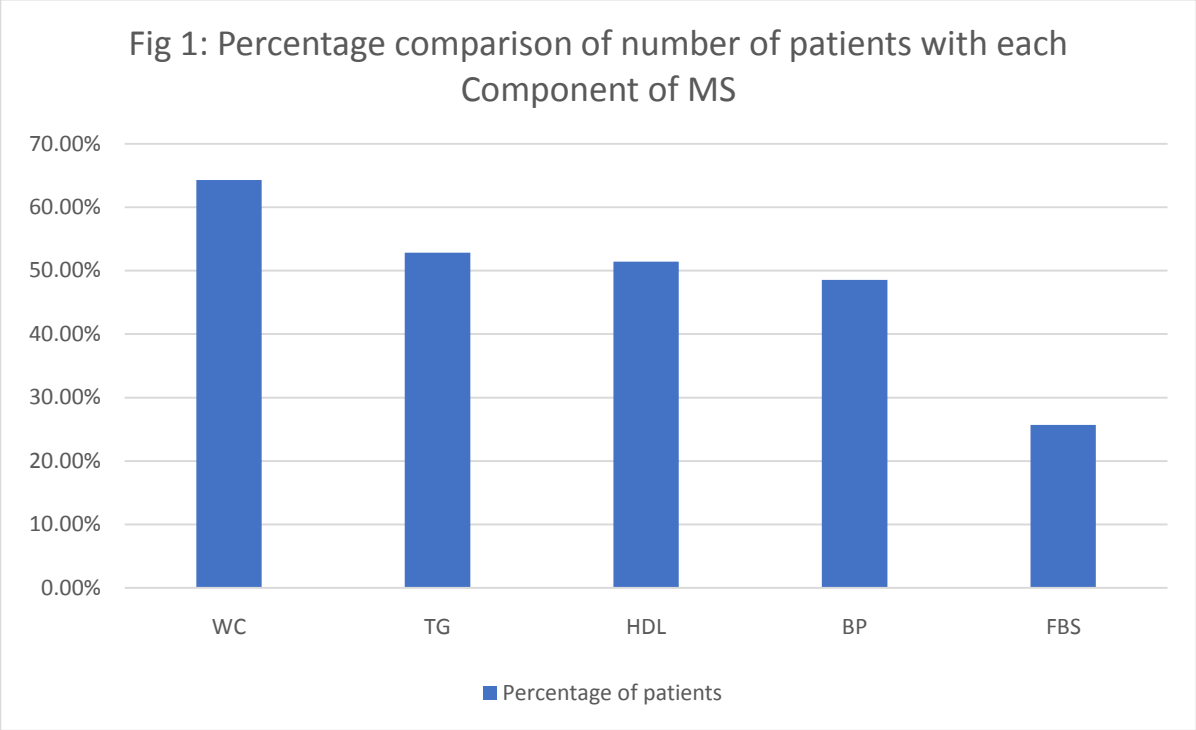
WC= Waist circumference, TG = Triglycerides, HDL = High density lipoprotein, BP = Blood pressure, FBS =



Fasting blood glucose

Metabolic Syndrome	Criteria fulfilled	Total	Percentage
No MS	0	7	10%
Pre MS - 1	1	17	24.29%
Pre MS - 2	2	9	12.86%
MS - Mild	3	16	22.85%
MS - Moderate	4	17	24.29%
MS - Severe	5	4	5.71%
Total		70	100%

Table3 : Metabolic syndrome (MS) criteria fulfilled by patients.

V. DISCUSSION

XP is a common manifestation of lipid abnormality, hormonal factors, local factors and macrophages, which usually appears most commonly in middle-aged females.[7]

Most studies have found increased LDL level and decreased HDL levels in XP cases. It is known to be associated with atherosclerosis, coronary artery disease (CAD), insulin resistance, DM, HTN, stroke, dyslipidemia and obesity. However, it is still unclear whether such lesions are markers of cerebrovascular disease (CVD) or MS.[8]

In our study, magnitude of patients suffering from XP was found to be 0.12%.In the study conducted by Jain et al,[4] 0.32% patients were suffering fromXP.The difference in the study is because majority of our study participants werefrom sub-urban and rural area, where patients are not much aware or bothered bythe disease itself.

In this study, the age of onset of XPrange from 16 to 65 years with a peak incidence in 4thand 5thdecades.Similarly, in study conducted by Nair PA et al,[9]the age of onset of XP ranged between 15 and 73 years, with a peak incidence in4th and 5thdecades.

In our study, there was female preponderance with female to male ratio being 2.69:1. This finding was in concordance withother studies where the ratio ranged from 2.07:1 to 4.43:1.[9,10]

While analysing the residential area of the study participants, we found thatmajority of the study subjects belonging to sub-urban area (52.86%), followed byrural (37.14%) and urban area (10%). The results in the study, conducted by NairPA et al,[9] shows occurrence in rural (55%) and urban area (54%).This findingsof ours, might be due to the fact that the institution is located in a sub-urban area.

While analysing the past history of significant illness, we found DM was themost prevalent (11.43%) followed by HTN (7.14%), thyroid dysfunction (4.28%)and dyslipidemia (1.42%).

However, in other studiesDM was reported in6% to 34.2% patients.[10-14]Previous history of HTN was seen in 26.7% to 37.7% patients in other studies.[10,11,12,15]

Furthermore, Dey A et al,[11] in their study revealed, Dyslipidemia in 60% cases,CAD in 6.56% of cases of XP. In the study, conducted by Jain A et al,[4] a total of42.4% of patients had associated systemicdiseases like HTN and DM.

In our study, there was family history of HTN in 17.14%,DM in 10%,XP in 5.71%, CVD in 4.28%, obesity in 4.28%, dyslipidemia in 2.85% and thyroid disorder in 1.42% patients.

Gangopadadhya et al.[10] reported Family history of HTN in 32.5%, XPin 27.5%, DM in 20%, heart disease in 20% and othertype of xanthoma in 2.5% of patients.

Duration of XP among study participants revealed that the majority of them(51.43%) were having the problem from 1 to 5 years. 45.71% of the patients werehaving XP from ≤1 year.This finding was similar to the study done by Reddy et al.[16] and Chhetri et al.[17]However, Jain A et al.[4] found majority of the patients (51.5%) had Xanthelasmaof <1 year duration.

In the present study we found that the lesion revealed majority of the patients(84.28%) had bilateral lesion. Patients with bilateral XP lesions had more prevalence of MS(57.63%) than patients with unilateral XP lesions (27.27%) but it was not found statistically significant.In other studies bilateral lesion was foundranging from39% to 76.72% patients.[4,8,11,12,14,17]

In our study, 48.57% patients were hypertensive. while increased SBP wasnoted in 47.14% and DBP in 41.42% XP patients.Dey A et al.[11]reported, HTN was found in 37.7% of XP cases.

In the current study, increased FBS is noted in 25.71% XP patients.While in other studies DM was found in variable number of patients ranging from 6% to 34.2%.[11,13,14]

In the current study,the level of total cholesterol wasincreased in 52.85% patients. There was decreased HDLC level in51.42% XP patients. Serum TG was also increased in 52.85% XPpatients; while Serum VLDL was increased in 48.6% XP patients.

Altered lipid levelswere seen in 50% to 60.6% of patients with XP inother studies.[4,16,18,19,20]Increased TG value in XP patients have been observed byGangopadadhyaet al.[10], Epstein et al.[15] and Kahán et al.[21] in 22.5%, 47% and 18.18% respectively.

GondaneS et al.[8] reported that the TG level was increased in 63% cases.They found increased LDLC levels in 71.2% cases. They also reported adecrease in HDLC in 46.6% cases; VLDL cholesterol was increased in 20.5% cases.Increased VLDL levels were also observed in other studies in XP patients.[3,4,22]

In our study, the mean level of total cholesterol, serum TG, serum HDLC, serum LDLC and serum VLDL was 216.3 mg/dl, 177.01mg/dl, 58.75 mg/dl, 122.91 mg/dl and 37.81 mg/dl respectively.

While Jain A et al.[4] reported increased mean cholesterol level to be 216.8mg/dl in XP cases. Likewise, the mean TG level (170.4mg/dl), LDL (mean=134.4mg/dl) and VLDL (mean=34.0mg/dl) too were higher in XP. Mean Serum HDL levels in XP patients was 40.5mg/dl.[4]

The prevalence of MS among XP patients was 52.86% in the present study which is slightly higher than study conducted by GondaneS et al.[8]whoreported MS was present in 45.2% in XP patients.In India, age adjusted prevalence of Metabolic syndrome was found to be approximately 25%.[23]In a community based study done in 2018-19 inthe state where current study was conducted, prevalence of metabolic syndrome was 32.8%.[24]

Among these 37 XP patients with MS, 16 (43.24%) were found to have 3 criterias, we labelled them in mild MS, 17 (45.95%) were found to have 4 criterias, we labelled them in moderate MS and 4 (10.81%) were found to have 5 criterias, we labelled them in severe MS.

In other 33 XP patients without MS, 17 were found to have 1 criteria, we labelled them in pre MS 1 and 9 were found to have 2 criterias, we labelled them in pre MS 2. 7 patients were found to have No MS (criteria 0).

From the above observation at the end of the study, it can be said that, one criteria of MS was fulfilled by 63 (90%) of the study participant while remaining 7 (10%) did not met any criteria of MS.

VI. CONCLUSION

At the end of the study, we come to the conclusion that:

1. Xanthelasma palpebrarum was more commonly encountered between the age group of 31-40 years with more frequent involvement of females.
2. Bilateral lesions were more commonly encountered and upper inner canthi were more frequently involved.
3. In the present study, the full-fledged metabolic syndrome was observed in more than half of patients. Only 10% of the patients had no components of metabolic syndrome.

Hence, we concluded that screening for the components of metabolic syndrome in patient with xanthelasma palpebrarum is very important to prevent the metabolic syndrome related complications.

VII. LIMITATIONS

1. Due to lack of facilities apolipoprotein E (E11:E111) {a secretory glycoprotein involved in the transport and redistribution of lipid between tissue-which is associated with an increased risk of atherosclerosis} could not be assessed.
2. Occurrence of the components of metabolic syndrome among non-xanthelasma individuals of similar age, sex and socio-economic status needs to be determined in order to substantiate the significance of the association of xanthelasma palpebrarum with metabolic syndrome.

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