

URIC ACID IS ASSOCIATED WITH BOTH, XANTHELASMATA AND DYSLIPIDEMIA

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ABSTRACT

Objective: To assess the association of uric acid with both, xanthelasma and the fasting blood lipids.

Material and Methods: This cross-sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar, Pakistan from January 2015 to July 2016 and included 60 cases with xanthelasma palpebrarum (XP) as the study group, and 60 age and sex matched individuals without xanthelasma palpebrarum (WXP), as the control group. Each participant had his/her fasting lipid profile determined, along with serum uric acid. The data was analyzed using SPSS version 16. Independent t-test and Pearson correlation tests were applied.

Results: The values of uric acid, fasting total cholesterol, LDL-C and TGs were higher, and HDL-C lower, in the XP group, than in WXP group, ($P < 0.001$). Serum uric acid correlated positively with serum total cholesterol, triglycerides and LDL-C ($P < 0.001$), and negatively with HDL-C, ($P < 0.001$). Moreover, fasting cholesterol level was higher in XP group ($M=208.32$, $SD=17.135$), than WXP group ($M=177.28$, $SD=8.203$), at a statistically significant level of, $t(84.69) = 12.65$, $P < 0.001$, Cohen's $D=2.31$.

Conclusion: Serum uric acid is higher in subjects with xanthelasmata. Moreover, serum uric acid has a positive correlation with both; LDL-c and TGs, but an inverse relation with HDL-c.

Key Words: xanthelasma palpebrarum, dyslipidemia, uric acid, atherosclerosis.

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INTRODUCTION

Xanthelasma palpebrarum is the most common cutaneous marker of an underlying lipid disorder. Approximately 50% of the patients with xanthelasma palpebrarum are hyperlipidemic.¹ As hyperuricemia is a component of metabolic syndrome, and the presence of both hyperlipidemia and hyperuricemia increases the chances of atherosclerotic heart disease.²

Xanthelasma is a discrete yellowish deposit of fat underneath the skin, mostly on or around the eyelids. There is a genetic component to the presence of xanthelasmata, and their mere presence is not sufficient to diagnose or predict an underlying lipid disorder.³

However, if the subject lacks a family history of xanthelasmata, the odds of underlying hypercholesterolemia increase remarkably.¹⁻³ Xanthelasmata are in-fact, the cutaneous manifestations of lipidosis in which lipids accumulate in foam cells within the skin, and are often associated with hyperlipidemias, of both primary and secondary types.⁴

Serum uric acid level has been linked with hyperlipidemia, and is considered as a component of metabolic syndrome.⁴ The coexistence of both hyperlipidemia and hyperuricemia increases the odds of atherosclerosis along with other risk factors like hypertension and obesity etc.⁵ Although, XP is a benign lesion causing no functional disturbance, it is a dermatological problem with a cosmetic concern.⁶

As is true of our setup, most of the patients with XP, do not have their lipid profile checked, routinely. Therefore, there was a need to know, whether routine assessment of the lipid profile in these cases is essential or not? Similarly, even if serum lipid profile is checked in people with xanthelasmata, their uric acid is usually not measured. Therefore, the current study was undertaken to document the frequencies of both, hyperlipidemia and hyperuricemia in subjects with xanthelasma palpe-

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brarum, and to evaluate an association between serum uric acid and the blood lipids.

MATERIAL AND METHODS

This was a cross-sectional, observational study conducted in the Department of Medicine of Khyber Teaching Hospital, Peshawar, from January 2015 to July 2016. This study was approved by the ethics review committee of the hospital. An informed written consent was obtained from every participant. The study group comprised of sixty subjects with clinically visible xanthelasma palpebrarum (XP) called as, the XP-group. For the sake of diagnostic clarity, an expert opinion was sought from a senior dermatologist, for every participant of the XP group. For the purpose of comparison, another group consisting of sixty age and sex matched individuals, without xanthelasma palpebrarum (WXP), was included as the control group.

All the patients included in the final study were recruited from the medical outpatient department, and were admitted, either to the department of medicine or dermatology, for the purpose of detailed clinical evaluation, and essential laboratory tests. Serum fasting cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and serum uric acid was measured for every participant, after an overnight fast. Fasting serum uric acid in the range of 2.5-6.5mg/dl was taken as normal. Similarly, fasting TGs in the reference range of 100-150mg/dl were regarded as normal. For fasting serum cholesterol, LDL-C and HDL-C, the optimal values were; <200mg/dl, <150 mg/dl and > 45mg/dl, respectively.

The inclusion criteria included; any gender or racial background, and age more than 18 years. Subjects with previous history of lipid or uric acid disorders, or on any lipid or uric acid lowering therapy were excluded from the study. Patients with co-morbidities such as, hypo or hyperthyroidism, nephrotic syndrome, current or ex-smokers, alcoholics, patients who used steroid therapy in the preceding one month, and females on any oral contraceptive pills, were excluded from the study. The data was obtained on a structured questionnaire specifically designed for this purpose including; the demographic data, previous medical/surgical history, history of medications (current or previous), list of co-morbidities and so forth.

The data was analyzed using SPSS version 16. Descriptive statistics' were applied to calculate the frequencies and percentages of hyperuricemia and hyperlipidemia in both the groups. The independent student t-test was used to compare the means of blood lipids and uric acid levels between the XP, and WXP groups. Lastly, Pearson correlation test was used to assess any association between fasting lipids and uric acid in the XP group.

RESULTS

This study included 60 participants in the xanthelasma palpebrarum (XP) group, and an equal number of age and sex matched individuals in without xanthelasma palpebrarum (WXP), group. Of the 60 participants in XP group, 53.3% were males, and 46.7% females. The WXP group comprised of 55% male, and 45% female population. Mean age of the subjects was 45 and 44

Table 1: Descriptive statistics of the fasting cholesterol, LDL, HDL, TGs and uric acid, outside the given normal cut-off points

Variable	Cut-off point	Percentage		P Value
		XP group	WXP Group	
Total Cholesterol	>200mg/dl	54%	1.7%	<0.001
LDL	>150mg/dl	54%	Approx 1.7%	<0.001
HDL	<45md/dl	31%	1.7%	<0.001
TGs	>150mg/dl	67%	5%	<0.001
Uric Acid	>6.5mg/dl	56%	Approx 3.3%	<0.001

Table 2: Independent t-test statistics

	Group	N	Mean	Std. Deviation	P Value
Total Cholesterol	XP	60	208.32	17.135	< 0.001
	WXP	60	177.28	8.203	< 0.001
LDL	XP	60	154.12	11.706	< 0.001
	WXP	60	132.20	6.446	< 0.001
HDL	XP	60	51.40	7.026	< 0.001
	WXP	60	60.75	3.419	< 0.001
TGs	XP	60	159.47	10.400	< 0.001
	WXP	60	130.10	8.046	< 0.001
Uric Acid	XP	60	6.61	.633	< 0.001
	WXP	60	5.61	.309	< 0.001

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Table 3: Pearson's correlation between serum uric acid and the fasting blood lipids

Uric Acid	Statistics	Total Cholesterol	LDL-C	HDL-C	TGs
	r value	0.95	0.95	-0.94	0.93
	P value	<0.001	<0.001	<0.001	<0.001

years (standard deviation ± 8.8 and ± 9.1) in the XP, and WXP groups, respectively. Fifteen percent of the patients in the XP group had a positive family history for xanthelasmata against 1.7% in the WXP group. Sixty percent of our participants in XP group had multiple xanthelasmata, and most of them (65%) were yellowish grey in color descriptive statistics of cholesterol and uric acid is shown in Table 1.

An independent student's t-test was run to compare the mean values of fasting lipid profile, and uric acid among the XP, and WXP groups. For fasting total cholesterol, levene's test for equality of variance was statistically significant, $P < 0.001$. Results indicated that fasting cholesterol level was higher in XP group ($M=208.32$, $SD=17.135$), than WXP group ($M=177.28$, $SD=8.203$) at a statistically significant level of $t(84.69)=12.65$, $P < 0.001$, Cohen's $D=2.31$. The results of independent t-test (Table 2), revealed a statistically significant difference between the values of fasting total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and uric acid (UA), between the participants with xanthelesma palpebrarum (XP group), and those without it (WXP group). It is worth noting that the values of uric acid along with fasting total cholesterol, LDL-C and TGs were statistically higher in the XP group. This was in sharp contrast to HDL-C, which was higher in the WXP group.

The Pearson's correlation test showed a statistically significant positive correlation of uric acid with fasting total cholesterol, LDL-C and TGs in the XP group. However, there was a strong negative correlation between uric acid and HDL-C Table 3.

DISCUSSION

Xanthelesmata which is rare in the general population with reported variable incidence of 0.56-1.5% is derived from the Greek word, "xanthos" (yellow) and "elasma" (beaten metal plate).¹⁰⁻¹¹

This most common cutaneous xanthoma, which represents a localized cutaneous phenomenon, may often signify a systemic hyperlipidemia and is associated with elevation of LDL, as is seen in pure hypercholesterolemia (such as FH) or Type III hyperlipoproteinemia.¹² In our study, vast majority of patients with xanthelasma palpebrarum had evidence of hyperlipidemia. The commonest abnormality seen was the mixed-type hyperlipidemia.

Xanthelasmata; usually, occur as bilateral symmetrical yellow plaques; often, near the medial canthus of the upper eyelid.¹²⁻¹³ Majority of subjects in our study had bilateral yellowish plaques. However, they were not symmetrical and were seen around both the medial canthus and the upper lateral eyelid.

This disorder typically presents in third to fifth decade of life, with an incidence of 1.1% in women and 0.3% in men. Incidence before age 40 can be an indication of familial hypercholesterolemia (FH).¹⁴ It is worth mentioning that, the mean age of patients with XP in our study group was 45 years, which is consistent with previous observations. Moreover, considering the increased incidence of dyslipidemia and hyperuricemia in the XP group, a higher risk of atherosclerosis in people with xanthelesma can be assumed.¹⁴⁻¹⁵

The definite etiology needs to be elucidated yet, but a list of different diverse factors such as lipid abnormalities, hormonal disorders, local factors, and macrophages are attributed to play a role in its etiopathogenesis. Histologically, xanthelasma is composed of foamy histiocytes, laden with intracellular fat deposits called as, xanthoma cells. These cells are primarily located within the superior reticular. dermis.^{13,14} The main lipid constituent that is deposited in both the hyperlipidemic and normo-lipidemic xanthelasmas is esterified cholesterol.¹⁵

Xanthelesma palpebrarum can run in the families.^{12,15} Fifteen percent of our patients in the XP group had a positive family history for xanthelasmata which is comparable with a study done by Jain et al.¹⁶ However, other studies showed a lower incidence.¹⁷ Sixty percent of our participant in XP group had multiple xanthelesma in contrast to 91% of the cases reported by Jain et al.¹⁶

Xanthelesma palpebrarum can be associated with other systemic diseases apart from hyperlipidemia.¹⁶⁻¹⁷ In our study the mean values of uric acid and total cholesterol along with LDL and TGs were remarkably higher in the XP group, in comparison to the WXP group. Similar studies done in the past showed an association of xanthelasmata with systemic diseases like hypertension, cardiovascular disease, diabetes, cholelithiasis and hyperuricemia.^{7,18}

Although, our study demonstrated a significant association of serum uric acid with both xanthelasmata and dyslipidemia, one of the limitations was a relatively smaller sample size. Secondly, the association between

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xanthelasmata and dyslipidemia has been established previously. Nevertheless, our study showed novelty by demonstrating a significant link between uric acid and both, xanthelasmata and dyslipidemia.

CONCLUSION

Serum uric acid has a significant association with both, xanthelasmata and dyslipidemia.

RECOMMENDATIONS

It is recommended that, people with xanthelasmata should not only be screened for dyslipidemia, but for hyperuricemia also.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Khan WM: Main idea.
Khan A: Data collection.
Khan M: Bibliography.
Ayub M: Follow-up.
Rashid A: Critical review.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.