Prevalence of metabolic syndrome and its relationship with mucosal involvement in lichen planus: an observational study

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Background: Lichen planus (LP) is a chronic inflammatory disorder involving the skin, mucosa, hair, and nails. Previous reports have shown a possible association between LP and metabolic derangement, leading to increased cardiovascular risk among these patients. Our study aimed to assess the prevalence of metabolic syndrome (MetS) and its components in LP patients and to study their relationship with mucosal involvement in LP.

Methods: We conducted a cross-sectional observational study of 123 LP patients. Demographic and clinical data were obtained, and evaluation was done for the presence of abdominal obesity, hypertension, hyperglycemia, and dyslipidemia. MetS was diagnosed according to the modified National Cholesterol Education Program: Adult Treatment Panel III (NCEP-ATP III) criteria for the South Asian population. Data analysis was done using appropriate statistical methods.

Results: The prevalence of MetS in LP patients was 31%. The mean age of LP patients having MetS was considerably higher than those without MetS (44.8 ± 13.6 vs. 33.3 ± 15.9 years; $P = 0.0002$). Although statistically insignificant, female patients and patients with mucosal involvement showed a higher prevalence of MetS. Central obesity, hypertension, hyperglycemia, and hypertriglyceridemia were more prevalent in mucosal LP patients than in those without mucosal lesions, with hyperglycemia having a significantly higher prevalence in mucosal LP (41% vs. 18%; $P = 0.015$).

Conclusion: Increased age, female gender, and mucosal involvement are important predictors of concurrent metabolic derangement in LP patients. Thus, these patients should be screened for the presence of MetS and its components.

Keywords: metabolic syndrome, hyperglycemia, obesity, hypertension, lichen planus, India

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INTRODUCTION

Lichenoid disorders are inflammatory dermatoses characterized clinically by papules and plaques and histologically by a band-like lymphocytic infiltrate in the papillary dermis [1]. Lichen planus (LP), the prototype of lichenoid dermatoses, is a chronic disorder of unknown etiology involving the skin, mucosa, and appendages. It affects about 0.5–1% of the population worldwide and is characterized by pruritic, violaceous, flat-topped papules and plaques [2,3]. It is believed to represent a T-cell-

mediated inflammatory response. This chronic inflammatory process and oxidative stress induction seen in LP may be linked to the development of metabolic derangement [4-6]. An association between LP and metabolic disorders has been reported in multiple studies worldwide [7-19].

Metabolic syndrome (MetS) refers to a cluster of abnormalities that increase the risk of morbidity and mortality from cardiovascular disease and diabetes [20]. The prevalence of MetS and its relationship with LP varies widely in published studies. In India, data on metabolic derangement in LP patients are scarce, with only a few of the related studies originating from eastern India. Our study was designed to assess the prevalence of MetS and its components in LP patients and to study their relationship with mucosal involvement in LP.

MATERIALS AND METHODS

This was a hospital-based cross-sectional observational study conducted at a tertiary care center in eastern India. All consecutive patients with a clinical diagnosis of LP, confirmed by histopathological examination wherever necessary, were selected from patients attending the dermatology outpatient department over a period of one year, starting from 1st March 2018. Based on the inclusion and exclusion criteria, a total of 123 patients were enrolled in the study after informed consent. The inclusion criteria for cases included new patients with clinical and/or histopathological diagnosis of classical or any morphological variant of LP. Patients on treatment or previously treated for LP, pregnant patients, and severely ill patients were excluded from the study.

Demographic and clinical data pertaining to age, gender, duration of illness, sites of involvement, and known history of hypertension, diabetes, or hyperlipidemia were obtained from the enrolled patients using an interviewer-administered questionnaire. The patients were clinically examined for morphological type of LP and mucosal involvement, including oral as well as genital lesions. Hair and nail involvement was also noted. Waist circumference was measured at the level of the umbilicus using a tape measure. Blood pressure (BP) was measured in the arm using a sphygmomanometer at least 15 minutes after rest in the sitting posture. Venous blood samples were collected after overnight fasting for 12 hours for estimation of fasting blood sugar (FBS) by the hexokinase method and serum triglyceride (TG) and serum high-density lipoprotein cholesterol (HDL-C) by enzymatic methods. MetS was diagnosed based on National Cholesterol Education Program: Adult Treatment Panel III (NCEP-ATP III) criteria with a modification in the criteria for central obesity for the South Asian population (including Indians), as shown in Table 1 [21,22]. Patients satisfying three or more of these criteria were diagnosed with MetS.

All data were tabulated in a Microsoft Excel sheet and statistically analyzed using the same software. Numerical variables were computed as mean and standard deviation, while categorical data were described through frequencies and percentages. For inferential statistics, we used t-tests and chi-squared tests for intergroup comparisons of continuous and categorical variables, respectively. *P*-values of less than 0.05 were taken as statistically significant.

The details of the study were discussed with all patients, and written informed consent was obtained from the participants. Ethical approval for the study was obtained from the Clinical Research Ethics Committee of the institution.

RESULTS

One hundred and twenty-three patients participated in this study. There were 57 (46%)

Table 1. Modified National Cholesterol Education Program: Adult Treatment Panel III criteria for diagnosis of metabolic syndrome

Central obesity	**Waist circumference** **≥ 90 cm for men** **≥ 80 cm for women**
Hypertension	Blood Pressure ≥ 130/85 mmHg or specific medication
Fasting blood sugar	≥ 100 mg/dl or specific medication or previously diagnosed type 2 diabetes
Serum triglyceride	≥ 150 mg/dl or specific medication
Serum high-density lipoprotein cholesterol	< 40 mg/dl in men < 50 mg/dl in women or specific medication

males and 66 (54%) females, with a male-to-female ratio of 1:1.16. The mean age of the patients was 36.9 ± 16.1 years. Most patients (41%; n = 51) were in the age group of 40–59 years. The duration of LP in the patients ranged from 1 to 144 months, with an average duration of 18.3 ± 25.7 months.

Among the study subjects, 89 patients (72%) had skin LP, 19 (16%) had mucosal LP, and 15 (12%) had both skin and mucosal involvement. Also, 13 patients (11%) showed nail involvement. The most common morphological was classical LP in 75 patients, followed by hypertrophic LP in 9 patients. Among the 28 patients with oral lesions, 23 had reticular, 4 had erosive, and 1 had plaque-like oral LP. Seven out of the eight patients with genital lesions had erosive LP, while one had annular LP.

Thirty-eight (31%) of the patients enrolled were found to have MetS. The prevalence among females was 35% as compared to 26% among males (P = 0.410). Table 2 compares various characteristics between LP patients with and without MetS. The mean age of LP patients having MetS was substantially higher than those lacking MetS (44.8 ± 13.6 vs. 33.3 ± 15.9 years; P = 0.0002). Prevalence was maximum in the age group of 50–59 years, while none of the patients below 20 years of age had MetS (Figure 1). Also, 41% of the patients with mucosal involvement had MetS as compared to 27% of those without any mucosal lesions (P = 0.191).

The LP patients with MetS showed a shorter mean duration of lesions and a higher prevalence of mucosal and nail involvement as compared to those without MetS. However, the P values were not significant in any of these cases.

Among the patients with MetS, the most common morphology of skin lesions was classical LP, followed by LP pigmentosus (Table 3). The

Table 2. Comparison of characteristics between lichen planus (LP) patients with and without metabolic syndrome (MetS)

	MetS Present (n = 38)	MetS Absent (n = 85)	*P*-value
Mean age ± SD (years)	44.8 ± 13.6	33.3 ± 15.9	0.0002
Mean duration of LP ± SD (months)	13.0 ± 15.2	20.7 ± 29.0	0.129
Oral lesions	13 (34%)	15 (18%)	0.073
Genital lesions	3 (8%)	5 (6%)	0.702
Nail involvement	6 (16%)	7 (8%)	0.346

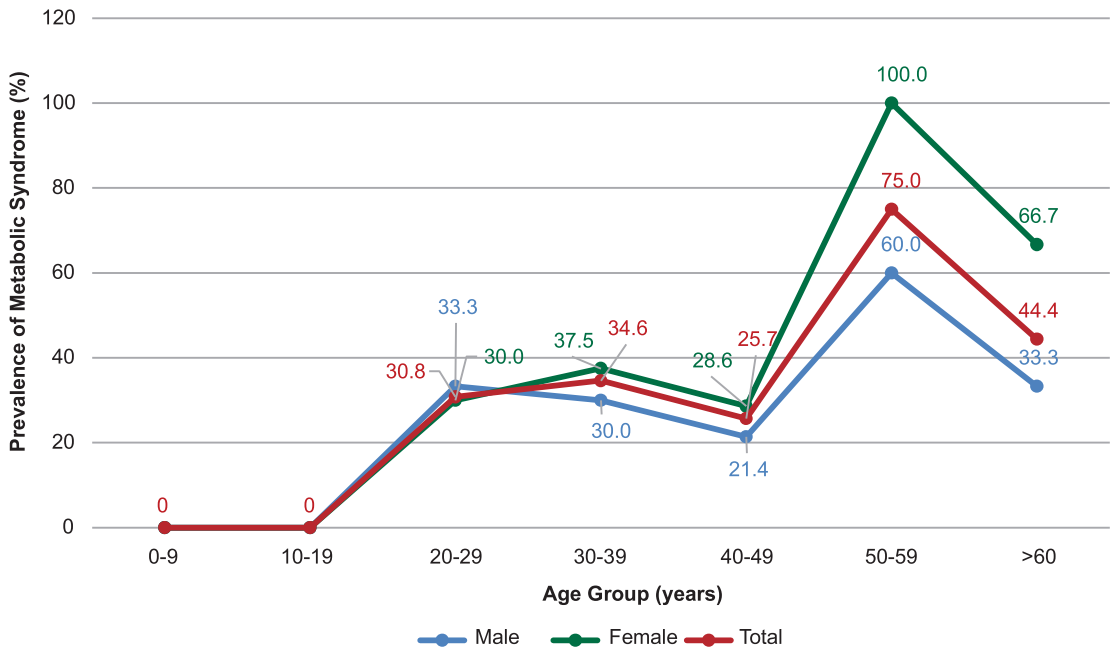

Figure 1. Line chart showing the age-specific prevalence of metabolic syndrome in the study population.

Table 3. Types of lichen planus (LP) in patients with metabolic syndrome

Type	Frequency (%)
Skin lesions (n = 32)	
Classic	27 (84)
Hypertrophic	1 (3)
LP Pigmentosus	3 (9)
Linear	0
Actinic	0
Bullous	1 (3)
Annular	0
Follicular	0
Oral lesions (n = 13)	
Reticular	10 (77)
Erosive	2 (15)
Plaque-like	1 (8)
Genital lesions (n = 3)	
Erosive	3 (100)
Annular	0

predominant type of oral LP in this group was the reticular type. Three patients with MetS had genital lesions, and all three had erosive LP.

The most prevalent component of MetS observed was central obesity in 77 patients (63%), followed by hypertension in 39 patients (32%). Central obesity, hypertension, elevated FBS, and low HDL-C were more prevalent in females, with the latter showing statistical significance ($P = 0.007$) (Figure 2). All the parameters of MetS, except low HDL-C, were more prevalent in LP patients with mucosal involvement than in those without mucosal lesions. The prevalence of elevated FBS was notably higher in patients with mucosal involvement (41% vs. 18%; $P = 0.015$) (Figure 3).

DISCUSSION

LP is a common, chronic inflammatory papulo-squamous disorder encountered in dermatological practice. Although its etiopathogenesis is not well understood, several potential pathogenetic mechanisms have been proposed, indicating that LP may serve as a reliable external marker of underlying immune and metabolic dysfunction [4,6,23,24].

Our study was conducted on 123 patients of LP attending the outpatient department in a tertiary care hospital in eastern India. Females outnumbered males to a small extent, with the maximum number of patients aged 40–59 years. These findings were comparable to most other Indian studies, such as those by Garg *et al.* and Ireddy *et al.* [3,23]. Morphologically, the predominant type of skin lesion was classical LP, and the predominant type of oral lesion was the reticular type. Similar findings have been reported by other authors [15,17].

The prevalence of MetS in the general population in various parts of India ranges from 11% to 41% [25]. A large community-based survey from eastern India reported the prevalence to be 33.5%

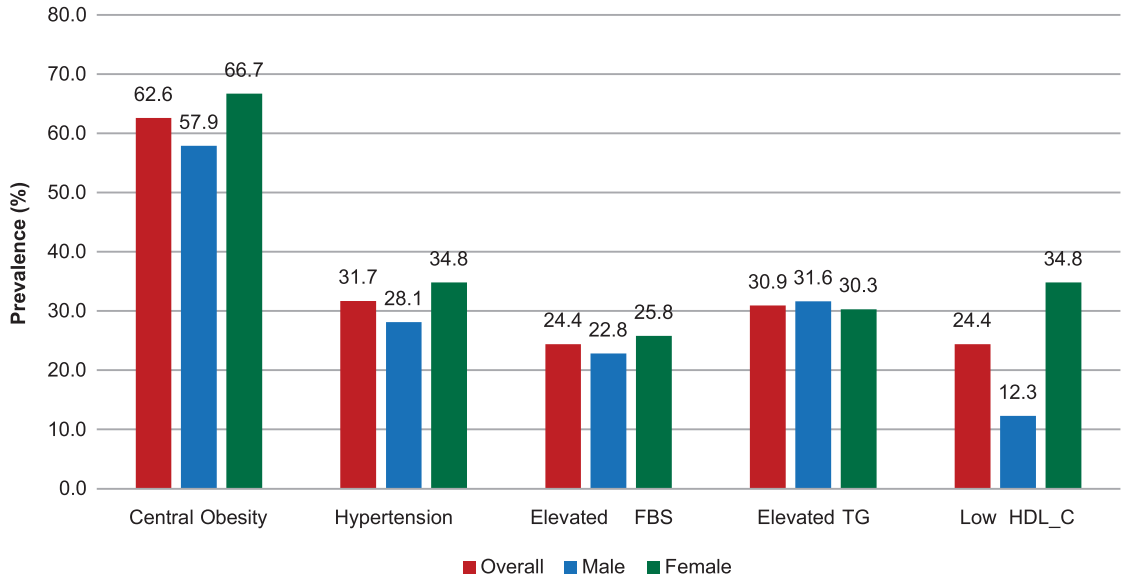

Figure 2. Bar graph showing the prevalence of metabolic syndrome parameters in the study population (FBS: Fasting Blood Sugar; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol)

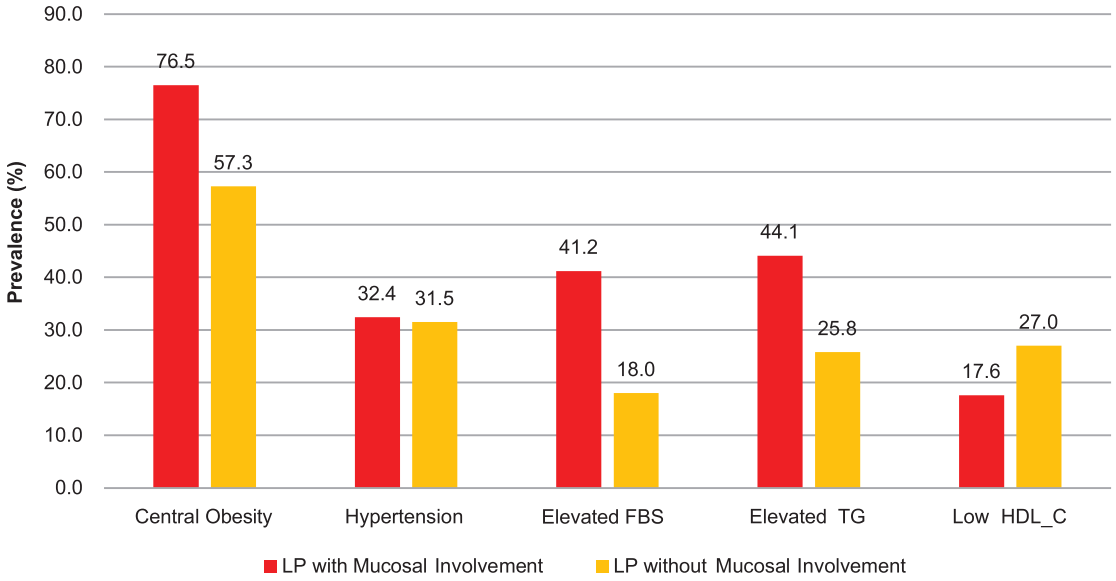

Figure 3. Bar graph showing prevalence of metabolic syndrome parameters based on mucosal involvement (FBS: Fasting Blood Sugar; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol LP: Lichen Planus)

overall [26]. Interestingly, the prevalence of MetS among LP patients in our study was in the same range as that reported in the general population. However, according to a recent systematic review, LP patients have a significantly higher prevalence of MetS (approximately twice) compared with the general population [27].

As mentioned in Table 4, studies from across the world have reported variable prevalence of MetS in LP, ranging from 6% to 48% [4,9,10,14-19]. The observed variation may be due to differences in study settings, sample sizes, patient selection, population genetics, dietary habits, physical activity levels, and MetS diagnostic criteria. The sample size in our study was more than most similar studies from our country, making our observations more significant.

Table 4. Comparison of prevalence of metabolic syndrome in lichen planus (LP) patients in previous studies

Study	Sample Size	Metabolic Syndrome (%)
Arias-Santiago *et al.*, 2011 [4]	100	27
Baykal *et al.*, 2015 [10]	79	26.6
Kuntoji *et al.*, 2016 [9]	50	6
Kurian *et al.*, 2017 [14]	40	45
Hashba *et al.*, 2018 [15]	70	35.7
Okpala *et al.*, 2019 [16]	90	18.9
Geetharani *et al.*, 2019 [17]	113	19
Singla *et al.*, 2019 [18]	100	43
Daye *et al.*, 2020 [19]	98	48
Present study	123	31

In our study, the mean age of LP patients with MetS was significantly higher than that in those without MetS. A Nigerian study by Okpala *et al.* reported similar findings, showing participants with LP and MetS to be significantly older than LP patients without MetS [16].

Krishnamoorthy *et al.* found the prevalence of MetS in patients of oral LP to be 27.27% [11]. A significantly higher prevalence of MetS was reported in LP patients with mucosal involvement by Baykal *et al.* (34.5 vs. 8.3%; $P = 0.032$) [10]. Hashba *et al.* and Daye *et al.* also reported a higher frequency of MetS in patients with oral involvement than those with isolated cutaneous lesions, although not statistically significant [15,19]. This was corroborated by the findings in our patients, with the prevalence of MetS being higher in patients with mucosal involvement than those without it, although insignificantly. Similarly, we found oral, genital, and nail involvement to be more common among LP patients with MetS. Contrary to this, Okpala *et al.* reported oral involvement to be more common in patients without MetS [16].

Baykal *et al.* reported a significantly longer duration of LP in patients with insulin resistance—a primary feature of MetS [10]. Similarly, in the study by Hashba *et al.*, the mean duration of LP in patients

with MetS was slightly higher than those without it [15]. Conversely, in our study, the mean duration of LP in patients with MetS was lower than those without it. This may be due to the fact that only newly diagnosed LP patients were taken into account, while relapsing and treatment-resistant chronic cases, in whom chronic inflammation and the associated metabolic derangement are likely to exist more frequently, were excluded from our study.

The high prevalence of central obesity and hypertension noted in our study can be explained by similar findings from a community-based survey done in eastern India by Prasad *et al.*, suggesting an overall high prevalence of these abnormalities in the general population [26]. Central obesity showed a consistently high prevalence among LP patients in other similar studies from our country [14,15]. The frequencies of hypertension and hypertriglyceridemia in our patients were also comparable with those reported by Singla *et al.* and Hashba *et al.*, respectively [15,18]. However, compared to both these studies, hyperglycemia and low HDL-C were relatively less common in our patients [15,18].

Out of 62 patients suffering from oral LP, 17 (27.4%) had type 2 diabetes mellitus, and 11 (17.7%) had impaired fasting glucose levels in a study by Romero *et al.* [28]. Lopez-Jornet *et al.* also reported a high prevalence of diabetes in oral LP [29]. Hashba *et al.* found increased FBS in 59% of patients with oral LP, compared to 52.6% of patients with skin LP [15]. In keeping with these findings, our study revealed a significant association between elevated FBS and the presence of mucosal lesions. This implies that underlying pathomechanisms may link mucosal involvement in LP to the occurrence of insulin resistance in these patients.

Our study had a few limitations. There was no control group, so the strength of the association between LP and MetS could not be determined. Also, as it was a cross-sectional study, so the directionality of the association could not be assessed, for which long-term prospective studies are required. Although the sample size was larger than most similar studies from our country, it could not be increased further due to limited time and resources, resulting in very few statistically significant correlations. Therefore, larger case-control studies are recommended to determine any association of MetS with LP and its various types, including mucosal LP.

CONCLUSION

Based on our study findings, routine screening for metabolic derangement should be considered in LP patients, especially in older patients and females. The presence of mucosal lesions could also serve as a guide to indicate the presence of metabolic abnormalities, especially hyperglycemia. Early detection and prompt treatment of these risk factors may go a long way in preventing such patients' subsequent development of cardiovascular disorders and diabetes mellitus.

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Conflict of interest: None declared.

REFERENCES

1. Piguet V, Breathnach SM, Cleach LL. Lichen planus and lichenoid disorders. In: Griffiths CEM, Barker J, Bleiker T, et al. (Eds). Rook's textbook of dermatology. Chichester, West Sussex, UK: John Wiley & Sons Ltd; 2016.
2. Payette MJ, Weston G, Humphrey S, et al. Lichen planus and other lichenoid dermatoses: Kids are not just little people. Clin Dermatol. 2015;33:631-43.
3. Garg VK, Nangia A, Logani K, et al. Lichen planus-a clinico-histopathological. Indian J Dermatol Venereol Leprol. 2000;66(4):193-5.
4. Arias-Santiago S, Buendia-Eisman A, Aneiros-Fernandez J, et al. Cardiovascular risk factors in patients with lichen planus. Am J Med. 2011;124:543-8.
5. Saleh N, Samir N, Megahed H, et al. Homocysteine and other cardiovascular risk factors in patients with lichen planus. J Eur Acad Dermatol Venereol. 2014;28:1507-13.
6. Panchal FH, Ray S, Munshi RP, et al. Alterations in lipid metabolism and antioxidant status in lichen planus. Indian J Dermatol. 2015;60:439-44.
7. Arias-Santiago S, Buendia-Eisman A, Aneiros-Fernandez J, et al. Lipid levels in patients with lichen planus: a case-control study. J Eur Acad Dermatol Venereol. 2011;25:1398-401.
8. Dreiher J, Shapiro J, Cohen AD. Lichen planus and dyslipidaemia: a case-control study. Br J Dermatol. 2009;161:626-9.

9. Kuntoji V, Kudligi C, Bhagwat PV, et al. Dyslipidemia and metabolic syndrome in patients with lichen planus: a case-control study. J Pak Assoc Dermatol. 2016;26:290-7.
10. Baykal L, Arıca DA, Yaylı S, et al. Prevalence of metabolic syndrome in patients with mucosal lichen planus: a case-control study. Am J Clin Dermatol. 2015;16:439-45.
11. Krishnamoorthy B, Suma GN, Mamatha NS, et al. Lipid profile and metabolic syndrome status in patients with oral lichen planus, oral lichenoid reaction and healthy individuals attending a dental college in Northern India – a descriptive study. J Clin Diagn Res. 2014;8:ZC92-5.
12. Lai YC, Yew YW, Schwartz RA. Lichen planus and dyslipidemia: a systematic review and meta-analysis of observational studies. Int J Dermatol. 2016;55:e295-304.
13. Yusuf SM, Tiijani UA, Maiyaki M B, et al. Dyslipidemia: prevalence and associated risk factors among patients with lichen planus in Kano, North-West Nigeria. Nig Q J Hosp Med. 2015;25:145-50.
14. Kurian G, Krishnan S, Shakthi P. A prospective case control study on metabolic syndrome in lichen planus in a tertiary care centre. Int J Res Dermatol. 2017;3:427-32.
15. Hashba H, Bifi J, Thyvalappil A, et al. Prevalence of metabolic syndrome in patients with lichen planus: a cross-sectional study from a tertiary care center. Indian Dermatol Online J. 2018;9:304-8.
16. Okpala IC, Akinboro AO, Ezejoifor IO, et al. Metabolic syndrome and dyslipidemia among Nigerians with lichen planus: a cross-sectional study. Indian J Dermatol. 2019;64:303-10.
17. Geetharani G, Sumithra S, Devaprabha S, et al. Eruptive lichen planus, a marker of metabolic syndrome. Indian J Dermatol. 2019;64:299-302.
18. Singla R, Ashwini PK, Jayadev B. Lichen planus and metabolic syndrome: is there a relation? Indian Dermatol Online J. 2019;10:555-9.
19. Daye M, Temiz SA, Işık B. The relationship between lichen planus and metabolic syndrome. J Cosmet Dermatol. 2021;20(8):2635-2639.
20. Grundy SM. Metabolic Syndrome: connecting and reconciling cardiovascular and diabetes worlds. J Am Coll Cardiol. 2006;471093-100.
21. Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Final report. Circulation. 2002;106:3143-421.
22. Misra A, Vikram NK, Gupta R, et al. Waist circumference cut-off points and action levels for Asian Indians for identification of abdominal obesity. Int J Obes (Lond). 2006;30:106-11.
23. Ireddy SG, Udbalkar SG. Epidemiological study of lichen planus. BMR Medicine. 2014;1:1-9.
24. Kar BR, Panda M, Patro N. Metabolic derangements in lichen planus - a case control study. J Clin Diagn Res. 2016;10:01-3.
25. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab. 2008;93(11_Supplement_1):s9-30.
26. Prasad DS, Kabir Z, Dash AK, et al. Prevalence and risk factors for metabolic syndrome in Asian Indians: a community study from urban Eastern India. J Cardiovasc Dis Res. 2012;3(3):204–11.
27. Ying J, Xiang W, Qiu Y, et al. Risk of metabolic syndrome in patients with lichen planus: a systematic review and meta-analysis. PLoS One. 2020;15(8):e0238005.
28. Romero MA, Seoane J, Varela-Centelles P, et al. Prevalence of diabetes mellitus amongst oral lichen planus patients. clinical and pathological characteristics. Medicina Oral. 2002;7:121–9.
29. Lopez-Jornet P, Camacho-Alonso F, Rodriguez-Martines MA. Alterations in serum lipid profile patterns in oral lichen planus: a cross-sectional study. Am J Clin Dermatol. 2012;13:399-404.