Original Research Article

Association of lichen planus with metabolic syndrome–acasecontrol study in a tertiary care center.

Nishant Saurabh Saxena[1] ,Nimisha Saxena[2] , Animesh Saxena[3], Harsh Sharma[*]

[1]Assistant Professor,[1]Dept. of ENT, G.S.V.M College and Hospital , Kanpur, Uttar Pradesh, India.

[2]Associate Professor,[2]Dept. of Biochemistry, K.D Medical College and Hospital Research Center, Mathura, Uttar Pradesh, India.

[3]Associate Professor, Department of Dermatology, P.M.C.H Bhopal, India

[4]Associate professor,*Dept. of Dermatology, K.D Medical College and Hospital Research Center, Mathura, UttarPradesh, India.

Corresponding Author – Dr. Harsh Sharma, Associate Professor, Dept. of Dermatology, K.D Medical College and Hospital Research Center, Mathura, Uttar Pradesh, India. Email I'd - drharsh1311@rediffmail.com

Abstract

Background: Lichen planus is an inflammatory papulosquamous dis- ease which affects skin and mucous membrane and cause metabolic derangements.

Methods: This is an hospital based case control study during a span of 2 year (Jan2018-Dec 2019) which includes 60 cases of lichen planus and 60 age and sex matched controls. Relevant clinical history and physical examination was done and collaborated with blood investigations. Diagnosis was made based on IDF criteria.

Results: No significant association can be established between lichen planus and metabolic syndrome (p=0.278) Although prevalence of hypertension was higher in cases as compared to controls (36% vs. 26%, p=0.027) , TG levels (12% vs. 6%, p=0.030 and low HDLC levels (47% vs. 33%, p=0.039). No significant association was established between FBS and waist circumference with lichen planus.

Conclusions: Although no significant association can be established between lichen planus and metabolic syndrome but its components such as hypertension, TG and HDLC were found to be associated with LP as per the study. Therefore screening of these parameters in LP patients is necessary to avoid future complications in these patients.

Keywords: Lichen planus, Metabolic syndrome, Hypertension, Triglyc- eride

Introduction

Lichen planus derives its nomenclature from a greekword "Leichen"(1) is an inflammatory papulosqua- mous disease affecting skin and mucous membrane a papulosquamous disease. Dr. Wilson described it as an inflammatory disorder involving stratified squa- mous epithelium of unknown etiology(2). In 1895, Weyl demonstrated Wickham Striae i.e (reticulate white lines) on the surface of lichen planus lesions(3) Lichen planus is an inflammatory disorder which af-fects skin and mucous surfaces and characterized by flat-topped violaceous polygonal papules which co-alesce to form plaques(4). It is an sub-acute chronic dermatosis of idiopathic origin and triggered by sev-eral factors such as drugs, chemical allergens and viruses (5,6).

It is an inflammatory disorder mediated by T cells causing alteration in lipid metabolism thereby increasing serum triglycerides and decrease in serum HDL levels (7). It also affects endocrine functions and cause diabetes mellitus which may contribute to development of lichen planus. In 1963, Grinspan showed the association of oral lichen planus and diabetes mellitus and hypertension and named the syndrome as Grinspan syndrome(8).

Metabolic syndrome is defined as group of disor- ders or derangements comprising of dyslipidemia, hypertension, impaired glucose tolerance and ab- dominal obesity. Metabolic syndrome is associated with many dermatological conditions such as psoriasis, androgenetic alopecia, SLE etc (9). Metabolic syndrome is also found to be associated

with lichen planus. International Diabetes Feder- ation Criteria has been used to define metabolic syndrome in this study. Chronic inflammation and elevated proinflammmatory

cytokines are the hall- mark of metabolic syndrome. Proinflammatory cy- tokines like Leptin, adiponectin, TNF-αnterleukin- 6,monocyte chemotactic protein-1 plays the major role in development of metabolic derangements. These cytokines produces insulin –resistance and metabolic complications like elevated blood pres- sure, dyslipidemia and heart disease. These are more often found to be increased in many dermatologicaldiseases(10).

Oxidative stress is also an important factor in de- velopment of metabolic syndrome. Oxidative stress results when the reactive oxygen species exceeds the capacity of antioxidants.One of the major source of ROS is xenobiotics which includes chemical cosmet- ics, environment pollutants, drugs and food flavoring agents. Skin is involved in metabolising these xeno- biotics and other endogenous bioactive substances from the body .It excretes these substances in the form of sebum. Derangements affecting the excre- tion of these in the form of sebum will increase circulating lipids and cholesterol and results in dys-lipidemia and metabolic distress. (9-11) .

Methods

This case control study was conducted in k.d medical and hospital and research centre in collaboration with G.S.V.M medical college kanpur .Patients attend- ing OPD in DVL and ENT (for oral lichen planus cases) were enrolled in the study for a period of 2 years (Jan 2018-Dec2019).Institutional ethics com- mittee was taken before start of the study .Patients above 18 years of age were taken and matched with the controls without any dermatological ailments. Pregnant women, lactating mothers and persons on immunosuppressant or on the treatments of lichen planus were excluded.120 patients were included in the study out of which 60 were included in the LP pa- tients and 60 were controls. Relevant clinical history and demographic data for patients were collected in each group Later the parameters of metabolic syndrome were measured in each patient of both groups. Several parameters which defines metabolic syndrome were measured like waist circumference ,blood pressure both systolic and diastolic and fasting glucose (12- hour fasting), lipid profile including serum choles- terol, LDLC,HDLC and TG levels. Waist circum- ference was measured at the mid-point between the lower margin of the last palpable rib and the iliac crest(12). Photographs of the lesions were taken. Prior to inclusion in the study informed consent hasbeen taken in both the groups .

Data for both the groups were taken in a proforma sheet and statiscally analysed using SPSS version 20 (IBM SPSS,US). Pearson's chi square test was used to statically analyse the results and find prevalence and association of metabolic syndrome in lichen planus patient group and controls without lichenplanus.

Results

The majority of patients belong to age group of 40sand 60s (Figure 1). Out of 60 patients of LP 18 (30%) were males and 42(70%) were females Out of the 40 cases of LP, 10 (25%) were males and 30 (75%) were females (Figure 2) with mean age of the studypopulation being 41.53±13.54 yrs.
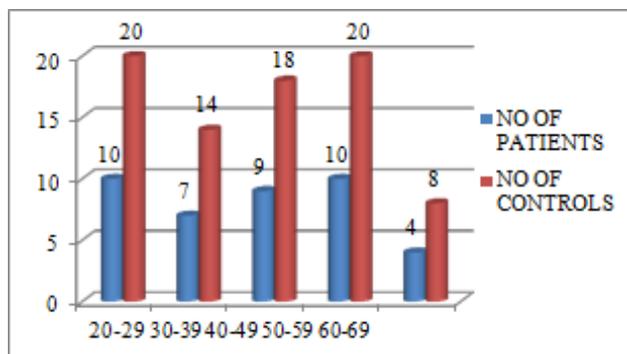
FIGURE 1: *Age distribution among patients with and without L Cl patterns of lichen planus in the study P*

Among the 60 patients with LP, 4 (7%) patients had oral lesions alone, 4 (7%) patients had scalp52 (86.6%) patients had skin lesions. 3 patients (5%) patients had nail involvement along with skin lesions and 3 (5%) patients had oral lesions along with skin lesions
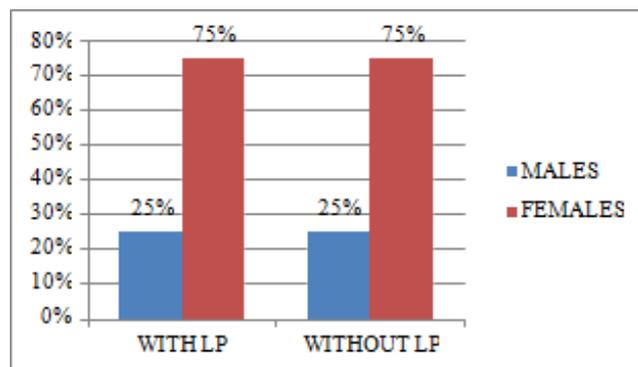

FIGURE 2: *Gender distribution among patients with and without LP*

Among 60 patients with LP, 20 (33%) patients had metabolic syndrome when compared to 40(67%) individuals without LP (p=0.278). Among patients with metabolic syndrome, majority of those with LP belonged to the age group between 50-59 years (38.88%) while those in control group belonged to 40-49 years and 50-59 years (28.12% each). Of the patients with LP, metabolic syndrome was found in 14 females (77.8%) and 4 males (22.2%) (p=0.714). In the control group, metabolic syndromewas present in 6 (19%) males and 26 (81%) females.

TABLE 1: Lichen planus and its associations

S. no	Parameter	Presen	Ab-sent	
1	Increased waist circumference	28	32	0.599
2	Hypertension	22	38	0.027
3	Raised FBS	19	41	0.359
4	Low HDLC level	28	32	0.039
5	Hypertriglyceri demia	12	48	0.03

lesions alone (lichen planopilaris) while remaining Among 60 LP patients 22 (36%) were of hyperten- sion and in control group 16 (26%) (p=0.027). of the 22 patients with hypertension in the LP group, 20(89.5%) were females and 2(10.5%) were males. Increased fasting blood sugar level in patients with LP were 21(35%) as compared to 33(55%) in con- trol groups respectively(p=0.359). Similarly Triglyc- eride levels were found to be raised in 12 (20%) patients with LP as compared to control 6 (10%) (p= 0.030). HDLC level was found to be low in patients with LP. Among 40 patients with LP, 28 (47%) as compared to 20(33%) individuals among the controls (p=0.039).. Waist circumference was found to be higher in 28 (47%) and 25 (42%) individuals. with and without lichen planus respectively (p=0.599) (Table 1).Hence hypertension, hypertriglyceridemia and low HDLC levels were found to have statistically significant association with lichen planus with p values of 0.027, 0.03 and 0.039 respectively.

Discussion

Lichen planus is an inflammatory disorder involving T cells for pathogenesis .It affects skin and mucous membrane. Its association with metabolic syndrome has been studied since long but there are several con- tradictions in various studies so more concrete and robust study with large study population is needed
.Metabolic syndrome comprises of increased blood pressure, elevated TG and low HDLC ,hypercholes- terolemia, deranged fasting blood sugar, central obe- sity. Few studies have shown that LP is associated with Hep C infection while few have disproved it.[13−15] One study has also showed an association between hashimotos thyroiditis and lichen planus.[16]

Few studies have shown higher association of LP with metabolic syndrome while some refutes the same(17).

This study was done to give some insight whether LP shows any association with metabolic syndromeor not .Though more studies are needed to potentiatethis association.

Demographic details

Age

In this study out of 60 patients with LP majority of patients fall in the age group of 40s and $\pm$ 60s .with

the mean age of patients with LP was 41.53 13.54 yrs (median= 41$\pm$and range=45) which was matched for age and gender with control group which showed mean age of 41.43 13.45 yrs (median= 41.50 and range=45).The results of this study were found to be similar with study done by Omal et al done in south Indian population(18) similarly the study done by Mehdipour also showed the same trend (19).

Maximun number of Patients with LP with metabolic syndrome fall into sixth decade while in the con- trol group maximum number of individuals with metabolic syndrome belong to fifth and sixth decade. While Prasad et al showed highest prevalence in seventh decade (20).

Gender

Out of 60 patients, 42 (70%) were females and 10 (30%) were males. Although in this study female predominance was seen but this was not found to be statiscally significant. Parihar et al also found female predominance in his study (1:0.8)(21). 14 females (77.8%) and 4 males (22.2%) were found to be associated with metabolic syndrome again this shows females are affected more with complications compared to males. Balasubramaniam et al showed in his study that 60% of females in India were foundto have metabolic syndrome(22).

Metabolic syndrome

Among the patients with LP; 14 females (77.8%) and 4 males (22.2%) had metabolic syndrome. While in control group metabolic syndrome was present in 6 (19%) males and 26 (81%) females. No significant association was found between LP and metabolic syndrome (p=0.278).

Similar to this study, one larger study with 100 participants was taken by Arias et al . In their study according to ATP III criteria for MS, only 27% of patients with lichen planus had MS while the control group had 20%.This was statiscally insignificantwith p value 0.310(7).

Baykal et al in a study showed that out of 79 patients of LP 26% had metabolic syndrome compared to 12% in control group. They have also shown that mucosal LP was more associated with metabolic syndrome(17).

Blood pressure

Out of 60 patients in study group 22 had hyperten- sion patients of which, 20(89.5%) were females and 2(10.5%) were males while only 16 had hypertension in control group. This was statiscally significant with p value 0.027 The mean systolic BP among the cases and controls were 125.7±12.9 mmHg and 117.58±15.3 mmHg respectively while the mean diastolic BP was 83.2±5.84 mmHg within the casesand 75.2±8.37 mmHg among the control group.

Similar results were observed by Baykel et al in their study with 26 (32.9%) of 70 LP patients suffering from hypertension with a p value of 0.027(17).

However this was not in accordance with the study done by Salvador Arias-Santiago et al were they could not prove any association between LP and hypertension(7).

Fasting blood sugar

In this study, increased fasting blood sugar level in patients with LP were 21(35%) as compared to 33(55%) in control groups respectively(p=0.359)this is statiscally The mean FBS among the LP patients was 103.03 29.25 mg/dl and the same among the control group was found to be 97.15 28.25 mg/dl.

But contrary to this Atefi et al have shown higher prevalence of diabetes mellitus in LP patients as compared to control(23).Findings similarto Atefi were found by Baykel et al(17). Grinspan also found higher prevalence of diabetes mellitusand hyperten- sion in patients with oral erosive LP and named it Grinspan syndrome(24).

Serum lipids

Similarly triglyceride levels were found to be raised in 12 (20%) patients with LP as compared to control 6 (10%) (p= 0.030). HDLC level was found to be low in patients with LP. Among 40 patients with LP, 28 (47%) as compared to 20(33%) individu- als among the controls (p=0.039). The mean values of triglyceride levels were 131.33 37.1 mg/dl and

116.71 37.7 mg/dl among cases and controls in this study as well The mean HDLC levels were 44.6 7.34 mg/dl and

46.76 6.26 mg/dl among the cases and controls respectively. Mehdipour et al carried a study with 88 participants Constructed three groups with 22 patients in each group.first group was of erosive oral LP, second of non-erosive oral LP and third of healthy individu- als.When compared to controls statiscally significant relation was found between increased TG and low HDLC levels in patients group with a p value of 0.00and 0.02 respectively(19).

Study done by Sarkar et al also supports this with the similar findings done on 25 LP patients with age and gender matched controls. Along with altered HDLC and triglyceride levels, LDL levels were also found to be higher in this study(25).

Waist circumference

Waist circumference was found to be higher in 28 (47%) and 25 (42%) individuals with and without lichen planus respectively (p=0.599) but this was statiscally insignificant as suggested by p value .

The mean waist circumferences of the patients with and without LP were found to be 86.63±12.07 cm and 86.86±9.03cm respectively.

Conclusion

Based on this study it can be concluded that asso- ciation of LP with metabolic syndrome was satatis- cally insignificant whereas individual parameters of metabolic syndrome when studied and compared with the control group showed different results .hy- pertension was statiscally significant in LP patients as compared to control group also the lipid profile was found to deranged more oftenly in LP patients significantly in patients with oral erosive LP as com- pared to control group whereas waist circumference and fasting blood sugar was not statiscally significant when compared with the control group. However screening of patients of LP for these parameters is important to prevent future comorbidities and ensurea better life.

Acknowledgements

References

1. Goldsmith LA, Fitzpatrick TB. Fitzpatrick's der- matology in general medicine. New York: McGraw-Hill Medical; 2012.

2. Gorouhi F, Davari P, Fazel N. Cutaneous and Mu- cosal Lichen Planus: A Comprehensive Reviewof Clinical Subtypes, Risk Factors, Diagnosis, and Prognosis. Sci World J. 2014;2014:e742826.

3. Oral Lichen Planus: An Update on Etiology, Patho- genesis, Clinical Presentation, Diagnosis and Man- agement.

4. Garg VK, Nangia A, Logani K, Sharma RC. Lichen Planus-a Clinico-histopathological. Indian J Derma-tol Venereol Leprol. 2000;66(4):193-5.

5. Rook's textbook of dermatology. In: Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Ninth edition. Chichester, West Sussex ; Hoboken, NJ: John Wiley & Sons Inc; 2016.

6. Burns T, Rook GA, editors. Rook's textbook of dermatology: in four volumes. 8th ed. Oxford: Wiley-Blackwell; 2010.

7. Arias-Santiago S, Buendía-Eisman A, Aneiros- Fernández J, Girón-Prieto MS, Gutiérrez-Salmerón MT, Mellado VG, et al. Cardiovascular risk fac- tors in patients with lichen planus. Am J Med. 2011;124(6):543–8.

8. Halimi S, Ferizi M, Gerqari A, Krasniqi N, Fer- iziM. GRINSPAN'S SYNDROME – a case report. Case Study Case Rep. 2016;6(3):73–8.

9. Padhi T, Garima. Metabolic syndrome and skin: Psoriasis and beyond. Indian J Dermatol. 2013;58(4):299.

10. Padhi T, Garima. Metabolic Syndrome and Skin: Psoriasis and Beyond. Indian J Dermatol. 2013;58(4):299–305.

11. Zhou S-S, Li D, Zhou Y-M, Cao J-M. The skin function: a factor of anti-metabolic syndrome. Dia- betol Metab Syndr. 2012;4:15.

12. Shen W, Punyanitya M, Chen J, Gallagher D, Albu J, Pi-Sunyer X, et al. Waist Circumference

Correlates with Metabolic Syndrome Indicators Bet-ter Than Percentage Fat. Obes Silver Spring Md. 2006;14(4):727–36.

13. Petti S, Rabiei M, De Luca M, Scully C. The mag- nitude of the association between hepatitis C virus infection and oral lichen planus: meta-analysis and case control study. Odontology. 2011;99(2):168–78.

14. Himoto T, Masaki T. Extrahepatic Manifesta- tions and Autoantibodies in Patients with Hepatitis C Virus Infection. Clin Dev Immunol. 2012;871401.

15. Das A, Das J, Majumdar G, Bhattacharya N, Neogi D, Saha B. No association between seroposi-tivity for Hepatitis C virus and lichen planus: A case control study. Indian J Dermatol Venereol Leprol. 2006;72(3):198–200.

16. Lo Muzio L, Santarelli A, Campisi G, Lacaita M, Favia G. Possible link between Hashimoto's thy-roiditis and oral lichen planus: a novel association found. Clin Oral Investig. 2013;17(1):333–6.

17. Baykal L, Arıca DA, Yaylı S, Örem A, Bahadır S, Altun E, et al. Prevalence of Metabolic Syndrome in Patients with Mucosal Lichen Planus: A Case– Con- trol Study. Am J Clin Dermatol. 2015;16(5):439–45.

18. Omal P, Jacob V, Prathap A, Thomas N. Preva- lence of oral, skin, and oral and skin lesions of lichen planus in patients visiting a dental school in Southern India. Indian J Dermatol. 2012;57(2):107–9.

19. Mehdipour M, Zenouz AT, Davoodi F, Gholizadeh N, Damghani H, Helli S, et al. Evalua- tion of the Relationship between Serum Lipid Profile and Oral Lichen Planus. J Dent Res Dent Clin Dent Prospects. 2015;9(4):261–6.

20. Prasad DS, Kabir Z, Dash AK, Das BC. Preva- lence and risk factors for metabolic syndrome in Asian Indians: A community study from urban East-ern India. J Cardiovasc Dis Res. 2012;3(3):204–11.

21. Parihar A, Sharma S, Bhattacharya SN, Singh UR. A clinicopathological study of cutaneous lichen planus. J Dermatol Dermatol Surg. 2015;19(1):21– 6.

22. Balasubramanyam A, Rao S, Misra R, Sekhar RV, Ballantyne CM. Prevalence of Metabolic Syn-drome and Associated Risk Factors in Asian Indians.J Immigr Minor Health. 2008;10(4):313–23.

23. Atefi N, Majedi M, Peyghambari S, Ghourchian
S. Prevalence of diabetes mellitus and impaired fast- ing blood glucose in patients with Lichen Planus. Med J Islam Repub Iran. 2012;26(1):22–6.

24. Bagewadi A, Bhoweer AK. Oral Lichen Planus and Its Association with Diabetes Mellitus and Hypertension. J Indian Acad Oral Med Radiol. 2011;23(3):300-3

25. Sarkar M, Dayal S, Samanta S, halaut VS, Malik I, Sehgal PK. Serum Leptin and Lipid Profile in Lichen Planus: A Case Control Study. Int J Health Sci Res IJHSR. 2015;5(10):129–35.