

## A correlation between oxidative stress and hypertriglyceridemia in lichen planus - A case control study

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### Abstract

**Introduction and Objective:** Chronic inflammation & lipid peroxidation plays a pivotal role in the etiopathogenesis of cardiovascular risks in many clinical conditions. Whereas, Lichen planus (LP), is a chronic skin inflammatory disorder which disturbs lipid metabolism & increases the lipid peroxides. However, there are limited data about the correlation between oxidative stress & hypertriglyceridemia in LP, hence the study was undertaken to 1) Estimate the levels of TG (triglycerides) & MDA (malondialdehyde) levels & 2) to correlate between the MDA & TG levels in LP patients.

**Materials and Methods:** A case control study was done at KIMS hospital, Hubli, which included 50 LP patients and 50 healthy individuals. Serum levels of TG (GPO-PAP method) and MDA (TBA method) was done.

**Result:** Patients with LP presented higher significant TG values (182.93 vs. 113 mg/ dl), MDA values (4.81 vs. 3.99 nmol/ml) vs. controls. Also, our study showed positive correlation between TAG & MDA levels which is statistically significant (0.012).

**Interpretation and Conclusion:** Thus, the present study showed increased levels of TG & MDA, indicating that hypertriglyceridemia & lipid peroxidation may have domino effect with each other due to chronic inflammation & thereby may increase the cardiovascular complications in LP patients.

**Keywords:** Atherosclerosis, Cardiovascular risks, Dyslipidemias, Chronic inflammation, Lichen planus, Oxidative stress.

### Introduction

Atherosclerosis, is one of the precursor to many diseases like stroke, peripheral vascular disease & myocardial infarction which increases impermanence across the worldwide. Overall, the disease is mainly due to the chronic inflammation, which is promoted by lipid accumulation & increased reactive oxygen species (ROS).<sup>1</sup> But many subclinical skin inflammatory diseases like atopic dermatitis, lichen planus undergo undiagnosed for cardiovascular risks where its etiopathogenesis remains baffled. Lichen planus (LP) is a cryptogenic inflammatory disorder which impinges mainly on skin, mucous membranes, nails, and hair.<sup>2</sup> Chronic inflammation, altered lipid metabolism and oxidative stress are accountable for increased frequency.<sup>3</sup> Psoriasis, another chronic inflammatory skin disorder which is alike LP in etiopathogenesis, due to dysregulated T-cell interactions there is over expression of pro-inflammatory cytokines that leads to the hyperproliferation of keratinocytes and activation of neutrophils in the epidermis which finally results in chronic T-cell activation, resulting in persistent cycle of inflammation.<sup>4,5</sup>

Not only that, this persistent inflammation causes the disturbances in lipid metabolism like low levels of High Density Lipoproteins – Cholesterol (HDL-C) or high levels of triglycerides.<sup>3,6</sup> Hypercholesterolemia & hypertriglyceridemia are contributing risk factors, that can act individually or together for the development of atherosclerosis.<sup>1</sup>

Origin of cellular degeneration in LP is believed to be subepithelial infiltration of T-lymphocytes that contributes

to cytokines production which in turn can stimulate production of ROS and cause oxidative damage to tissues.<sup>7,8</sup>

Oxidative stress represents as lipid peroxidation in the cell membranes<sup>9</sup> which alters the lipid rich membrane fluidity and their signalling efficiency, leading to inflammatory changes and to aberrant cell proliferation responses. MDA (Malondialdehyde), is one of the end products of polyunsaturated fatty acid peroxidation & commonly used as a biomarker for oxidative stress.<sup>10-12</sup> It has been proposed that a derangement in the elimination of ROS through sebum results in an increased blood level of circulating lipids and cholesterol, thereby increasing the risk of dyslipidemia.<sup>13,14</sup>

Thus, chronic inflammation, lipid disturbances and lipid peroxidation may form a vicious cycle in the etiopathogenesis of LP, hence the present study was done to know the levels of TG & MDA & to correlate between the oxidative stress & hypertriglyceridemia in LP patients.

### Materials and Methods

**Study Participants:** This case-control study was done at KIMS, Hubli. Ethical clearance was obtained from the Institutional Ethical Clearance Committee. Convenient sampling method was done as exact prevalence was unknown.

The study group consists of 50 diagnosed LP patients from the Dermatology Department OPD and the 50 healthy controls. Both the cases and controls are interviewed to obtain relevant data after taking informed consent.

### Inclusion Criteria:

**Cases:** 1) > 18 years of either sex. 2) Newly diagnosed LP patients. 3) LP patients who stopped therapy.

**Control:** 1) >18years of either sex. 2) Healthy individuals (without any skin manifestations/inflammatory diseases/cardiovascular/hypothyroidism/DM/HTN)

**Exclusion Criteria:**

1) Lichenoid drug eruption 2) Receiving treatment for LP such as systemic corticosteroids, retinoic acid, methotrexate. Diagnosis was made based on clinical symptoms and confirmed by histopathological features. Data were also gathered on age, sex, habits like smoking, alcohol consumption & hypothyroidism, personal history of cardiovascular disease & whether the patients were on antihypertensive, cholesterol lowering drugs. Weight and height was taken, thereby body mass index (BMI) was measured by the formula: weight in kg/ height in m<sup>2</sup>.

The dyslipidemia was considered if one of the following parameters were present: 1) Triglycerides >150mg/dl; 2) Total cholesterol > 200mg/dl; 3) LDL-C >130mg/dl; or 4) the patient received treatment for dyslipidemia. In our study we are measuring only triglycerides to consider dyslipidemia.

**Method of Collection of Sample:** After relevant history taking and informed consent, 5 ml of fasting venous blood were collected, allowed blood to clot and serum was separated & analyzed for TG, MDA levels

**Measurement of Triglycerides:** Triglycerides were estimated by the GPO-PAP (glycerol phosphate oxidase-phenol antiaminopyrine) method by using standard kits, ERBA diagnostics on the fully automated analyzer.

**Measurement of Malondialdehyde:** MDA was done by TBA (thiobarbituric acid) assay on spectrophotometer at 535nm

**Statistical Analysis**

The statistical analyses were performed with the IBM SPSS software version 20.0 Independent sample student t test was used to compare mean values of variables & expressed as mean±SD. Pearson's correlation co-efficient was used to measure the relationship between TG & MDA levels. P<0.05 was considered significant in all analyses.

**Results**

A total of 100 individuals was studied, 50 with LP and 50 healthy controls. Among 50 cases, 29 were males and 21 were females.

Table 1 shows higher mean of height, weight & BMI in cases than controls which is statistically highly significant at p<0.0001

**Table 1: Mean values of age, height, weight & BMI among cases & controls**

	Cases		Controls		Significant level
	MEAN±SD	t value	MEAN±SD	t value	
AGE (yrs.)	46.58±15.04	21.89	48±14.1	23.82	0.0001
HEIGHT (cms)	158.62±16.99	65.78	161.24±7.56	150.74	0.0001
WEIGHT (kgs)	62.55±11.28	31.18	59.97±8.32	50.95	0.0001
BMI	29.40±38.04	5.46	23.07±2.89	56.3	0.0001

Values are expressed as mean ± SD

**Table 2: Descriptive statistics of cases**

Parameters	N	Minimum	Maximum	Mean ± sd
Triglycerides (mg/dl)	50	44	576	182.93±127.2
MDA (nmol/ml)	50	3.32	6.31	4.81±0.82

N- number of cases

**Table 3: Descriptive statistics of controls**

Parameters	N	Minimum	Maximum	Mean±SD
TAG (mg/dl)	50	43	210	113.52±43.0
MDA(nmol/ml)	50	3.13	5.22	3.99±0.55

N-number of controls

**Table 4: Comparison between serum levels (mean±SD) of TG & MDA in cases & controls.**

Parameters		Mean±SD	't' value	'p' value
TAG (mg/dl)	Cases	182.93±127.2	18.63	.0001
	Controls	113.52±43		
MDA (nmol/ml)	Cases	4.81±0.82	51.13	.0001
	Controls	3.99±0.55		

It is observed from table 4, that patients showed higher mean TG and MDA levels than the controls which was highly significant (p<0.0001) by application of student's t test.

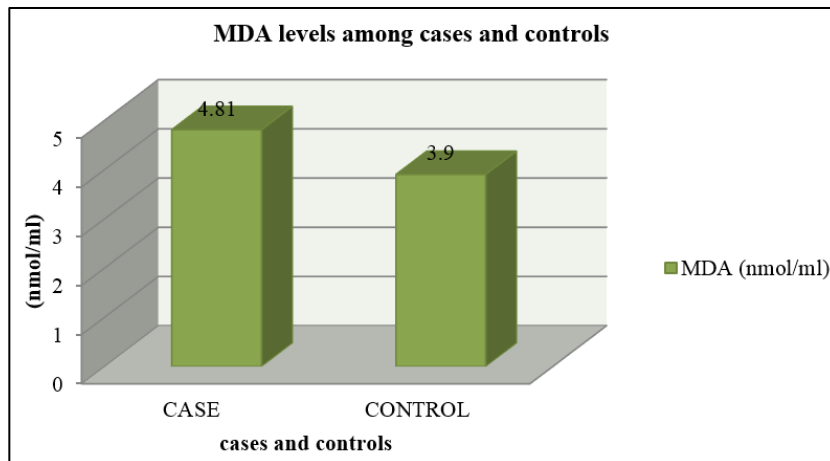


Fig. 1: Comparison of MDA levels among cases & controls

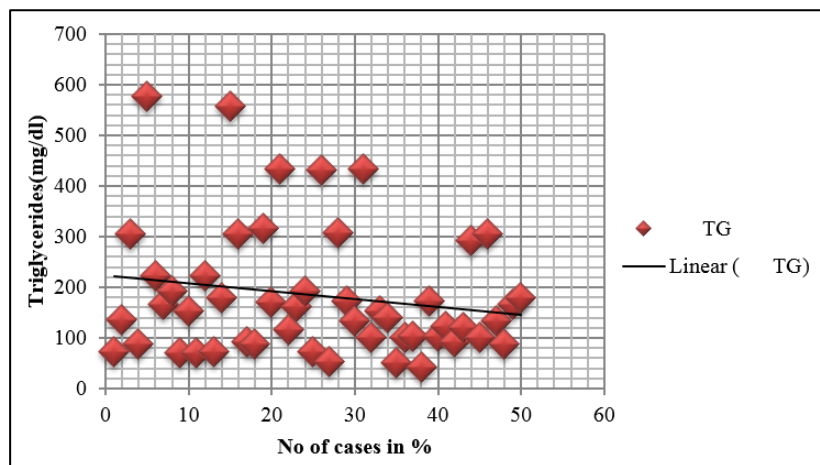


Fig. 2: Scatter diagram showing distribution of cases as per their TG

Most of the cases (50%) had Triglycerides ranging between 100-200mg/dl

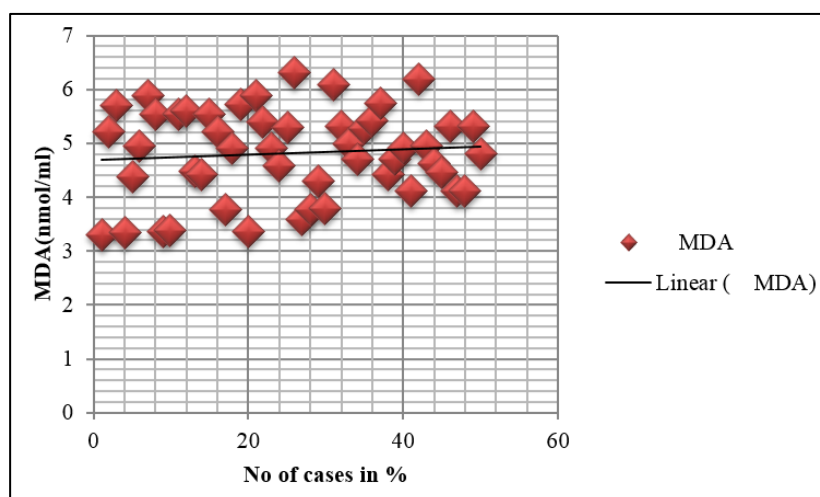


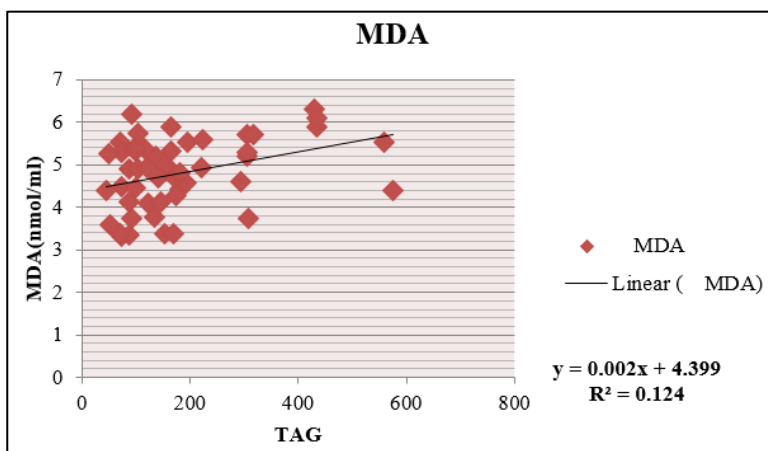
Fig. 3: Scatter diagram showing distribution of cases as per their MDA

(40%) of the cases had MDA levels ranging between 4-5 nmol/ml

**Table 5: Pearson’s correlation between serum TG & MDA levels among cases**

Parameters	MDA Levels	
	r value	p value
TAG	0.3	0.012*

It is observed from the table that there is positive correlation between TG and MDA levels with r values of 0.3 respectively which is statistically significant (< 0.012).



**Fig. 4: Pearson’s correlation co-efficient between serum TG levels with MDA levels among cases**

**Dicussion**

LP is an idiopathic chronic inflammatory skin disorder and its etiopathogenesis are clearly unknown. It is believed to be T-cell immune mediated, where it stimulates the many proinflammatory mediators like cytokines, interleukins etcinturn causes the alterations in the lipid metabolism like hypertriglyceridemia. Also, the local production of inflammatory mediators can stimulate the production of ROS which damages the cell membrane by lipid peroxidation and thereby causing the disequilibrium between the pro-oxidants and antioxidants.

Table 1, showed higher mean values of weight and BMI in lichen planus patients than the controls which was statistically highly significant p (<0.0001). Increased BMI is one of the contributing risk factor for cardiovascular disease. Present study showed higher mean values of about 29.4 which is in the range of overweight. Also, our present study showed higher triglycerides values among LP patients which is one of independent marker for dyslipidemia & may contribute to the progression of atherosclerosis. Study by Melita Vuksic Polic et al,<sup>15</sup>,= showed strong connection between the imbalanced concentrations of one or more serum lipids like hypertriglyceridemia and the occurrence of LP. Another similar case-control study by SalvdorAriaset al,<sup>16</sup> included 200 patients, showed higher mean values of TAG with a positive correlation with cytokines, CRP.

Psoriasis, an autoimmune disorder quite similar to LP in etiopathogenesis. Since it is a T-cell immune mediated disorder, attacks on keratinocytes leading to generation of ROS & releases pro-inflammatory cytokines like TNF-α, IL-6, IL-10, IL-4 which are linked to cause dyslipidemia.<sup>22</sup> Several other studies by Zari Javidiet al,<sup>17</sup> Mallbris L et al,<sup>18</sup> Pietrazak A et al,<sup>19</sup> Jochen Schmitt et al,<sup>20</sup> Isabela

Guimaraes Ribeiro Baeta et al<sup>21</sup> have shown that psoriasis has been linked to dyslipidemia.

Present study also showed higher mean MDA levels in lichen planus patients (4.81±0.82 vs 3.99±0.55) which is highly significant (p<0.0001) and shows that oxidative stress may play a role in pathogenesis.In systematic review by Shovana et al<sup>23</sup>found that there is increased levels of MDAin eight studies & have role in the pathophysiology of oral lichen planus.

Oxidative stress where there is an increase in free radicals, which damages the cell membrane of the cell and thereby altering the functions. Cellular degeneration in LP is thought to be the sub epithelial infiltration of T-lymphocytes, which promote the formation of cytokines. These cytokines stimulate the production of ROS and products of lipid peroxidation triggering apoptosis that is a hallmark feature of lichen planus. Also, our study showed positive correlation which was statistically significant between triglycerides & malondialdehydein LP patients. As levels of triglycerides increases, the levels of malondialdehyde were increased which shows hypertriglyceridemia & oxidative stress interrelate with each other in its etiopathogenesis.

**Conclusion**

Thus, our study emphasizes that chronicinflammation in LP act as vicious cycle between hypertriglyceridemia & oxidative stress, where these factors can accelerate the cardiovascular risks in these patients. By knowing that, these factors may have role in etiopathogenesis would be helpful in LP patients for routine screening of dyslipidemia & thereby reduce the risk & complications of cardiovascular disease later in life as an early intervention.

**Conflict of Interest:** None.

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