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Original Article

Dermatology Section

Atherogenic Index of Plasma: A Marker for Undetectable Dyslipidaemia among Lichen Planus Patients

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ABSTRACT

Introduction: Lichen Planus (LP) is a chronic inflammatory cutaneous disease. Some studies investigated its association with Dyslipidaemia as a main contributing factor for cardiovascular insults. Atherogenic Index of Plasma (AIP) is a strong factor for suspecting that risk.

Aim: To investigate lipid profile and calculate AIP in LP patients to early detect atherogenic Dyslipidaemia, if present.

Materials and Methods: This case-control study investigated 40 LP patients and 20 age, gender and body mass index (BMI) matched healthy volunteers. Lipid profile of all subjects was evaluated. AIP was estimated as Log {Triglycerides (TGs)/ High Density Lipoprotein-Cholesterol (HDL-C)} and accordingly, patients were categorised into high, medium and low cardiovascular risk patients.

Results: Dyslipidaemia was detected in 47.5% of patients, while all control subjects had normal lipid profile ($p<0.001$). High Total Cholesterol (TC) and Low Density Lipoprotein-Cholesterol (LDL-C) mean values were significantly associated with LP patients as compared to controls ($p<0.001$ for both), while no significant differences regarding HDL-C and TG levels have been detected. AIP was significantly elevated in LP patients compared to controls ($p=0.002$). Most of the patients (72.5%) have high cardiovascular risk versus 30% of controls ($p=0.004$). About one-third of the high cardiovascular risk patients (31.9%) had no dyslipidemia. High risk patients tend to be of older age with no significant differences regarding gender or disease duration.

Conclusion: AIP is a good predictor of cardiovascular risk in LP patients even in presence of normal lipid profile and should be evaluated in every case to permit earlier management.

Keywords: Cholesterol, Chronic inflammatory cutaneous, Lipoprotein

INTRODUCTION

LP is a chronic, inflammatory cutaneous disease. It also affects the oral and genital mucosa, scalp, and nails [1].

It is an immune-mediated disease; in which Langerhans cells stimulate T-lymphocytes. These stimulated lymphocytes are epidermotropic in nature. It attacks Keratinocytes (KCs), producing reactive oxygen species. During this process, KCs generate inflammatory mediators that potentiate the lymphocytotoxic process. Some investigators proved the association between LP and Cardiovascular Disease (CVD) since inflammation produces disturbances of lipid metabolism which accelerates the Cardiovascular (CV) risk secondary to dyslipidaemia [2].

Lipid profile is known to be a significant predictor for many abnormalities such as dyslipidaemia, hypertension, atherosclerotic vasculature and CVD. Alterations in lipid levels make the individuals more susceptible to endothelial dysfunction and atherosclerotic CVD [3]. The newly-addressed lipid profiles: non-HDL-C, TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C ratios are proposed to be more helpful than the ordinary ones in CVD risk suspicion [4]. Many researches have been investigated on the relationship between TGs and HDL-C. It was proved that the ratio of TGs/HDL-C (atherogenic index of plasma AIP), is a strong predictor of myocardial infarction [5] and atherosclerosis [6].

There are few studies about the relationship between LP and atherogenic lipid profile [2,7,8]. Hence, in the present study authors aimed to investigate the lipid profile and AIP in LP patients in a trial to get benefit from following up of patients for early diagnosis of dyslipidaemia and lowering CV risks.

MATERIALS AND METHODS

A case-control study was conducted on all consecutive LP patients who attended the Dermatology Clinic, Ashmoun General Hospital, Egypt during the period between January and October 2013. Every subject signed a consent form which was approved by the Ethical Research Committee of Menoufia Faculty of Medicine in accordance with Helsinki Declaration (revised in 2000). The study included two groups:

- Patients' group: It included 40 adult patients with LP.
- Control group: It included 20 matched healthy subjects (regarding age, gender and body mass index (BMI)) who were selected from volunteers and blood bank attendants.

Any patient under systemic or topical treatment for LP (within the last four weeks) was excluded. Patients receiving medications that may cause lichenoid drug eruption (non-steroidal anti-inflammatory drugs, beta blockers, thiazide diuretics, angiotensin-converting enzyme inhibitors gold, antimalarial agents, penicillamine, and quinidine) were excluded. In addition, overweight and obese persons (BMI≥25), smokers, alcoholics, hypertensives, diabetics, patients having chronic liver, cardiovascular or thyroid disease or receiving medications that may affect serum lipid level (lipid lowering agents, Isotretinoin, etc.) were not included in the study.

Complete history, general and dermatologic examinations were done for all subjects. Diagnosis of LP was done clinically. BMI was estimated as kg/m^2 [9].

Sample Collection and Biochemical Analysis

Five millilitres of venous blood was withdrawn, under aseptic conditions, after 12 hours-fast. The blood samples were centrifuged at 5000 rpm for five minutes. Serum was frozen (-20°C) to be analysed for TC, TGs, and HDL-C levels within a week using the following methods:

TC: enzymatic methods of Allain CC et al., using Randox England Kit [10].

HDL-C: HDL-C precipitant method [11].

TGs: using enzymes [12].

LDL-C: Friedewald formula [13].

Estimation of AIP: Log (TGs/HDL-C) [14].

Measured parameters were classified according to the following estimated values [Table/Fig-1][13,15-17]:

Dyslipidaemia was diagnosed when TGs >150 mg/dL and/or TC >200 mg/dL and/or LDL-C >130 mg/dL [2].

LDL-C [13]	Normal: 66-130 mg/dL	High: 130-190 mg/dL	Very high >190 mg/dL.
TC [15]	normal: <200 mg/dL	Borderline: 200-239 mg/dL	High: ≥240 mg/dL
TGs [16]	Normal: 35-135 mg/dL	Borderline: 135-149 mg/dL	High: >150 mg/dL.
HDL-C [17]	Normal: >65 mg/dL	Borderline: 45-65 mg/dL	Low: <45 mg/dL

[Table/Fig-1]: Measured parameters were classified according to the following estimated values.

AIP identifies low CV risk if ranging between -0.3- 0.1, medium CV risk if lies between 0.1- 0.24 and high CV risk if it was more than 0.24 [14].

STATISTICAL ANALYSIS

Data were analysed by SPSS version 11 program. Variables were compared using Mann-Whitney test, Student's t-test and Kruskal-Wallis test. Correlations among quantitative variants were assessed using Spearman's correlation coefficient (r). Statistically significant results were considered if p-value was <0.05.

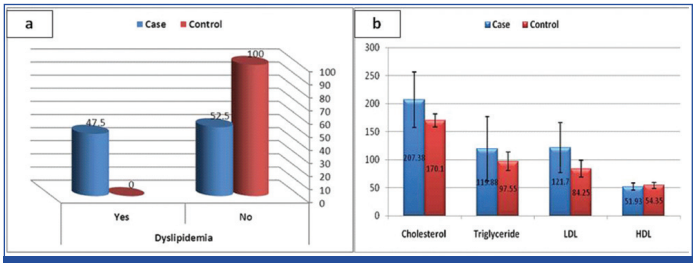
RESULTS

Clinico-demographic data are shown in [Table/Fig-2]

Comparison between LP patients and controls with regard to lipid profile and Dyslipidaemia: Highly significant difference was detected between LP patients and healthy controls regarding dyslipidaemia since 19 patients (47.5%) had dyslipidaemia while all control subjects (100%) had normal lipid profile (p<0.001) [Table/Fig-3a]. Higher mean values of TC (p<0.001), and LDL-C (p<0.001) were significantly associated with LP patients' group, while there were no significant differences between both groups regarding HDL-C and TG levels (p>0.05). However, mean values of TGs tended to be elevated in patients compared to controls (p=0.07) [Table/Fig-3b].

Variables	Cases n=40	Controls n=20	p-value
Age/year			
Mean±SD	38.95±10.73	34.10±9.76	0.095
Range	20-60	20-54	
BMI			
Mean±SD	23.73±1.47	23.55±1.54	0.67
Range	20-25	20-25	
Duration of disease			
Mean±SD	3.28±2.60	_	
Range	0.42-10	_	
Variables	**N (%)**	**N (%)**	**p-value**
Gender			
Male	13 (32.5)	10 (50)	0.19
Female	27 (67.5)	10 (50)	
Affected Site			
Trunk	2 (5.0)	_	
Extremities	19 (47.5)	_	
Trunk and extremities	19 (47.5)	_	
Nail affection			
Yes	3 (7.5)	_	
No	37 (92.5)	_	
Mucosal affection			
Yes	4 (10)	_	
No	36 (90)	_	
Family history			
Yes	2 (5.0)	_	
No	38 (95.0)	_	

[Table/Fig-2]: Demographic and clinical data of the studied subjects.
X±SD mean±standard deviation



[Table/Fig-3]: Comparison between case and control groups regarding: (a) Dyslipidaemia; and b) lipid profile.

Comparison between LP patients with Dyslipidaemia and those without regarding age, gender and disease duration: There was no significant difference between dyslipidaemic and non dyslipidaemic LP patients regarding age, gender and disease duration (p>0.05) [Table/Fig-4].

	The studied Cases				p-value
	With Dyslipidaemia n=19		Without dyslioidemia n=21		
Age/year					
Mean±SD	40.16±9.35		36.02±10.97		0.16
Range	20-56		20-60		
Duration					
Mean±SD	3.71±2.24		2.88±2.88		0.13
Range	0.5-8		0.42-10		
	No	%	No	%	
Gender					
Male	8	42.1	5	23.8	0.22
Female	11	57.9	16	76.2	

[Table/Fig-4]: Comparison between case with Dyslipidaemia and those without Dyslipidaemia as regards age, gender and disease duration.
X±SD mean±standard deviation

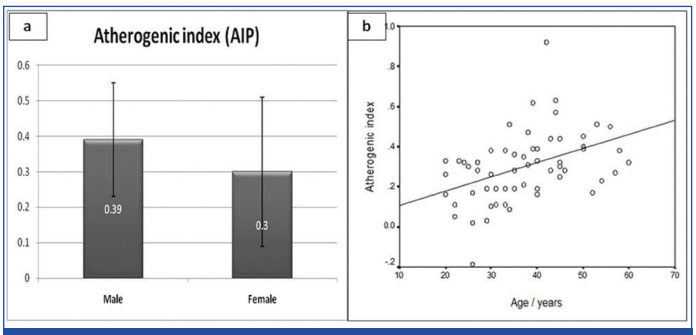
Comparison between patients and controls with regard to AIP: AIP was significantly elevated in LP cases compared to control group (p=0.002) [Table/Fig-5]. Also, a significant difference was found between both groups regarding atherogenic index categories; since 72.5% of LP patients were of high CV risk versus 30% of controls, while 10% of LP patients were of low CV risk versus 40% of controls (p=0.004) [Table/Fig-5].

	Case n=40	Control n=20	p-value
AIP			
Mean±SD	0.33±0.20	0.12±0.22	0.002*
Range	-0.19-0.92	-0.26-0.39	
	N (%)	N (%)	
Atherogenic index categories			
Low risk	4 (10)	8 (40)	0.004*
Medium risk	7 (17.5)	6 (30)	
High risk	29 (72.5)	6 (30)	

[Table/Fig-5]: Comparison between case and control groups regarding atherogenic index of plasma.
AIP atherogenic index of plasma, X±SD mean±standard deviation, *significant

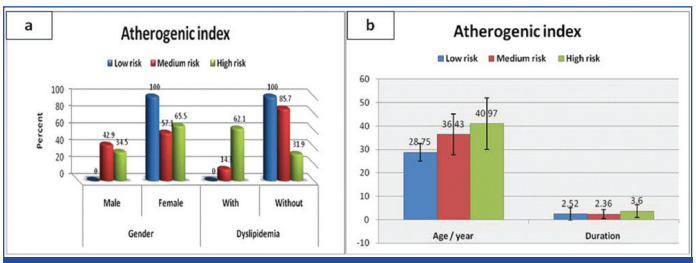
AIP in relation to clinical parameters of LP patients: There was insignificant difference in AIP of both genders (p>0.05) [Table/Fig-6a]. A highly significant positive correlation was identified between

AIP and age of patients (p<0.001) [Table/Fig-6b]. However, no significant correlation has been detected between AIP and disease duration (p>0.05).



[Table/Fig-6]: (a) Demonstration of AIP in male and female lichen planus patients; (b) correlation between AIP and age of patients.

Significant differences were found among atherogenic index categories of cases regarding dyslipidaemia. A total of 62.1% of high CV risk patients had dyslipidaemia, while none of the low-risk patients had dyslipidaemia (p=0.01) [Table/Fig-7a]. No significant differences have been detected between atherogenic index categories of cases with regard to gender and disease duration (p>0.05 for both) [Table/Fig-7a,b]. However, there was a tendency of high risk patients to be of older age. Mean age was 40.97±11.03 in high risk patients versus 28.75±3.77 in low risk patients (p=0.06) [Table/Fig-7b].



[Table/Fig-7]: Comparison among AIP categories of patients regarding clinical parameters: (a) gender, Dyslipidaemia; (b) age and disease duration.

DISCUSSION

In the current study, dyslipidaemia was diagnosed in 47.5% of patients versus none of the controls. Among LP patients, no significant difference was detected between dyslipidaemic and non dyslipidemic cases as regards to age, gender and disease duration. Therefore, there is an association between LP and dyslipidaemia when controlling age, gender and BMI. LP patients had higher serum cholesterol and LDL-C than those of the controls and tended to have higher TG mean values than controls. This agrees to results of Arias-Santiago S et al., [2] in cases with classic LP and Krishnamoorthy B et al., in oral LP [2,18].

López-Jornet P et al., found that LP cases and controls are in different regarding TC or LDL-C but HDL-C was significantly decreased and TGs were significantly elevated in oral LP compared to healthy subjects [19]. This controversy may be attributed to the differences in the studied populations and the clinical types since all of their patients had oral LP with or without cutaneous LP.

AIP, the log transformed ratio TG/HDL-C, is the best method to determine cholesterol etherification rate in HDL-C plasma (FERHDL) which is considered as a functional risk marker for CAD and thus a better indicator of CV risk than individual lipid parameters [20] and can significantly predict atherosclerosis [6,21].

To the best of authors knowledge, AIP (Log TG/HDL-C) has not been studied before in LP patients. In the present study, despite the non significant differences between LP patients and controls regarding TG and HDL-C serum levels, there was a highly significant difference between both with regard to AIP. Also, authors have observed that despite absence of dyslipidaemia in all control subjects, 30% of them were of high CV risk.

This was in agreement with Nwagha UI and Igweh JC, who stated that AIP could be the alternative to diagnose atherogenic risk in cases where other lipid measures appear normal [22]. This was proved in hypertensive menopausal women, since, AIP level approximated high risk values, with apparently insignificant changes in the routine lipid parameters.

Also, the present study showed a significant difference between LP patients and controls with regard to atherogenic index categories, since most of LP patients (72.5%) were of high risk; however the majority of controls (40%) were of low-risk. This may explain the high prevalence of CVD among LP patients.

In the present study, AIP showed a highly significant positive correlation with patients' age. Also, there was a tendency of high risk patients to be of older age. That was in agreement with Bakry OA et al., who demonstrated a similar finding in females with androgenetic alopecia. Therefore, ageing is an independent risk factor for having atherogenic Dyslipidaemia (AD) [23].

LIMITATION

Patients were picked from one dermatology clinic and the resulting data may not be generalisable to other settings. The small sample size and absence of further investigations to assess cardiovascular insults may limit the conclusions of the study. However, the objective nature of the diagnostic tool used in the study and the biological plausibility of its results support the data and the inference obtained from the study.

CONCLUSION

Dyslipidaemia is prevalent among LP patients with no gender differences. AIP (Log TG/HDL-C) could be a better indicator of CV risk in those patients especially in presence of normal lipid profile. The present results may support the recommendation that serum lipid parameters and AIP have to be investigated in all LP patients to ensure earlier identification of previously undiagnosed hyperlipidemia in order to start proper management.

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