ORIGINAL ARTICLE

Study of Insulin Resistance and Dyslipidemia in Psoriasis Patients in a Tertiary Care Hospital, South India

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Abstract:

Background: Psoriasis is a chronic immune mediated inflammatory skin disease with a prevalence of 1–3% in the general population. In recent years, psoriasis has been recognized as a systemic disease associated with metabolic syndrome or its components such as: obesity, insulin resistance, hypertension and atherogenic dyslipidemia. *Aim & Objectives:* To investigate the metabolic state in psoriatic patients in order to clarify the association of psoriasis with insulin resistance and dyslipidemia. *Material and Methods:* The study included 52 psoriasis patients who attended the Outpatient Department of Dermatology at Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, Karnataka, India. The cases were divided into mild (n=28) and severe (n=24) category based on the Psoriasis Area and Severity Index (PASI) score. Fifty healthy controls were also included in the study. Fasting blood glucose, fasting insulin, insulin resistance by Homeostasis Model Assessment (HOMA-IR) method and lipid profile were measured in both cases and controls. *Results:* The fasting insulin levels and insulin resistance measured by HOMA-IR method were significantly ($P<0.05$) higher in mild and severe psoriasis cases when compared to healthy controls. Total Cholesterol, triacyl glycerol, LDL-Cholesterol levels were significantly ($P<0.05$) higher in mild and severe psoriasis cases in comparison with controls. HDL-Cholesterol levels were significantly ($P<0.05$) lower in both mild and severe cases when compared to controls. *Conclusion:* Our findings in this study showed that psoriasis is associated with components of metabolic syndrome like insulin resistance and atherogenic dyslipidemia which are considered to be predisposing factors for diabetes mellitus and cardiovascular diseases. The early detection of insulin resistance and dyslipidemia in psoriasis patients could help them reduce the risk of development of diabetes mellitus and cardiovascular diseases by modifying life style and dietary habits.

Keywords: Psoriasis, Insulin Resistance, Dyslipidemia, Metabolic Syndrome

Introduction:

Psoriasis is a chronic, inherited, and autoimmune inflammatory skin disorder affecting approximately 1-3% of the general population [1]. Psoriasis is a systemic disease in which up to 20-30% of patients show systemic involvement like, atherosclerotic cardiovascular diseases, arthritis, metabolic syndrome which includes components such as obesity, dyslipidemia, Insulin Resistance (IR) and Diabetes Mellitus (DM). It has a significant impact on patient's quality of life [2]. Studies have reported that insulin resistance in psoriasis is a part of its pathogenesis where both share common pathway induced by interleukin-1β [3]. Changes in plasma lipid and lipoprotein composition in patients with psoriasis may be the

reason for the increased risk of atherosclerosis [4]. Several studies from western countries have reported association of insulin resistance and dyslipidemias in psoriasis; however the studies of insulin resistance and dyslipidemia in psoriasis in India are scarce. Hence we conducted this case-control study to establish the same.

Materials and Methods:

This case-control study was conducted at Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, Karnataka, India during the period of 1st March to 31st October 2015. The study included 52 Psoriasis patients attending the outpatient department of dermatology. Of the 52 cases, 28 were mild cases (PASI score<3) and 24 severe cases (PASI score < 10) depending on the Psoriasis Area and Severity Index (PASI) as per the British Association of Dermatologists Guidelines [5]. The study also included 50 controls that were selected randomly from various other outpatient departments. Written informed consent was taken from each subject and our study was approved by ethical committee of the Institute.

Inclusion criteria:

Newly diagnosed psoriatic patients who have not received any treatment for psoriasis or lipid lowering drugs were included in this study.

Exclusion criteria:

All the factors for secondary hyperlipidaemia were excluded such as hypertension, diabetes, obesity and hypothyroid etc. Patients suffering from other inflammatory disorders like rheumatoid arthritis, asthma and atopic dermatitis were also excluded from study.

Methodology:

In both controls and cases, 7 ml of venous blood was drawn with aseptic precautions in the fasting state i.e. after an overnight fasting for 10-12 hrs. Out of 7 ml venous blood drawn, 2 ml was transferred into EDTA vacutainer and 5ml into plain vacutainer. Plasma and serum were separated respectively by centrifuging the samples. Fasting plasma glucose levels were estimated by glucose oxidase method in ERBA Chem 7 semi-auto analyzer using ERBA reagents.

The Fasting Insulin levels were measured in the serum by the Electrochemiluminescence Immunoassay (ECLIA) method in Cobas e 411 analyzer using Roche reagents. Serum total Cholesterol, Triacyl glycerol, HDL-cholesterol and LDL-cholesterol were measured by standard enzymatic methods in ERBA Chem 7 semi-auto analyzer using ERBA reagents. IR was calculated using the Mathew's formula. Homeostasis Model Assessment [HOMA-IR] = Fasting glucose (mmol/L) x Fasting insulin (μU/mL) / 22.5[6].

In both controls and cases, Body Mass Index (BMI) and blood pressure were measured. The statistical data was analyzed by students't' test with 'p' value <0.05 as significant using SPSS software version 16.

Results:

The general demographic characteristic features of controls and cases are shown in table 1 of the 50 controls, 26 were males and 24 were females and their mean age was 33.32±7.25 years. In mild and severe psoriasis cases the male to female ratio was 17/11 with mean age 38.85±10.67 years and 14/10 with mean age 40.37± 9.40 years respectively. Sex did not show any significance between controls

and cases (p=0.73). The body mass index was significantly (p<0.01) higher in mild and severe Psoriasis cases when compared to control subjects.

Table 2 shows comparison of various laboratory parameters between controls and cases. The fasting plasma glucose, fasting insulin, insulin resistance, total cholesterol, triacyl glycerol and LDL-cholesterol were significantly (p<0.001) higher in mild and severe psoriasis cases when compared with control subjects. The HDL-cholesterol levels were significantly (p<0.01) lower in mild and severe cases when compared to controls.

Table 1: Descriptive Characteristics of Cases and Controls

Characteristic	Controls (N=50)	Mild Cases (N=28)	Severe Cases (N=24)	Chi-Square χ 2	P value
Age (Years)	32.32 ±7.25	38.85±10.67	40.37± 9.40	8.782	<0.001
Sex (M/F)	26 / 24	17 / 11	14 / 10	0.6293	0.73^{NS}
BMI	23.19 ± 2.98	25.24 ± 3.77	25.94 ± 3.06	7.173	<0.01
Systolic BP	124.93±19.06	131.41±22.88	134.32±27.56	1.676	0.19^{NS}
Diastolic BP	73.83±12.26	84.72±21.66	85.24±23.89	4.719	<0.05

BMI-Body Mass Index, M-Male, F-Female, NS= Not Significant

Table 2: Comparison of Parameters between Controls and Cases

Parameter	Controls (N=50)	Mild Psoriasis Cases (N=28)	Severe Psoriasis Cases (N=24)	P value
FPG (mmol/l)	5.19±0.52	5.72±0.60	5.77±0.54	<0.001
F.Insulin (mIU/ml)	6.77±1.00	8.25±1.10	10.78±1.98	<0.001
HOMA-IR	1.55±0.33	2.21±0.43	2.75±0.51	<0.001
Total Cholesterol (mg/dl)	178.14±21.12	185±25.45	203.21±34.32	<0.001
TAG (mg/dl)	167.74±24.04	179.61±37.20	213.33±34.32	<0.001
HDL-C (mg/dl)	43.99±4.70	41.07±6.44	38.79±6.68	<0.01
LDL-C (mg/dl)	100.67±16.78	112.79±17.27	122.97±17.38	<0.001

FPG=Fasting Plasma Glucose, TAG= Triacyl Glycerol, HDL-C= HDL Cholesterol, LDL-C= LDL Cholesterol

Table 3 shows comparison of insulin resistance and lipid profile between mild and severe psoriasis cases. The fasting insulin, insulin resistance (HOMA-IR), total cholesterol, triacyl glycerol and LDL-cholesterol, were significantly in severe psoriasis cases compared to mild cases. However, fasting plasma glucose and HDL-C levels did not show significant difference (p>0.05) between mild and severe psoriasis cases.

Table 3: Comparison of Insulin Resistance and Lipid Profile between Mild and Severe Psoriasis Cases

Parameter	Mild cases	Severe cases	P value
FPG (mmol/l)	5.72±0.60	5.77±0.54	0.71 NS
F.Insulin (mIU/ml)	8.25±1.10	10.78±1.98	<0.001
HOMA-IR	2.21±0.43	2.75±0.51	<0.01
Total Cholesterol (mg/dl)	185±25.45	203.21±34.32	<0.05
TAG (mg/dl)	179.61±37.20	213.33±34.32	<0.001
HDL-C (mg/dl)	41.07±6.44	38.79±6.68	0.22 NS
LDL-C (mg/dl)	112.79±17.27	122.97±17.38	<0.05

NS= Not Significant

Discussion:

Psoriasis is a chronic immune-mediated skin disease characterized by hyper proliferation of keratinocytes which is initiated and maintained by inflammatory mediators [7]. Psoriasis, which was primarily considered a cutaneous disease, is recently being identified with systemic inflammation [8]. There is a complex network of inflammatory and immune cells, cytokines, chemokines and growth factors, all of which interact with one another to initiate a cascade of inflammatory events resulting in T-cell infiltration in the epidermis and dermis [9, 10].

Psoriatic patients have an increased prevalence of the core components of metabolic syndrome including; obesity, dyslipidemia, non alcoholic fatty liver disease, IR and DM [11].

The findings in our study clearly demonstrate the presence of insulin resistance among the mild and severe psoriasis cases in comparison with the

control subjects. The insulin resistance was also significantly higher in severe psoriasis cases compared to mild cases. Our results correlated with studies done by Boehncke *et al* [12], Uysal *et al* [13] and Farhad Malekzad *et al* [14].

The probable mechanism involved in the development of insulin resistance in psoriasis is through the activation of different kinases by pro-inflammatory cytokines containing IL-1β, IL-17A, IL-22, IL-23 and TNF-α. The same mechanism is also involved in the formation of atheromatous plaques leading to cardiovascular diseases [3]. The degree of insulin resistance and dyslipidemia are directly proportional to the severity of psoriasis which substantiates our finding that insulin resistance and dyslipidemia were more in severe cases than the mild cases [3].

Dyslipidemia which refers to increased triacyl glycerol levels and decreased HDL-Cholesterol levels was observed among mild and severe psoriasis cases in our study. The degree of dyslipidemia was significantly higher in severe cases when compared to mild cases. The findings in our study are consistent with previous studies on dyslipidemia in psoriasis [13, 15, 16] and its association with severity [15-17].

The exact mechanism for occurrence of dyslipidemia in psoriasis is not clear, however it is thought to be induced by several environmental and immunological factors such as TNF-α and IL-6 [18].The lipids present in the scales of psoriasis have shown increased levels of cholesterol and low free fatty acids. During exfoliation there is loss of cholesterol from the scales. This could be the reason for increased synthesis of serum cholesterol causing dyslipidemia [17]. Furthermore the chronic nature of the disease influences lifestyle, smoking, increased alcohol intake, and stress increase the oxidative damage in the body. This leads to oxidation of LDL-Cholesterol which accumulates in the blood vessels leading to atherosclerosis.

Limitations:

The limitation of our study is that age and sex are not matched in the control groups.

Conclusion:

Our study showed that psoriasis is not only confined to skin but also associated with systemic involvement in the form of insulin resistance and dyslipidemia considered to be risk factors for cardiovascular diseases and diabetes mellitus. Therefore we emphasize early screening of Psoriasis patients for insulin resistance and dyslipidemia, which could help them in reducing the risk of cardiovascular diseases. Thus decreasing the morblity and mortality of psoriasis patients associated with cardiovascular co-morbidities through dietary and lifestyle modifications.

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