ORIGINAL RESEARCH PAPER

Biochemistry

CORRELATION BETWEEN INSULIN RESISTANCE AND PATTERN OF DYSLIPIDAEMIA IN PSORIASIS.

Dr. Suparna Dhara	Demonstrator, Dept. of Biochemistry, North Bengal Medical College, Susrutanagar, Darjeeling, West Bengal.
Dr. Indrajit Nath	Assistant Professor, Dept. of Biochemistry, North Bengal Medical College, Susrutanagar, Darjeeling,
Dr. Anindya Dasgupta*	Dept. of Biochemistry, Calcutta National Medical College, Kolkata-14 *Corresponding Author

ABSTRACT

Objectives: The present study was aimed to assess the relationship between the pattern of dyslipidaemia and body fat deposition with insulin resistance in Psoriatic patients.

Material &methods: Body mass index (BMI) and waist circumference(WC) were measured in 40 psoriaitic patients against matched controls. Fasting Blood Glucose (FBG) and Triglyceride(TG),Cholesterol(CHOL), Low density lipoprotein(LDL), Very low density lipoprotein(VLDL), and High density lipoprotein(HDL) were measured by spectrophotometry. Insulin resistance was assessed by measuring the HOMA-IR values.

Results: FBG, WC and HDL between this two groups were statistically not significant (p value=0.271, 0.21 and 0.72 respectively). On the other hand, BMI, HOMA-IR, TG, CHOL, LDL and VLDL levels were significantly higher in the case group (p < 0.05). Bivariate correlation analysis showed HOMA IR to be significantly associated with FBG, BMI, WC, Total CHOL and LDL (but not with VLDL, TG and HDL values.

Conclusion: mainly an increased insulin resistance that is directly related to significantly elevated levels of abdominal obesity and LDL cholesterol levels reflects metabolic derangements in psoriatic patients in this region. We suggest regular monitoring of psoriatic patients for these parameters to avoid the impending cardiovascular risks in them.

Introduction

Psoriasis is a common chronic, disfiguring, inflammatory and proliferative condition of the skin in which both genetic and environmental influences have critical role [1]. It is a multifactorial disease with phenotypic diversity and genetic heterogeneity [2]. As it affects approx 2-3% of global population [3, 4], it poses substantial contribution for overall morbidity for human suffering. Moreover, although manifested most prominently as a skin disorder, this disease is confounded by several systemic complications some of which become more lethal than its dermatological component. The disease is characterised by T-cell mediated hyperproliferation of keratinocytes, angiogenesis with vasodilatation and excess Th-1 and Th-17 mediated inflammatory processes based on a complex genetic background [5]. The pro inflammatory molecules released during chronic inflammation leads to the presence of one or more disorders co-occuring with psorisis, such as atherosclerosis, atherogenesis, insulin resistance, hypertension, obesity, dyslipidaemia, metabolic syndrome and Diabetes mellitus type2..Some recent studies also reported higher prevalence of insulin resistance in these patients. A well established pathway linked atherosclerosis to obesity via overproduction of tumor necrosis factor(TNF-a),which also contribute to insulin resistance and development of type 2 diabetes melitus[6,7]. Studies have documented the risk of psoriasis to be directly related to the body mass index(BMI) reflecting a casual relationshop between obesity and psoriasis[8]. On the other hand the chronic inflammatory nature of psoriasis and dyslipidaemia have been suggested to be contributing risk factors for the development of atherosclerosis, coronary artery disease and myocardial infarction resulting in increased cardiovascular morbidity[9,10,11]. From these results we hypothesized that there is an association of insulin resistance , dyslipidaemia and central obesity with the disease process in the psoriatic patients. Accordingly, we made an effort to assess the association of these parameters with psoriasis in our region through evaluating FBG, IR, Lipid profile parameters,BMI and WC in them.

2. Materials & methods:
2.1. Selection of cases and controls:
The present hospital based, cross sectional study was undertaken in the Departments of Dermatology & Biochemistry, Burdwan Medical College & Hospital, and Burdwan. 40 patients suffering from psoriasis (clinically and histopathologically confirmed) attending the dermatology Out Patient Department (OPD) with age > 15 years, duration of disease < 2 years (to avoid the metabolic complications of immunosuppressive therapy), not receiving any systemic treatment were selected as the case group by the method of convenience. Age and sex-matched 46 healthy persons attending OPD for cosmetic purposes (Melasma, acquired and congenital melanocytic nevus, epidermal nevus, and milia) were included in the study as control subjects. Patients suffering from diseases that cause secondary hyperglycemia and dyslipidaemia, such as cushing syndrome, hyperthyroidism, corticosteroid therapy etc. and patients also suffering from nephrotic syndrome, chronic renal failure, liver disease, connective tissue disorder were excluded from study. Obese patients (BMI > 30kg/m2), patients on medications such as beta blockers, thiazides, retinoids, cyclosporine, hypoglycaemic drugs, hypolipidaemic drugs, pregnancy and lactating mothers and patient having history of smoking and alcoholism were also excluded.

2.2. Measurement of study parameters:
Fasting plasma glucose level were measured by standard photometric technique following the glucose oxidase peroxidise (GOD-POD) method. Serum insulin was assayed by ELISA from Accubind (USA). Insulin resistance was calculated by the homoeostatic model assessment (HOMA) from the values of fasting glucose levels and serum insulin. For this calculation we took the help of HOMA calculator. (HOMA Calculator 2.2.2, UK, released in December 2007). As HOMA is a steady state model, only clinically realistic values that would be seen in a fasting subject were used (plasma glucose 63mg/dl to 450mg/dl and Plasma insulin 2.79 µIU/ml to 55.76 µIU/ml). Lipid profile parameters level were measured by standard photometric technique following the Cholesterol oxidase peroxidise method(CHOD-PAP) for CHOL, Glycerol 3 phosphate oxidase (GPO) for TG, Direct method for HDL and LDL. All clinically diagnosed cases of psoriasis were confirmed by histopathology.

2.3. Data analysis:
The data obtained were analysed for differences between mean values of the case and control group.Correlation analysis was done to find any association. Statistical analyses were performed with the help of SPSS software version 17.0 for Windows 10. For all

statistical analyses, the p value was considered significant at p < 0.05 for 95% confidence interval.

2.4. Ethical permission: The study protocol strictly adhered to the revised Helsinki declaration for human studies and Institutional ethical clearance was obtained before the start of the study.

3. Results:

Table 1: Independent sample t test for different parameters in case and control groups

Parameters	Case (N=40) Mean (SD)	Control (N=46) Mean (SD)	T	P value
FBG (mg/ dl)	90.475 (10.205)	93.782 (16.282)	- 1.109	0.271
Insulin (µIu/ml)	33.523 (16.12)	8.3 (4.08)	10.247	< 0.001*
HOMA-IR	4.14 (1.98)	1.097 (0.577)	9.929	<0.001*
BMI	24.013 (2.572)	22.852 (2.78)	1.999	0.049*
WC (cm)	86.525 (10.043)	84.13 (7.47)	1.264	0.210
Cholesterol(mg/ dl)	201.27 (39.81)	164.56 (23.66)	5.275	<0.001*
Triglyceride(mg/ dl)	166.37 (45.87)	144.82 (25.62)	2.734	0.008*
HDL Cholesterol (mg/dl)	42.7 (4.96)	44.47 (3.75)	- 1.88	0.63
LDL Cholesterol (mg/dl)	123.85 (37.25)	91.12 (15.3)	5.45	<0.001*
VLDL Cholesterol (mg/dl)	33.27 (9.17)	28.96 (5.12)	2.734	0.008*

*Difference is significant (p < 0.05) at confidence interval (CI) of 95%

In the case group serum insulin level and insulin resistance marker HOMA-IR were found to be significantly raised than those of control group (p <0.001). However, fasting blood glucose level did not show any significant difference between the case and control groups (p = 0.271).

BMI was significantly higher in psoriatic group than in age- and sex-matched control (p=0.049) without any significant increase in the WC parameter indicating a definite increase in overall body weight without any marked change in abdominal obesity (p = 0.21).

Among the Lipid profile parameters , Total CHOL and LDL were found to be significantly raised than those of control group (p <0.001).Triglyceride and VLDL were also raised than in control group(p=0.008). However, HDL level did not show any significant rise (p=0.63).

Table 2: Correlation of IR with other parameters

Parameters	Pearsons correlation (r value)	Significance
FBG(mg/dl)	0.921	<0.001*
BMI	0.986	<0.001*
WC	0.978	<0.001*
Cholesterol	0.941	<0.001*
Triglyceride	-0.114	0.483
HDL Cholesterol	0.247	0.124
LDL Cholesterol	0.928	<0.001*
VLDL Cholesterol	0.114	0.483

The correlation analysis in Table 2 showed the correlation of IR with all other parameters. The results revealed that obesity of both type i.e. general as well as abdominal fat deposition were significantly associated with IR in the psoriatic patients. FBG ,Total CHOL and LDL Cholesterol were also associated significantly with IR in this group.

Figure:1

Association between Insulin Resistance ,LDL Cholesterol & Total. Cholesterol
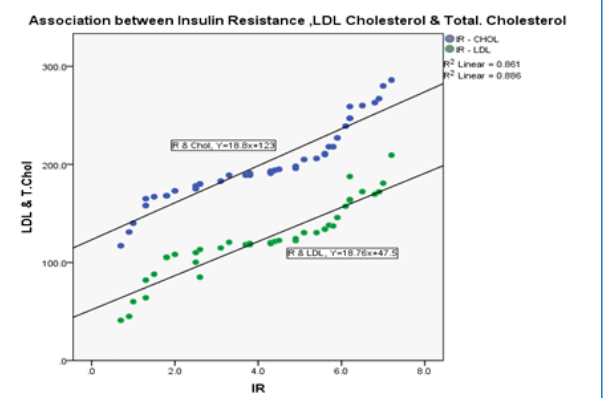
4. Discussion

In the present study,we found significantly higher degree of insulin resistance along with an increased BMI, Total CHOL, TG , LDL and VLDL Cholestereol in the case group (Table 1).On the contrary HDL Cholesterol does not differ significantly between case and control group. The increasing risks for developing atherosclerosis and cardiovascular diseases in psoriasis are attributed to many metabolic complications like diabetes mellitus, obesity, and dyslipidaemia. The results of our present study signified that these metabolic abnormalities in psoriasis may be confounded through an increased insulin resistance and abnormal lipid profile. The increased insulin resistance in our study group was found significantly associated with FBG ,both overall and abdominal obesity, Total cholesterol and LDL as evident from correlation analysis(Table 2). Our findings are corroborated by several studies worldwide that have shown raised serum insulin, HOMA-IR, BMI, WC, Total CHOL,TG,LDL and VLDL in psoriatic patients. Studies conducted by Boehncke S. et al on psoriasis patients showed signs of insulin resistance along with definite correlations between BMI and HOMA (P < 0·02)[12]. P. Krishnamoorthy et al reported that psoriasis patients had more insulin resistant (HOMA-IR: 3.5 vs 1.4, P<0.001) and higher waist circumferences (40 cm vs 35.5 cm, P<0.001) than their normal counterparts [13]. Study of VaishaliDhat et al. (2016) found that psoriasis patients have raised total CHOL, LDL, TG and decreased HDL[14] .Study of Rocha-Pereira et al (2001) also showed similar type of results[15]. On the other hand study of Piskin et al. (2003) have found normal HDL and raised all other parameters of lipid profile [16]. The association between abdominal fat accumulation and risk of chronic disease, including type 2 DM and coronary artery disease has long been recognised. Insulin resistance may be a key factor in this link. Psoriasis is associated with an inflammatory cytokines [17, 18]. These cytokines might play an important role in increasing insulin resistance in them. For example, TNF may lead to insulin resistance through a variety of pathways such as impairing insulin signalling by inhibiting the tyrosine kinase activity of the insulin receptor; by activating peroxisome proliferator-activated receptor (PPAR) which promotes epidermal proliferation and modulates adipogenesis and glucose metabolism; and by suppressing adiponectin secretion from adipocytes, which is an important anti-inflammatory molecule that also functions in regulating insulin sensitivity [19-21] . This change in TNF- level with the duration of psoriasis could provide more definitive answer to hyperlidaemia in psoriasis patients. Impairment in insulin receptor function results in abnormal glucose tolerance, conditions commonly associated with obesity and insulin resistant states. Moreover it is also known that insulin increases LDL receptor expression [22-24]. Thus Insulin resistance is associated with LDL accumulation in blood vessels as a result of poor clearance by functionally impaired LDL receptor [25,26]. This in turn predisposes to atherosclerosis and

cardiovascular diseases. Thus insulin resistance and dyslipidaemia causes the increased risk of cardiovascular morbidity and atherosclerosis in our study population.

Conclusion: The present study provided important insights into the association of insulin resistance , increased body fat deposition and dyslipidaemia in patients of psoriasis that may herald an impending risk factor for cardiovascular disease in future. It will be therefore prudent to follow-up and monitor psoriasis patients for cardiovascular disease and metabolic syndrome with its sequelae. Our study also suggested that psoriasis is no longer a disease of skin; rather it has far reached implications involving some other vital organ systems. An appropriate knowledge regarding the biochemical basis of this association will help to develop a better understanding of the disease process and to make substantial modifications in the management and prognosis of psoriasis.

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