International Journal of Advances in Medicine
Bari R et al. Int J Adv Med. 2022 Jun;9(6):689-693
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20221352

Original Research Article

Insulin resistance in psoriasis: prevalence and prospects from a tertiary care centre

Ranajit Bari[1]*, Kuntolika Mani[2], Mrinmoy Adhikary[3], Shubhankar Chowdhury[1], Jyothi Chowdhury[4], Gobinda Chatterjee[5]

[1]Department of Endocrinology, [2]Department of Physiology, [5]Department of Dermatology, Institute of Post Graduate Medical Education and research, Kolkata, West Bengal, India
[3]Department of Community Medicine, Murshidabad Medical College, Berhampore, West Bengal, India
[4]Department of Pathology, Institute of Child Health, Kolkata, West Bengal, India

Received: 10 April 2022
Revised: 30 April 2022
Accepted: 05 May 2022

***Correspondence:**
Dr. Ranajit Bari,
E-mail: dr.ranajit@gmail.com

ABSTRACT

Background: Psoriasis is a chronic autoimmune inflammatory disorder of skin. Though the exact etio-pathogenesis is not well-understood, several studies hypothesised it as a complex interaction between genetics, immunology, and environment. Hence, we aimed to assess the insulin resistance among psoriasis patients and to correlate the insulin resistance with the disease severity, and inflammation.
Methods: A tertiary hospital-based observational study was conducted for a year (2016-2017) at dermatology and endocrinology OPD, IPGMER and SSKM Hospital, Kolkata. The eligible participants were selected after applying the inclusion and exclusion criteria. After obtaining the written informed consent, basic demographic details were collected and examined for certain physical and biochemical parameters. Data was entered in Microsoft excel and analysed using SPSS software. Appropriate statistical analysis was carried out.
Results: A total of 48 cases and 40 controls participated in the study. The median fasting insulin ($p<0.001$), HOMA-IR ($p<0.001$), and hs CRP ($p=0.047$) in cases were significantly higher than controls. There were significant differences of HOMA-IR within three groups of psoriasis. There was a positive correlation and statistically significant between PASI and HOMA-IR (rho=0.469, p value=0.001) and between PASI and fasting insulin (rho-0.528, p value<0.001).
Conclusions: Chronic psoriasis patients were more insulin resistant and significantly correlated with the disease severity index.

Keywords: Psoriasis, Hospital-based study, Cross-sectional, Insulin resistance, Inflammation

INTRODUCTION

Psoriasis is a chronic, non-communicable, relapsing autoimmune inflammatory disorder of skin and prone among genetically susceptible individuals.[1] The global prevalence of psoriasis varied from 0.14% to 1.99%.[2] The established risk factors for psoriasis were genetic factors, smoking, obesity, drug, alcohol, vitamin D deficiency, infection, stress, trauma.[3-12] Insulin has a role in skin homeostasis mechanism. It regulates the equilibrium between proliferation and differentiation of dermal structures. In psoriasis, high levels of pro-inflammatory cytokines activate p38MAPK, which induces insulin resistance (IR) by serine phosphorylation of IRS, leading to blockade of differentiation and proliferation of basal keratinocytes. Subsequently Boehncke et al found the relationship between psoriasis and insulin resistance in

other way as they got elevated resistin level in patients with psoriasis. They suggested cytokine-induced IR might contribute to epidermal dysfunction and therefore the development of psoriasis.[13] Naturally controversy and confusion arises whether IR is a cause or effect of psoriasis. In 2012, Buerger et al emphasize the IR as a cause of development of psoriasis as they described IL-1 beta to induce insulin resistance via p38MAPK.[14] Insulin resistance (IR) is defined as impaired biologic response to either endogenously secreted or exogenously administered insulin, manifested by decreased insulin stimulated glucose transport, metabolism of adipocytes and skeletal muscle, and increased hepatic glucose output.[15] The gold standard method for measuring IR focuses on maintaining a normal blood glucose level in a hyperinsulinemic state, known as euglycemic hyperinsulinemic clamp.[16] It is a labour intensive and time consuming process, not applicable for routine screening and large scale epidemiological studies. Other direct methods for assessment of IR like insulin sensitivity test (IST), insulin tolerance test (ITT) are not feasible in routine clinical practice. Homeostatic model assessment of insulin resistance (HOMA-IR) is a mathematical model of glucose insulin interaction first described in 1985 by Matthews et al. The denominator 22.5 is a normalizing factor i.e. normal insulin×glucose. Therefore, normal HOMA-IR is 1. It can be used in large studies. Boehncke et al. measured insulin resistance by OGTT and HOMA-IR. They noted that the severity of psoriasis measured by PASI was correlated with insulin resistance.[17] There are only few published studies in this regard in India when compared to global studies. The relationship of IR with the disease severity i.e. using psoriasis area severity index (PASI) and inflammation are less explored in Indian context. Against the aforesaid background, this study was conducted to assess the insulin resistance among psoriasis patients and to correlate the insulin resistance with the disease severity, and inflammation.

METHODS

An observational study was conducted for a period of one year (2016 to 2017) in a tertiary care hospital. The inclusion criteria were patients aged more than 18 years, duration of disease more than 6 months and without any systemic therapy in past one month. The patients with acute psoriasis, severe pustular psoriasis, know case of diabetes or cardiovascular disease, any history of acute illness, pregnancy and lactation were excluded. Patients attending the dermatology and endocrinology outpatient department at IPGMER and SSKM Hospital, Kolkata were selected consecutively and screened for the eligibility criteria. Those who fulfilled the criteria were enrolled for the study. Forty-eight consecutive patients of psoriasis vulgarise diagnosed by the dermatologist from the OPD were recruited after considering proper inclusion and exclusion criteria. Informed consent was taken in their own language. Forty age, sex, and BMI matched subjects who attended with non-inflammatory disorder of skin and patients of primary hypothyroidism on regular levothyroxine therapy with normal thyroid stimulating hormone (TSH) level for at least one year were recruited as control in the same procedure. So, there were 48 cases and 40 controls with total sample of 88.

PASI (psoriasis area severity index) was measured by dermatologist . This is currently the gold standard score for the assessment of extensive psoriasis. Four sites of affection, the head (h), upper limb (u), trunk (t) and lower limbs (l), were separately scored by using three parameters, erythema, induration and desquamation, each of which was graded on a severity scale of 0 to 4, where 0=nil, 1=mild, 2=moderate, 3=severe and 4=very severe. The area-wise percentage involvement of the involved sites was calculated as: 1=less than 10% area; 2=10-29%; 3=30-49%; 4= 0-69%; 5=70-89%; and 6=more than 90%. The final formula for PASI score = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + Iu + Du) Au + 0.3 (Et + It+ Dt) At + 0.4 (El + Il + Dl) Al. The maximum score of PASI is 72. PASI 75 is a 75% reduction of baseline PASI score. It is commonly considered as a denominator for satisfactory results of any treatment modality for psoriasis.

BMI (body mass index) was calculated by following formula- BMI=weight (kg)/height (m^2). Blood samples were collected after 12 hours of fasting. Following blood parameters were tested: Fasting glucose: Fasting glucose was measured from serum sample by GOD-POD method. Fasting insulin: by chemiluminescent immunometric assay by Immulite 1000 HsCRP: by nephelometric technology, BN ProSpec®, SIEMENS indirect serum marker of inflammation. Homeostatic model assessment of insulin resistance (HOMA-IR): It was calculated by the formula. HOMA-IR=Glucose×insulin/22.5 (glucose in mmol/l) or HOMA-IR=Glucose×insulin/405 (glucose in mg/dl).

Study technique

Forty-eight patient of psoriasis were recruited into the study after satisfying inclusion and exclusion criteria. Proper informed consent was taken in their own language. They were undergone thorough history taking on duration of disease, course of illness, concomitant illness, h/o addiction, especially smoking, family h/o diabetes mellitus, psoriasis, and cardiovascular illness. In physical examination the aforementioned parameters were examined properly. Blood samples were drawn after 12 hours of fasting to examine glucose, insulin. HOMA-IR was calculated as mentioned earlier.

Statistical analysis

Data analysis was done using IBM SPSS software vs.22. Chi square test for comparison of categorical variables, unpaired t-test for comparison of numerical variables were used as appropriate. To compare HOMA-IR within subgroups, analysis of variance (ANOVA) test and to compare HOMA-IR in between 3 subgroups least

significance difference (LSD) test were used. A value of 2.5 was taken as cut off for insulin resistance (IR) i.e. values with HOMA≥2.5 were categorised as insulin resistant.[18,19] Correlations between variables were assessed using spearman's rank correlation, p value≤0.05 was considered to be significant.

RESULTS

There were 48 cases and 40 controls participated in the present study. Males were predominant in both the groups. There was significant proportion of current smoker and hypertensive on treatment in psoriasis group as compared to control (Table 1).

Table 1: Comparison of baseline categorical variables between cases and controls.

Variables	Case n=48 (%)	Control n=40 (%)	P value by Chi-square
Age in years (mean±SD)	44.7±15.2	44.6±10.2	0.98
Sex			
Male	38 (79.2)	30 (75)	0.64
Female	10 (20.8)	10 (25)	
Alcohol intake	8 (16.7)	4 (10)	0.36
Current smoker	25 (52.1)	6 (15)	<0.001
Family history of diabetes	8 (16.7)	5 (12.5)	0.58
Hypertensive on treatment	6 (12.5)	0 (0.0)	0.02

There were no significant differences of age, sex, BMI between case and control, as they were matched for these characteristics. The median fasting insulin (p<0.001), HOMA-IR (p<0.001) (Figure 1), and hsCRP (p=0.047) in cases were significantly higher than controls (Table 2). There was statistically significant positive correlation between psoriasis area severity index (PASI) and insulin resistance (HAOMA-IR) (Spearman's rho 0.469, p value-=0.001) (Figure 2). Three subgroups of psoriasis patients depending on severity scale (PASI score), mild (<10), moderate (10-20) and severe (>20). There were 42% cases of mild psoriasis, 31% cases of moderate psoriasis and 27% cases of severe psoriasis (Figure 3). There were significant differences of HOMA-IR within three groups of psoriasis (Table 3). the mean of HOMA-IR of severe psoriasis group (by LSD) was significantly greater than both the means of HOMA-IR in case of mild and moderate psoriasis groups. The mean difference of HOMA-IR between type 1 and type 2 psoriasis were reported by Student t-test. It was found that type 2 psoriasis had significantly higher insulin resistance than type 1 psoriasis (p value=0.02).

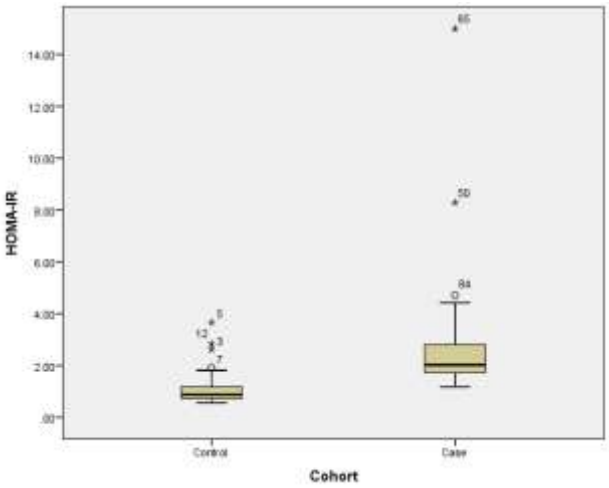

Figure 1: Comparison of HOMA-IR between case and control.

Among cases, 29.2% were IR and in controls, 7.5% were IR. There were statistically significant higher insulin resistant subjects in psoriasis group compared to control (p value=0.010) (Table 4). There was statistically significant positive correlation between psoriasis area severity index (PASI) and insulin resistance (HOMA-IR) (rho=0.469, p value=0.001) and between PASI and fasting insulin (rho=0.528, p value<0.001). CRP was taken as marker of inflammation. There was no significant correlation between CRP and HOMA-IR both in case (rho=0.101, p=0.50) and control (rho=0.03, p=0.90). There was no significant correlation between PASI and hsCRP (CRP) in case (rho=0.097, p=0.51).

Table 2: Comparison of study parameters between cases and controls.

Parameters	Cases (n=48)		Controls (n=40)		Mann-Whitney U value	P value
	Median	IQR	Median	IQR		
Fasting insulin	8.95	7.62-11.7	3.94	3.25-5.18	165.5	<0.001
HOMA-IR	2.02	1.72-2.82	0.88	0.72-1.20	194.00	<0.001
CRP	0.68	0.30-1.30	0.30	0.30-0.52	725.50	0.047

Table 3: Comparison of HOMA-IR within PASI subgroups of cases (N=48).

HOMA-IR in cases								
PASI score	N	Mean	SD	95% confidence interval for mean		Minimum	Maximum	P value by ANOVA
				Lower bound	Upper bound			
Mild (<10)	20	1.88	0.51	1.64	2.12	1.187	2.96	0.01
Moderate (10-20)	15	2.33	0.81	1.88	2.78	1.17	4.1	
Severe (>20)	13	4.13	3.75	1.86	6.4	1.49	14.99	
Total	48	2.63	2.18	2.00	3.27	1.17	14.99	

Table 4: Insulin resistance in case and control.

Group	Insulin non-resistant N (%)	Insulin resistant N (%)	Total	P value
Case	34 (70.8)	14 (29.2)	48 (100)	0.010
Control	37 (92.5)	3 (7.5)	40 (100)	
Total	71 (80.7)	17 (19.3)	88 (100)	

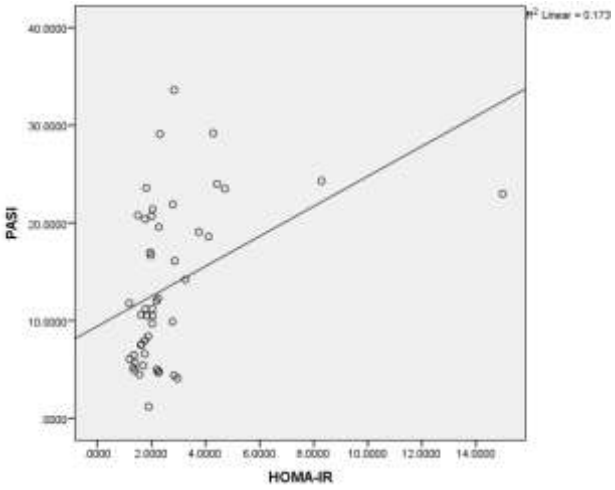

Figure 2: Correlation between psoriasis area severity index (PASI) and HOMA-IR.

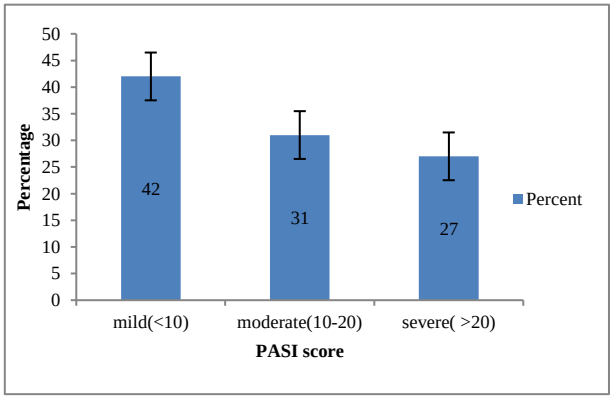

Figure 3: Subgroups of psoriasis patients based on PASI score.

DISCUSSION

In our study, we included 48 patients of chronic plaque psoriasis as case and 40 age, sex, matched control subjects. In comparison to control subjects, patients with psoriasis had significantly higher levels of fasting insulin and HOMA-IR. Patients with psoriasis also had significantly higher levels of hsCRP in comparison to controls which is a reflection of inflammation due to psoriasis. Similar finding was reported by Uysal et al, Dhara et al.[20,21] In the present study, type 2 psoriasis patients had significantly higher HOMA-IR than type 1 psoriasis which coherent with Ucak et al.[22] There were significant differences of HOMA-IR within three groups of psoriasis patients. Patients with severe psoriasis had significantly higher insulin resistance (HOMA-IR) in comparison to mild and moderate psoriasis.

HOMA-IR in patients with psoriasis was significantly correlated with disease severity score (PASI) which was in line with Uysal et al. [20] We accepted HOMA-IR value of 2.5 for insulin resistance in our Indian population according to study by Sing et al.[18,19] Taking that cut off value, 29.17% of our cases and 7.5% of the control subjects were insulin resistant (p value=0.01). So there were significantly higher insulin resistant subjects in psoriasis group compared to age, sex and BMI matched control population. Ucak et al had taken HOMA-IR cut off 3.2, they found 22.9% of cases and 2.5% of control were insulin resistant.[22] In our study mean disease duration was 7.6 years. There was no significant correlation of disease duration with HOMA-IR and PASI. Disease duration having no effect on insulin resistance supports the finding as studied by Ucak et al.[22]

Limitations

As it was a hospital-based study, the study findings could not be generalised. HOMA-IR was an indirect mathematical model assessment of insulin resistance. Further, a longitudinal study needs to be done to explore the natural pathophysiology of the disease and its variation with insulin resistance.

CONCLUSION

Patients with chronic plaque psoriasis were more insulin resistant compared to age, sex, body mass index (BMI)

matched healthy control subjects. Insulin resistance (HOMA-IR) was significantly correlated with disease severity index (PASI). However, inflammation (CRP) was not significantly correlated with disease severity index (PASI) and insulin resistance (HOMA-IR). Type II Psoriasis was associated with significantly higher insulin resistance than type I psoriasis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Griffiths CEM, Barker JNWN. Pathogenesis and clinical features of psoriasis. Lancet. 2007;370:263-71.
2. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. Global psoriasis atlas. national, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:590.
3. Gladman DD, Anhorn KA, Schachter RK, Mervart H. HLA antigens in psoriatic arthritis. J Rheumatol. 1986;13(3):586.
4. Trembath RC, Clough RL, Rosbotham JL, Jones AB, Camp RD, Frodsham A, et al. Identification of a major susceptibility locus on chromosome 6p and evidence for further disease loci revealed by a two stage genome-wide search in psoriasis. Hum Mol Genet. 1997;6(5):813.
5. Mallon E, Bunce M, Wojnarowska F, Welsh K. HLA-CW*0602 is a susceptibility factor in type I psoriasis, and evidence Ala-73 is increased in male type I psoriatics. J Invest Dermatol. 1997;109(2):183.
6. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ Psoriasis and smoking: a systematic review and meta-analysis. Br J Dermatol. 2014;170(2):304-14.
7. Li W, Han J, Choi HK, Qureshi AA Smoking and risk of incident psoriasis among women and men in the UnitAm J Epidemiol. 2012;175(5):402-13.
8. Henseler T, Christophers E Disease concomitance in psoriasis. J Am Acad Dermatol. 1995;32(6):982.
9. Augustin M, Glaeske G, Radtke MA, Christophers E, Reich K, Schäfer I. Epidemiology and comorbidity of psoriasis in children Br J Dermatol. 2010;162(3):633-6.
10. Cullen G, Kroshinsky D, Cheifetz AS, Korzenik JR. Psoriasis associated with anti-tumour necrosis factor therapy in inflammatory bowel disease: a new series and a review of 120 cases from the literature Aliment Pharmacol Ther. 2011;34(11-12):1318-27.
11. Qureshi AA, Dominguez PL, Choi HK, Han J, Curhan G. Alcohol intake and risk of incident psoriasis in US women: a prospective study. Arch Dermatol. 2010;146(12):1364.
12. Poikolainen K, Karvonen J, Pukkala E. Excess mortality related to alcohol and smoking among hospital-treated patients with psoriasis Arch Dermatol. 1999;135(12):1490.
13. Boehncke WH, Boehncke S and Buerger C. Beyond immunopathogenesis. Insulin resistance and "epidermal dysfunction" Hautarzt. 2012; 63:178-83.
14. Claudia B. Interleukin-1b interferes with epidermal homeostasis through induction of insulin resistance: implications for psoriasis pathogenesis. J Investigat Dermatol. 2012;132:2206-14.
15. Warram JH, Martin BC, Krowelski AS, et al. Slow glucose removal rate and hyperinsulinemia precede the development of type II diabetes in the offspring of diabetic parents. Ann Intern Med. 1990;113:909-91.
16. DeFronzo RA, Tobin JD, Andres R: Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979;237:E214-23.
17. Boehncke S, Thaci D, Beschmann H, Ludwig RJ, Ackermann H, Badenhoop K and Boehncke WH. Psoriasis patients show signs of insulin resistance. Br J Dermatol. 2007;157:1249-51.
18. Yashpal S, Garg MK, Tandon N, Marwaha RK. A study of insulin resistance by homa-ir and its cut-off value to identify metabolic syndrome in urban Indian Adolescents. J Clin Res Pediatr Endocrinol. 2013;5(4):245-51.
19. Rhea F, Sadlier M, Connolly M, Marie A. Tobin Psoriasis and insulin resistance: a review. J Diab Res Clin Metab. 2014;2050-0866-3-3.
20. Uysal S, Yilmaz FM, Karatoprak K, Artüz F, Cumbul NU. The levels of serum pentraxin3, CRP, fetuin-A, and insulin in patients with psoriasis. Eur Rev Med Pharmacol Sci. 2014;18:3453-8.
21. Dhara S, Dasgupta A, Rout JK, Banerjee U, Dasgupta S. Clinico-biochemical correlation between psoriasis and IR. Indian J Clin Biochem. 2015;30:99-103.
22. Ucak S, Ekmekci T, Basat O, Koslu A, Altuntas Y. Comparison of various insulin sensivity indices in psoriatic patients and their relationship with type of psoriasis. JEADV. 2006;20:517-22.

Cite this article as: Bari R, Mani K, Adhikary M, Chowdhury S, Chowdhury J, Chatterjee G. Insulin resistance in psoriasis: prevalence and prospects from a tertiary care centre. Int J Adv Med 2022;9:689-93.