Risk factors for cardiovascular diseases and metabolic syndrome in psoriatic patients: case - control study

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ABSTRACT

Background: Psoriasis has an increased likelihood of comorbidities compared with healthy controls such as **cardiovascular diseases and metabolic syndrome.**

Objectives: To investigate the risk factors that increases the incidence of cardiovascular diseases and metabolic syndrome in Iraqi patients with psoriasis.

Patients & methods: a case- control prospective study enrolled 80 patients with psoriasis and 80 normal individuals as a control group. Psoriasis severity was assessed using PASI(psoriasis area severity index) score, in both groups, blood pressure, BMI(body mass index) & waist circumference were measured, laboratory tests including fasting blood sugar & lipid profile were done. For comparison between the 2 groups, Fisher s exact test were performed.

Results: In psoriatic group, calculation of (BMI), showed that 19 (23.8%) were obese, 34 (42.5%) over weight, 27 (38.8%) normal weight. Thirty four patients (42.5%) had an elevated blood pressure, both were significantly correlated with the severity of psoriasis.44 (55%) have abnormal lipid profile, 17 (21.3%) elevated cholesterol, 17(21.3%) had raised LDL & 32 (40%) had low HDL. These were correlated with the severity of psoriasis. Eight (10%) patients had elevated VLDL & 13 (16.3 %) had elevated TG. Twelve (15%) patients had elevated FBS.33 (41.25%) patients were having Metabolic syndrome and the risk was increased with the duration of psoriasis. Comparing with the control group, psoriatic patients were at risk of developing hyperglycemia & hyperlipidemia with statistically significant elevation of fasting blood sugar, cholesterol, LDL, & reduced HDL.

Conclusions: Compared with the control group, psoriatic patients in our population had an atherogenic lipid profile with increased prevalence of risk factors for cardiovascular diseases & metabolic syndrome & this was directly correlated with the severity and duration of the disease.

Key words: risk factors, cardiovascular, psoriasis

عوامل الخطورة للإصابة بأمراض القلب والشرايين ومتلازمة الايض عند المرضى المصابين بداء الصدفية : دراسة مقارنة

المقدمة: ان المرضى المصابين بداء الصدفية تزداد لديهم احتمالية الاصابة بالأمراض المصاحبة كأمراض القلب والشرايين ومتلازمة الايض ، لذلك صمم هذا البحث لدراسة عوامل الخطورة التي تزيد من احتمالية الاصابة بأمراض القلب والشرايين ومتلازمة الايض عند مرضى الصدفية

طريقة العمل: اشتملت الدراسة على ٨٠ مريض بداء الصدفية و ٨٠ اشخاص اصحاء كمجموعة ضبط، تم قياس شدة المرض باستخدام مقياس" باسي سكور "، وفي كلتا المجموعتين تم قياس: الضغط، مؤشر كتلة الجسم، محيط الخصر، نسبة السكر في الدم ونسبة انواع الدهون في الدم. تم اعتماد فحص" فشر اكزاكت" للمقارنة بين المجموعتين.

النتائج: اظهرت الدراسة ان ٢٣.٨% من مرضى الصدفية يعانون من السمنة و٤٢.٥% من فرط الوزن فبما سجل ارتفاع ضغط الدم عند ٤٢.٥% من المرضى وكانت هذه النتائج تتناسب طرديا مع شدة المرض. كانت بنسبة الدهون في الدم مرتفعة بنسبة ٥٥% من المرضى وكما يلي: ارتفاع نسبة الكولسترول عند ١٧ مريض (٢١.٣%) وارتفاع نسبة الكولسترول واطئ الكثافة عند١٧(٢١.٣%) وانخفاض نسبة الكولسترول عالي الكثافة في ٣٢(٤٠%) وكانت هذه النتائج تتناسب طرديا مع شدة المرض، ارتفاع نسبة الكولسترول الشديد التوطئة في ١٠% فيما سجل ارتفاع التراكليسيرايد عند ١٦.٣% وارتفاع نسبة السكر عند١٥% من المرضى كما اظهرت النتائج ان ٣٣ (٤١.٢٥%) من المرضى يعانون من متلازمة

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الايض وتزداد الخطورة طرديا مع فترة الاصابة بالصدفية وبالمقارنة مع مجموعة الضبط فان مرضى الصدفية اكثر عرضة للإصابة بارتفاع نسبة السكر ونسبة انواع الدهون في الدم مع فارق احصائي مهم .

الاستنتاجات: بالمقارنة مع الناس الاصحاء فان مرضى داء الصدفية اكثر عرضة لمخاطر الاصابة بأمراض القلب والشرايين ومتلازمة الايض وهذه الخطورة تتناسب طرديا مع فترة وشدة المرض

INTRODUCTION

Psoriasis is a chronic, relapsing, genetically determined, inflammatory and proliferative disease of the skin, characterized by well-defined erythematous plaques bearing large adherent silvery scales.[1] It affects about 1- 3% of the world's population.[2] Psoriasis is considered as a disorder of keratinocyte proliferation in the epidermis secondary to activated lymphocytes in the dermis. However, the precise mechanism and sequence of interactions between keratinocytes and immune cells is not yet fully understood. Psoriasis is characterized by main pathogenic changes[3]: Epidermal hyper proliferation with loss of differentiation, dilatation and proliferation of dermal blood vessels & accumulation of inflammatory cells, particularly neutrophils and T-lymphocytes. It has been demonstrated that patients with immune _mediated inflammatory diseases, such as psoriasis, have an increased likelihood of comorbidities compared with healthy controls.[4,5] The prevalence of arthritis, depression, suicidal ideation, inflammatory bowel diseases, and lymphoma appears higher in psoriatic patient compared with general population.[6-8] In recent years, there is an accumulating evidence suggesting that psoriasis is a multi-systemic disease, and frequently associated with comorbidities such as cardiovascular diseases and metabolic syndrome[9,10], therefore this study was arranged to investigate the prevalence of risk factors that increases the incidence of cardiovascular diseases and metabolic syndrome in Iraqi patients with psoriasis, and to compare the result with the normal group.

PATIENTS AND METHODS

A cross sectional comparative outpatient based study recruiting 80 patients with psoriasis and 80 normal individuals as a control group matched for the same age and sex. All patients were selected during their consultation to the Department of Dermatology and Venereology at Basra General Hospital, Basrah, Southern Iraq, and all participants gave informed consent. Inclusion criteria were all patients with mild to sever psoriasis including pustular and erythrodermic psoriasis and their age above 15 years old. Patients & normal control who were a known case of cardiovascular diseases or diabetes, and those with family history of medical illnesses, smokers, alcoholics, patients on retinoid or cytotoxic therapy, and pregnant women were excluded. PASI score (Psoriasis Area and Severity Index) was applied to all patients with psoriasis to evaluate the disease severity. [11] Blood pressure (Bpr), body mass index measurement (BMI), and waist circumference were measured for both groups. BMI ranged from 25 to 29.9 was regarded as overweight & 30 and above were Obese .Normal value for the waist circumference was less than 102 cm in male & less than 88 in female. [12] Laboratory measurements were done after an average fasting 12-14 hours using spectrophotometer and enzymatic method for the estimation of serum glucose level & lipid profile which includes total serum cholesterol, triglycerides, HDL, VLDL, and LDL[11,12]**:** Statistical analysis were performed using SPSS version 15.0, Statistical significance was set at $P < 0.05$. For comparison between patients and control group, the Fisher's exact test & chi-square test were performed.

RESULTS

For each group, they were 52 (65%) males and 28(35%) females, their ages ranged from 15-65 years with a mean age of 35.8 ± 12.2 year for both sexes. In patients group; psoriasis varied in severity from mild 10 (12.5%), moderate 29 (36.25%) to sever 41 (51.25%) and the duration of the disease ranged from < 1 year in10 (12.5%) patients, 1-10 years in 42(52.5%) and less than 10 years in 28(35%) patients. (Table-1).

Table 1. Distribution of patients numbers according to duration & severity of psoriasis:

Duration of psoriasis in years	No. of patients	Severity of psoriasis		
		Mild	Moderate	Sever
< 1 year	10 (12.5%)	1	5	4
1 _ 10 years	42(52.5%)	7	16	19
> 10 years	28 (35%)	2	8	18
Total	80 (100%)	10	29	41

Through the calculation of the body mass index (BMI), 19 (23.8%) were obese, 34 (42.5%) over weight, 27 (38.8%) normal weight. While in control group**;** 5 (6.3%) were obese, 30 (37.5%) over weight & 45(56.3%) normal weight, in comparison with the control group, psoriatic patients tended to be more obese than normal control group ($P < 0.05$). Thirty four (42.5%) of psoriatic patients had an elevated blood pressure & only 13 individuals (16.3%) of the control had a raised blood pressure. Compared with the control group, psoriatic patients were at more risk for developing hypertension ($P < 0.05$) (Table-2) & both the high blood pressure & BMI were significantly associated with the severity of psoriasis ($P < 0.05$), (Table-4).

The results of blood analysis showed that 44 (55%) of psoriatic patients had abnormal lipid profile, 17 (21.3%) patients had elevated serum cholesterol and 17(21.3%) had raised LDL & 32 (40%) patients had decreased level of HDL. These findings were directly correlated with the severity of psoriasis ($P < 0.05$), (Table-3). In addition 8 (10%) patients had an elevated level of VLDL and 13 (16.3%) had raised triglyceride (TG). Twelve (15%) patients had high fasting blood sugar (FBS) that are statistically not significantly increased with the severity of psoriasis (P value > 0.05).(Table-3).

Table 2. Relation of elevated blood pressure(Bp) and body mass index (BMI)with the severity of psoriasis.

variables	Total number	No. of patients according to severity of psoriasis			P value
		Mild	Moderate	Sever	
elevated Bp.	34 (42.5%)	1 (10%)	5 (17%)	28 (68.3%)	0.000
normal weight	27 (38.8%)	10 (37.03)	15 (55.5%)	2 (7.4%)	
over weight	34 (42.5%)	0 (0.00%)	13 (38.2%)	21(61.7%)	
obese	19 (23.7%)	0 (0.00%)	1 (5.2%)	18(94.7%)	0.000

Table 3. Relation of serum lipid levels & FBS with severity of psoriasis.

Abnormal analysis	Total number No. (%)	No. of patients according to severity			P value
		Mild psoriasis No. (%)	Moderate psoriasis No. (%)	Sever psoriasis No. (%)	
1. Increase cholesterol	17 (21)	0 (0)	3 (17.6)	14 (82.3)	0.012
2. increase LDL	17 (21)	0 (0)	3 (17)	14 (82.3)	0.012
3. Increase VLDL	8 (10)	0 (0)	4 (50)	4 (50)	0.45
4. Decrease HDL	32 (40)	0 (0)	4 (12.5)	28 (87.5)	0.000
5. Increase TG.	13 (16.3)	0 (0)	5 (38.4)	8 (61.5)	0.32
6. Increase FBS	12 (15)	0 (0)	2 (16.6)	10 (83)	0.48

Table 4. Comparison of the elevated Bpr. and BMI between patients and control groups.

DATA	Patients No. (%)	Control No. (%)	P value
Elevated Bp.	34 (42.5)	13 (16.3)	0.000
BMI: normal weight	27 (33.75)	45 (56.3)	0.002
Over weight	34 (42.5)	30 (37.5)	
Obese	19 (23.8)	5 (6.3)	

Considering blood analysis of the control group; 6(7.5%) had elevated fasting blood sugar ,19 (23.8%) had abnormal lipid profile: 4 (5%) had increase serum cholesterol, 4(5%) with raised LDL, 4 (5%) had low level of HDL, 2(2.5%) had increased VLDL, and 5 (6.3 %) had raised TG (Table-5). Comparing with control group, psoriatic patients were at risk for developing hyperglycemia & hyperlipidemia with statistically significant elevation of fasting blood sugar, cholesterol, LDL, & reduced HDL level (P-value < 0.05). (Table-5).

Table 5. Comparison of serum lipids & FBS levels between patients and control groups.

DATA	Patients No. (%)	Control No. (%)	P value
1. increase cholesterol	17 (21.3)	4 (5)	0.04
2. increase LDL	17 (21.3)	4 (5)	0.04
3. increase VLDL	8 (10)	2 (2.5)	0.98
4. decrease HDL	32 (40%)	4 (5%)	0.000
5. increase TG	13 (16.3%)	5 (6.3%)	0.78
6.increase FBS	12 (15 %)	6 (7.5 %)	0.210

According to the National Cholesterol Education Program Adult Treatment Panel III that defines the diagnosis of metabolic syndrome [12], 33 (41.25%) of our patients were diagnosed as having Metabolic syndrome and the risk was increased with the duration of psoriasis (6% of patients with duration less than 1year compared to 57.5% with more than 10 years duration).

DISCUSSION

Although psoriasis is a chronic inflammatory disease of skin, It is considered now as a systemic condition analogues to other inflammatory immune disorders such as rheumatoid arthritis and systemic lupus erythematosus.[13] Recently, an accumulative evidence from published studies suggested the association of psoriasis with established co morbidities that increases the risk of cardiovascular diseases including components of metabolic syndrome such as hypertension, diabetes, dyslipidemia and obesity.[14,15] Furthermore, inflammation was shown to be a key factor in atherogenesis providing a unifying mechanism for the association between atherosclerosis and chronic inflammatory immune diseases [16]. In psoriasis, Inflammation results in a lymphocytes cytokines milieu, such as TNF-α and IL-6 and other signs of systemic inflammation, such as increased C- reactive protein levels or platelets activation. These factors seem to play a major role in the development of atherosclerosis and ultimately myocardial infarction.[17] The result of our study clearly demonstrated that psoriatic patients have an increased prevalence of co morbidities that are associated with risk of cardiovascular disease as compared to normal control group, in addition we reported a direct correlation between severity of psoriasis and the prevalence of these co-morbidities. An increased risk of hypertension was demonstrated in our psoriatic patients as compared to control group and the risk was significantly correlated with the severity of the disease and this was similarly reported in published studies,[14,15] however in these studies only women with psoriasis were included and a direct association between psoriasis severity and risk of hypertension was not found. The observed association in our study could be explained by the systemic chronic inflammation in psoriasis, [18] the systemic medication used in psoriasis therapy may have a hypertensive adverse effect and lack of exercise owing to physical and social discomfort in psoriatic patients.[19] Although statistically not significant our finding confirmed that psoriatic patients have an elevated risk of diabetes in comparison with non-psoriatic control group and this was similarly reported by other studies,[20-22] and it also strengthen the concept of insulin resistance as a consequence of chronic inflammation associated with psoriasis. Boehnck[23] et al found that the metabolic state in psoriasis to be shifted toward insulin resistance. Further supportive evidence comes from the anti-psoriatic effect of thiozilidinediones, oral hypoglycemic drugs used in type II diabetes mellitus. [24] Although psoriatic patients who received systemic medication for psoriasis were excluded, many of them were on long term topical steroid therapy especially those with extensive skin involvement, therefore the possibility of systemic absorption of topical steroid when applied for long period of time over a large body surface area could, in part, explain the observed increased risk of diabetes in our patients, supporting this, most of our patients did not rigorously adhere to the guidelines of using topical corticosteroid. The study clearly demonstrate a high prevalence of metabolic syndrome in psoriatic patients as compared to control group, furthermore, the risk of metabolic syndrome was higher with the longer duration and with more severe form of psoriasis. These results were comparable with recent studies.[22,25,26] Considering the individual component of metabolic syndrome, obesity was significantly more prevalent in psoriatic patients compared with non-psoriatic control group especially those with sever disease and this finding was similarly reported in other studies.[14,22] The frequent association between psoriasis and development of obesity is not well understood. The more recent observation was focused on the effect of leptin, a hormone that regulates energy intake and expenditure and

adipose metabolism. In one study, serum leptin level and leptin receptor expression in skin were elevated in patients with severe psoriasis,[27] and another study found that psoriasis was significantly associated with hyperleptinaemia independent of gender, metabolic syndrome and obesity, suggesting that leptin has mechanistic role in contributing to the development of obesity and metabolic syndrome in patients with psoriasis.[28] The results of our observation clearly demonstrate a dyslipidemic profile in psoriatic patients and this was significantly correlated with the severity of the disease. Our results also showed a significant difference in the mean level of total cholesterol & LDL between patients and control, moreover there was a significant decrease of HDL cholesterol in the serum of psoriatic patients when compared to control group. In addition, TG and VLDL were also higher in patients with psoriasis although statistically not significant. There is abundance of published data clearly demonstrate an abnormal lipid profile in patients with psoriasis.[29,30] Our results were in consistence with the most recent Iraqi study[31] that showed an atherogenic lipid profile in psoriatic patients compared with matched control especially those with sever disease. The increased vulnerability of psoriatic patients to develop hyperlipidemia is not well explained, some abnormalities in the digestive system has been suggested depending on the finding of structural and functional abnormalities in nearly all the segment of gastro intestinal tract. [32] In addition activation of immune system in psoriasis may cause some changes in patient lipid profile. [30]

In conclusion, psoriatic patients in our population have an increased prevalence of risk factors for cardiovascular diseases compared to normal control and this risk was directly correlated with the severity and duration of the disease. There was an atherogenic lipid profile in patients with psoriasis (raised serum cholesterol, LDL, VLDL and TG with reduction in HDL level). Early recognition of these changes with adequate treatment might reduce the risk of developing cardiovascular diseases in psoriatic patients. Treatment with lipid lowering agents, control of hypertension, diabetes and obesity may significantly reduce the morbidity associated with psoriasis and may improve the psoriatic lesions clinically. Further study focusing on the therapeutic effect of lipid lowering agents in the treatment of psoriatic lesions is highly recommended.

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