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INVESTIGATIVE REPORT

Psoriasis and the Metabolic Syndrome

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Previous reports have shown a possible association between psoriasis and obesity, ischaemic heart disease, hypertension or diabetes mellitus. However, most of these studies were uncontrolled and were based on small sample sizes. We therefore investigated the association between psoriasis and the metabolic syndrome in a case control study. Case patients were defined as patients with a diagnosis of psoriasis vulgaris. Control patients were subjects who underwent hernioplasty or appendectomy. We used data mining techniques utilizing the database of the southern district of Clalit Health Services. The proportions of patients with diseases that belong to the metabolic syndrome were compared between case and control patients by univariate analyses. χ^2 tests were used to compare categorical parameters between the groups. Logistic regression models were used to measure the association between psoriasis and the metabolic syndrome. A total of 340 patients with psoriasis and 6643 controls were included in the study. The mean age of case patients was 47.7 years (SD 10.7 years). There were 50.3% men and 49.7% women. Ischaemic heart disease was present in 23.5% of the patients with psoriasis, compared with 17.2% of the controls (p=0.003). Diabetes mellitus was present in 27.9% of the patients with psoriasis, compared with 19.5% of the controls (p <0.001). Hypertension was present in 44.4% of the patients with psoriasis, compared with 37.2% of the controls (p=0.007). Obesity was present in 29.4% of the patients with psoriasis, compared with 23.5% of the controls (p=0.012). Dyslipidaemia was present in 50.9% of the patients with psoriasis, compared with 44.2% of the controls (p=0.015). The association between psoriasis and the metabolic syndrome was pronounced after the age of 50 years and in men. Multivariate models adjusting for age and gender demonstrated that psoriasis was associated with an increased risk for ischaemic heart disease (odds ratio (OR) 1.4 95% confidence interval (CI) 1.0–1.8), diabetes mellitus (OR 1.5 95% CI 1.2–2.0), hypertension (OR 1.3 95% CI 1.0–1.7), obesity (OR 1.3 95% CI 1.0–1.7) and dyslipidaemia (OR 1.2 95% CI 1.0–1.6). Our findings demonstrate a possible association between psoriasis and the metabolic syndrome. Further studies are needed to establish this observation.

Key words: psoriasis; metabolic syndrome; epidemiology.

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The metabolic syndrome is a combination of diabetes mellitus, hypertension, obesity and hyperlipidaemia. The prevalence of the metabolic syndrome in the USA is estimated to be up to 15% of the population. The pathophysiology of the metabolic syndrome is complex and has been only partially elucidated. Most patients have a degree of insulin resistance, but there is debate as to whether this is the cause of the metabolic syndrome or a by-product of a generalized metabolic derangement. There is a role for systemic inflammation, as a number of inflammatory markers are often increased in patients with the metabolic syndrome (e.g. C-reactive protein, interleukin (IL)-6, or tumour necrosis factor (TNF)-α) (1–3). Recent studies have demonstrated patients with inflammatory diseases, such as systemic lupus erythematosus and rheumatoid arthritis, have an increased risk for diseases in the spectrum of the metabolic syndrome (4, 5). In the last decade it has become evident that psoriasis is an inflammatory disease attributed to alterations in the immune system, involving T lymphocytes (6, 7). Previously, several reports have demonstrated a possible association between psoriasis and diabetes mellitus, cardio-vascular diseases (including hypertension, myocardial infarction and heart failure) and obesity (8–30). However, most of the studies were anecdotal, were based on small sample sizes, or were not controlled. The purpose of the current study was to assess the association between psoriasis and the metabolic syndrome using data mining techniques utilizing the database of "Clalit Health Services" (CHS).

METHODS

This study was designed as a retrospective case-control study using data mining techniques utilizing the CHS database.

The study was conducted in the southern district of CHS, the largest managed care organization in Israel. In the southern district of Israel, CHS serves a population of approximately 470,000 enrolees. The dermatology service in the southern district of CHS includes 17 active dermatologists working in 23 clinics, from Ashkelon in the north to Sapir in the south, accounting for approximately 110,000 patient-physician encounters annually. CHS has a comprehensive computerized database that

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has continuous real-time input from pharmaceutical, medical and administrative computerized operating systems. The diagnoses of components of the metabolic syndrome – diabetes, hypertension, dyslipidaemia and obesity are captured routinely during the everyday practice of CHS family physicians, entered into the computerized system and undergo a process of precise validation for each case.

Case patients were defined as having psoriasis. The diagnoses of psoriasis were retrieved from the computerized database of Soroka University Medical Center. The diagnoses of psoriasis were made by hospital physicians. The control group consisted of subjects without a diagnosis of psoriasis who underwent hernioplasty or appendectomy, sampling the general population.

The proportions of patients with diseases in the metabolic syndrome were compared between case and control patients by univariate analyses. χ^2 tests were used to compare categorical parameters between the groups. *t*-tests were used to compare continuous parameters between the groups. Logistic regression models were used to measure the association between psoriasis and the metabolic syndrome. Statistical analysis was performed using SPSS software.

RESULTS

The study included 340 patients with psoriasis and 6643 controls. The mean age of case patients was 47.7 years (SD 10.7 years, range 24–70 years). The mean age of the controls was 47.0 years (SD 11.0 years, range 22–70 years). In the case group, there were 171 men (50.3%) and 169 women (49.7%). In the control group, there were 3458 men (52.1%) and 3185 women (47.9%).

The proportions of ischaemic heart disease, diabetes mellitus, hypertension, obesity and dyslipidaemia and smoking were increased in patients with psoriasis compared with the control group. The proportions of peripheral vascular disease, cerebro-vascular accidents and carotid artery stenosis were not increased in patients with psoriasis compared with the control group (Table I).

The association between psoriasis and ischaemic heart disease was pronounced in men and above the age of 50 years (Table II), whereas the association between psoriasis and diabetes mellitus was pronounced in men and above the age of 35 years (Table III).

Table II. *Proportion of ischaemic heart disease in patients with psoriasis and in the control group, stratified by age and gender*

	Patients with psoriasis (*n*=340)	Controls (*n*=6643)	OR (95%CI)	*p*
Total	80 (23.5%)	1143 (17.2%)	1.5 (1.1–1.9)	0.003
Age (years)				
<35	0 (0%)	26 (2.5%)	1.0 (1.0–1.0)	ns
35–50	22 (13.8%)	334 (11.4%)	1.0 (1.0–1.0)	ns
50–65	50 (39.7%)	702 (29.0%)	1.2 (1.0–1.4)	0.012
>65	8 (72.7%)	81 (33.8%)	2.4 (0.9–6.4)	0.019
Gender				
Men	54 (31.6%)	798 (23.1%)	1.5 (1.1–2.1)	0.012
Women	26 (15.4%)	345 (10.8%)	1.5 (1.0–2.3)	0.077

OR: odds ratio; CI: confidence interval; ns: not significant.

The association between psoriasis and hypertension, dyslipidaemia and obesity was prominent after the age of 35–50 years (data not shown). The association between psoriasis and smoking was observed in men and women and above the age of 18 years (data not shown). Multivariate models adjusting for age and gender demonstrated that psoriasis was associated with an increased risk for ischaemic heart disease, diabetes mellitus, hypertension, obesity and dyslipidaemia and smoking (Table IV).

DISCUSSION

In the current study it was observed that psoriasis was associated with ischaemic heart disease, diabetes mellitus, hypertension, dyslipidaemia, obesity and smoking. The association was pronounced in men and after the age of 35–50 years. Our study supports a previous observation by Henseler & Christophers (14), Herron et al. (15), Mallbris et al. (22) and other uncontrolled reports that have been published previously (21, 22, 28). Thus, although our study was conducted retrospectively, our findings demonstrate a possible association between psoriasis and the metabolic syndrome.

The metabolic syndrome is a combination of diabetes mellitus type II (or insulin resistance), hypertension,

Table I. *Proportion of diseases in the metabolic syndrome, smoking and obesity in patients with psoriasis and in the control group – univariate analyses*

	Patients with psoriasis (*n*=340)	Controls (*n*=6643)	OR (95% CI)	*p*
Ischaemic heart disease	80 (23.5%)	1143 (17.2%)	1.5 (1.1–1.9)	0.003
Diabetes mellitus	95 (27.9%)	1298 (19.5%)	1.6 (1.2–2.0)	< 0.001
Hypertension	151 (44.4%)	2468 (37.2%)	1.4 (1.1–1.7)	0.007
Dyslipidaemia	173 (50.9%)	2935 (44.2%)	1.3 (1.1–1.6)	< 0.015
Obesity	100 (29.4%)	2935 (23.5%)	1.4 (1.1–1.7)	< 0.012
Smoking	118 (34.7%)	1648 (24.8%)	1.6 (1.3–2.0)	< 0.001
Peripheral vascular disease	15 (4.4%)	242 (3.6%)	1.2 (0.7–2.1)	ns
Cerebro-vascular accident	15 (4.4%)	256 (3.9%)	1.2 (0.7–2.0)	ns
Carotid artery stenosis	5 (1.5%)	89 (1.3%)	1.1 (0.4–2.7)	ns

OR: odds ratio; CI: confidence interval; ns: not significant.

Table III. *Proportion of diabetes mellitus in patients with psoriasis and in the control group, stratified by age and gender*

	Patients with psoriasis (*n*=340)	Controls (*n*=6643)	OR (95% CI)	*p*
Total	95 (27.9%)	1298 (19.5%)	1.6 (1.2–2.0)	<0.001
Age (years)				
<35	2 (4.7%)	68 (6.5%)	0.7 (0.2–3.0)	ns
35–50	33 (20.6%)	461 (15.7%)	1.4 (0.9–2.1)	ns
50–65	53 (42.1%)	695 (28.7%)	1.8 (1.2–2.6)	0.001
>65	7 (63.6%)	74 (30.8%)	3.9 (1.1–13.8)	0.023
Gender				
Men	48 (28.1%)	653 (18.9%)	1.7 (1.2–2.4)	0.003
Women	47 (27.8%)	645 (20.3%)	1.5 (1.1–2.1)	0.018

OR: odds ratio; CI: confidence interval; ns: not significant.

central obesity, and combined hyperlipidaemia (elevated low-density lipoprotein (LDL); decreased high-density lipoprotein (HDL); elevated triglycerides). The diagnosis of the metabolic syndrome has been revised recently by the International Diabetes Federation (31) as central obesity (according to ethnicity specific waist circumference) plus any 2 of the following criteria:

1. Raised triglycerides:
   >150 mg/dl (1.7 mmol/l)
   Specific treatment for this lipid abnormality.
2. Reduced HDL-cholesterol:
   <40 mg/dl (1.03 mmol/l) in men
   <50 mg/dl (1.29 mmol/l) in women
   Specific treatment for this lipid abnormality.
3. Raised blood pressure:
   Systolic >130 mmHg
   Diastolic >85 mmHg
   Treatment of previously diagnosed hypertension.
4. Raised fasting plasma glucose:
   Fasting plasma glucose >100 mg/dl (5•6 mmol/l)
   Previously diagnosed type 2 diabetes.

Diseases associated with the metabolic syndrome are polycystic ovarian syndrome, haemochromatosis, acanthosis nigricans and fatty liver. The diseases that comprise the metabolic syndrome are treated separately. However, drugs that decrease insulin resistance (metformin and thiazolidinediones) not only reduce hyperglycaemia, but may also cause improvement in blood pressure and lipid profile (1–3).

Table IV. *Logistic regression models of the association between diseases in the metabolic syndrome and psoriasis (multivariate analyses)*

	OR; 95% CI
Ischaemic heart disease	1.4; 1.0–1.8*
Diabetes mellitus	1.5; 1.2–2.0
Hypertension	1.3; 1.0–1.7
Dyslipidaemia	1.2; 1.0–1.6
Obesity	1.3; 1.0–1.7

OR: odds ratio; CI: confidence interval.
*In each model, the odds ratios are adjusted with age, gender and smoking status.

Previous studies have shown an increased risk of atherosclerosis in patients with inflammatory diseases such as systemic lupus erythematosus and rheumatoid arthritis (6, 7). Inflammation was shown to be a key factor in atherogenesis, providing a unifying mechanism for explaining the association between atherosclerosis and chronic inflammatory diseases involving inflammatory cytokines, T cells and macrophages. It is possible that psoriasis is an inflammatory disease that is associated with atherosclerosis, similar to the association of atherosclerosis and systemic lupus erythematosus and rheumatoid arthritis.

In the present study, 104/340 patients with psoriasis (30.6%) were hospitalized for psoriasis, which occurred due the sampling process of hospital-based information systems. As patients who are hospitalized are known to have more concomitant diseases, a possible bias might have been introduced into the study. However, even when the data analyses was repeated using strata of psoriasis patients who were hospitalized for psoriasis or patients who were never hospitalized for psoriasis, the results were not significantly different between the strata.

It is important to emphasize that association alone, and not causality, was proven. Further prospective studies are needed to establish this novel observation. If this observation is accurate, psoriasis may take a role as a new risk factor for diseases such as ischaemic heart disease. In addition, we suggest that patients with psoriasis should be evaluated for the concomitant presence of diseases, such as ischaemic heart disease, hypertension and diabetes mellitus and obesity. In our service, at the southern district of CHS, we plan a targeted intervention program in patients with psoriasis in order to identify and treat diseases that are in the spectrum of the metabolic syndrome and to promote smoking cessation.

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