Prevalence of the Metabolic Syndrome in Psoriasis

Results From the National Health and Nutrition Examination Survey, 2003-2006

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Objectives: To estimate the prevalence of the metabolic syndrome among individuals with psoriasis and to examine the association between these 2 conditions in the general US population.

Design: Cross-sectional health survey of a nationally representative random sample of the noninstitutionalized civilian US population.

Setting: The National Health and Nutrition Examination Survey, 2003-2006.

Participants: The study included 6549 participants aged 20 to 59 years.

Main Outcome Measures: Prevalence of the metabolic syndrome defined by the revised National Cholesterol Education Program Adult Treatment Panel III definition and odds ratios for associations after adjustment for age, sex, race/ethnicity, smoking status, and C-reactive protein levels.

Results: The prevalence of the metabolic syndrome was 40% among psoriasis cases and 23% among controls. According to 2008 US census data, the projected number of patients with psoriasis aged 20 to 59 years with the metabolic syndrome was 2.7 million. The univariate and multivariate odds ratios for patients with psoriasis and the metabolic syndrome were 2.16 (95% confidence interval, 1.16 to 4.03) and 1.96 (1.01 to 3.77), respectively. The most common feature of the metabolic syndrome among patients with psoriasis was abdominal obesity, followed by hypertriglyceridemia and low levels of high-density lipoprotein cholesterol.

Conclusions: The prevalence of the metabolic syndrome is high among individuals with psoriasis. Given the serious complications associated with the metabolic syndrome, this frequent comorbidity should be recognized and taken into account in the long-term treatment of individuals with psoriasis.

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P SORIASIS IS A CHRONIC, INflammatory disease of the skin that affects approximately 2% of the population[1-4] and poses a lifelong burden for those affected.[1] A survey by the National Psoriasis Foundation found that 75% of patients with psoriasis reported a moderate to large negative impact of the disease on the quality of their life, with an alteration of everyday activities.[5]

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The negative impact of psoriasis may not be limited to its cutaneous or psychosocial manifestations. Previous studies have suggested a link between psoriasis, a common inflammatory disorder, and individual components of the metabolic syndrome, such as obesity, hypertension, diabetes, and dyslipidemia.[6-11] However, data on the association between psoriasis and the metabolic syndrome defined by a standard definition[12] are scarce,[13] as reflected in a recent review.[14] We are aware of only 1 prior study that examined this association, based on hospital patients in northern Italy.[15] Using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, that study reported a 65% increased risk of the metabolic syndrome developing among patients with psoriasis compared with patients with other skin diseases.[15] To date, to our knowledge, no population-based data are available. Therefore, it remains unknown whether the association exists in the context of the general population and, if so, by what magnitude.

Recent studies have estimated a prevalence of 15% to 24% for the metabolic syndrome in the general population.[16,17] Because the implications of the metabolic syndrome for the overall health of indi-

Table 1. Characteristics of the Study Participants According to Presence of Psoriasis

Variable	Psoriasis (n=71)	No Psoriasis (n=2385)	P Value
	(95% CI)[a]	(95% CI)[a]	
Age, y	41.7 (38.9-44.4)	38.6 (38.1-39.2)	.04
Male sex	46.4 (34.7-58.2)	50.1 (48.0-52.1)	.55
Non-Hispanic white	83.1 (72.9-93.3)	69.8 (65.1-74.5)	.008
Smoking status			.55
Never smoker	47.4 (33.8-61.0)	53.3 (50.3-56.2)	
Former smoker	25.1 (15.3-34.9)	18.7 (16.3-21.1)	
Current smoker	27.5 (15.0-40.1)	28.0 (25.0-31.1)	
CRP, mg/dL	0.6 (0.4-0.8)	0.4 (0.4-0.5)	.14
Waist circumference, cm	101.8 (97.9-105.7)	96.0 (95.2-96.9)	.003
BMI	30.3 (28.7-31.9)	28.1 (27.7-28.5)	.01
Systolic blood pressure, mm Hg	122.1 (118.5-125.7)	117.9 (117.3-118.6)	.02
Diastolic blood pressure, mm Hg	74.1 (70.9-77.4)	70.9 (70.2-71.7)	.06
Triglycerides, mg/dL	173.9 (125.1-222.6)	136.4 (129.0-143.8)	.12
HDL-C, mg/dL	53.7 (48.8-58.6)	54.8 (53.9-55.8)	.64
Fasting glucose, mg/dL	96.5 (94.2-99.1)	95.9 (94.9-96.8)	.58

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol.

SI conversion factors: To convert fasting glucose, HDL-C, and triglycerides to millilmoles per liter, multiply by 0.0555, 0.0259, and 0.0113, respectively, and to convert CRP to nanomoles per liter, multiply by 95.24.

[a]Values are means (95% CI) or proportions (95% CI) as appropriate for the variable. Data are presented incorporating sample weights and are adjusted for clusters and strata of the complex sample design of the National Health and Nutrition Examination Survey.

viduals are substantial and psoriasis is a common skin disorder, we sought to assess the prevalence of the metabolic syndrome and its associated components among individuals with psoriasis and to compare them with individuals without psoriasis in the general population using data from the National Health and Nutrition Examination Survey (NHANES), 2003-2006.

METHODS

STUDY POPULATION

Since 1999, NHANES has been conducted every 2 years[16] using a multistage, stratified design. In the 2 cycles from 2003-2004 and 2005-2006, a total of 6549 participants aged 20 to 59 years were asked whether they had been diagnosed as having psoriasis. Approximately half of all participants were then randomly assigned to participate in a fasting laboratory study. In this study, we analyzed data for all of the 2456 individuals without a prior diagnosis of diabetes who attended the medical examination, had fasted prior to the blood collection, had answered the question about psoriasis, and who had complete information for the variables presented in **Table 1**. The NHANES study underwent institutional review board approval, and written informed consent was obtained from the participants before initiation of the study.

ASSESSMENT OF THE METABOLIC SYNDROME

Our primary definition of the metabolic syndrome was based on the revised criteria from NCEP ATP III.[12] According to the revised NCEP ATP III criteria, participants with 3 or more of the following criteria were defined as having the metabolic syndrome: abdominal obesity (waist circumference, >102 cm in men and >88 cm in women); hypertriglyceridemia (triglycerides, ≥150 mg/dL [to convert to millimoles per liter, multiply by 0.0113]); low levels of high-density lipoprotein cholesterol

(<40 mg/dL [to convert to millimoles per liter, multiply by 0.0259] in men and <50 mg/dL in women); high blood pressure (≥130/85 mm Hg); and high fasting glucose levels (≥100 mg/dL [to convert to millimoles per liter, multiply by 0.0555]). We also reported our results using the original NCEP ATP III criteria, which use a different cutoff for the fasting glucose levels (ie, ≥110 mg/dL) but are otherwise identical to the revised criteria.[17] Fasting glucose levels were measured using a hexokinase method. Triglycerides were measured enzymatically in serum using a series of coupled reactions. High-density lipoprotein cholesterol levels were measured using a direct immunoassay method (Roche/Boehringer-Mannheim Diagnostics, Indianapolis, Indiana). Details regarding the laboratory procedures for all of these tests have been published elsewhere.[16] Because our purpose was to identify individuals with the metabolic syndrome, who would be at a higher risk of developing type 2 diabetes mellitus (or cardiovascular outcomes) in the future, we excluded diabetic individuals from our analysis. We performed a sensitivity analysis with which we repeated the main analysis with the diabetic individuals included.

ASSESSMENT OF PSORIASIS

During the home interview, all participants aged 20 to 59 years were asked, "Have you ever been told by a health care provider that you had psoriasis?" Such a self-report of psoriasis has been used to estimate the prevalence of psoriasis in the US population[18] and has also frequently been used in previous epidemiological studies of psoriasis.[19-22]

STATISTICAL ANALYSIS

All statistical analyses were performed using the survey commands of Stata, version 11 (StataCorp, College Station, Texas), to incorporate sample weights and to adjust for clusters and strata of the complex sample design. The prevalence of the metabolic syndrome was calculated according to the presence of psoriasis. Logistic regression was performed to evaluate the asso-

Table 2. Prevalence of the Metabolic Syndrome According to the Presence of Psoriasis in the National Health and Nutrition Examination Survey (NHANES), 2003-2006[a]

| | Revised NCEP ATP III Definition | | | | Original NCEP ATP III Definition | | | |
| | | | OR (95% CI) | | | | OR (95% CI) | |
Variable	Psoriasis, %	No Psoriasis, %	Unadjusted	Multivariate[b]	Psoriasis, %	No Psoriasis, %	Unadjusted	Multivariate[b]
Total (N=2456)	39.9	23.5	2.16 (1.16-4.03)	1.96 (1.02-3.77)	31.4	17.1	2.22 (1.22-4.02)	2.02 (1.07-3.83)
Male (n=1183)	30.6	26.6	1.22 (0.52-2.85)	1.08 (0.45-2.58)	28.8	18.8	1.74 (0.72-4.25)	1.60 (0.64-3.99)
Female (n=1273)	47.9	20.4	3.53 (1.61-7.78)	2.80 (1.12-6.96)	33.7	15.4	2.79 (1.36-5.70)	2.21 (0.94-5.18)

Abbreviations: CI, confidence interval; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; OR, odds ratio.
[a] Data are presented incorporating sample weights and adjusted for clusters and strata of the complex sample design of NHANES.
[b] Multivariate OR refers to ORs obtained using a logistic regression model after adjustment for age, sex, race/ethnicity, smoking status, and C-reactive protein levels. When subgroups were looked at by sex, this variable was removed from the multivariate model.

ciation between psoriasis and the presence of the metabolic syndrome, and the results were expressed as odds ratios (ORs), first without adjustment and then with adjustment of the covariates. Age and race/ethnicity are known to affect the prevalence of the metabolic syndrome and were included as covariates in multivariate models along with sex.[23] Smoking status and inflammation (measured by C-reactive protein [CRP] levels) were also entered as covariates because of their known associations with insulin sensitivity, diabetes, and weight.[24-27] Serum levels of glucose, triglycerides, and high-density lipoprotein cholesterol; waist circumference; and blood pressure are all part of the definition of the metabolic syndrome and were therefore excluded from the multivariate model.[17] We plotted histograms with normal density plots to compare the frequency of the metabolic syndrome features between patients with psoriasis and controls and evaluated the statistical significance of the trend using the Pearson χ^2 test. For all measures, 95% confidence intervals (95% CIs) were calculated. All P values are 2-sided.

RESULTS

The mean age of the overall population was 39 years; 50% of the participants were male; 70% were white; and the mean body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) was 28. The prevalence of psoriasis in this population was 4% (95% CI, 3%-5%), and the characteristics of the study population according to presence of psoriasis are shown in Table 1. The mean age of the participants with psoriasis was 42 years; 46% were male; 83% were white; and the mean BMI was 30. Age, BMI, waist circumference, and systolic blood pressure were significantly higher in individuals with psoriasis compared with those without psoriasis (P=.04, .01, .003, and .02, respectively).

The prevalence of the metabolic syndrome according to the revised NCEP ATP III criteria was 40% among individuals with psoriasis and 23% among individuals without psoriasis (**Table 2**). The OR for patients with psoriasis and the metabolic syndrome was 2.16 (95% CI, 1.16-4.03) on univariate analysis and 1.96 (95% CI, 1.02-3.77) after adjustment for age, sex, race/ethnicity, smoking, and serum CRP levels. The corresponding ORs for the original NCEP ATP III criteria were 2.22 (95% CI, 1.22-4.02) and 2.02 (95% CI, 1.07-3.83). When we removed CRP measurements from the multivariate models, the ORs did not change materially. The

prevalence of the metabolic syndrome among women with psoriasis was higher than that among men with psoriasis, whereas the prevalence among female controls was lower than that among male controls (Table 2). The multivariate ORs using the revised criteria for the metabolic syndrome were 2.21 (95% CI, 0.94-5.18) among women and 1.60 (95% CI, 0.64-3.99) among men (P for interaction by sex, 0.1). Repeating this analysis with diabetic individuals included did not materially affect the point estimates presented above.

When we applied these data to the 2008 US census population estimate, 6.6 million (95% CI, 4.8-8.3) individuals aged 20 to 59 years were estimated to have psoriasis in the United States, and 2.7 million (95% CI, 1.6-3.6) of these individuals with psoriasis were estimated to have the metabolic syndrome, an excess of 1 million patients compared with the expected value among individuals without psoriasis.

The prevalence of individual components of the metabolic syndrome according to presence of psoriasis is shown in **Table 3**. The most common abnormal metabolic feature among individuals with psoriasis was abdominal obesity, which was present in 63% of patients, followed by hypertriglyceridemia and low high-density lipoprotein cholesterol levels. The **Figure** illustrates a higher prevalence of individuals meeting the NCEP ATP III criteria and a shift to the right of the frequency distribution of the metabolic syndrome components. No elements of the metabolic syndrome were present in 28% of individuals without psoriasis, whereas 13% of those with psoriasis were free of any components of the metabolic syndrome (P=.004). The difference in the frequency distribution of metabolic components between the 2 groups was statistically significant (P=.02).

COMMENT

In this nationally representative sample of US men and women, we found that 40% of US adults with psoriasis had the metabolic syndrome. Compared with individuals without psoriasis, the prevalence was nearly double among those with psoriasis, and the excess prevalence remained substantial after adjustment for covariates such as age, sex, smoking status, and CRP levels. Based on these data, it is estimated that of the 6.6 million adults (age

Table 3. Prevalence of Individual Metabolic Abnormalities of the Metabolic Syndrome According to Presence of Psoriasis in the National Health and Nutrition Examination Survey (NHANES), 2003-2006 [a]

Variable	% (95% CI)		OR [b] (95% /CI)
	Psoriasis	No Psoriasis	
Abdominal obesity	62.9 (51.3-74.5)	47.9 (45.3-50.5)	1.72 (1.03-2.86)
Hypertriglyceridemia	44 (33.8-54.2)	27.2 (24.9-29.6)	2.08 (1.39-3.11)
Low HDL cholesterol	33.9 (23.7-44.1)	23.9 (21.3-26.4)	1.63 (0.98-2.71)
High blood pressure	28.4 (14.8-41.9)	22.2 (20.4-24)	1.33 (0.63-2.79)
High fasting glucose, original	8.4 (1.4-15.4)	8.0 (6.5-9.4)	1.01 (0.44-2.36)
High fasting glucose, modified	30.5 (16.9-44.1)	28.5 (25-32)	1.06 (0.56-1.99)

Abbreviations: CI, confidence interval; HDL, high-density lipoprotein; OR, odds ratio.
[a] Data are presented incorporating sample weights and adjusted for clusters and strata of the complex sample design of NHANES.
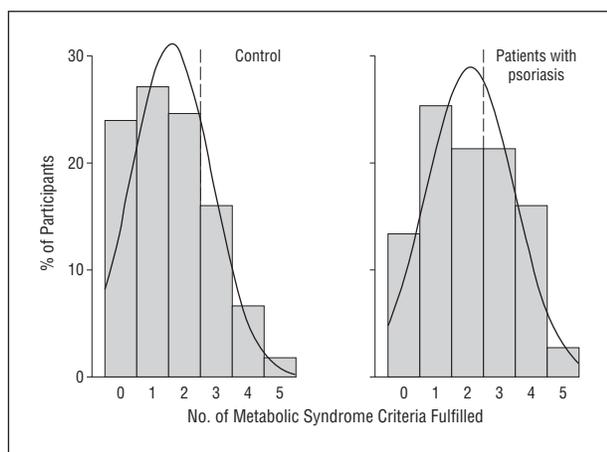[b] Odds ratios are adjusted for age, sex, and race/ethnicity.

Figure. Frequency distribution of the metabolic syndrome components according to the presence of psoriasis. The dashed vertical line marks the cutoff for the definition of the metabolic syndrome, with the columns to the right of this line representing those patients meeting the modified National Cholesterol Education Program Adult Treatment Panel III criteria. The solid line represents the normal density plot, showing a shift toward the right among patients with psoriasis.

range, 20-59 years) with psoriasis in the United States, 2.7 million have the metabolic syndrome, or nearly a million more individuals than would be expected from individuals without psoriasis. This prevalence estimate for psoriasis is consistent with previous reports.[20]

These findings may partially explain the increased future risk of cardiovascular-metabolic morbidity and mortality among individuals with psoriasis reported in previous studies. For example, large population-based cohort studies in the United Kingdom demonstrated increased risks of myocardial infarction, stroke, and cardiovascular mortality in patients with severe psoriasis.[18,28,29] These findings have been supported further in a recent meta-analysis of cardiovascular disease in psoriasis.[30] Furthermore, women with psoriasis showed a 63% increased risk of future diabetes compared with women without psoriasis.[9] Finally, patients with severe psoriasis were found to die about 3 to 4 years earlier than patients without psoriasis.[31] As these cardiovascular outcomes are known complications of the metabolic syndrome, its increased presence in psoriasis may contribute to the increased risk of these complications seen in individuals with psoriasis.

Our findings also have important clinical implications. First, a diagnosis of psoriasis should trigger a high clinical suspicion and investigation for a potential coexistence of the metabolic syndrome. If present, the syndrome needs to be recognized as a potentially more life-threatening factor than psoriasis given the serious associated complications.[31] The cornerstones of treatment of the syndrome are the management of weight and ensuring appropriate levels of physical activity as demonstrated by studies showing that dietary modification and enhanced physical activity may delay or prevent the transition from impaired glucose tolerance to type 2 diabetes mellitus.[32] These lifestyle interventions, particularly weight reduction, may even enhance the efficacy of psoriasis treatment, as demonstrated in a recent randomized trial[33] and by case reports of dramatic improvement of psoriasis after gastrectomy for obesity.[34]

The close association with the metabolic syndrome and its complications may become relevant when determining long-term therapeutic options in the psoriasis population. For example, tumor necrosis factor blockers may decrease insulin resistance in patients with psoriasis,[35,36] and although the association between tumor necrosis factor treatments and weight gain have not been reported in randomized trials, 2 recent articles suggested that these treatments are associated with weight gain, with no clear difference in lipid profile.[37,38] These data call for larger-scale studies to determine how individual treatment regimens affect the metabolic syndrome and cardiovascular disease risk in patients with psoriasis. Furthermore, it would also be valuable to study whether aggressive preventive treatment results in better cardiovascular-metabolic outcomes for patients with psoriasis.

We found that abdominal obesity and disturbances in lipid profiles were the most important factors leading to the increased prevalence of the metabolic syndrome in this study. The aforementioned hospital-based case-control study using the NCEP ATP III criteria also found that the metabolic syndrome in patients with psoriasis was primarily driven by obesity and high triglyceride levels,[15] and a recent meta-analysis found that many studies have shown an increased prevalence of traditional cardiovascular risk factors, but not all found an association with diabetes.[39] As central obesity is associated with abnormal levels of various inflammatory markers, including tumor necrosis factor α and interleukin 6,[32] it is con-

ceivable that these factors may contribute to the pathogenesis of psoriasis. Indeed, 2 large cohort studies found that obesity is associated with the future development of psoriasis.[7,40] On the other hand, the close association between psoriasis and the metabolic syndrome could be explained by shared genetic risk loci, as recent genome-wide association studies indicate. For example, *CDKAL1* has been associated with both psoriasis and type 2 diabetes mellitus, and *PTPN22* has been associated with many diseases, including psoriasis and type 1 diabetes mellitus.[41] It would be interesting to see whether these genotypes modify the association between psoriasis and the metabolic syndrome.

The strengths and limitations of our study deserve comment. This study was performed in a nationally representative sample of US men and women; therefore, the findings are likely to be generalizable to US men and women. Our data seem to suggest that the association between psoriasis and the metabolic syndrome is present in women only, but because of small subgroup sizes, this finding should be interpreted with caution. Similar to other population-based epidemiological studies of psoriasis,[1,4,22] the self-reported diagnosis of psoriasis by a physician in this study was not validated with an examination by a dermatologist. However, it is unlikely that misclassification of the diagnosis would explain the substantial associations observed in this population study. It remains conceivable that the results may even be more striking with more specific case definitions of psoriasis. Nonetheless, confirming these results using such specific case definitions of psoriasis would be valuable. The current study intended to provide national estimates of the prevalence of the metabolic syndrome among individuals with psoriasis and the magnitude of the cross-sectional association between the 2 conditions. Both aims were well served by the NHANES study design. Potential temporal relationships between these disorders should be addressed by longitudinal studies.

In conclusion, these findings from a nationally representative sample of US adults show a doubling in the prevalence of the metabolic syndrome among patients with psoriasis independent of age, sex, race/ethnicity, smoking status, and CRP levels. These findings estimate that 2.7 million patients with psoriasis aged 20 to 59 years are affected by the metabolic syndrome. Given its associated serious complications, this comorbidity needs to be recognized and taken into account when treating individuals with psoriasis.

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PRACTICE GAPS

Lack of Appropriate Screening for the Metabolic Syndrome in Patients With Psoriasis Risks Underrecognition and Undertreatment of Important Comorbidities

Recent advances have solidified our understanding that psoriasis is an important systemic inflammatory disease. Specifically, characterization of the inflammatory cells and the cytokine milieu, as well as an appreciation of increased cardiovascular risk factors, vascular disease, and mortality, has been profound. In this issue of the *Archives*, Love and colleagues remind us of the presence of these important cardiovascular risk factors, some of which cluster as the so-called metabolic syndrome. They estimate that nearly 2.7 million adults with psoriasis in the United States have the metabolic syndrome, representing a unique challenge and an opportunity.

Although dermatology researchers have led these advances, there are significant barriers to the incorporation of this knowledge into daily practice. First, physicians must be active learners who give careful attention to the evidence in the literature. The relationship between psoriasis and cardiovascular risk factors has become a particularly hot topic for several years, so, while the average dermatologist is conversant with this topic, it is the unusual dermatologist who has acted on it. To bridge this potential gap, educational programs should be developed aimed at affecting patient care through courses and continuing medical education at local or national meetings. Some such programs do exist; eg, a consensus statement that provides guidance with regard to comorbidities and screening guidelines has been released by the National Psoriasis Foundation.[1]

Practice Gaps Poll results available at www.archdermatol.com

On a practical level, many dermatologists, even those who are well versed, may be uncomfortable or uncertain how to screen for the individual components of the metabolic syndrome. Although dermatology has its ear-