Psoriasis and the Risk of Diabetes and Hypertension

A Prospective Study of US Female Nurses

Abrar A. Qureshi, MD, MPH; Hyon K. Choi, MD, DrPH; Arathi R. Setty, MD, MPH; Gary C. Curhan, MD, ScD

Objective: To evaluate the independent association between psoriasis and risk of diabetes and hypertension.

Design: A prospective study of female nurses who were followed up from 1991 to 2005.

Setting: Nurses' Health Study II, a cohort of 116 671 US women aged 27 to 44 years in 1991.

Participants: The study included 78 061 women who responded to a question about a lifetime history of physician-diagnosed psoriasis in 2005. Women who reported a diagnosis of diabetes or hypertension at baseline were excluded.

Main Outcome Measure: New diagnosis of diabetes or hypertension, obtained from biennial questionnaires.

Results: Of the 78 061 women, 1813 (2.3%) reported a diagnosis of psoriasis. During the 14 years of follow-up, a total of 1560 incident cases (2%) of diabetes and 15 724 incident cases (20%) of hypertension were documented. The multivariate-adjusted relative risk of diabetes in women with psoriasis compared with women without psoriasis was 1.63 (95% confidence interval, 1.25-2.12). Women with psoriasis were also at an increased risk for the development of hypertension (multivariate relative risk, 1.17; 95% confidence interval, 1.06-1.30). Age, body mass index, and smoking status did not significantly modify the association between psoriasis and risk of diabetes or hypertension (P values for interaction, \( \neq .07 \)).

Conclusions: In this prospective analysis, psoriasis was independently associated with an increased risk of diabetes and hypertension. Future studies are needed to find out whether psoriasis treatment will reduce the risk of diabetes and hypertension.


PSORIASIS IS A CHRONIC INFLAMMATORY skin disease that affects between 1% and 3% of the population and poses a lifelong burden. Recent studies indicate that psoriasis is associated with an increased risk of comorbidity and mortality. Systemic inflammation in psoriasis and an increased prevalence of unhealthy lifestyle factors have been independently associated with obesity, insulin resistance, and an unfavorable cardiovascular risk profile. Diabetes and hypertension are responsible for major morbidity and mortality in the United States. Previous cross-sectional studies have demonstrated that individuals with psoriasis have a higher prevalence of obesity, diabetes, and hypertension. Individuals with mild psoriasis had a slightly higher risk of diabetes (relative risk [RR], 1.13) and hypertension (RR, 1.03) after adjustment for age, sex, and body mass index (BMI). In a case-control study from Israel, the risk of diabetes (RR, 1.27) was higher in individuals with psoriasis. Among a group of psoriatic individuals in Italy, diabetes mellitus occurred more frequently in those younger than 50 years. Individuals with psoriasis were more likely to have cardiovascular risk factors, including hypertension, and myocardial infarctions at a younger age.

For editorial comment see page 467

More than 80% of individuals with diabetes develop hypertension, and approximately 20% of individuals with hypertension develop diabetes. In patients with hypertension and diabetes, the pathogenesis of cardiovascular disease is multifactorial, but recent evidence points toward the presence of a low-grade inflammatory process. Inflammatory markers (eg, C-reactive protein) have been shown to predict the development of diabetes and hypertension. To our knowledge, this is the first study to prospectively examine the association between psoriasis and diabetes or hypertension in a cohort of US women.

Author Affiliations: Channing Laboratory, Department of Medicine (Drs Qureshi, Choi, Setty, and Curhan), and Department of Dermatology (Dr Qureshi), Brigham and Women’s Hospital and Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health (Dr Curhan), Boston, Massachusetts.
Table 1. Baseline Characteristics of Women Who Self-reported a Diagnosis of Psoriasis Between 1991 and 2005

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No (n=76,248)</th>
<th>Yes (n=1,813)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>36.2</td>
<td>36.4</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>23.6</td>
<td>24.4</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>66</td>
<td>56</td>
</tr>
<tr>
<td>Current</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Past</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>Mean alcohol intake, g/wk</td>
<td>3.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Mean physical activity, METS/wk</td>
<td>21</td>
<td>20</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); METS, metabolic equivalent hours.

Table 2. Age-Adjusted and Multivariate Relative Risks (RRs) for the Development of Diabetes and Hypertension Among Women With Psoriasis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No of cases</th>
<th>Person-years, millions</th>
<th>Age-adjusted RR</th>
<th>Multivariate RRb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1500</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60</td>
<td>1.32 (1.19-1.45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15,338</td>
<td>0.99</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>386</td>
<td>1.32 (1.19-1.45)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

a Excluding any individuals with concomitant diabetes and hypertension.

b Simultaneously adjusted for age, smoking status (never, current, past), body mass index (calculated as weight in kilograms divided by height in meters squared) (21.0-22.9, 23.0-24.9, 25.0-27.4, 27.5-29.9, 30.0-34.9, and ≥35.0), alcohol intake (1-4, 5-9, 10-14, 15-29, and ≥30 g/wk), and physical activity in quintiles of metabolic equivalent hours per week.

ASSIGNMENT OF PSORIASIS

In 2005, NHS II participants were asked whether they had ever received a physician diagnosis of psoriasis and, if so, the date of diagnosis. Of the 84,039 women who responded to the psoriasis question in 2005, a total of 2,169 reported a physician diagnosis of psoriasis. After women with diabetes or hypertension at baseline in 1991 were excluded, 78,061 women remained in the analysis, 1813 of whom reported psoriasis. Therefore, 356 women with psoriasis were excluded because of baseline diabetes or hypertension. For this study, follow-up was started in 1991 because it is the first year for which we have corresponding information on smoking and alcohol status.

ASSIGNMENT OF DIABETES AND HYPERTENSION

Self-reported incident hypertension and incident diabetes cases were recorded from 1991 to 2005. We excluded women who first reported concomitant diabetes and hypertension on the same questionnaire during follow-up so that diabetes and hypertension could be evaluated as independent outcomes. Previously, medical record review confirmed a documented blood pressure reading greater than 140/90 mm Hg in 100% of women in the NHS I who reported hypertension; also, self-reported hypertension was predictive of subsequent cardiovascular events.21

COVARIATES

Date of birth and height were reported on the 1989 questionnaire. The participants reported their current weight on the biennial mailed questionnaires. The baseline and biennial follow-up questionnaires asked about smoking status and alcohol intake. Physical activity was defined as the number of metabolic equivalent hours per week; specifically, the number of metabolic equivalent hours was calculated as a product of the time invested in an activity every week and the energy expenditure required by the activity.

RESULTS

Women accrued person-time from the return of the 1991 questionnaire until they reported a diagnosis of diabetes or hypertension or were censored at the end of the follow-up period in 2005. New psoriasis diagnoses were updated every 2 years. We used Cox proportion hazards modeling to estimate the age-adjusted and multivariate RRs of incident diabetes and hypertension in women who had reported a physician diagnosis of psoriasis compared with those who did not. We categorized BMI (calculated as weight in kilograms divided by height in meters squared) at baseline and at each questionnaire cycle into 6 categories (<21.0, 21.0-22.9, 23.0-24.9, 25.0-29.9, 30.0-34.9, and ≥35.0). To minimize residual confounding by BMI in categories, we also considered BMI as a continuous variable. Smoking status was categorized (never, current, or past), as was alcohol intake (1-4, 5-9, 10-14, 15-29, and ≥30 g/wk). Physical activity was categorized in quintiles of metabolic equivalent hours per week. We explored potential interactions by age (<45 years vs ≥45 years), BMI (<25.0 vs ≥25.0), and smoking status (never, current, or past) by testing the significance of interaction terms added to our final multivariate models. For all rate ratios, we calculated 95% confidence intervals (CIs). All statistical analyses were performed using SAS software, version 9.1 (SAS Institute Inc, Cary, North Carolina). The institutional review board of Partners Health Care System, Boston, Massachusetts, approved this study.

OVER THE 14-YEAR FOLLOW-UP, 1560 INCIDENT CASES OF DIABETES AND 15,724 INCIDENT CASES OF HYPERTENSION OCCURRED. THERE WAS NO SUBSTANTIAL DIFFERENCE IN THE MEAN AGE BETWEEN WOMEN WITH AND WITHOUT PSORIASIS (Table 1). MEAN BMI, ALCOHOL INTAKE, AND PROPORTIONS OF CURRENT AND PAST SMOKERS WERE HIGHER IN THE PSORIASIS GROUP. AMONG WOMEN WITH PSORIASIS, THERE WERE 60 INCIDENT CASES (3.3%) OF DIABETES. COMPARED WITH WOMEN WITHOUT PSORIASIS, THE AGE-ADJUSTED RR OF DIABETES IN WOMEN WITH PSORIASIS WAS 2.08 (95% CI, 1.60-2.69) (Table 2). THIS RR REMAINED SIGNIFICANTLY HIGHER THAN THAT FOR WOMEN WITHOUT PSORIASIS (Table 3).
cantly elevated (RR, 1.63; 95% CI, 1.25-2.12) after further adjustment for BMI, smoking status, alcohol intake, and physical activity. None of the 60 women who reported psoriasis and diabetes had type 1 diabetes.

Of women with psoriasis, 386 (21.3%) developed incident hypertension. This proportion of women with hypertension and psoriasis represented an increased risk of hypertension (age-adjusted RR, 1.32; 95% CI, 1.19-1.45) that was attenuated but remained significant after multivariate adjustment (RR, 1.17; 95% CI, 1.06-1.30). We also evaluated possible effect modification by age, BMI, and smoking status in multivariate models. The association between psoriasis and risk was not modified by BMI for diabetes (P = .65) or hypertension (P = .07). There was also no effect modification by smoking status for diabetes or hypertension (P ≥ .50). Because women with psoriasis may be more likely to see a physician, and therefore more likely to be diagnosed as having diabetes or hypertension, we performed additional analyses after limiting the population to those women who underwent at least 1 physical examination during follow-up. There was no material change in the results.

This prospective study demonstrated an increased risk of diabetes and hypertension in women with psoriasis, even after adjustment for age, BMI, alcohol intake, and smoking status. Therefore, our study advances previous findings from cross-sectional studies and emphasizes the need to better understand the mechanisms that underlie these associations.

The risk of diabetes among individuals with psoriasis has been shown in cross-sectional studies to be elevated, with an RR between 1.27 and 2.48, consistent with our prospective study. Although obesity and the metabolic syndrome had been proposed as an explanation for this increased risk, we found that the risk of diabetes was independent of BMI. Inflammation could be a biologically plausible mechanism underlying this association; insulin resistance has previously been attributed to inflammation, and elevated C-reactive protein levels are predictive of diabetes. Alternatively, therapy for psoriasis may promote development of diabetes, especially if patients were treated with systemic steroids. In our study, information on psoriasis-related therapy was not available. Nonetheless, systemic steroids are not the standard of care for psoriasis in the United States and are typically avoided in patients with psoriasis owing to the potential for disease worsening. The topical steroids that are often used in the treatment of psoriasis may be systemically absorbed if they are used on large body surface areas for extended periods. The long-term use of topical steroids on large body surface areas could explain the observed increase in risk for diabetes, although adherence with long-term topical steroids use is generally low.

An increased risk of hypertension of 1.2- to 2-fold has been reported in cross-sectional studies. In our study, individuals with psoriasis were at a slightly increased risk for hypertension. Although psoriasis and hypertension share common risk factors, such as smoking and obesity, we observed an independent association between psoriasis and hypertension after adjusting for smoking status and BMI. Potential explanations for this association include systemic inflammation and psoriasis treatment. As mentioned above, psoriasis is a chronic inflammatory disease, and inflammation is a risk factor for hypertension. In one study, although the risk for other cardiovascular risk factors was higher in severe psoriasis, a similar association between psoriasis severity and risk of hypertension was not found. Previous work has shown that elevated levels of C-reactive protein were associated with a 52% increase in the risk of hypertension developing in women. Systemic therapy for psoriasis with medications such as cyclosporine may increase the risk of hypertension directly, albeit this risk is low; we did not have data on therapy in our study, but long-term cyclosporine use in psoriasis is not common. Individuals with psoriasis may also be less likely to exercise owing to physical or social discomfort, thereby increasing their risk for hypertension. In our study, we controlled for physical activity and found no material change in risk for hypertension.

Our study was predominantly restricted to white women. Therefore, we cannot generalize these results to men or other racial groups. Our study was observational; thus, we cannot rule out the possibility that unmeasured factors might have contributed to the observed associations. While we observed no material change in the results that excluded the individuals who underwent at least 1 physical examination during follow-up, we cannot eliminate potentially increased ascertainment of our outcomes among women with psoriasis. A major strength of the study was the detailed collection of information on BMI, smoking status, and alcohol. Similar to other epidemiological studies of psoriasis, we did not confirm the nurses’ self-reported physician diagnosis of psoriasis clinically with an examination by a dermatologist. Previous validation studies in the NHS I for another skin condition, ie, basal cell carcinoma, found self-reports to be more than 90% accurate. While we expect the overall accuracy of self-reported physician diagnosis of psoriasis to be high among registered nurses, the corresponding accuracy against a dermatologist’s examination is not available. Confirming our results using more specific case definitions of psoriasis and evaluating for various psoriasis subtypes, severity, and treatment effects would be valuable.

In conclusion, our prospective study indicates that women with psoriasis have an increased risk for diabetes and hypertension, confirming the findings from previous cross-sectional studies. These data illustrate the importance of considering psoriasis a systemic disorder rather than simply a skin disease. Further research is needed to better understand the mechanisms underlying these associations and to find out whether psoriasis therapy can reduce the risk for diabetes and hypertension.

Accepted for Publication: July 25, 2008.

Correspondence: Abrar A. Qureshi, MD, MPH, Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital, 45 Francis St, 221L, Boston, MA 02115 (abrar.qureshi@channing.harvard.edu).

©2009 American Medical Association. All rights reserved.
Author Contributions: Dr Qureshi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Qureshi, Choi, Setty, and Curhan. Acquisition of data: Qureshi, Choi, and Curhan. Analysis and interpretation of data: Qureshi, Choi, and Curhan. Drafting of the manuscript: Qureshi and Choi. Critical revision of the manuscript for important intellectual content: Qureshi, Choi, Setty, and Curhan. Statistical analysis: Qureshi and Curhan. Obtained funding: Qureshi. Administrative, technical, or material support: Qureshi, Setty, and Curhan. Study supervision: Qureshi, Choi, and Curhan.

Financial Disclosure: Dr Qureshi has been a consultant and speaker for Abbott, Amgen, and Genentech.

Funding/Support: This work was partly supported by grants KO7CA108977/NCI (Dr Qureshi) and CA050385/NCI from the National Cancer Institute.

Role of the Sponsors: The sponsor had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Additional Contributions: Elaine Coughlan-Gifford assisted with data analysis and programming.

REFERENCES