SHORT COMMUNICATION

Body Composition, Cardiometabolic Risk Factors and Comorbidities in Psoriasis and the Effect of *HLA-C*06:02* Status: The HUNT Study, Norway

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Psoriasis is a chronic inflammatory skin disease with a prevalence that varies across the world (1). Prevalence estimates in Norway are high, ranging from 5.8% to 11.4% (2, 3). Observational studies have associated psoriasis with multiple comorbidities, including obesity (4). However, detailed characterization of body composition in a large psoriasis sample is lacking (5). Recent awareness of multimorbidity has focused attention on closer clinical surveillance and the development of clinical guidelines for the management and treatment of psoriasis (4). As several studies are based on hospital records, there is less information about the comorbid burden and related comorbidities in a general population with higher prevalence estimates of psoriasis, making optimal clinical surveillance unclear. *HLA-C*06:02* is the major genetic contributor in psoriasis and *HLA-C*06:02* status is associated with disease endotypes, comorbidities and response to systemic treatments (6–8). This makes *HLA-C*06:02* a potential biomarker of disease trajectories, comorbid burden and treatment efficacy (6, 7).

The aim of this study was to assess the overall prevalence of psoriasis, and to estimate the associations of psoriasis with body composition parameters assessed by bioelectrical impedance analysis, as well as the associations with cardiometabolic risk factors and comorbidities in a large population-based study (the fourth wave of the Trøndelag Health Study (HUNT4, 2017–2019)) in Norway. Furthermore, this study aimed to investigate the recently reported association of *HLA-C*06:02* status with anthropometric measures, comorbidities, and, for the first time, its association with detailed body composition parameters.

METHODS AND RESULTS

Data from the fourth wave of the Trøndelag Health Study (HUNT4, 2017–2019) were utilized. All inhabitants in the Nord-Trøndelag region of Norway, aged 20 years or older, were invited and 56,042 (54.0%) participated (9). Classification of psoriasis and comorbidities were defined by self-reported disease and/or biochemical measurements. Body composition of all participants was assessed using bioelectrical impedance analysis. Genotyping was performed using a custom Illumina HumanCoreExome array (UM HUNT Biobank v.2.0) (10). Individuals with psoriasis were classified as either *HLA-C*06:02*-positive (≥1 copies of the rs4406273-A allele) or *HLA-C*06:02*-negative (0 copies). A full methodological description is given in Appendix S1, Tables SI–IV and Fig. S1. The prevalence of psoriasis was 6.6%, of which 26.6% were positive for *HLA-C*06:02* (Table SI). Individuals with psoriasis had higher mean levels of total body fat (33.3% vs 31.5%) and visceral fat (138.4 vs 125.4 cm^2), as well as lower levels of skeletal muscle mass (36.8% vs 37.8%) compared with individuals without psoriasis (Table SIII). Individuals with psoriasis had higher mean systolic blood pressure (132.0 vs 131.1 mmHg), triglycerides (1.8 vs 1.7 mmol/l), HbA1c (36.4 vs 35.3 mmol/mol) and high-sensitivity CRP (hsCRP) (3.1 vs 2.7 mg/l). In participants with psoriasis, *HLA-C*06:02*-positive individuals had a tendency towards lower levels of visceral fat (132.0 vs 137.1 cm^2), and lower hsCRP (2.6 vs 3.3 mg/l) (Table SIV).

Individuals with psoriasis more often had a history of myocardial infarction (adjusted prevalence ratio (aPR) 1.54), angina pectoris (aPR 1.55), heart failure (aPR 1.56), atrial fibrillation (aPR 1.41), apoplexia (aPR 1.63), asthma (aPR 1.51), chronic obstructive pulmonary disease (COPD) (aPR 1.89), diabetes (aPR 1.61), hypothyroidism (aPR 1.32), hyperthyroidism (aPR 1.58), migraine (aPR 1.41), renal disease (aPR 1.63) and gout (aPR 1.83) (Table SV). *HLA-C*06:02*-positive psoriatic individuals had higher prevalence of atrial fibrillation (aPR 3.96) and slightly lower prevalence of migraine (aPR 0.73) compared with *HLA-C*06:02*-negative individuals (Table SVI).

DISCUSSION

The self-reported prevalence of psoriasis in HUNT4 was 6.6%, higher than what has been reported for western Europe (1). This high prevalence may partly be explained by the identification of milder psoriasis, not typically included in hospital-based studies (2). Adipose tissue has the capability to induce an inflammatory state, which, in turn, may contribute to the development of psoriasis and comorbidities (5, 11). As adiposity is a modifiable risk factor for both psoriasis and comorbidities, there are clear implications of evaluating different types of adiposity independently. Body composition evaluation is superior to BMI, as it provides information on distribution of body fat and skeletal muscle mass, valuable gauges of metabolic health. Previous studies comparing body composition in psoriasis and controls have been limited by small sample size (≤242 individuals with psoriasis) (5).

In the current study, body composition analyses included 3,219 individuals with psoriasis and 45,816 controls, and it was observed that individuals with psoriasis had more body fat, particularly visceral fat. This is corroborated by a recent systematic review (5). *HLA-C*06:02*-positivity was associated with a tendency towards a lower levels of visceral fat, in line with previous studies investigating BMI and waist circumference (6), as well as lower levels of hsCRP. Individuals with psoriasis had lower levels of skeletal muscle mass compared with controls. Sustained inflammation may give loss of muscle mass and strength (5), and may partly explain this observation.

Increasing attention has been given towards the association between psoriasis and comorbidities. This has been important to improve quality of life and to reduce the risk of overall mortality among patients with psoriasis (4). Obesity is shown to reduce the effect of biologic treatment, and this knowledge has been expanded to include other metabolic comorbid conditions (12). Personalized management of psoriasis requires robust biomarkers. Genetic markers may predict comorbidities and treatment efficacy, improving treatment outcome (6, 7). When investigating associations between *HLA-C*06:02* status and comorbidities, the current study found increased prevalence of atrial fibrillation and decreased prevalence of migraine in *HLA-C*06:02*-positive psoriatic individuals. However, the confidence intervals are wide, and these results should be interpreted with caution. Douroudis et al. (6) found that *HLA-C*06:02*-negativity was associated with higher prevalence of cardiovascular and thyroid disease, findings which were not replicated in the current study.

A major strength of this study is the population-based design with a high participation rate of 54.0%. Combining genetic data and information on comorbidities increases the novelty of these results, as this aspect has sparsely been studied previously. This study also had several limitations. We did not investigate subtypes or severity of psoriasis. Furthermore, the analyses were limited to diseases included in the cluster questionnaire in HUNT4. Many disease outcomes were self-reported, introducing the possibility of misclassification, which varies across the included comorbidities (9). However, the psoriasis question in HUNT has been validated with a positive predictive value of 78% (2). There is also a risk of ascertainment bias, which may introduce false-positive associations between psoriasis and comorbidities. The descriptive statistics on cardiometabolic risk factors were only standardized for age and it is likely that other factors (such as medication, smoking and exercise) could influence these results. While we were able to adjust for, for example, education and smoking when estimating PR, residual confounding may still occur. The study includes several comparisons, but given the descriptive nature of the study, it was not adjusted for multiple testing.

In conclusion, the results of this study support the importance of addressing psoriasis as a systemic disease that requires holistic and multidisciplinary care. The results highlight the importance of cardiometabolic risk factors and prevention of comorbidities, both for the hospital-based dermatologist and the general practitioner treating patients in a general population.

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The authors have no conflicts of interest to declare.

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