

## Comorbidities of Prurigo Nodularis in Finland Between 1996 and 2019

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Prurigo nodularis (PN) is a chronic pruritic skin disorder with an estimated prevalence of 6–72 per 100,000 individuals worldwide. PN is found in all age groups, with the highest incidence in people aged over 50 years. The clinical picture of PN is characterized by lichenoid or excoriated nodules, typically appearing on the trunk or extensor side of the extremities (1).

Recent studies have reported an association between PN and various comorbidities (2, 3) such as hypertension, lipid disorders and type 2 diabetes (3), as well as autoimmune conditions, such as coeliac disease and type 1 diabetes (3, 4). Similar to other dermatological diseases, PN is often accompanied by psychiatric disorders (3).

Very few studies have been conducted on comorbidities of PN in Northern Europe (5). The present study was designed to evaluate the comorbidities associated with PN in Northern Finland.

### PATIENTS AND METHODS

Patient records were collected from the database of Oulu University Hospital (OUH) using the International Statistical Classification of Diseases (ICD-10) code for PN. The study included all patients with ICD-10 code L28.1 registered in their records after 1 January 1996 and who were either admitted to OUH or had visited an outpatient clinic by 31 December 2019. All records were manually checked by the authors for demographics, pre-selected comorbidities, and treatments used for PN. Records of deceased patients were included. The study was approved by the medical director of OUH.

The overall prevalence of comorbidities was calculated. Data are presented as means, standard deviation (SD) and range, and as proportions for categorical variables. A  $\chi^2$  test was used to test differences between the sexes. Statistical analyses were performed using SAS software package (version 9.4, SAS Institute, Inc., Cary, NC, USA) and a *p*-value of 0.05 was considered statistically significant.

### RESULTS

The demographics of the study population are shown in **Table I**. A total of 223 patients (72.9%) had at least one comorbid disease. Somatic comorbidities were found in 71.6% (*n*=219) of patients. All investigated somatic and psychiatric comorbidities are shown in **Fig. 1A**. Dermatological comorbidities were found almost half of the patients (*n*=127; 41.5%) and a quarter of those (26.8%; *n*=34) presented with more than one dermatological comorbidity (Fig. 1B). Psychiatric comorbidity affected

**Table I. Demographics of the study population**

Characteristics	
Study population, <i>n</i>	306
Female/male, <i>n</i>	184/122
Age, years, mean $\pm$ SD (range)	68.6 $\pm$ 13.9 (18–96)
Age at diagnosis, years, mean $\pm$ SD (range)	56.7 $\pm$ 15.1 (10–93)
Smoking status, <i>n</i> (%)	
Yes, current/previous	69 (22.5)
No or data not available	237 (77.5)

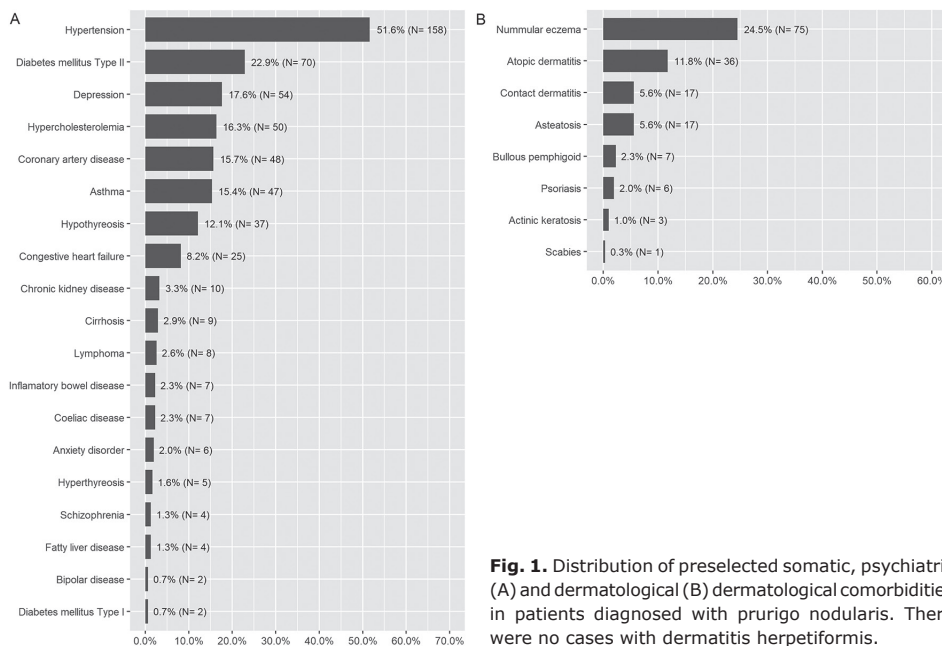
SD: standard deviation.

19.3% (*n*=59) of patients. There was a predominance of psychiatric comorbidities in females compared with males (26.1% of females and 9.1% of males, *p*<0.001). However, significant differences between the sexes were not seen in other comorbidity groups (data not shown).

### DISCUSSION

This study found that as many as 72.9% of patients with PN had at least one comorbidity. In a German study 87% of patients with PN were found to have one or more comorbidities (6). This slight discordance may be explained by differences in the comorbidities selected: infectious diseases were included in the German study (6). The current findings are in line with previous reports from 2 large American studies (2, 3). However, in the current study, hypothyroidism was more common than reported in a large health claim database-based study from the USA (*n*=7,095), which reported the prevalence of thyroid diseases as 1.0% (3, 6). Interestingly, the prevalence of hypothyreosis in Finland does not differ from other countries (7). Of the more uncommon comorbidities, coeliac disease was more prevalent in our data (2.3%), compared with the US study (0.37%) (3, 6). This difference can be explained by the high overall prevalence of coeliac disease in Finland (8). Surprisingly, the current study population lacked cases with dermatitis herpetiformis, despite the fact that its prevalence in Finland is among the highest in the world (9).

Previously, atopic dermatitis (AD) and psoriasis have been reported to be associated with PN (3, 10), but, overall, there are few studies reporting dermatological comorbidities with PN (2, 3, 6). The most common dermatological comorbidities with PN in the current study were “nummular eczema or widespread nummular eczema” and AD. In previous studies, the prevalence of AD in patients with PN varies from 3.3% to 15.3% (2, 3, 5, 6). Despite



**Fig. 1.** Distribution of preselected somatic, psychiatric (A) and dermatological (B) dermatological comorbidities in patients diagnosed with prurigo nodularis. There were no cases with dermatitis herpetiformis.

the fact that the incidence of bullous pemphigoid (BP) was increasing in Finland during the study period (11), only 2.3% of cases in the current study had a comorbid diagnosis of BP.

Previous studies have shown that PN is associated with psychiatric disorders (12). We found that as many as 19.3% of patients had 1 or more psychiatric comorbidities. This is comparable to psychiatric morbidity overall among adult patients with AD in Finland (13). In the current study, depression was the most common psychiatric comorbidity (17.6%), being more prevalent than in Danish study ( $n=877$ ; 8.5%) (12) and, in general, Finnish population (14). However, the US study ( $n=909$ ) reported an even higher (23.9%) prevalence of depression (2), although another US study reported a collective prevalence of 17.3% for “mood disorders” without specifying the individual prevalence of depression (3). Although our finding of the prevalence of depression differs from that of the Danish study, the prevalence of anxiety in the current study (2.0%) corresponds to that (2.1%) of the Danish study (12). Conversely, a German claims database study reported a very high prevalence of anxiety (10.6%) (5).

Previously, an American study ( $n=695$ ) identified that subjects with PN were more than 4 times more likely to have malignancy than were matched controls (15). Several lymphomas ( $n=8$ ; 2.6%) were found in the current study population. A US study ( $n=7,095$ ) reported that lymphoma of any type was found in 0.52% of patients with PN (3). In another smaller US study that analysed malignancies more closely ( $n=695$ ), lymphomas were the second most common group of malignancies after the skin tumours (15), but the authors did not report exact prevalence rates. A higher prevalence of lymphomas in the present study than in the US study may reflect the fact that

the current study population was gathered from a tertiary referral hospital rather than from health insurance claims (3).

The current study has some limitations. Only certain pre-selected comorbidities were looked for, which makes direct comparisons with previous studies difficult. In addition, data were collected from the patient records of a university hospital, lacking information from primary care. One strength of the current study was that the PN diagnosis was recorded in a specialist clinic, and so benefitted from a standardized practice, ensuring high-quality patient records.

Although all the patients in the current study were of Caucasian origin, the results can be generalized to other populations (2, 3).

In conclusion, it is important for physicians treating patients with PN to take into account the high risk of comorbidities.

*The authors have no conflicts of interest to declare.*

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