Epidemiological data of 290 pemphigus vulgaris patients: a 29-year retrospective study

**Background:** Pemphigus vulgaris (PV), an autoimmune blistering disease involving the skin and mucosa, is traditionally considered to be prevalent among Jews, particularly those of Ashkenazi origin. Israel, where the Ashkenazi and non-Ashkenazi Jewish population live alongside a large Arab minority, is a particularly interesting place for epidemiological studies of PV. **Objectives:** To characterise the epidemiological and clinical parameters of PV patients from a single tertiary medical centre in Israel. **Materials & methods:** Data was retrieved retrospectively from the medical records of newly diagnosed PV patients referred to the Sheba Medical Center between 1980 and 2009. **Results:** A total of 290 PV patients were diagnosed during the study period. The mean age at diagnosis was 49.7 years (range: 10-92 years) and a female predominance was identified (1.54:1; \(p<0.001\)). Among the Jewish patients, the ratio of Ashkenazi to non-Ashkenazi was 1.23:1, which was not statistically significant in comparison to the ratio of the general Jewish population in Israel (\(p=0.289\)). We describe the comorbidities found among the patients. Disease severity at diagnosis was not found to be related to the epidemiological parameters examined. **Conclusion:** Studies from different countries reveal variations in the clinical and epidemiological characteristics of the disease. The epidemiology of PV in Israel, a Middle-Eastern country with a Western lifestyle and a diverse ethnic population, shows some characteristics that represent an “admixture” between European and Middle-Eastern or Asian countries. The associated comorbidities of PV emphasize the need for dermatologists to keep a high index of suspicion and actively evaluate patients to determine their presence. **Key words:** bullous disease, comorbidity, epidemiology, pemphigus vulgaris
Patients and methods

The computerised database at the Sheba Medical Center was searched for all patients with PV who were either admitted to the Department of Dermatology or visited the outpatient clinic between 1980 and 2009. Diagnoses were based on: (i) appearance of mucosal and/or cutaneous involvement that was clinically compatible with PV (blisters or erosions); (ii) histopathology showing suprabasal acantholysis in the epidermis; and (iii) direct immunofluorescence demonstrating IgG (with or without C3) intercellular deposition throughout the epidermis in a “chicken wire” pattern.

Patients with other forms of pemphigus disease besides PV (pemphigus foliaceus or IgA pemphigus), as well as those with equivocal diagnosis, were excluded. Patients’ files were retrospectively analysed, and the following epidemiological and clinical data were retrieved from the medical records: age at diagnosis, sex, ethnic origin, site of initial lesion, associated illness at diagnosis, and mortality rate. For Jewish patients, the ethnic origin was classified as Ashkenazi, Sephardic non-Ashkenazi, or mixed, based on place of birth or paternal origin.

During the first visit, the severity of the disease was determined, as previously described [9], as mild (score of 1-3), moderate (4-6), or severe (7-9) by an experienced clinician based on three parameters: number of erosions (<5, 5-10, or >10, corresponding to a score of 1, 2, or 3 points, respectively), body surface area (percentage) involved (<1, 1-10, or 11-30, corresponding to a score of 1, 2, or 3 points, respectively), and daily prednisone dosage (mg/d) (<30, 30-59, or ≥60, corresponding to a score of 1, 2, or 3 points, respectively).

The study was approved by the institutional ethical committee (no. 7172).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL, USA) version 15.0 for Windows was used for data entry and analysis. Normally distributed numerical data was summarised by its mean values and standard deviation. The relationships between sex, origin, or site of lesions at presentation, and severity of the disease, were evaluated using a chi-squared test (χ²). Evaluation of ethnic origin distribution between PV patients and the general population was performed using Fisher’s exact test. All analyses of paired data were performed using a paired t-test. Confidence intervals were extended to a level of 95%. A p value below 0.05 was accepted as statistically significant.

Results

Our database included 375 diagnosed pemphigus patients, from which 290 PV patients were included in the study. The others were diagnosed as having other pemphigus forms or an equivocal diagnosis that did not meet the criteria for inclusion as specified above. The age, sex, origin, and initial site of lesions among the PV patients are provided in table 1.

Sex distribution and age at onset

The female-to-male ratio in our study sample was 1.54:1 (176 females, 114 males; p<0.001). The average age at diagnosis was 49.7 years (SD ± 16.1 years), with an almost identical median age of 50 years. The youngest patient was 10 years old and the oldest 92. For both genders, the risk of onset peaked during the fifth and sixth decade of life, with no significant difference in mean age found between males and females (50 years and 49.5 years, respectively). Twenty-eight percent of the patients were diagnosed before the age of 40, but the disease was very rare under the age of 20. The age distribution at onset for all patients is illustrated in figure 1.

Ethnicity and origin

Ethnicity and origin data was available for 227 of the patients, as shown in table 1. Of these, 217 were Jews and 10 were Arabs (4.4%). Among the Jewish patients, the ratio of Ashkenazi to non-Ashkenazi patients was 1.23:1. This value was compared to the Ashkenazi to non-Ashkenazi ratio among the Jewish population in Israel (1.17:1), as calculated based on data from the Israel Central Bureau of Statistics [10], and was found not to be statistically significant (Fisher’s exact test, p = 0.289). Differentiation between Ashkenazi and non-Ashkenazi Jews in the general population was based on place of birth (or paternal place of birth), as was described for PV patients in this study.

Clinical presentation, comorbidities, and mortality

The sites of involvement at onset were reliably documented for 264 patients. A total of 110 patients (42%) presented with mucosal lesions only, while 100 patients (38%) had mucocutaneous lesions and 54 patients (20%) had only cutaneous lesions.

The initial prednisone dose given at disease presentation was documented for 192 patients; 144 patients (75%)