

## RISING DERM STARS

### Association of Pemphigus and Pemphigoid with Osteoporosis and Pathological Fractures

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**Background:** Pemphigus and pemphigoid are two groups of autoimmune bullous disease (AIBD) associated with high morbidity and mortality. While there is no cure for either condition, a mainstay for treatment is long-term systemic corticosteroids that can decrease bone mineral density (BMD). Patients with pemphigus and pemphigoid likely have additional risk factors for decreased BMD, including chronic inflammation.

Osteoporosis and skeletal fractures resulting from decreased BMD can lead to significant morbidity, hospitalization, decreased quality of life, and mortality. However, no large-scale studies have rigorously examined the association of AIBD with osteoporosis and fractures.

**Objective:** The goal of our study was to determine whether pemphigus and pemphigoid are associated with osteoporosis and fracture in the U.S. population and how this affects admission rates and cost of care.

**Methods:** We performed a cross-sectional study of 198,102,435 children and adults, including 4,502 with pemphigus and 8,863 with pemphigoid, from the 2006-2012 National Emergency Department Sample (NEDS), which is comprised of 20% of all emergency care visits throughout the United States.

**Results:** Patients with pemphigus or pemphigoid were more likely to be female, older, evenly distributed across income quartiles, use Medicare as the primary source of payment, and have a history of long-term steroid use. A pooled analysis across all 7 years showed that patients with pemphigus had significantly higher odds (multivariate logistic regression including age, sex, primary payer, income quartile, history of long-term steroids; OR, 95% CI) of diagnosis with osteopenia (2.200, 1.590-3.045), osteoporosis (2.536, 2.159-2.978), osteomalacia (29.699, 4.049-217.834), and pathologic fracture (2.035, 1.422-2.912)

Similarly, patients with pemphigoid had significantly higher odds of diagnosis with osteoporosis (1.550, 1.392-1.727) and pathologic fracture (1.517, 1.222-1.884). Patients with pemphigus additionally had significantly higher odds of diagnosis with femur fracture (1.459, 1.125-1.893) and vertebral fracture (1.464 1.060-2.023).

Significant two-way interactions were detected between both pemphigus and pemphigoid and history of long-term steroid use on osteopenia, osteoporosis, and pathologic fracture. The rate of inpatient admission (% frequency, 95% CI) in patients with both pemphigus and fracture (96.4, 89.4-100.0) and pemphigoid and fracture (90.9,

80.4-100.0) was significantly higher than in those without fracture. The yearly inflation adjusted cost of combined ED and inpatient care was consistently and significantly higher in patients with pemphigus or pemphigoid and fracture compared to those without fracture.

**Limitations:** Data on severity and treatments of pemphigus and pemphigoid were not available.

**Conclusion:** Pemphigus and Pemphigoid were associated with an increased risk of osteoporosis and pathologic fractures. This remained significant even after controlling for history of long-term steroid use, suggesting other disease intrinsic and extrinsic factors may underlie this increased risk (e.g. chronic inflammation, medication, lifestyle). Patients with either pemphigus or pemphigoid and fracture also had higher admission rates and higher overall inflation adjusted cost of care. We propose that patients with pemphigus and pemphigoid constitute a significant, previously underrecognized public health burden due to risk for fractures, and they may benefit from early interventions (i.e. early bone density scans, adjustments in steroid dose, vitamin supplementation, referral to endocrinologist) from their primary physician – the dermatologist.