

Hereditary Angioedema, C1-INH Replacement Therapy, and Coexisting Autoimmune Disorders: Findings From a Claims Database

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INTRODUCTION

- Autoimmune diseases are a leading cause of morbidity and mortality in the United States, with an overall estimated prevalence of 4.5% (6.4% in females and 2.7% in males).^{1,2}
- Autoimmune diseases are often associated with dysregulation of complement.^{3,4}
- Complement activation must be tightly regulated to avoid excessive consumption of complement and tissue injury.³ The classical pathway is regulated/inhibited by C1-inhibitor (C1-INH), which inhibits C1.⁵
- In hereditary angioedema with C1-INH deficiency (C1-INH-HAE), failure to inhibit C1 leads to increased consumption of C4 and C2. Deficiency of these components may promote deposition of immune complexes into tissues and contribute to development of autoimmune disease.^{5,6}
- There is a potential similarity between secondary deficiency of C1r, C1s, and C2 in HAE and the effects of primary deficiency (ie, due to genetic mutations) of these components.^{3,7} We hypothesize that the secondary deficiency due to HAE has effects on autoimmunity analogous to those of the primary deficiency.
- To clarify the association between C1-INH deficiency and autoimmune diseases we compared coexisting autoimmune diseases claims frequency between patients with C1-INH-HAE treated with plasma-derived C1-INH (pdC1-INH), which corrects the underlying C1-INH deficiency, versus other non-C1-INH therapies.

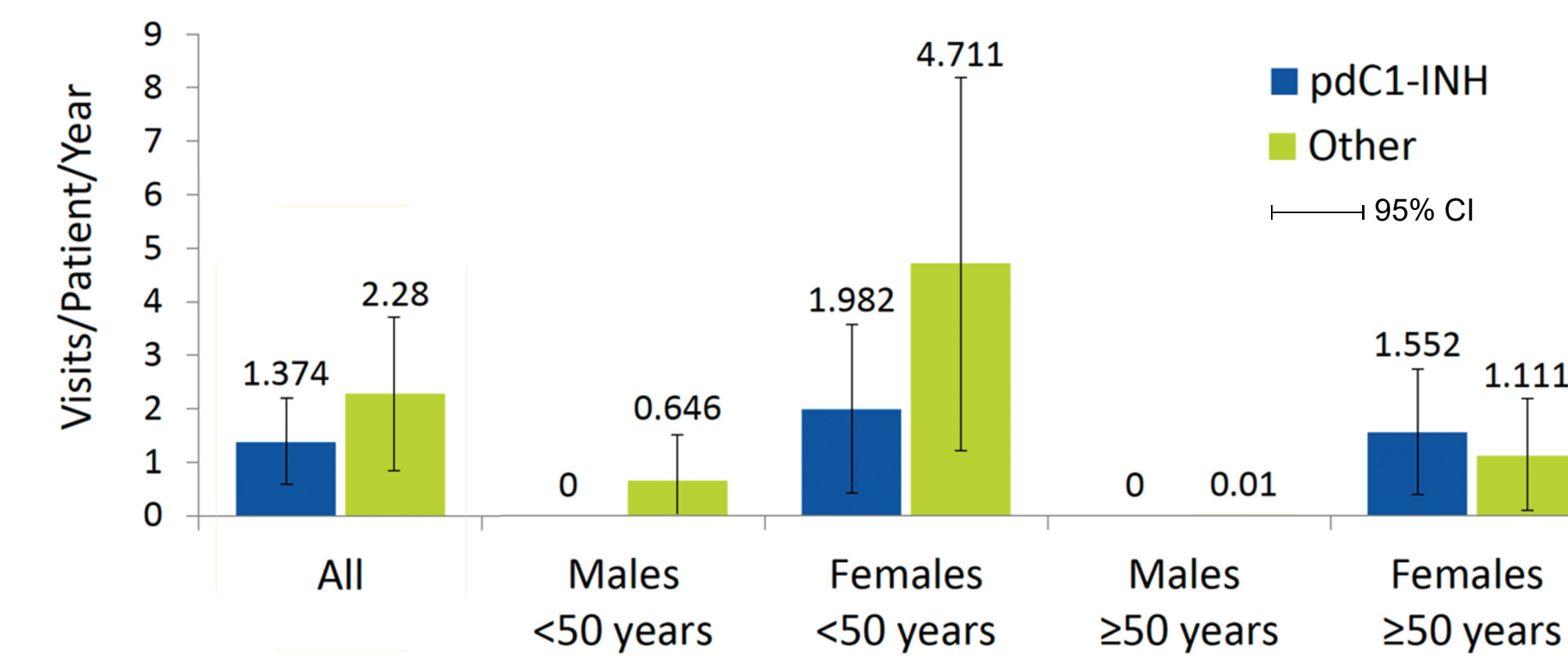
METHODS

- Patients with C1-INH-HAE were identified in the IMS Health PharMetricsPlus claims database between January 2012 and December 2016 by the ICD (International Classification of Diseases) 9/10 diagnosis code, and classified by their HAE treatment as “pdC1-INH” or “other (non-C1-INH)” treatments.
- The index date was the first claim for HAE treatment. For patients using C1-INH, the first fill was the index date even if other HAE medications had been used previously. Continuous enrollment in the health plan for ≥12 months following the index date was required.
- Frequency of visit claims for autoimmune conditions was identified based on diagnostic codes (primary or secondary).
- Mean visits per patient per year by treatment group, and stratified by gender and age group (<50 years vs ≥50 years) were summarized for autoimmune conditions.

RESULTS

- A total of 589 patients with HAE were identified; 69% were female and 38% were aged ≥50 years. Of the 589 patients, 276 (729 patient-years) were treated with pdC1-INH and 313 (860 patient-years) received other (non-C1-INH) treatments.
- Of the 589 patients, 76 (12.9%) had at least 1 visit for

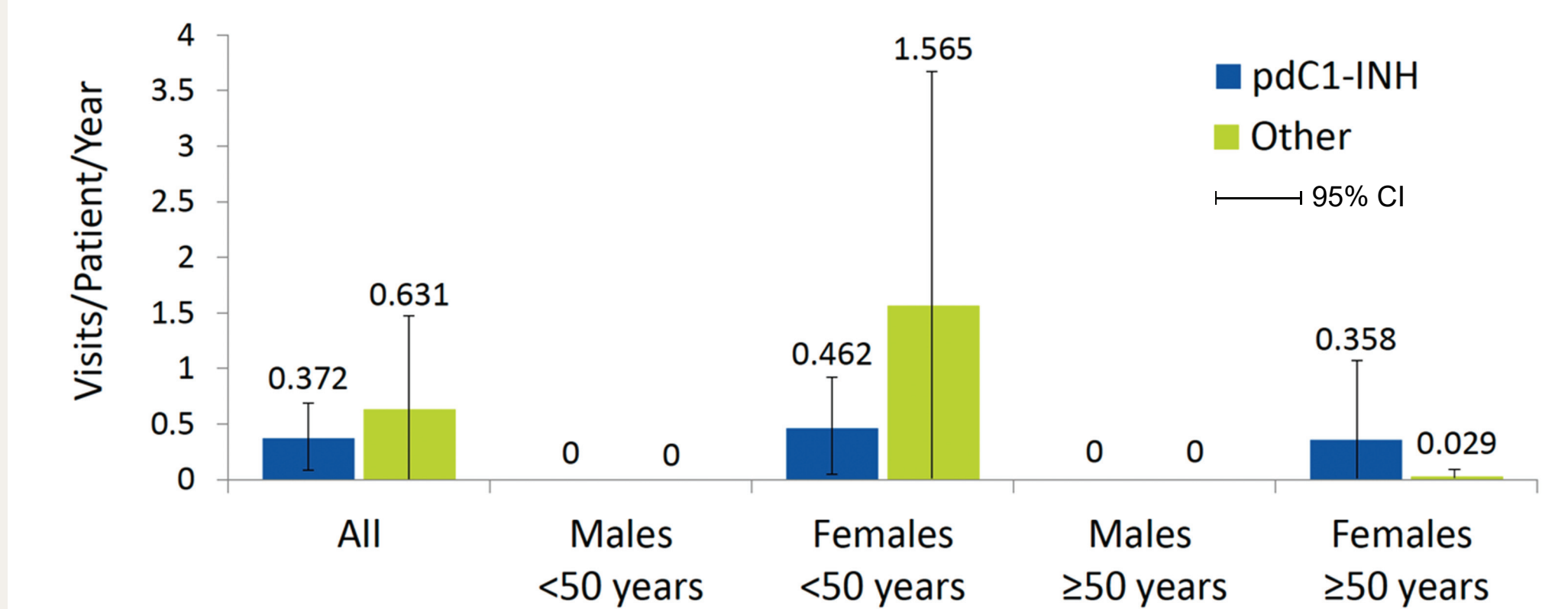
Figure 1. Mean Visits per Patient per Year for Any Coexisting Autoimmune Condition



a coexisting autoimmune disorder. These data are consistent with the literature regarding autoimmunity in patients with HAE.^{5,6}

- The most common coexisting autoimmune conditions were lupus, alopecia, rheumatoid arthritis, sicca (Sjögren’s syndrome), and connective tissue disorders. These data are also consistent with the literature.^{5,8}
- The mean (95% CI) number of visits for autoimmune diagnoses per patient per year was numerically lower among patients treated with pdC1-INH (1.37 [0.56, 2.19]) compared to patients treated with non-C1-INH treatments (2.28 [0.83, 3.73]) (**Figure 1**).
- Regardless of treatment received or age group, the mean (95% CI) number of visits for coexisting autoimmune disorders per patient per year was higher in females than in males (**Figure 1** and **Figure 2**).

Figure 2. Mean Visits per Patient per Year for Lupus



CONCLUSIONS

- C1-INH replacement therapy may have a modulating effect on the occurrence of autoimmune disease.
- Further research is needed to elucidate the potential role of C1-INH replacement therapy in modulating the severity and risk of a concomitant autoimmune disorder in patients with C1-INH-HAE.

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