Global Frequency and Diagnosis of Hereditary Angioedema with Normal C1INH: A Real World ACARE Survey

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Rationale

- The pathophysiology of hereditary angioedema (HAE) Type 1 (HAE-C1INH-Type1) and 2 (HAE-C1INH-Type2) is well characterized; however, HAE associated with normal C1INH activity (HAE-nC1INH) is frequently of unknown etiology[1]
- While a recent study provided prevalence estimates of HAE-nC1INH in the United States (US) leveraging claims data,[2] a global standardized algorithmic diagnostic approach for HAE-nC1INH is lacking, limiting precise prevalence estimates to inform management[1]

Objectives

- To assess the global frequency of presumptively diagnosed HAE-nC1INH
- To characterize the diagnostic pathway of patients with HAE-nC1INH, including types of testing and time to diagnosis

Methods

- Board-certified HAE-treating physicians, practicing at accredited Angioedema Centers of Reference and Excellence (ACAREs), completed a 27-item online survey based on personal recall between December 2022 and April 2023
- Participating physicians were required to have treated at least 1 patient with presumptive HAE-nC1INH in the past 12 months
- All participants provided informed consent prior to initiating the survey and provided consent for their data to be used anonymously or in aggregate
- The analysis was performed using descriptive statistics

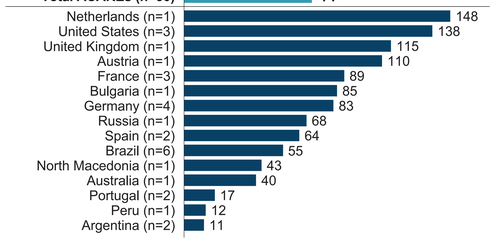
Results

- Thirty physicians from 30 global ACAREs in 15 countries reported a mean treatment volume of 71 patients with all types of HAE within the previous 12 months (min: Argentina n=11; max: Netherlands n=148) (**Table 1, Figure 1**)

Table 1. Physician-respondent characteristics

Characteristic	ACARE (N=30)
Specialty, n (%)	
Allergy and/or immunology	19 (63.3)
Dermatology	7 (23.3)
Internal medicine	3 (10.0)
Otolaryngology	1 (3.3)
Years in practice, mean (range)	25 (6–45)

Figure 1. Average total HAE patient volume over prior 12 months[a]



[a]Average number of patients per center treated for any type of HAE (confirmed or suspected); n represents the number of centers per country.

Figure 2. Estimates of HAE subtypes by country

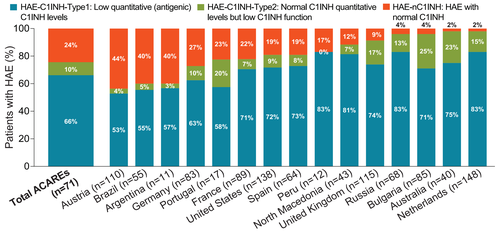


Figure 3. Estimates of HAE subtypes among adult and pediatric patients

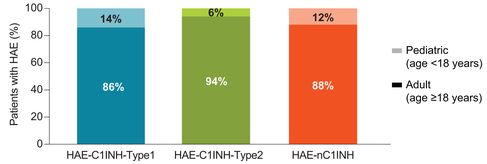
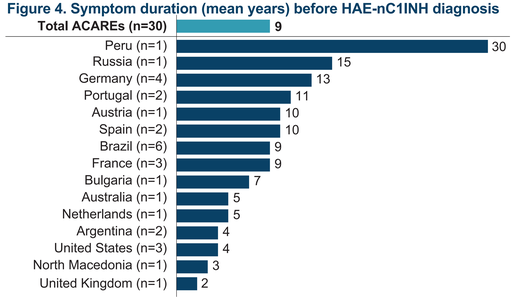


Figure 4. Symptom duration (mean years) before HAE-nC1INH diagnosis



Time to diagnosis was defined as the time from which symptoms were experienced to receiving a clinical diagnosis.

Figure 5. Mean number of HAE-nC1INH diagnostic criteria assessed

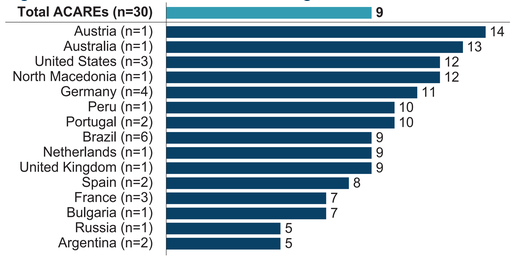
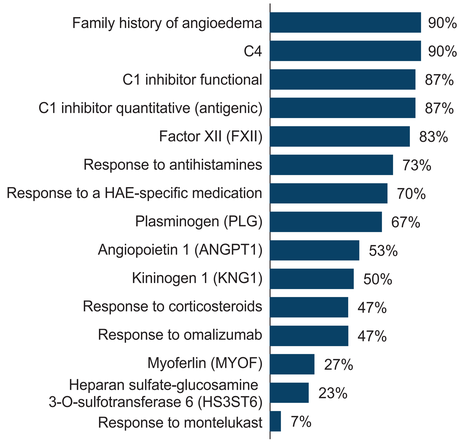
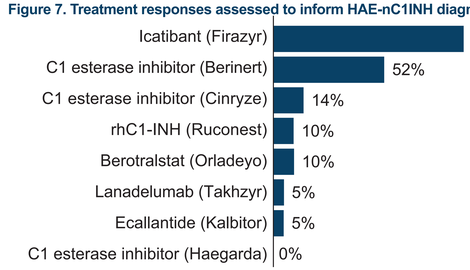


Figure 6. HAE-nC1INH diagnostic criteria utilized (n=30)



Physicians were asked to select which criteria they typically assess to make a diagnosis of HAE-nC1INH (multiple selections allowed).

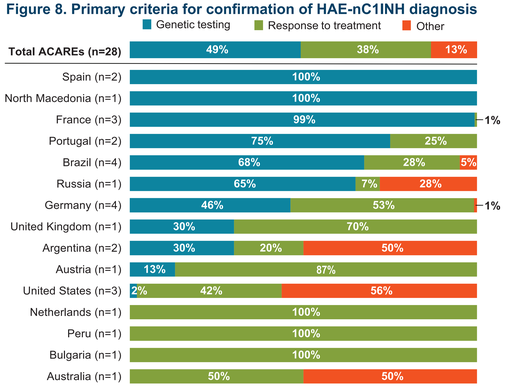
Figure 7. Treatment responses assessed to inform HAE-nC1INH diagnosis[a]



[a]Among those assessing response to HAE-specific medication to inform diagnosis (n=21).
rhC1-INH, recombinant human C1INH.

- Utilization of genetic testing (other than Factor XII) for diagnosis was highly variable across countries (**Figure 8**)

Figure 8. Primary criteria for confirmation of HAE-nC1INH diagnosis



Physicians were asked, "To the best of your recollection what percentage of patients were primarily confirmed using each of the following," and asked to select from a list of criteria. Twenty-eight of 30 physicians responded to the question.

Conclusions

- **The frequency of HAE-nC1INH may be greater than previously reported and varied widely across countries, potentially due to regional genetic differences, variable diagnostic criteria utilized, or other unknown factors**
- **These findings highlight variable clinical approaches and substantial delays in the diagnosis of HAE-nC1INH**
- **Reliable, validated, and easily accessible biochemical biomarkers are needed to improve accurate diagnosis and clinical management of people living with HAE-nC1INH**

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1. Maurer M, et al. *Allergy*. 2022;77(7):1961-1990.
2. Riedl MA, et al. *J Allergy Clin Immunol Pract*. 2023;11(8):2450-2456.e6.

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