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Advocacy in Action: International Patient Group Improves Hereditary Angioedema Diagnosis and Care Across the Asia–Pacific

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To the Editor,

Hereditary angioedema (HAE) is a rare genetic disorder, where early detection and treatment can significantly improve patient outcomes and reduce mortality [1]. Although the Asia–Pacific (APAC) represents half of the world's population, the prevalence of HAE has been reported to be only 0.2 per million (compared to 'global' prevalence of around 20 per million) [2, 3]. Even within APAC, there are disparities in reported HAE prevalence even within the same countries/ethnicities, suggesting that genetics alone cannot account for this difference [1, 2]. Moreover, despite mortality rates of up to 30% in countries without HAE-specific medications, these drugs are available only in a minority of APAC countries [2, 4]. Hence, there is a pressing need to reduce disparities in HAE care, especially within the APAC region [5–7].

Patient advocacy and support groups play a crucial role in improving patient support, awareness and advocate for the accessibility of medications, especially for rare diseases. HAE international (HAEi) was established in 2004 with the aim to raise awareness and improve the lives of HAE patients. HAEi's goal is to connect HAE patient advocacy groups and recognised HAE contacts (collectively referred as PAG). With support from HAEi, HAE PAG have been established in 11 countries in

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Summary

- Hereditary angioedema advocacy groups were associated with increasing prevalence and access to HAE-specific medications.
- Impact of hereditary angioedema advocacy groups were greater among countries with emerging economies.

APAC. The objective of this study is to evaluate the impact of these PAGs on the diagnosis and treatment of HAE in the APAC region.

An electronic questionnaire was developed after several rounds of drafting by a designated steering committee (J.C.Y.W., D.C., F.W., P.H.L.) and reviewed by all authors. This questionnaire was distributed to HAE-experienced physicians of APAC countries with HAE PAG using SurveyMonkey (Momentive Inc., California, USA) between September and November 2023. Country representatives were asked regarding the following: (1) prevalence, (2) access to diagnostic tests, (3) HAE-specific medications and (4) physician perception of HAEi support in their respective region. Responses from before and after the establishment of the first PAG in their region are available in the online repository (https://osf.io/gzk53). 'HAE medications' were defined as HAE-specific on-demand medications (C1-esterase inhibitor [C1-INH], icatibant or ecallantide) or prophylaxis (C1-INH, berotralstat or lanadelumab) which were registered or available in respective countries. Non-HAE-specific or investigational medications which were used off-label or as part of research were excluded. 'HAEi resources' included any physician-orientated tools developed by HAEi (such as the 'HAE TrackR' and 'HAE companion' applications, as well as 'HAEi Research Methodologies'). Participant countries were classified 'advancing economies' and 'emerging economies' [8]. Data on specific populations (for individual country, and the Hong Kong Special Administrative Region [SAR] of China) for calculation of prevalence rates were extracted [9]. Fisher's exact test was used to compare the availability of diagnostic tests and HAE-specific medications between emerging and advanced economies. Exact Poisson method was used to compare the prevalence rates of participant countries. Statistical analysis was performed using IBM SPSS version 22 (SPSS Inc., Chicago, IL, USA) and Prism 10 (GraphPad Software, Boston, MA, USA). The significance level for all tests was set at $p < 0.05$.

Eleven regions participated in the study, with five (45.5%) countries (Australia, Japan, New Zealand, Singapore and South Korea) classified as advanced economies and six (54.5%) (China [Hong Kong SAR], India, Malaysia, Nepal, Philippines, and Thailand) as emerging economies. Figure 1A illustrates a summary timeline of when each surveyed country established its first HAE PAG. At the time of survey, the median duration

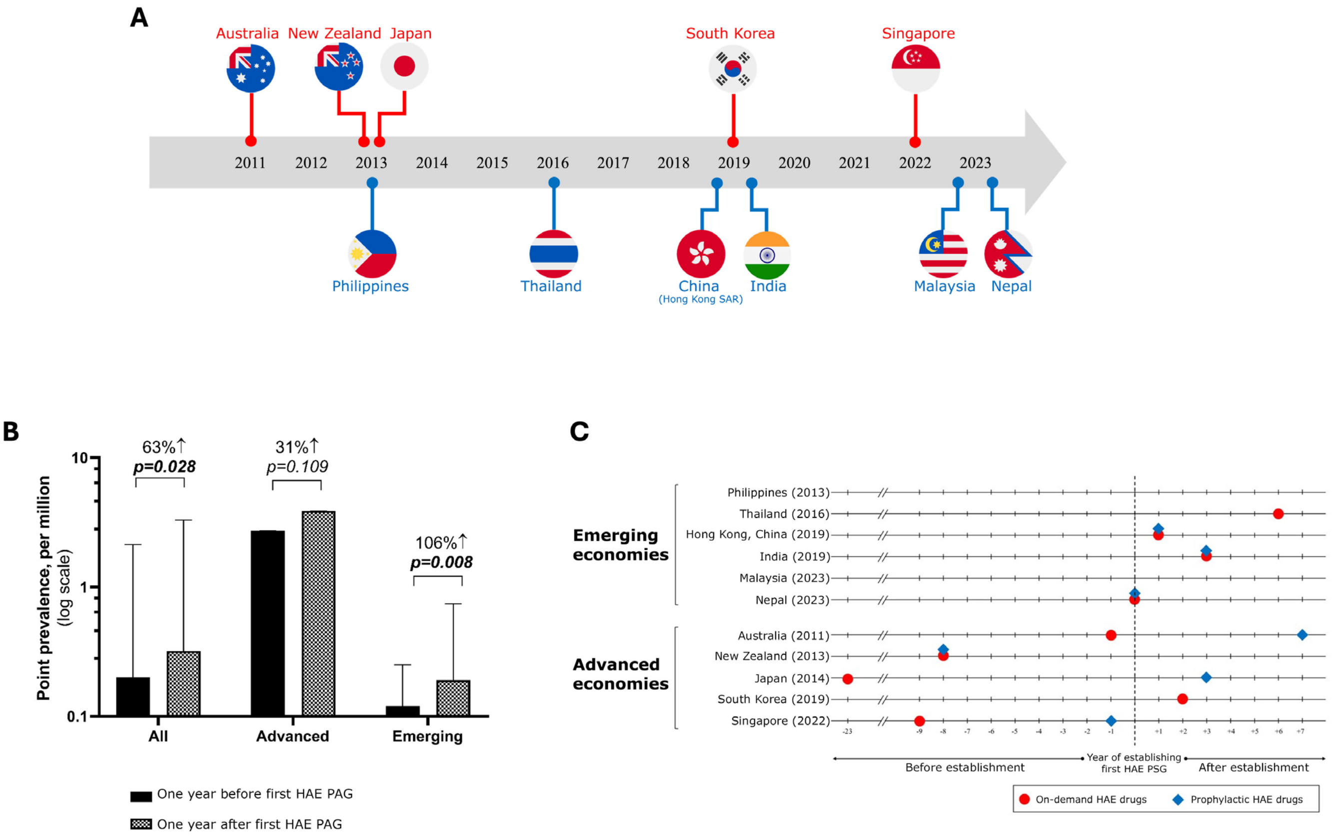

FIGURE 1 | Summary timelines and comparisons of HAE prevalence and medication access in relation to establishment of patient advocacy groups. (A) Timeline of establishment of first HAE PAG among countries of advanced and emerging economies; (B) comparison of HAE prevalence one-year before versus after PAG establishment among countries with advanced and emerging economies; and (C) availability of HAE-specific medications relative to PAG establishment.

since PAG establishment was 4.0 (0–12) years. Countries with advanced economies reported longer duration than those with emerging economies, but did not reach statistical significance (8.4 ± 4.7 vs. 5.2 ± 3.9 years, $p = 0.243$).

Among nine representatives with complete data (available in online repository: https://osf.io/gzk53), there was an increase in reported prevalence of 0.12 per million (63.0%, $p = 0.008$) 1 year following establishment of PAG. Subgroup analysis revealed that this increase was mainly contributed by emerging economies (0.12–0.19 per million, $p = 0.028$) (Figure 1B).

Before PAG establishment, 4 (36.4%) of 11 countries had access to HAE-specific medications (Advanced: 4 (80%), Emerging: 0, $p = 0.015$). Post establishment, these medications became available in 9 (81.2%) of 11 countries (Advanced: 5 (100%), Emerging: 4 (66.6%), $p = 0.455$). Figure 1C summarises the availability of HAE-specific medications relative to HAEi support for the first PAG among surveyed countries.

The majority (72.7%) of participants reported that 'HAEi made a positive difference in education and awareness' and had used HAEi resources in their respective countries. Almost half (45.4%) agreed that 'it was easier to find or gain access to tests since gaining support from HAEi' (Advanced: 20.0% vs. Emerging: 66.7%, $p = 0.122$), and more than one-third (36%) agreed 'HAEi made connections to find routes to diagnostic testing easier' (Advanced: 20.0% vs. Emerging: 50.0%, $p = 0.303$).

Our study had limitations, especially with our questionnaire being prone to recall bias. The small sample size only represents the perspective of physicians in evaluating the impact of HAE PAG. Also, the full impact of recently established PAGs may not be evident yet as the duration of PAG engagement varies.

This study is, to our knowledge, the first to assess the real-world impact of PAG on HAE diagnosis and care. We demonstrate that establishment of HAE PAG was associated with increased reported disease prevalence, medication access and awareness, particularly in emerging economies of the APAC region. Therefore, maintaining a focus on building and supporting HAE PAG will be vital for driving lasting effects and reducing regional disparities. We anticipate that this study's insights could also apply to other rare diseases, thereby reducing health disparities globally.

Author Contributions

All authors contributed to the study conception and design. Study design and material preparation were performed by P.H.L. and D.C. Data analysis and the first draft of the manuscript was written by J.C.Y.W., C.C.W.T. and K.C.W.L.; and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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