

Burden of Hereditary Angioedema Attacks in Adolescents

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Introduction

- Hereditary angioedema (HAE) is characterized by recurrent and unpredictable episodes of subcutaneous or submucosal swelling, which are debilitating and potentially fatal
- The onset of HAE symptoms typically occurs during childhood and may intensify significantly during puberty¹⁻³
 - Consequently, adolescents with HAE may face a substantial burden
- The current analysis examined the burden of HAE attacks in adolescent patients compared to adults

Methods

- People with Type 1 and 2 HAE were recruited between April and June 2023 by the US Hereditary Angioedema Association
- The study aimed to recruit approximately 80% adults and 20% adolescents
- Participants completed a 20-minute, self-reported, online survey that asked about their last treated HAE attack
- Participants were ≥12 years old and had to have treated ≥1 HAE attack within the prior 3 months using an approved on-demand therapy
- Quality of life (QoL) was assessed at the time of the last treated attack and "today" (i.e., current QoL), utilizing the EuroQol Five-Dimensions Five-Levels (EQ-5D-5L)
- Descriptive analyses were performed

Results

Table 1. Participant Demographics at the Time of Survey

| | Total (n = 94) | Adults (85% n = 80) | Adolescents (15% n = 14) |
|--|----------------|-----------------------|----------------------------|
| Current Mean Age, (SD) | 39.4 (17.4) | 43.8 (15.0) | 14.4 (1.5) |
| Mean Age of Diagnosis, Years (SD) | 18 (12.6) | 20 (12.5) | 6 (4.1) |
| Gender | | | |
| Male | 28% | 21% | 64% |
| Female | 72% | 79% | 36% |
| Race/Ethnicity | | | |
| White | 87% | 89% | 79% |
| Hispanic or Latino | 9% | 8% | 14% |
| Black/African American | 3% | 3% | 7% |
| American Indian or Alaskan Native | 2% | - | 14% |
| Asian | 3% | 4% | - |
| Other | 1% | 1% | - |
| HAE Type | | | |
| Type 1 | 81% | 81% | 79% |
| Type 2 | 19% | 19% | 21% |
| On Long-Term Prophylaxis | 54% | 54% | 57% |
| Physician Diagnosed Depression, % | 25% | 26% | 14% |
| Physician Diagnosed Anxiety, % | 30% | 29% | 36% |
| Days Since Last Treated Attack, Median (IQR) | 14 (7,28) | 14 (7,28) | 14 (18,28) |

- Respondents included 14 (15%) adolescents with an average age of 14 years and 80 (85%) adults with an average age of 44 years (Table 1)
- Respondents were predominately female (72%) and White (86%). A larger proportion of the adolescent patients were male (64%) compared to adult patients (21%)
- At the time of their most recent treated attack, 54% and 57% of adults and adolescents, respectively, were on non-androgen, long-term prophylaxis
- The duration of the last HAE attack for adolescents was median 2 days (IQR = 1-3 days) and for adults median 1 day (IQR = 1-2 days)

Figure 1. Long-Term Prophylaxis at Time of Last Treated Attack (n = 51)

| Long-Term Prophylaxis | Adults (n = 43) | Adolescents (n = 8) |
|--|-----------------|---------------------|
| Lanadelumab | 63% | 25% |
| Subcutaneous Human C1 Esterase Inhibitor | 26% | 13% |
| Bertralstat | 9% | 38% |
| Intravenous Human C1 Esterase Inhibitor | 2% | 25% |

- Among those on long-term prophylaxis at the time of the last treated attack, lanadelumab was the most common treatment among adults, whereas adolescents were most often treated with bertralstat (Figure 1)

Figure 2. On-Demand Therapy Used for Last Treated Attack

| On-Demand Therapy | Adults (n = 80) | Adolescents (n = 14) |
|--------------------------------------|-----------------|----------------------|
| Icatibant | 77% | NA* |
| Recombinant C1 Esterase Inhibitor | 13% | 50% |
| Plasma Derived C1 Esterase Inhibitor | 9% | 50% |
| Ecallantide | 3% | 0% |

*Not approved for patients under 18 years old

- The initial on-demand treatment was most commonly icatibant (branded and generic) for adults and recombinant C1 esterase inhibitor or plasma derived C1 esterase inhibitor for adolescents (Figure 2)

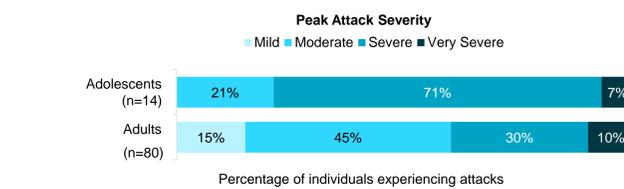
Figure 3. Initial Site of Attack of Last Treated Attack

| Initial Site of Attack | Adults (n = 80) | Adolescents (n = 14) |
|------------------------|-----------------|----------------------|
| Abdominal/Stomach | 58% | 71% |
| Peripheral | 21% | 14% |
| Face/Tongue | 10% | 7% |
| Throat | 6% | 7% |
| Genitals | 4% | 0% |

- Over two-thirds of adolescents (n = 10) and 59% of adults (n = 47) reported that the last treated attack originated in the abdomen
- Symptoms spread from the initial site to another site in 28% of adults (n=22) and 43% of adolescents (n=6)

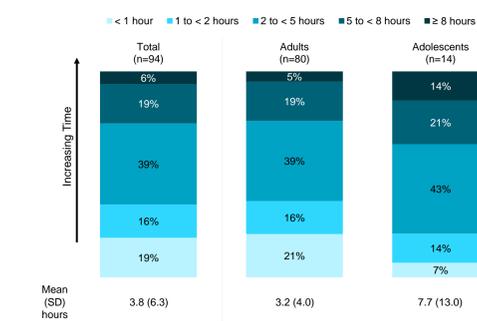
Results

Figure 4. Peak Attack Severity



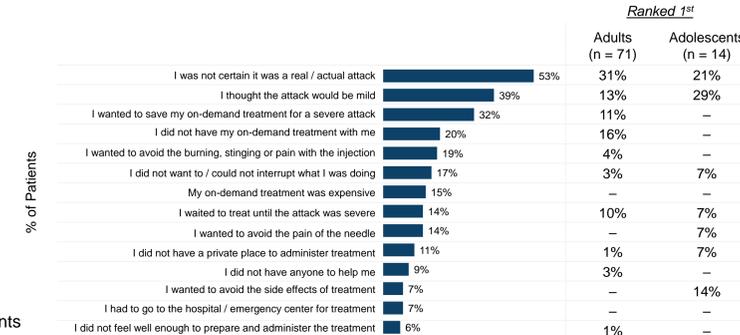
- For attack severity, 78% of adolescents rated their last attacks as severe or very severe, compared to 40% of adults (Figure 4)
- 29% of adolescent vs 5% of adult patients indicated they required emergency visit or hospitalization for their last attack

Figure 5. Time to On-Demand Treatment



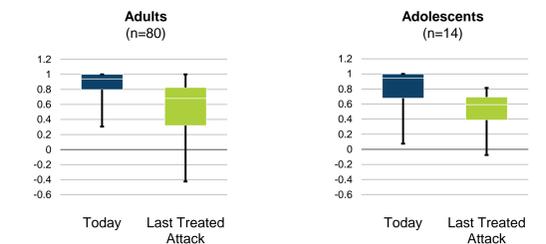
- The median recorded time from attack onset to on-demand treatment was 4 hours (interquartile range [IQR] = 2-5 hours) for adolescents and 2 hours (IQR = 1-4 hours) for adults (Figure 5)

Figure 6. Barriers to Treating HAE Attacks Sooner



- As seen in Figure 6, uncertainty as to whether they were experiencing an attack or believing that the attack would be mild were ranked as the primary reasons for not initiating treatment of the attack earlier (adolescents 21% and 29%; adults 31% and 13%)

Figure 7. EQ-5D-5L Index Values Today and Last Treated Attack



- Median EQ-5D-5L score (Figure 7) were meaningfully lower (based on minimal important difference: 0.08) at the time of the attack (adolescents, median = 0.59, IQR = 0.39-0.69; adults, median = 0.68, IQR = 0.32-0.83) than patients' current scores (adolescents, median = 0.94, IQR = 0.68-1.0; adults, median = 0.94, IQR = 0.80-1.0)

Conclusions

- The results of our study suggest that the burden of HAE attacks may be disproportionately severe for adolescents
- Specifically, the adolescents in our cohort reported higher anxiety, attack treatment delays, proportion of patients with peak attack severity as severe and very severe, emergency visits or hospitalizations, and impact on QoL during attacks compared to adults
- Taken together, these findings suggest that adolescents with HAE may experience enhanced morbidity from HAE attacks and associated on-demand therapy
- Our investigation would support expanding efforts targeted towards improving the recognition and treatment of HAE attacks among adolescents and alternatives to currently approved on-demand treatments

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Disclosures

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