Epidemiology of Hereditary Transthyretin (hATTR) Amyloidosis: A Real-World Analysis of a US Commercially Insured Population

Sheila R. Reddy, PhD, RPh[1], Spencer Guthrie, MBA[2], Eunice Chang, PhD[1], Ryan Tieu, MS[1], Marian H. Tarbox, MPP[1], Michael R. Pollock[3]

[1]Partnership for Health Analytic Research, LLC, Beverly Hills, CA, USA; [2]Aurora Bio INC, San Francisco, USA; [3]Akcea Therapeutics, Boston, MA, USA

BACKGROUND

- Hereditary transthyretin (hATTR) amyloidosis is a rare genetic, progressive, and fatal disease caused by buildup of misfolded transthyretin protein (amyloid) in organs and tissues[1]
- The recent incidence of hATTR amyloidosis in the US is not well documented[2,3]
  - The most frequently cited estimate in current literature is from 1996 and reports the US incidence of hATTR amyloidosis to be one in 100,000 individuals[4,5]
  - However, rates are most likely underestimated due to a lack of awareness and diagnostic uncertainty[2,6]

OBJECTIVE

- To generate a recent US estimate of diagnosed incidence of hATTR amyloidosis, focusing on patients with hATTR-associated polyneuropathy and/or mixed phenotype

METHODS

- Retrospective study using IBM® MarketScan® Commercial and Medicare Supplemental databases* from 01/01/2013 – 12/31/2017

Patient identification of incidence cases

- Included adult patients (≥18 years of age at index) newly diagnosed with hATTR amyloidosis (incident cases) in the calendar year (CY) of 2016
  - ≥1 medical claim with a relevant diagnosis code for amyloidosis (ICD-10-CM: E85.0-4, E85.89, E85.9; excludes light chain and wild type) in CY2016 AND ≥1 occurrence of qualifying criteria for hATTR any time during study period:
    - ≥15 days diflunisal use without >30-day gap OR liver transplant (patients with claim with code E85.1 or E85.2 at any time did not require additional qualifier)
- Disease-free enrollees: All enrollees who were continuously enrolled and without a diagnosis code of amyloidosis (including ICD-9-CM amyloidosis codes: 277.30, 277.31, 277.39) in CY2015

Study measures

- Annual diagnosed incidence defined as:
  - Number of new cases of hATTR in CY2016 divided by total at-risk (disease-free) patient-years from 01/01/2016 to either diagnosis (cases) or enrollment end (non-cases) in CY 2016, whichever occurred first
  - Incidence reported as cases per million person-years (PMPY)
  - Enrollment was continuous during at-risk period

Statistical analysis

- Incidence rates stratified by age group and gender
- All data transformations and statistical analyses were performed using SAS® version 9.4

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RESULTS

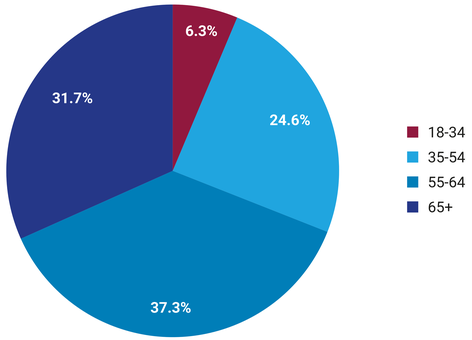
- Annual diagnosed incidence of hATTR in 2016 was 9.0 patients PMPY (**Table 1**)
- Incident cases were concentrated in older age groups (65+ years: 23.3, 55-64 years: 14.6, 35-54 years: 5.8, 18-34 years: 2.2 PMPY) and slightly more common among females than males (9.6 vs. 8.3 PMPY) (**Table 1, Figures 1-3**)

Table 1. hATTR Amyloidosis 2016 Incidence by Demographic Groups

	N	Number of Case per Million Person-Years
All	142	9.0
Age group		
18-34	9	2.2
35-54	35	5.8
55-64	53	14.6
65+	45	23.3
Gender		
Female	80	9.6
Male	62	8.3

hATTR: hereditary transthyretin.

Figure 1. Age Distribution among New Cases of hATTR in 2016



hATTR: hereditary transthyretin.

Figure 2. Gender Distribution among New Cases of hATTR in 2016

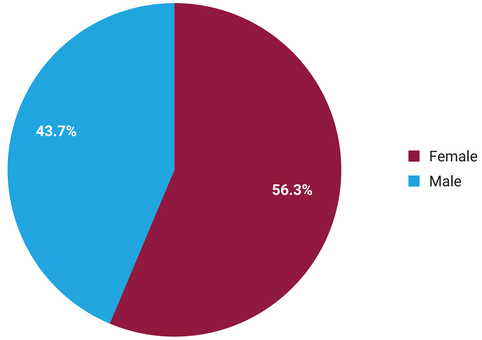


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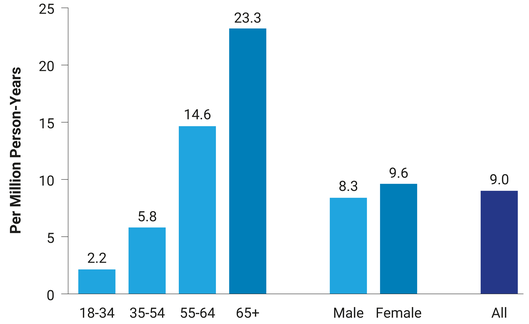
Figure 3. 2016 hATTR Incidence



hATTR: hereditary transthyretin.

LIMITATIONS

- Estimation of hATTR incidence using claims has not been previously validated; such estimation is difficult due to diagnostic challenges such as lack of awareness of the disease and, until recently, the absence of medical coding specific to the different types of transthyretin amyloidosis, including hATTR and wild-type ATTR amyloidosis (ATTRwt)
- This database has an underrepresentation of senior patients (65+) as it does not include all patients covered by Medicare[7]
  - Based on our results, as seniors (65+) have the highest rate of new cases of hATTR, the overall incidence in 2016 is likely underestimated
- We found a higher incidence of hATTR in females than males, in contrast with other studies that report higher hATTR rates among males

CONCLUSIONS

- The epidemiology of hATTR amyloidosis is not well understood or quantified
- This study reveals a small but meaningful number of new patients diagnosed with hATTR in the US in 2016: an incidence rate of 9.0 cases PMPY indicates about 2,245 new hATTR patients in 2016
- Consistent with previous studies, new cases are predominately of advanced age
- Future estimation of prevalence is planned

References

1. Ihse E, et al. J Pathol. 2008;216(2):253-261.
2. Gertz MA. Am J Manag Care. 2017;23(7 Suppl):S107-S112.
3. Nienhuis H, et al. Kidney Dis (Basel). 2016;2(1):10-19.
4. Ando Y, et al. Orphanet J Rare Dis. 2013;8:31.
5. U.S. National Library of Medicine. Transthyretin amyloidosis [Internet]. Genetics Home Reference. 2019 [cited 2019 Sep 10]. Available from: https://ghr.nlm.nih.gov/condition/transthyretin-amyloidosis#sourcesforpage
6. Hawkins P, et al. Ann Med. 2015;47(8):625-638.
7. Cantillon DJ, et al. JACC Clin Electrophysiol. 2017;3(11):1296-1305.

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http://bit.ly/2mMGzAg

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