Increasing Prevalence and Incidence of AL Amyloidosis Among Older Adults in the US

Preeti S. Bajaj, PhD[1]; Michael S. Broder, MD, MSHS[2]; Ashis K. Das, MBBS, MPH, PhD[2]; Eunice Chang, PhD[2]; Marian H. Tarbox, MPP[2]; Ansgar Conrad, PhD[1]; Anita D'Souza, MD, MS[3]

[1] Prothena Biosciences Inc, South San Francisco, CA, USA; [2] PHAR (Partnership for Health Analytic Research), Beverly Hills, CA, USA; [3] Medical College of Wisconsin, Milwaukee, WI, USA.

BACKGROUND & OBJECTIVE

- Amyloid light chain (AL) amyloidosis is a rare, progressive, and typically fatal disease caused by toxic, soluble amyloidogenic light chain aggregates and insoluble light chain amyloid deposits that infiltrate multiple organs and progressively affect organ structure and function.[1]
- Diagnosis often occurs in adults over the age of 60; however, recent estimates of prevalence and incidence of AL amyloidosis in this population are limited.[2-8]
  - The specific AL amyloidosis International Classification of Diseases, Tenth Edition, Clinical Modification (ICD-10-CM) diagnosis code, E85.81, was not introduced until 2017. Thus, real-world data prior to this time was limited and relied on non-specific ICD-9-CM diagnosis codes to identify patients.
- We aimed to provide comprehensive estimates of overall and age-, sex-, and race-specific AL amyloidosis prevalence and incidence in older US adults using nationally representative data.

METHODS

Study design and data source

- Cross-sectional, retrospective cohort study using 2018-2020 data from the Medicare 100% Research Identifiable Files (RIFs), which cover 100% of Medicare beneficiaries and contain patient-level information on demographics, enrollment, and administrative claims data.[9, 10]

Patient population

- Patients with AL amyloidosis were defined as Medicare beneficiaries enrolled in Medicare fee-for-service (FFS) ≥65 years with ≥1 inpatient or ≥2 outpatient claims for AL amyloidosis (ICD-10-CM diagnosis code E85.81) in any diagnosis field during each calendar year.
- Yearly (2018-2020) prevalent beneficiaries had AL amyloidosis in the calendar year of interest and continuous annual enrollment in Medicare FFS during that calendar year.
- Yearly (2019-2020) incident beneficiaries had newly diagnosed AL amyloidosis in the calendar year of interest (no AL amyloidosis diagnosis code in the prior year) and continuous enrollment in Medicare FFS in the previous year.

Outcomes and statistical analysis

- Annual prevalence (per 100,000) was calculated using the number of prevalent beneficiaries divided by the number of total beneficiaries who met the enrollment requirement during the same period.
- Prevalent beneficiaries could be included in multiple years and the denominator for the cohort was estimated using an enhanced 5% sample of all Medicare beneficiaries each year.
- Annual incidence (per 100,000 person-years) was calculated using the number of incident beneficiaries divided by the total at-risk person-years.
  - The at-risk population included beneficiaries who were both continuously enrolled with Medicare FFS and had no AL amyloidosis diagnosis in the year prior.
  - For non-incident beneficiaries, the at-risk person-time was the duration of enrollment during the calendar year. For incident beneficiaries, the at-risk person-time was the duration of time from January 1st of the diagnosis year up to the diagnosis date.
- Rates were stratified by age group (65-74, 75-84, ≥85), sex, and race.
- Data transformations and statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC).

RESULTS

- The inclusion/exclusion criteria resulted in the identification of:
  - 1,510 prevalent beneficiaries in 2018, 1,926 in 2019, and 2,214 in 2020; and
  - 716 incident beneficiaries in 2019; and 751 in 2020 with AL amyloidosis (Table 1).
- Across years, a greater proportion of AL amyloidosis patients were male, White, and from the Midwest region of the US.
- The prevalence of AL amyloidosis among older adults increased during the study period, and incidence increased slightly (Table 2).
  - Prevalence: 9.92 in 2018, 12.27 in 2019, and 14.01 cases per 100,000 in 2020 (Figure 1).
  - Incidence: 5.01 in 2019 to 5.12 cases per 100,000 person-years in 2020 (Figure 2).
  - Increases in epidemiology estimates were observed among the following subgroups: those aged 75-84 (prevalence) and ≥85 (incidence) years, males, and Black beneficiaries.
- The analysis is focused on only the subset of patients, based on a number of inclusion and exclusion criteria, for whom we had sufficient claims records to reliably assess incidence/prevalence; therefore, patient counts are likely underestimated and calculated rates are expected to be more reliable estimates of incidence/prevalence.
- Based on a prevalence of 14.01 per 100,000 and an estimated 57 million US adults ≥65 years old, we estimate that the US prevalence of AL amyloidosis among adults above the age of 65 years is approximately 8,000 individuals.

RESULTS (continued)

Table 1. Demographics of Medicare FFS beneficiaries with AL amyloidosis

	Selected prevalent cases			Selected incident cases	
	2018	2019	2020	2019	2020
N	1,510	1,926	2,214	716	751
Age, mean (SD)	73.8 (5.6)	74.1 (5.8)	74.4 (6.1)	76.0 (6.1)	76.4 (6.5)
65-74, n (%)	880 (58.3)	1,098 (57.0)	1,236 (55.8)	327 (45.7)	320 (42.6)
75-84	559 (37.0)	720 (37.4)	822 (37.1)	315 (44.0)	340 (45.3)
85+	71 (4.7)	108 (5.6)	156 (7.0)	74 (10.3)	91 (12.1)
Female, n (%)	666 (44.1)	864 (44.9)	953 (43.0)	327 (45.7)	300 (39.9)
Race, n (%)					
White	1,291 (85.5)	1,660 (86.2)	1,878 (84.8)	619 (86.5)	627 (83.5)
Black	111 (7.4)	131 (6.8)	171 (7.7)	63 (8.8)	83 (11.1)
Other/Unknown	108 (7.2)	135 (7.0)	165 (7.5)	34 (4.7)	41 (5.5)
Region, n (%)					
Midwest	488 (32.3)	633 (32.9)	692 (31.3)	228 (31.8)	208 (27.7)
Northeast	337 (22.3)	432 (22.4)	464 (21.0)	153 (21.4)	164 (21.8)
South	398 (26.4)	485 (25.2)	613 (27.7)	201 (28.1)	242 (32.2)
West	287 (19.0)	376 (19.5)	445 (20.1)	134 (18.7)	137 (18.2)

Table 2. Prevalence and incidence rates of AL amyloidosis among Medicare FFS beneficiaries

	Prevalence per 100,000 population			Incidence per 100,000 person-years	
	2018	2019	2020	2019	2020
Overall (Age ≥65 years)	9.92	12.27	14.01	5.01	5.12
Age group, years					
65-74	10.52	12.62	13.95	4.49	4.21
75-84	11.34	14.16	16.15	6.29	6.67
85+	3.68	5.65	8.43	3.73	4.64
Gender					
Female	7.46	9.41	10.32	3.90	3.49
Male	13.40	16.31	19.19	6.59	7.44
Race					
White	9.44	11.78	13.25	4.81	4.75
Black	15.29	18.20	24.66	9.56	12.94
Other/Unknown	13.28	15.27	17.72	4.46	4.97
Region					
Midwest	11.58	14.24	15.74	5.76	5.09
Northeast	11.56	14.86	15.79	5.70	6.02
South	7.21	8.52	10.66	3.84	4.52
West	11.14	14.18	16.39	5.57	5.49
Age group * Gender					
65-74 years old					
Female	8.25	9.68	10.60	3.38	2.85
Male	13.59	16.61	18.49	6.00	6.08
75-84 years old					
Female	8.43	11.48	12.08	5.37	5.09
Male	15.20	17.70	21.56	7.50	8.75
85+ years old					
Female	2.46	3.67	5.04	2.41	2.08
Male	6.24	9.67	15.15	6.40	9.68

Figure 1. Prevalence per 100,000

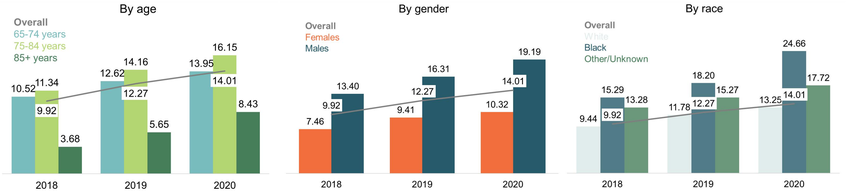
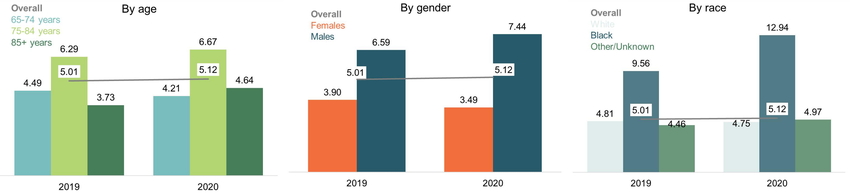


Figure 2. Incidence per 100,000 person-years



LIMITATIONS

- Limitations of the study include:
  - Possible miscoding, a common limitation of claims data research, leading to possible misidentification; however, our methodology for identifying amyloidosis patients is consistent with previously published work using claims data.[11-14]
    - To mitigate this potential limitation, we conducted a sensitivity analysis examining different inclusion criteria and specific treatment utilization rates to confirm that the included study patients were not likely to be transthyretin amyloidosis (ATTR) patients.
  - Potentially underestimated prevalence and incidence rates due to the following:
    - The recent addition of the specific AL amyloidosis ICD-10-CM code, which could require time for uptake and appropriate use.
    - Patients with AL amyloidosis who did not receive care during the study period, who were misdiagnosed, or who were experiencing symptoms but had yet to be diagnosed would not have been identified as having AL amyloidosis.
    - The inclusion/exclusion criteria excluded patients with shorter survival (known to be the case for patients with advanced stage disease), resulting in selection bias.
    - Reported prevalence and incidence rates do not reflect patients not covered by Medicare FFS.

CONCLUSIONS

- AL amyloidosis affects approximately 10-14 per 100,000 older US adults, or an estimated 8,000 individuals within the Medicare population over 65 years of age.
- The prevalence and incidence of AL amyloidosis appear to be increasing, particularly in those with advanced age, among males, and among Black beneficiaries.
- Further research focused on diagnostic patterns, clinical characteristics, and outcomes in these high-risk populations is needed.

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AUTHOR DISCLOSURES

This analysis was supported by Prothena Biosciences Ltd (Dublin, Ireland), a member of the Prothena Corporation plc group. PS Bajaj and A Conrad are employees of Prothena Biosciences Inc and hold stock in Prothena Corporation plc. MS Broder, AK Das, E Chang, and MH Tarbox are employees of PHAR, which received funding from Prothena to conduct the research described. A D'Souza is an employee of the Medical College of Wisconsin and was paid by Prothena to consult as a subject matter expert.