Determinants of higher costs and inpatient hospitalization among patients with AL amyloidosis

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BACKGROUND

- Amyloid light chain (AL) amyloidosis is a rare, progressive, and typically fatal disease caused by underlying plasma cell dyscrasia.[1]
  - Staging is based on cardiac and hematologic biomarkers that indicate severity of disease including the presence and severity of heart damage.[2]
- Clinical and economic burden have been shown to be higher in persons with AL amyloidosis compared to those without.[3-8]
  - However, the impact of factors such as disease severity has not been examined.
  - Additionally, 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, many published estimates of healthcare resource utilization (HCRU) and costs are based on populations identified using non-specific ICD-9-CM diagnosis codes.
- We aimed to examine determinants of healthcare costs and inpatient hospitalization in AL amyloidosis, using the ICD-10-CM code specific for AL amyloidosis.

METHODS

Study design and data source

- Retrospective analysis using 2019 data from the Merative® MarketScan® Commercial and Medicare Supplemental and the IQVIA Pharmetrics Plus® databases.

Patient population

- Adult patients (existing or newly diagnosed) with ≥1 inpatient or ≥2 outpatient claims for AL amyloidosis (ICD-10-CM code E85.81) in any diagnosis field during 1/1/2019-12/31/2019 in the United States.
- Continuous enrollment in a health plan in the calendar year was required.

Outcomes and statistical analysis

- To identify the determinants of higher costs and hospitalization, linear and logistic regression models, respectively, were conducted using a forward selection method.
  - For both models, the base model included: age groups, gender, region, and advanced disease (defined as the presence of advanced cardiac or renal conditions - heart failure, myocardial infarction, chronic kidney disease [stages 4 & 5, pulmonary hypertension, sudden cardiac death/cardiac arrest], or use of cardiac stent or dialysis) as the independent variables.
  - Variables that most improved the fit among the following characteristics and comorbidities were sequentially added: provider specialty of hematologist/oncologist, individual classifications in the Charlson Comorbidity Index (a total of 18 variables including one cancer variable excluding multiple myeloma), monoclonal gammopathy of undetermined significance, hypothyroidism, Waldenström's macroglobulinemia, hypotension, hyperlipidemia, carpal tunnel syndrome, hepatomegaly, purpura, claudication, stroke, and peripheral neuropathy.
  - Apart from age, gender, region, and severity of AL amyloidosis, all other independent variables in the final model were considered significant with a p-value <0.05.
- Data transformations and statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC).

RESULTS

- We identified 591 patients with AL amyloidosis: mean age 60.8 years, 42.6% females **(Table 1)**.

Table 1. Demographic and clinical characteristics of patients with AL amyloidosis (2019)

N	591
Age, mean (SD) [median]	60.8 (9.9) [61]
18-34, n (%)	5 (0.8)
35-54	130 (22.0)
55-64	309 (52.3)
65+	147 (24.9)
Female, n (%)	252 (42.6)
Region, n (%)	
Midwest	192 (32.5)
Northeast	122 (20.6)
South	204 (34.5)
West	73 (12.4)
Insurance type, n (%)	
Commercial	387 (65.5)
Medicare	110 (18.6)
Other	94 (15.9)
Advanced AL Amyloidosis,[a] n (%)	
Non-advanced	248 (42.0)
Advanced	343 (58.0)
Charlson Comorbidity Index, mean (SD) [median]	4.0 (2.7) [4]
Congestive heart failure, n (%)	288 (48.7)
Chronic pulmonary disease	139 (23.5)
Renal disease	252 (42.6)
End stage renal disease	58 (9.8)
Multiple myeloma	336 (56.9)

[a] Defined as the presence of advanced cardiac or renal conditions - heart failure, myocardial infarction, chronic kidney disease (stages 4 & 5, pulmonary hypertension, sudden cardiac death/cardiac arrest), or use of cardiac stent or dialysis.

RESULTS (CONTINUED)

- Mean (SD) total all-cause cost was $143,594 (171,486.4) and 39.1% of patients had a hospitalization.
- Determinants of higher healthcare costs included: having advanced AL amyloidosis ($57,280 higher than non-severe, p<0.001); and being younger than 65: 18-34 (estimate: $145,893 higher than ≥ 65, p=0.028), 35-54 ($88,638 higher, p<0.001), or 55-64 ($69,901 higher, p<0.001) **(Table 2)**.
  - Myocardial infarction, multiple myeloma, and other specific comorbid conditions were associated with higher costs (all p<0.05).
- Determinants of hospitalization included: having advanced AL amyloidosis (odds ratio: 3.01, p<0.001), myocardial infarction (2.49, p=0.004), cerebrovascular disease (2.14, p=0.042), chronic pulmonary disease (2.49, p<0.001), connective tissue/rheumatic disease (3.54, p=0.015), mild liver disease (2.25, p=0.017), diabetes with chronic complications (3.43, p=0.001), hypotension (2.30, p=0.002), hepatomegaly (7.05, p<0.001), and purpura (2.84, p<0.001) **(Table 2)**.

Table 2. Determinants of all-cause costs and inpatient hospitalization

	All-cause costs[a]		All-cause inpatient hospitalization[b]	
Effect	**Estimate (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
Age		<0.001[d]		0.250[c]
18-34 vs 65+	$145,893 (16029 – 275757)	0.028	2.47 (0.25 – 24.80)	0.442
35-54 vs 65+	$88,638 (52329 – 124948)	<0.001	1.66 (0.90 – 3.08)	0.107
55-64 vs 65+	$69,901 (40316 – 99487)	<0.001	1.61 (0.98 – 2.65)	0.059
Female vs Male	$-28,805 (-52938 – -4672)	0.019	1.26 (0.84 – 1.90)	0.260
Region		0.225[d]		0.263[c]
Midwest vs South	$104 (-29140 – 29349)	0.994	0.71 (0.43 – 1.17)	0.179
Northeast vs South	$8,002 (-24895 – 40900)	0.633	0.97 (0.57 – 1.66)	0.922
West vs South	$38,912 (-775 – 78600)	0.055	0.57 (0.29 – 1.12)	0.104
Advanced [e] vs non-advanced AL amyloidosis	$57,280 (31551 – 83008)	<0.001	3.01 (1.94 – 4.66)	<0.001
Myocardial infarction, yes vs no	$51,154 (13083 – 89225)	0.009	2.49 (1.34 – 4.61)	0.004
Cerebrovascular disease, yes vs no	-	-	2.14 (1.03 – 4.47)	0.042
Chronic pulmonary disease, yes vs no	-	-	2.49 (1.56 – 3.96)	<0.001
Connective tissue/rheumatic disease, yes vs no	-	-	3.54 (1.27 – 9.83)	0.015
Mild liver disease, yes vs no	-	-	2.25 (1.16 – 4.38)	0.017
Diabetes with chronic complications, yes vs no	-	-	3.43 (1.64 – 7.16)	0.001
Peripheral vascular disease, yes vs no	$56,075 (21517 – 90633)	0.002	-	-
Paraplegia or Hemiplegia, yes vs no	$159,194 (40973 – 277415)	0.008	-	-
Multiple myeloma, yes vs no	$83,044 (58839 – 107249)	<0.001	-	-
Cancer excluding multiple myeloma, yes vs no	$60,173 (32990 – 87355)	<0.001	-	-
Hypotension, yes vs no	$60,256 (28725 – 91787)	<0.001	2.30 (1.37 – 3.85)	0.002
Hepatomegaly, yes vs no	-	-	7.05 (2.63 – 18.93)	<0.001
Carpal tunnel syndrome, yes vs no	$64,749 (5198 – 124301)	0.033	-	-
Purpura, yes vs no	$54,014 (19389 – 88639)	0.002	2.84 (1.60 – 5.03)	<0.001

95% CI: 95% confidence interval. [a] Final linear regression model. To identify the risk factors, both models used a forward selection method by always including age (in year), gender, region, and severity of AL amyloidosis as independent variables, and sequentially added variables among selected characteristics and comorbidities (described in Methods). Besides age, gender region, and severity of AL amyloidosis, all remaining independent variables in the final models are significant (p<0.05). [b] Final logistic regression model. [c] Wald Chi-square test of Type III analysis of effects. [d] F-test of Type III sum of squares. [e] Defined as the presence of advanced cardiac or renal conditions - heart failure, myocardial infarction, chronic kidney disease (stages 4 & 5, pulmonary hypertension, sudden cardiac death/cardiac arrest), or use of cardiac stent or dialysis.

LIMITATIONS

- Limitations include possible miscoding, a common limitation of claims data research, leading some patients to possibly have been misidentified; however, our methodology for identifying amyloidosis patients is consistent with previously published work using claims data.[4,5,8-10]
- Increased age was associated with decreasing costs, which may be due to trends in treatment, with older people getting less aggressive treatment such as hematopoietic stem cell transplant; however, we are unable to confirm reasons for this trend in this study.
- Results may not be generalizable to other populations not covered by commercial and Medicare supplemental insurance.

CONCLUSION

- Younger age, advanced disease, and associated specific comorbidities are associated with higher healthcare costs and/or hospitalization in persons with AL amyloidosis.
- Results from our study may inform policy efforts to contain healthcare costs and reduce utilization for persons with AL amyloidosis, including in individuals with advanced disease.

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AUTHOR DISCLOSURES

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