Healthcare Resource Utilization in Alpha-Mannosidosis: Results from an International Caregiver Survey

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Introduction

- Alpha-mannosidosis (AM) is an ultra-rare autosomal lysosomal storage disorder caused by mutations in the *MAN2B1* gene which result in loss of activity of the alpha-mannosidase enzyme.
- AM affects between approximately 1/500,000 to 1/1,000,000 live births, and main clinical manifestations include immunodeficiency and high propensity to infections, skeletal abnormalities, mobility issues, hearing and speech impairments, intellectual disability, and psychological disorders.[1-3]
- Long term-prognosis is poor, with many patients becoming wheelchair dependent as a result of slow neuromuscular and skeletal deterioration.[4]
- Treatment options include hematopoietic stem cell transplantations (HSCT) and enzyme replacement therapy (ERT).[5]
- To date, there are no studies on the economic burden of AM.

Objective

- The primary aim of this study was to investigate the natural history and assess the worldwide economic burden of AM.

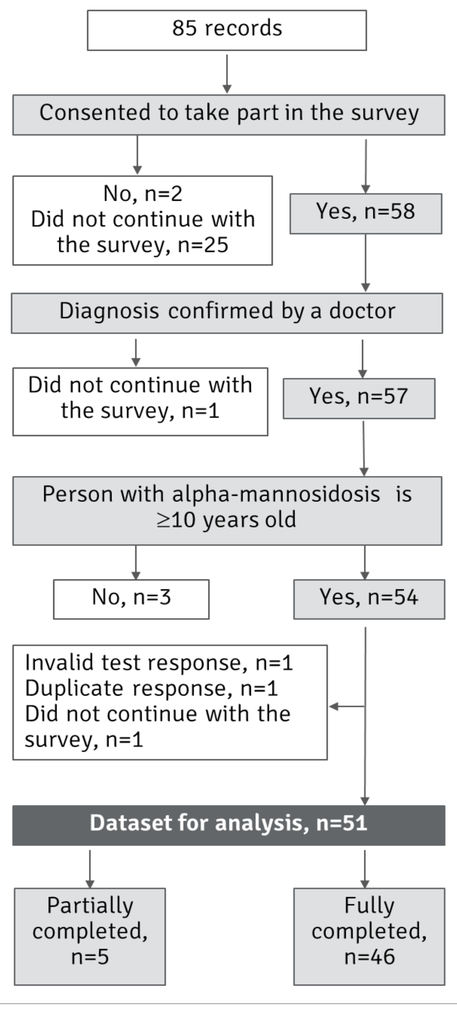
Methods

- An international online survey was conducted between November 2022 and February 2023 in patients aged ≥10 years or caregivers of patients with a confirmed diagnosis of AM.
- The study included untreated patients, patients receiving HSCT including bone marrow transplantation (BMT), and patients treated with ERT.
- Both qualitative and quantitative analyses were undertaken.

Results

- Overall, 3 patients and 48 caregivers from 18 different countries participated in the survey (**Figure 1**).
- The median age of patients treated with ERT was 21.1 years, compared with 13.6 years for patients treated with BMT/HSCT, and 29.2 years for untreated patients (**Table 1**).

Figure 1. Patient Attrition



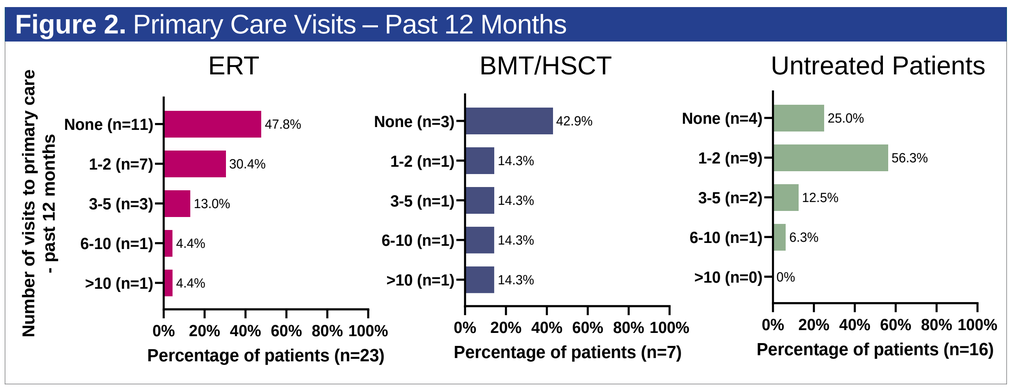
- The median age at which symptoms were noticed was 1.5 years for patients treated with ERT, compared with 0.7 years for patients treated with BMT/HSCT, and 2.4 years for untreated patients (**Table 1**).
- Median age at diagnosis was 6.6 years for patients treated with ERT, compared to 2.8 years for patients treated with BMT/HSCT, and 10.3 years for untreated patients (**Table 1**).

Table 1. Baseline Demographics

	ERT (n=26)	BMT/HSCT (n=7)	Untreated Patients (n=18)
Sex, n			
Males	15	3	8
Females	11	4	10
Age at time of survey			
Median	21.1	13.6	29.2
Mean±SD	24.9±10.8	15.9±4.9	26.4±7.8
Range	10.3–45.7	11.4–24.2	11.7–38.4
Age symptoms first noticed			
Median	1.5	0.7	2.4
Mean±SD	2.6±4.5	2.4±4.0	5.8±7.2
Range	0.0–23.5	0.0–11.3	0.3–24.1
Age at diagnosis			
Median	6.6	2.8	10.3
Mean±SD	8.3±7.2	3.8±3.0	11.3±7.0
Range	0.0–27.2	1.3–9.8	2.6–24.1
Age treatment started			
Median	17.0	3.2	-
Mean±SD	18.9±9.7	4.0±2.4	-
Range	5.3–37.5	1.6–7.8	-
Treatment length			
Median , years	5.3	10.4	-
Mean±SD	6.0±4.4	12.0±6.5	-
Range	0.3–12.5	4.3–22.2	-

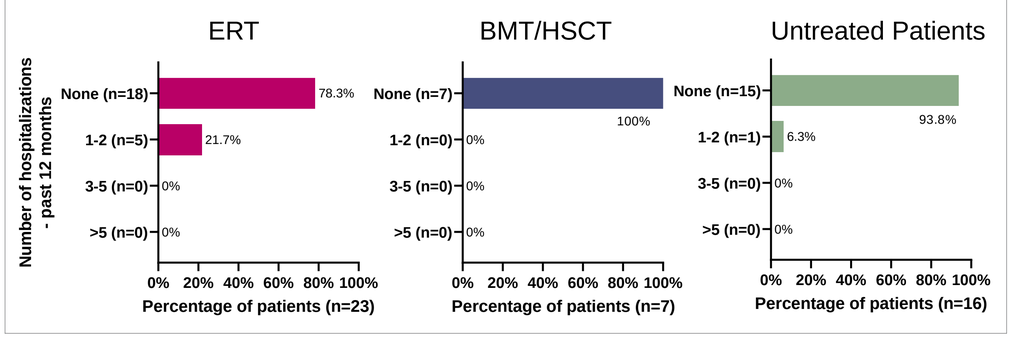
- For patients treated with ERT, 47.8% (n=11) had not visited their primary care doctor in the past 12 months, and 30.4% (n=7) had visited primary care 1–2 times (**Figure 2**).
- For patients treated with BMT/HSCT, 42.9% (n=3) had not visited their primary care doctor in the past 12 months, and 14.3% (n=1) had visited primary care 1-2 times (**Figure 2**).
- For untreated patients, 25.0% (n=4) had not visited their primary care doctor in the past 12 months, and 56.3% (n=9) had visited primary care 1–2 times (**Figure 2**).

Figure 2. Primary Care Visits – Past 12 Months



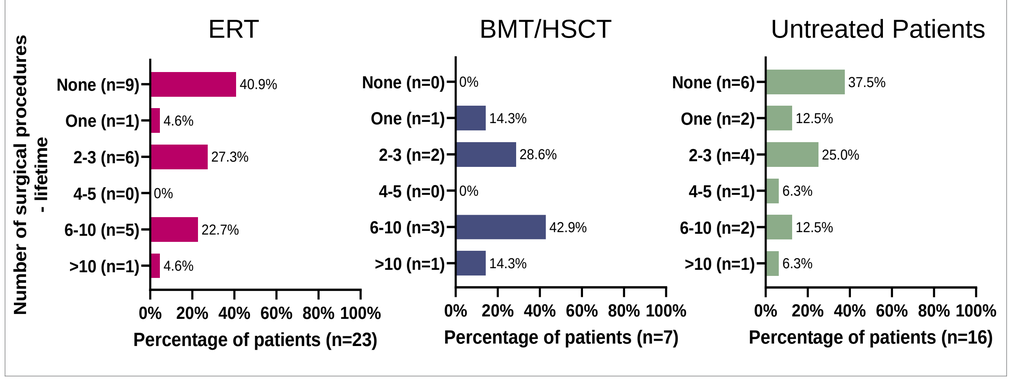
- No patients treated with BMT reported a hospitalization in the past 12 months, while 21.7% of patients treated with ERT and 6.3% of untreated patients reported 1-2 hospitalizations in the past 12 months (**Figure 3**).

Figure 3. Hospitalizations – Past 12 Months



- More patients with ERT reported never having an AM-related surgery over their lifetime (40.9%) compared to patients treated with BMT/HSCT (0%) or untreated patients (37.5%) (**Figure 4**).

Figure 4. Surgical Procedures - Lifetime



Discussion

- This study found that patients treated with BMT/HSCT had a lower median age at disease onset and diagnosis than those treated with ERT and untreated patients. Moreover, the time between diagnosis and treatment for BMT/HSCT treated patients was shorter compared with ERT-treated patients.
- Based on the lower median age at first symptoms and at diagnosis in patients receiving BMT and the shorter delay between diagnosis and treatment initiation, BMT may have been chosen due to differences in disease severity or due to clinicians' determination that BMT may be more successful in those diagnosed in early childhood.
- Differences in hospital and primary care visits between groups may be related to treatment received. ERT patients may have a higher ratio of hospital to primary care visits as a function of requiring hospital visits for infusion.
- Understanding the factors that drive these differences in healthcare resource utilization between groups remain to be determined (treatment type and set of symptoms and severity).

Limitations

- Sample sizes for this study were small, few patients were treated with BMT/HSCT.
- Specialty physician and/or physical therapy visits were also not captured in this data set.
- The results may have been impacted by recall bias since participants were asked to consider a 12-month period. Most data refer to the last 12 months leading up to the survey, thus recall biases cannot be excluded in all three groups.

Conclusions

- There are varying levels of healthcare resource utilization for patients with AM due to the heterogenous severity and phenotype of the disease. This is the first study reporting the remarkable economic burden of AM and suggests an unmet need for improved disease management in a substantial proportion of AM patients.

References

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