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Investigating the impact of early versus late diagnosis in Fabry disease on healthcare resource utilization and associated costs in Greece

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BACKGROUND

Fabry Disease (FD) is a rare inherited disease, caused by reduced or absent activity of α-galactosidase A enzyme. It can affect multiple systems of the human body, either at the same time (classical phenotype) or a single organ (non-classical phenotype)[1]. Due to its rarity and diverse manifestation, it is a major diagnostic challenge, often leading to delayed diagnosis, when the disease has progressed significantly[2].

OBJECTIVE

In this context, the aim of the present study was to assess the differences in healthcare resource utilization and associated costs between patients with early versus late clinical diagnosis of Fabry disease.

METHODS

Due to scarcity of relevant local clinical data, partly because of the disease rarity, the expert panel methodology was employed. The expert panel consisted of 8 hospital physicians (5 nephrologists, 2 neurologists, 1 cardiologist), with long term experience managing patients with FD.

A questionnaire based on an extensive literature review, concerning FD patient characteristics and resource use (medication, physician visits, tests, hospitalization, dialysis), was developed by the research team. Then, a pilot-testing was done with one of the experts, and the finalized questionnaire was used for the expert panel input. Cost data regarding lab and physical tests, medication (acquisition and administration) and hospitalization in ward derived from local official sources[3-9], while cost data for Intensive Care Unit (ICU) and dialysis were sourced from the international literature[10-11]. The analysis was held under the third-party payer perspective (social insurance) and, thus, only direct costs were included. All cost data refer to year 2022.

RESULTS

The expert panel analysis indicated nephrology as the most utilized medical specialty by FD patients (followed by cardiology and neurology) (Table 1). On average, classical FD patients are estimated to annually make 2.64 visits in early and 7.56 visits in late diagnosis to nephrologists. The respective visits of non-classical FD were 1.69 (early diagnosis) and 2.63 (late diagnosis) visits per year.

Concerning utilization of lab examinations, FD patients with late diagnosis perform almost all tests at significantly higher frequency compared to FD patients with early diagnosis, especially in classical FD.

Table 1. Average annual frequency of physician visits per phenotype and early/late diagnosis of adult Fabry patients

	Classical Fabry		Non-classical Fabry	
Specialty	Early diagnosis	Late diagnosis	Early diagnosis	Late diagnosis
Nephrologist	2.64	7.56	1.69	2.63
Cardiologist	2.21	5.07	1.31	1.88
Neurologist	2.14	4.79	1.31	1.88
Ophthalmologist	1.07	1.50	0.63	0.69
Otorhinolaryngologist	0.64	0.79	0.50	0.56
Rheumatologist	0.21	0.36	0.13	0.19

Regarding medication, agalsidase alfa is the medication with the highest proportion of utilization in all patient groups, ranging from 37.86% in non-classical early diagnosed FD to 47.14% in classical late diagnosed FD (Table 2).

It should be noted that a small proportion of patients does not receive any kind of treatment for FD, mainly for personal reasons. According to the expert panel, these patients generally do not consult healthcare professionals and do not monitor their condition with tests etc; thus, these patients were not included in the cost analysis.

Table 2. Distribution of treatment options per phenotype and early/late diagnosis

	Classical Fabry		Non-classical Fabry	
	Early diagnosis	Late diagnosis	Early diagnosis	Late diagnosis
ERT- Agalsidase alfa	45.00%	47.14%	37.86%	42.14%
ERT- Agalsidase beta	38.57%	40.71%	29.29%	33.57%
Oral Chaperone Therapy	13.57%	9.29%	25.71%	18.57%
No treatment for disease management	2.86%	2.86%	7.14%	5.71%
Total	100%	100%	100%	100%

In a 5-year time period, 26.88% of classical FD patients with early and 43.13% with late diagnosis are expected to be hospitalized, while 2.13% and 10.63%, respectively, are expected to require admission to ICU (Table 3). For non-classical FD, these proportions are 17.75% in early and 30.63% in late diagnosis, respectively, for hospitalization in general ward and 1.25% in early and 5.75% in late diagnosis for ICU.

Lastly, 17.00% of early and 29.00% of late diagnosed classical FD patients and 7.50% of early and 14.00% of late diagnosed non-classical FD patients are estimated to be on dialysis.

Table 3. Hospitalization of adult Fabry patients, for reasons related to the disease, in a 5-year time frame

	Classical Fabry		Non-classical Fabry	
	Early diagnosis	Late diagnosis	Early diagnosis	Late diagnosis
Proportion of patients expected to be hospitalized at least once within a 5-year timeframe	26.88%	43.13%	17.75%	30.63%
Mean number of hospitalizations in a 5-year period	1.94	4.00	1.50	5.31
Mean duration (in days) of hospitalization (per case)	4.06	6.13	3.25	7.31
Proportion of patients expected to need admission to ICU (among those hospitalized)	2.13%	10.63%	1.25%	5.75%
Mean number of days in ICU in a 5-year period (per patient, among those who will need admission to ICU)	10.33	10.80	7.50	9.67

The mean weighted annual cost of late diagnosis patients was estimated to be higher by 7,404.78€ in classical (156,572.64€ in early vs 163,997.42€ in late) and 3,538.74€ in non-classical FD (152,980.07€ in early vs 156,518.81€ in late) (Table 4). The main cost contributor in all patient groups is medication, accounting for more than 88% of the total cost, followed by dialysis.

Table 4. Mean weighted annual total cost per patient with Fabry disease

	Classical Fabry		Non-classical Fabry	
	Early diagnosis	Late diagnosis	Early diagnosis	Late diagnosis
Examinations	536.55€	671.92€	525.37€	660.61€
Physician visits	89.10€	200.70€	55.70€	78.30€
Medication	146,200.55€	145,662.75€	148,096.16€	147,093.49€
Hospitalization in ward	217.16€	726.10€	100.77€	615.56€
Hospitalization in ICU	131.06€	683.85€	55.84€	331.21€
Dialysis	9,398.13€	16,032.10€	4,146.23€	7,739.64€
Total	**156,572.64€**	**163,997.42€**	**152,980.07€**	**156,518.81€**

CONCLUSIONS

According to the study results, late diagnosis of Fabry disease results in higher use of healthcare resources, both for the classical and non-classical phenotypes, with the differences being greater in the classical type of the disease. International research has documented that early initiation of treatment in Fabry disease can affect positively the improvement and/or maintenance of long-term renal function[12].

Overall, the present study highlights the importance of early diagnosis in FD, since late diagnosis is shown to result in higher healthcare resource use and costs.

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