Healthcare resource utilization and cost of care for Gaucher patients in Iran

Majid Davari¹ · Azita Nabizadeh¹ · Maliheh Kadivar² · Akbar Abdollahi Asl¹ · Peymaneh Sarkheil³

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Abstract

Introduction Gaucher disease (GD) is an inherited recessive enzyme deficiency with a multisystem condition. The Iranian government covers the therapeutic expenditure of GD patients as it is not affordable for the patients. The aim of this study is to identify the main components of the cost of care in Gaucher patients (GPs) in Iran.

Methods The Gaucher patients were identified from the Iran Food and Drug Administration (IFDA) national registry database. The direct medical costs, including medication, diagnostic services, and physician visits were considered. The prices of therapeutic and diagnostic services were extracted from Iranian medical tariff book 2014–15. Iran Food and Drug Administration determined the cost of medications.

Results 164 Gaucher patients have been registered in Iran. A valid and reliable diagnostic tests are not used to identify the type of GD. The average health care cost per annum was 20,758 USD per patient, which is higher than 4 GDP per capita in Iran. Medication cost constitutes 95.2% of the total cost. The average cost of each GP was \$1,473,818 in his/her total life.

Conclusion GD is amongst the high-cost diseases and should be managed effectively. The application of oral medication for eligible GPs could improve allocative efficiency in GD management significantly. A sound, valid and reliable national clinical guideline could improve the efficiency of healthcare resources effectively. Selecting appropriate strategies for reducing the birth of a child with Gaucher, could support allocative efficiency of the limited resources effectively.

Keywords Health care · Gaucher disease · Cost · Resource utilization · Iran

Introduction

Gaucher disease (GD) is one of the inherited lysosomal storage disorders that results from the autosomal recessive deficiency of glucocerebrosidase. The deficiency of this enzyme halts the metabolism of macromolecules and leads to the accumulation of glucosylceramide which is responsible for necrotic complications [1, 2]. GD diagnosis is either by identification of the

mutation in the *GBA* or demonstrating a deficient enzyme activity in peripheral blood leucocytes or other nucleated cells [3, 4].

There are three types of GD (type 1 to 3). Type 1 GD, non-neuropathic form, includes more than 90% of cases with the prevalence of 1/20000–1/40000. Type 2 and type 3 GD are primarily neuropathic conditions with an estimated prevalence of 1/100000 for each [5–7]. The symptoms of GD include anemia, thrombocytopenia, bone involvement, hepatomegaly, Splenomegaly, lung, heart, kidney involvements, and growth disorders [8–13].

Enzyme replacement therapy (ERT) provides excess exogenous enzyme to hasten the breakdown of macromolecules and removes the stored substrate. The primary manifestations of types 1 and 3 GD are managed with ERT (Imiglucerase) but type 2 GD is not currently treatable [14–17].

Evidences for efficacy of ERT and SRT in GD are unusually sparse. Evaluating the process and the cost of management of Gaucher disease, which is one of the high-cost disease in Iran and in many other countries seems rational.

The aim of this study is to identify the main components of the cost of care in Gaucher patients (GPs) in Iran.

✉ Azita Nabizadeh
a-nabizadeh@razi.tums.ac.ir

¹ Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

² Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran

³ Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Method

The demographic characteristics of patients and the healthcare resource utilization are studied in this cost analysis study. The analysis was performed based on healthcare payer perspective. Therefore, only direct medical cost based on the Iranian medical tariff book 2014 were calculated.

Data source

The Gaucher patients were identified from Iran Food and Drug Administration (IFDA) national registry database. The healthcare service the patients received were taken from the department of special disease. Iran Food and Drug Administration's (IFDA) database was used for extracting the medications prescribed for GD. The 2017 exchange rate from the central bank of Iran was used to convert Iran Rials to US Dollar [1 USD = 34,117 Iranian Rials].

Cost analysis

The direct medical cost was calculated in three different categories. The medication cost is calculated based on the dosage and the price of Imiglucerase. The costs incurred during lab test and imaging were grouped under diagnostic costs. The cost of the physician visits was named as therapeutic cost. The total cost was the sum of the three categories.

Results

The electronic registry of GPs started from January 2015 in Iran. The review of IFDA database showed that 164 patients with GD were registered by September 2017; 85 female and 79 male. The summary characteristics of GPs are shown in Table 1.

Cerezyme® (Imiglucerase for injection), as the only medicine for GPs in Iran, is ordered, financed and distributed to the patients by IFDA. The MOH has defined a service package including a vast range of laboratory, diagnostics and in/out patient services for GPs in Iran. Since the treatment expenditures are very high, all therapeutic expenditures of the patients with GD are covered by the national healthcare system in Iran.

Until 2016, only Cerezyme® had been prescribed for all types of GPs in Iran. However, Abcertin® (Imiglucerase for injection) has entered into Iranian pharmaceutical market since 2016. This entrance led to a decline in Cerezyme® price sharply (49/5%). The summary of medications and their related costs are presented in Table 2.

The review of the process of patient registration showed that a valid and reliable diagnostic tests are not used to identify the type of GD. Thus all patients are registered in one category.

Table 1 Gaucher patient's characteristics

Characteristic	n (%)
Total patient	164
Median age	12
Male	79(48)
Female	85(52)
Current age distribution(yr.)	
Birth to 5	60(36.7)
5.1 to 10	33(20.2)
10.1 to 15	32(19.5)
15.1 to 20	10(6.1)
20.1 to 25	13(7.9)
25.1 to 30	4(2.4)
30.1 to 35	4(2.4)
35.1 to 40	3(1.8)
40.1 to 45	2(1.2)
45.1 to 50	2(1.2)
5 0.1 to 55	1(0.6)

In Iran, the ministry of health (MOH) provides the service for GD patients in special public clinics found throughout various cities in the country. Patients usually referred to the clinics in their vicinity for medications and health care services. The important point in disease management is that treatment protocols are not based on local, and even international, clinical guidelines.

Medication cost constitutes 95.2% (19,763 USD) of the total cost. Diagnostic services incurred an annual cost of 717 USD which was followed by therapeutic services at 278 USD per patient per year (Tables 3 and 4). The percentage share of each component of the cost is illustrated in Fig. 1.

Discussion

In the current study, the core components of the cost of GD treatment that need a considerable attention in Iran were identified. This may also have some lessons for other countries. The average direct medical cost of GD per patient was \$20,758 per annum, which is higher than 4 GDP per capita in Iran. The treatment of GPs starts

Table 2 List of medications and their related cost (USD)

Medicine	Number of vials	Annual cost (USD)	Annual cost per patient(USD)
Cerezyme	1791	1,259,900	a
Abcertin	7683	2,139,359	a
Total	9474	3,399,258	19,763

a. There was no detailed information on the number of Cerezyme and Abcertin use by each patient

Table 3 The type and frequency of physician visits and their annual costs

Physicians visit	Visit Frequency	cost (USD)	Percentage of total cost (%)
Hematologist	12	159	0.76
Orthopedic	1	13	0.06
Endocrinologist	4	53	0.25
Gastroenterologist	4	53	0.25
Total		278	1.34

mainly from child hood in Iran (Table 1) and their life expectancy are usually 4 years shorter than normal population [18]. Since the life expectancy in Iran is 75 years [19], each GP would be \$1,473,818 in his total life, which is terribly high. This may encourage health policy makers to think about methods for preventing the borne of such patients.

The review of the databases and patient profiles showed that a valid diagnostic test was not carried out to identify GPs and to classify different types of GDs effectively. Thus, while the treatment protocols for different types of the GD differ significantly, all patients were registered as a single group and were treated equally. This could be considered as one of the potential sources of

wasting resources. This is because, for example, despite the fact that type 2 GD is untreatable, all of GPs receive Imiglucerase, which is one of the high-cost medicines in Iran and perhaps in many other countries.

Furthermore, our data showed that a considerable number of patients had been wrongly diagnosed as a GP and then had taken wrong medications for years. For instance, one of the cases without GD had taken medications for 10 years at the cost of \$207,580. There are currently two tests available for detecting GP; enzymatic and genetic tests. The price of diagnostic tests varies from \$350 (for mutation detection) to \$1000 (for sequencing). However, considering the fact that the role of a diagnostic test for detecting right patients and their type of disease is crucial for efficient managing GD, the selection of an accurate and reliable test is of utmost importance.

Comparison between the cost drivers of MPS patients in Iran and England showed that while the medication costs are much closed to each other, the average annual costs of the MPS-I in the UK were almost 2 times higher than it in Iran. Nonetheless, it is important to note that comparing the net costs between the countries may cause misunderstanding and does not show the impact of the cost for each country. Therefore, to standardize the expenditures, it is better to express the costs based on GDP/Capita of the countries.

Table 4 The type and frequency of diagnostic services and their annual costs

Category	Item	Utilization frequency	Annual cost per capita(USD)	Percentage of total cost per capita (%)
Laboratory	Hemoglobin	2	1	0.004
	Platelet	2	1	0.007
	Chitotriosidase, PARC/CCL18	a	250	
	Beta-glucosidase	b	200	
	mutation analysis	b	350	
	Other	1	39	0.19
Imaging	Spleen volume	2	15	0.071
	Liver volume	2	18	0.088
	Spine(sagittal T1 weighted)	1	48	0.230
	Femora(coronal T1 and T2 weighted)	1	48	0.230
	Lateral spine;AP of entire femora	1	34	0.161
	DXA spine and hip	1	9	0.042
Cardiopulmonary	FVC	0.5	14	0.069
	Peak expiratory flow rate	0.5	5	0.022
	Echocardiogram	0.5	465	2.241
	Echocardiography	0.5	3	0.0152
	High-resolution chest computed tomography	0.5	16	0.077
Total			717	3.452

a. This test is not carried out in Iran

b. Enzymatic and genetic tests are done by the importing company for free

Fig. 1 The percentage share of Gaucher cost drivers

The results showed that medication costs had the largest share of healthcare resources at \$19,763 (95%) annually followed by diagnostic services at \$717 (3.5%). The smallest cost share of Gaucher services belongs to physician visits with an annual cost per capita of \$278 (1.5%). These figures show clearly that medication cost encompasses the vast majority of the resources used for GPs, and thus any program for improving the efficiency of GD management should target the medication therapy of GPs.

Two brand names of Imiglucerase are now available in the pharmaceutical market in Iran; Cerezyme and Abcertin. Since the price of these brands is different, the IFDA could consider cost-effectiveness analysis for selecting and supporting one of them for GPs. This could improve the efficiency of GD management.

In addition to the selection of brand-name medicines, it is also important to consider the method of treatment. Currently, the ERT and substrate reduction therapy (SRT) are the two approaches for the primary prevention of the manifestations of GD. ERT is done usually by an intravenous infusion of a solution containing the enzyme, whereas SRT is an oral administration that blocks the production of glucocerebroside. The duration of therapy, the convenient administration and the associated quality of life makes SRT preferable over ERT. Miglustat and Eliglustate are two form of SRT which are currently approved for treatment of GD [20].

A considerable number of patients have eligibility for taking oral medications (SRT) with acceptable efficacy. Bouwein showed that ERT and SRT have similar efficacy [21]. He stated that oral medication, SRT, is even

preferable because of ease of consumption and crossing blood-brain barrier. The difference in the prices of the two medications is also an important advantage of SRT comparing to ERT [21]. The price of SRT is almost one-third of ERT [21]. Nonetheless, patients with heart, liver or kidney failures, pregnant and breastfeeding women, young kids and the elderly above 65 have difficulty in taking oral medications [20]. However, since these patients comprise about 30% of the total GP population, the budget impact of shifting from ERT to SRT would be substantial. We, therefore, conclude that application of oral medication for maintenance therapy, after the therapeutic targets have been attained with ERT, in eligible GPs is one of the effective strategies for improving allocative efficiency in GD management. In the southern states of Brazil, the implementation of standard guideline saved 3 million USD with a compromise in the health status [22]. Such national clinical guideline should be based on an economic evaluation of the available alternatives and should encompass a whole process of the GD management; from diagnostic tests for approving the disease, medicine selection, and patients' eligibility for receiving specific services.

All cost estimates in our investigation were based on data of patients' profiles. Since the frequency of the use and the cost of diagnostic and therapeutic services were not in the patient's profile, these data were obtained from interview with clinicians. We suggest the future studies on this topic in addition to this method use questionnaires to obtain information on the last 12 months of patient

follow-up. One of the advantages of this mode of data collection is that patients and their caregivers are more likely to have reliable information on ancillary therapy, such as physical therapy, speech and the duration of use of medical devices.

Conclusion

GD is amongst the high-cost diseases and should be managed effectively. The annual cost of treatment for a patient is higher than 4 GDP per capita. The medication cost of GD had 95% of the share of healthcare resources. The application of oral medication for eligible GPs could improve allocative efficiency in GD management significantly. A sound, valid and reliable national clinical guideline could improve the efficiency of healthcare resources effectively. Since the average cost of a GP is terribly high, it worth to think about strategies for preventing the borne of such patients.

Limitation

Our study has three limitations. First, since the frequency of the use and the cost of diagnostic and therapeutic services were not recorded in the patient's profiles, these data were obtained from interview with clinicians. As a result, our cost information may not be completely accurate. However, as the costs of diagnostic and therapeutic services were only 5 Percent of the total cost of MPS-1 patients, we do not expect that this inaccuracy would affect our results significantly. Second, as all information about the patients, like weight and type of disease, was not recorded accurately in the patients' profiles, we could not perform a statistical analysis to reveal the association between characteristics of the patients and their health care costs. Finally, the absence of a single and comprehensive data source for all estimates was the third limitation of this study, which may decrease the accuracy of the results. Nonetheless, we tried to double check patients' data with both IFDA and the clinic to minimize this inaccuracy as much as it was possible.

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Compliance with ethical standards

Ethical approval The study was approved by the Faculty of pharmacy and Research Ethics Committee of the Tehran University of Medical Sciences.

Conflicts of interests The authors declare that they have no competing interests.

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