Health care resource utilization and cost of care for haemophilia A and B patients in Iran

Article *in* Transfusion and Apheresis Science · January 2016

DOI: 10.1016/j.transci.2016.01.025

CITATIONS
3

READS
78

7 authors, including:

Zahra Gharibnaseri
National Institute for Health Research,Tehran, Iran
15 PUBLICATIONS **56** CITATIONS
SEE PROFILE

Majid Davari
Tehran University of Medical Sciences
56 PUBLICATIONS **316** CITATIONS
SEE PROFILE

Majid Cheraghali
Baqiyatallah University of Medical Sciences
71 PUBLICATIONS **1,059** CITATIONS
SEE PROFILE

Roya Ravanbod
Tarbiat Modares University
29 PUBLICATIONS **97** CITATIONS
SEE PROFILE

ARTICLE IN PRESS

Transfusion and Apheresis Science ■■ (2016) ■■–■■

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Health care resource utilization and cost of care for haemophilia A and B patients in Iran

Zahra Gharibnaseri [a,b], Majid Davari [a,b,*], Abdolmajid Cheraghali [c], Peyman Eshghi [d], Roya Ravanbod [e], Ramin Espandar [f], Razieh Hantooshzadeh [g]

[a] Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[b] Pharmaceutical Management and Economics Research Center (PMERC), Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[c] Department of Pharmacology, University of Baqiyatallah Medical Sciences, Tehran, Iran
[d] Pediatric Congenital Hematologic Disorders Research Center, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[e] Department of Physical Therapy, Biomechanical Research Laboratory, Tarbiat Modares University, Tehran, Iran
[f] Department of Orthopedics, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[g] Ministry of Health and Medical Education, Tehran, Iran

ARTICLE INFO

Article history:
Received 1 October 2015
Received in revised form 27 December 2015
Accepted 13 January 2016

Keywords:
Health care
Haemophilia
Cost
Resource utilization
Iran

ABSTRACT

Background: Despite the fact that the total therapeutic expenditure of haemophilia is paid by the national health system in Iran, a limited number of research has been performed to evaluate the economic burden of haemophilia. It is even more important when considering the fact that "prophylaxis" has never been used as the main treatment protocol in haemophiliacs in the country, causing high arthropathy rates. The aim of this study is to evaluate the cost drivers in the treatment of haemophilia A and B patients in Iran.
Methods: The national registry database of Ministry of Health (MoH) was queried to identify total number of individuals characteristics diagnosed with Factor VIII and IX deficiency. The service package defined by the department for special diseases was used as the reference for the type and frequency of health care utilization in haemophiliacs in Iran. The direct medical costs including prescription, medical intervention, inpatient, outpatient and diagnostics services and arthroplasty were considered. The prices were extracted from Iranian medical tariff book 2014–15. Medication cost was obtained from the Iranian Food and Drug Organization.
Results: Among 8,337 patients registered with bleeding disorders, 3,948 and 848 were identified with haemophilia A and B respectively, of whom 856 (18%) patients had inhibitor at any time in the past. In the two groups, 2,328 (59%) and 452 (53%) patients suffered from severe, 686 (17%) and 186 (22%) from moderate and 902 (23%) and 185 (22%) from mild type of haemophilia. The average annual health care cost for every patient was USD 15,130, mostly allocated to medication USD 10,180 (67%), followed by therapeutic services USD 4,775 (32%) while diagnostic services stood third USD 177 (1%).
Conclusions: There is an urgent need for developing clinical practice guidelines for treatment protocols, procedures and supportive care in haemophilia management in Iran.

1. Background

Haemophilia is a group of bleeding disorders which lead to heavy and prolonged bleedings [1], inherited as an

* Corresponding author. Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran. Tel.: +982164121137; fax: +982166482606.
E-mail address: m-davari@tums.ac.ir (M. Davari).

http://dx.doi.org/10.1016/j.transci.2016.01.025
1473-0502/

X-linked recessive trait. The two most common types of haemophilia – A and B – are more likely to occur in male offspring.

The prevalence of haemophilia A (per 100,000 males) shows variation from 0.05 in Nigeria to 38.6 in Iceland [2]. Despite the fact that the accepted prevalence rate for rare diseases varies from one country to another ranging from 1/1,000 to 1/200,000 [3–5], haemophilia A and B in Iran with an estimated prevalence rate of 14 and 2.5 in 100,000 males, respectively, are listed in rare disease category [6].

There is a low desirability for clinical and experimental researches on rare diseases, thus requiring additional support from health authorities. This has resulted in rare diseases to be often called as "orphan diseases" in spite of the fact of distinct definitions [7]. Certain orphan diseases have been categorized as "special disease" in Iran and are currently governed by Management Center for Transplantation and Special Diseases (MCTSD) affiliated to Ministry of Health (MoH), deputy of curative affairs [8,9]. Currently, special diseases include multiple sclerosis, kidney transplantation, dialysis, thalassaemia and haemophilia [10].

Cost analysis studies have a considerable role in presenting reliable and valid data which could facilitate policymaking by clarifying total costs of illnesses as well as the identification of the main drivers of diagnostic and treatment costs [11]. These could help policymakers to focus more on issues where there is a need for cost containment policies, efficiency, and resource allocation [12,13]. This study aims to identify the main cost drivers of haemophilia A and B in Iran.

2. Method

In order to fulfil the purpose of this study, a prevalence approach was used and multiple data sources were aggregated for higher validity. In this study, both demographic and health resource utilization information were addressed. Health care costs were assessed from the payer perspective. The direct medical costs were taken into account, primarily based on the Iranian medical tariff book 2014.

2.1. Classifying costs

Health resources were categorized to three subgroups including medications, diagnostic and therapeutic services. The frequency of use as well as the cost of each item has been indicated for calculating total cost. Medication subgroup covered the number and cost of the factor concentrates (VII, VIII and IX). Diagnostic services included laboratory tests and imaging services. The components of therapeutic subgroup were physician visits, orthopaedic interventions and supportive services such as dentistry.

2.2. Data source

The national registry database of MoH was queried to identify individuals characteristics diagnosed with factor VIII and IX deficiency as well as the medical services provided for these patients and the frequency of health care utilization in each service which is based on standard practice. Patients were categorized based on the severity of disease and whether they had developed inhibitors or not. The medications used in both haemophilia A and B were extracted from Iranian Food and Drug Organization's database (FDO). The price year for the cost analysis was 2014 and prices were converted from Iranian Rials to USD based on the official exchange rate declared by central bank of Iran through the mentioned year [1 USD = 26,200 Iranian Rials] [14].

Table 1
Distribution of patients with different severity level based on percentage of normal factor activity in blood.

Severity level (% of normal factor activity in blood)	Number of haemophilia A (%)	Number of haemophilia B (%)
Severe (<1%)	2,328 (59)	452 (53)
Moderate (1–5%)	686 (17)	186 (22)
Mild (>5%)	902 (23)	185 (22)
Total	3,948	848

3. Result

More than 8,000 patients were registered with bleeding disorders. Among which 3,948 and 848 patients were identified with haemophilia A and B respectively. Other bleeding disorders sum up to 40% of the population. The percentage breakdown of overall haemophilia patients by severity can be seen in Table 1. The total number of haemophilia patients who had developed inhibitor at any time in the past was 856 (18%).

Clotting factors are ordered and financed by the MoH and provided by the FDO. The MoH is responsible for distributing the clotting factors among clinical settings throughout the country. The MoH has also defined a service package for haemophiliac patients in Iran which includes a vast range of laboratory, diagnostics and in/outpatient services.

The results show that the most utilized resource belongs to the medication category taking up an average annual amount of USD 10,180 per patient. Therapeutic services stand on the next position with an annual cost of USD 4,775 per patient and diagnostics take up USD 177 annually per capita. The percentage share in each group has been illustrated in Fig. 1.

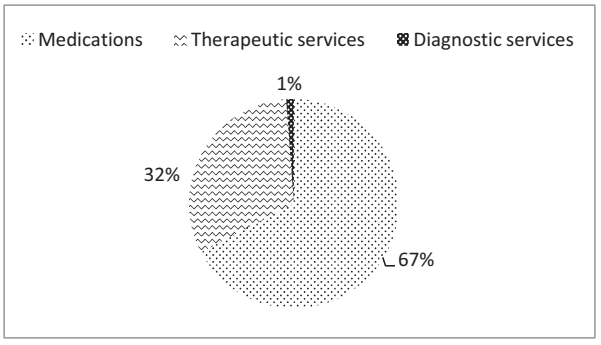

Fig. 1. Percentage share of haemophilia cost drivers.

Please cite this article in press as: Zahra Gharibnaseri, et al., Health care resource utilization and cost of care for haemophilia A and B patients in Iran, Transfusion and Apheresis Science (2016), doi: 10.1016/j.transci.2016.01.025

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

Medications	Number of vials consumed	Annual cost per capita (USD percentage from total cost)
Factor VIII (250 and 500 UI/vial)	410,721	5,141.90 (34.27)
Factor IX	52,127	787.35 (5.25)
Factor VII*	57,071	2,763.56 (18.42)
Activated prothrombin complex concentration	23,586	1,487.88 (9.92)
Total		10,180.69 (67.86)

* Based on FDO data, "antihaemophilic factor VII 1.2 mg vial" has been distributed through the market and not the recombinant form.

The cost drivers within each group are displayed in Tables 2, 3 and 4 (based on health care service package).

As evidenced by above figures, the top five cost drivers include:

1. Factor VIII concentrates (34.3%)
2. Bypassing agents (28.4%)
   i. Factor VII (18.4%)
   ii. APCC (activated prothrombin complex concentrate) (10%)
3. Total joint arthroplasty (23.1%),
4. FIX (5.3%)
5. Dentistry (1.54%)

Haemophilia patients are registered by MoH and covered by special disease insurance. These two sectors are the main payers of health care cost in haemophilia society; however, a small percentage is paid by charities.

MoH manages services through one or few clinics distributed through capital cities in Iran. Patients are referred to these clinics where they can receive their medications and other health care resources.

4. Discussion

The main objective of this study was to evaluate the main cost drivers of haemophilia A and B in Iran. Based on the data obtained from MoH and FDO's databases, the average annual cost of haemophilia care (per patient) was USD 15,130 in 2014.

The study found that the average annual health care cost was most often allocated to medication costs, USD 10,180 (67%), followed by therapeutic services, USD 4,775.37 (32%). Diagnostic services with an annual cost per capita of USD177 (1%) were ranked third. It is obvious that medication costs took up the largest portion of health care resources allocated to haemophilia treatments. This could emphasize the demand for reevaluation of policies and strategies regarding haemophilia to ensure the best available treatments as well as control potential medication wastage. It is also recommended to take into account the healthy life years gained alongside the costs to get a better view of the situation. This study can be considered as an update on the study of Karimi and colleagues, which was performed on 88 patients with haemophilia A selected from 170 patients in Fars haemophilia society in 2007. Karimi's study showed that the average annual cost of care for a patient with haemophilia A was equal to USD 8,510. This study also showed that medication costs made up 99% of total costs [15]. However, it is worth to mention that, due to different methodology, no head to head comparison can be made between the results of these two studies. Retrospective chart reviewing as used in Karimi's study can have

Table 3
The type and frequency of therapeutic services and their related annual costs.

Category	Items	Utilization frequency	Annual cost per capita (USD)	Percentage of total cost per capita (%)
Physician visits	Physical therapy	30	144.44	0.93
	Haematologist	4	14.44	0.09
	Orthopaedic	4	11.84	0.08
	Infectious disease specialist	1	2.96	0.02
	Psychiatrist	0.5	2.89	0.02
	Physiatrist	0.5	2.41	0.02
	Gastroenterologist	0.5	1.81	0.01
	Total		182.28	1.17
Orthopaedic interventions	Total joint arthroplasty (prosthesis and hospitalization)	0.30	3,611.11	23.14
	Synoviorthesis	0.10	96.30	0.62
	Rifampin administration	0.10	4.81	0.03
	Phosphorus radioisotopes administration	0.10	4.81	0.03
	Total		3,861.48	24.74
Supportive services	Dentistry	2.00	240.74	1.54
	Peginterferon Alfa-2a (Pegasys®) resistant HepC/Telaprevir, Boceprevir	0.01	166.67	1.07
	Clotting factor administration	15.00	150.22	0.96
	Platelet filters	0.5	120.37	0.77
	Hepatic C treatment	0.1	18.52	0.12
	Plasmapheresis	0.1	14.44	0.09
	Fibrin glue	0.1	9.63	0.06
	Cryoprecipitate transfusion	0.5	5.01	0.03
	Platelet transfusion	0.5	5.01	0.03
	Blood transfusion	0.1	1.00	0.01
	Total		731.61	4.69
Total			4775.37	30.6

Please cite this article in press as: Zahra Gharibnaseri, et al., Health care resource utilization and cost of care for haemophilia A and B patients in Iran, Transfusion and Apheresis Science (2016), doi: 10.1016/j.transci.2016.01.025

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

Category	Items	Annual utilization frequency rate	Annual cost per capita (USD)	Percentage of total cost per capita (%)
Laboratory tests	Quantitative PCR	1.0	87.90	0.56
	Qualitative PCR	1.0	27.02	0.17
	Interpreting PCR	1.0	8.40	0.05
	HbsAg	1.0	5.11	0.03
	Anti-HBs	1.0	5.11	0.03
	Anti-HBc	1.0	5.11	0.03
	Anti-HCV	1.0	5.11	0.03
	Anti-HIV	1.0	5.11	0.03
	Inhibitor	1.0	5.03	0.03
	CBC	4.0	2.24	0.01
	Factor level	1.0	1.74	0.01
	PTT	1.0	0.70	0.00
	Alkaline phosphatase	1.0	0.62	0.00
	ALT/SGPT	1.0	0.62	0.00
	Total		159.82	0.98
Prenatal tests			14.38	0.09
	Mutation analysis	0.05	16.08	0.10
	Fetus phenotypic analysis	0.05	9.08	0.06
	Fetal sex determination	0.05	2.89	0.02
	Total		28.05	0.18
Imaging	Radiology/MRI/CT scan	0.5	2.41	0.02
Total			176.61	1.09

certain benefits including taking advantage of practical data. While the possibility of selection bias and missing unrecorded data could be two important limitations of Karimi's study, using the national databank registry and numerating all haemophiliac patients' data can be seen as an advantage in our study. Taking a wide range of non-factor costs into account can also be viewed as another strength of our study design.

Inappropriate process in registering data was one of the major problems in delivering health care services for haemophilia patients. For example cost factors were not differentiated by geographical distribution which could have been used in assessing access to medical services throughout the country. It seems that developing electronic health records could improve health care delivery for these patients.

Regarding the top five cost drivers, it has been made visible that total joint arthroplasty cost counts for a substantial portion of total costs which should be taken into further consideration to examine whether it is being overused or not, compared to other haemophiliac societies. This high rate can be suggestive of improper use of other services such as physical therapy or clotting factor usage protocols (prophylaxis vs. on-demand) [16,17]. During data collection, the researchers met multiple cases which had been considered by their physicians as potential candidates for total joint replacement. However, these patients had been able to overcome joint damages by attending regular physiotherapy.

It should be kept in mind that the MoH spends a significant share of the gross domestic product (GDP) as compensations to haemophilia patients accidentally infected with HIV and/or HCV through contaminated blood products [18–20]. Therefore, there is a serious need for assessing the cost-effectiveness of different proposals in order to find the most efficient methods for taking care of haemophilia patients.

Nevertheless, our study has some limitations. It should be noted that not every cost data has been extracted from patients' usage. Instead an overall case count has been performed. This limitation restrains further analysis of the situation such as considering non-medical costs which could be helpful to analyze the results from different perspectives, as well as estimating the difference of costs between patients subgroups – based on severity or inhibitors.

In summary, the total average cost per haemophilia patient was USD 15,000 in Iran 2014. Factor concentrates make up 67% of the total expenditure, pointing out an urgent need for reevaluating treatment protocols and procedures. It is also recommended that the MoH develop clinical practice guidelines with a particular focus on supportive care in order to improve resource allocation as well as patient care in haemophilia society. In addition, developing electronic health records is another means for improving health care delivery through patients' registration.

Funding Sources

No funding has been received for this study.

Acknowledgements

The authors would like to thank the staffs from the FDO who have helped us collect related data from the organization database.

References

[1] Ingram G. The history of haemophilia. J Clin Pathol 1976;29(6):469–79.
[2] Stonebraker JS, Bolton-Maggs PH, Michael Soucie J, Walker I, Brooker M. A study of variations in the reported haemophilia A prevalence around the world. Haemophilia 2010;16(1):20–32.
[3] European Organisation for Rare Diseases (EURORDIS). Rare diseases: understanding this public health priority. 2005.

Please cite this article in press as: Zahra Gharibnaseri, et al., Health care resource utilization and cost of care for haemophilia A and B patients in Iran, Transfusion and Apheresis Science (2016), doi: 10.1016/j.transci.2016.01.025

[4] de Vrueh R, Baekelandt ERF, de Haan JMH. Background Paper 6.19 Rare Diseases, 2013, 9–10.
[5] La Regina M, Nucera G, Diaco M, Procopio A, Gasbarrini G, Notarnicola C, et al. Familial Mediterranean fever is no longer a rare disease in Italy. Eur J Hum Genet 2003;11(1):50–6.
[6] Mehdizadeh M, Kardoost M, Zamani G, Baghaeepour MR, Sadeghian K, Pourhoseingholi MA. Occurrence of haemophilia in Iran. Haemophilia 2009;15(1):348–51.
[7] Stolk P, Willemen MJ, Leufkens HG. Rare essentials: drugs for rare diseases as essential medicines. Bull World Health Organ 2006;84:745–51.
[8] Aghighi M, Heidary Rouchi A, Zamyadi M, Mahdavi-Mazdeh M, Rajolani H, Ahrabi S, et al. Dialysis in Iran. Iran J Kidney Dis 2008;2(1):11–5.
[9] Eshghi P, Mahdavi-Mazdeh M, Karimi M, Aghighi M. Haemophilia in the developing countries: the Iranian experience. Arch Med Sci 2010;6(1):83–9.
[10] Iran Health Insurance Organization. Special diseases, <http://th.ihio.gov.ir/Portal/Home/Default.aspx?CategoryID=508a3651-81f7-4ae0-95dd-a0b89a82c2fb#>; 1996 [accessed 07.07.15].
[11] McGinnis M, Olsen L, Goodby AW. Clinical data as the basic staple of health learning: creating and protecting a public good: workshop summary. National Academies Press; 2010.
[12] Simoens S. Health economic assessment: a methodological primer. Int J Environ Res Public Health 2009;6(12):2950–66.
[13] Rezvanfar MA, Kebriaeezadeh A, Moein M, Nikfar S, Gharibnaseri Z, Abdollahi-Asl A. Cost analysis of childhood asthma in Iran: a cost evaluation based on referral center data for asthma and allergies. J Res Pharm Pract 2013;2(4):162–8.
[14] Central Bank of Iran. Foreign exchange rates, <http://www.cbi.ir/ExRates/rates_en.aspx>; 2015 [accessed 28.07.15].
[15] Karimi M, Rahmani S, Ardeshiri R, RahmanAttar A, Pasalar M. Cost of care in Iranian hemophilic patients. Iran Red Crescent Med J 2007;9(3):154–7.
[16] Ravanbod V, Torkaman G, Baghaee Pour MR. The effect of steady-state bicycle exercise on the activity level of F-VIII in patients with mild and moderate haemophilia A. Physiol Pharmacol 2003;7(2):149–56.
[17] Eshghi P, Khanali L, Abed-Saeedi J, Farahani H, Abdolah Gorgi F, Habib-Panah B, et al. The effect of on demand and prophylactic therapeutic methods on quality of life among hemophilic children. Iran J Blood Cancer 2013;5(2):57–60.
[18] Cheraghali AM, Eshghi P. Cost assessment of implementation of immune tolerance induction in Iran. Value in Health Reg Issues 2012;1(1):54–8.
[19] Cheraghali AM. Availability of blood components and plasma derived medicines in Iran. Transfus Apher Sci 2007;37(1):3–7.
[20] Cheraghali A, Eshghi P, Abolghasemi H. Social consequences of infected haemophilia cases in the Islamic Republic of Iran. East Mediterr Health J 2011;17(6):552–6.

Please cite this article in press as: Zahra Gharibnaseri, et al., Health care resource utilization and cost of care for haemophilia A and B patients in Iran, Transfusion and Apheresis Science (2016), doi: 10.1016/j.transci.2016.01.025