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Hemophilia in Jordan: An Economic Burden Dilemma of Rare Disease

Ibrahim Alabbadi[1]*, Abdel Karim Al-Oweidi[2], Amirah Daher[2], Ayah BaniHani[3], Abdallah Awidi[2]

[1] Faculty of Pharmacy, The University of Jordan, Amman, Jordan.
[2] Faculty of Medicine, The University of Jordan, Amman, Jordan.
[3] International Society for PharmacoEconomics and Outcomes Research (ISPOR)-Jordan Chapter-General Secretary.

ABSTRACT

Jordan is an upper-middle-income country with high expenditures on pharmaceuticals. The development of new rare disease (e.g. hemophilia) therapies has encountered significant obstacles with respect to economic the cost of the disease and treatment. The aim of this overview was to estimate current annual spending on hemophilia treatment in Jordan and estimate the financial impact of adapting a new medication (Emicizumab) recently used for treating hemophilia patients in Jordan. **Methods:** based on the literature review, direct medical costs were quantified, required items' costs from the actual practice in Jordan were elicited from an expert panel, and a focus group meeting with the same was conducted one month later to determine the current estimated number of hemophilia Patients in Jordan, identify current treatment on demand quantities and their prices. All related medical costs were also identified (e.g. bleeding, the estimated number of hospital days, and/or Intensive Care Unit per bleeding episodes). Estimation of the annual consumption of current on-demand treatment quantities and cost were calculated and compared with scenarios of adding the new therapy (Emicizumab). **Results**: showed that the financial impact of using Emicizumab S.C. instead of Recombinant Factor VIIa I.V. on the budget of the Jordanian government will be 425,747 JOD ($601,338) annually. **Conclusions**: the economic advantages of a new hemophilia treatment might be very substantial for patients.

Keywords: Hemophilia, Jordan, Economic burden, 2019.

INTRODUCTION

Jordan is an upper middle-income country located in the western Asia part of the Middle East in an area of political instability, with a population of 10.554 million (4.966 million females=47.1% and 5.588 million males=52.9%) and an average annual live birth of 197,280 (2019). The Gross Domestic Product (GDP) amounted to be 31.435 billion JODs ($ US$44.4 billion), and Jordan GDP Per Capita reached 2,990 JOD ($4,222) in 2019. Jordan has a small economy with limited natural resources[(1)]. The total expenditure on health in Jordan amounted to be 2.566 billion JOD ($ 3.6 billion), and the per capita expenditure was 255 JOD ($ 361) in 2017 accounted for 8.9 percent of the GDP which is considered high for an upper middle-income country.

Expenditures on pharmaceuticals were high and reached 593 million JOD (US $ 838 million) in 2017 accounting for 2.05 % of the GDP and 23.13 % of the total health expenditures. Public expenditures on curative care accounted for 73.7 % while expenditures on primary care accounted for 19.6 % in 2017[(2)].

The health sector in Jordan is subdivided into multiple health providers including public, private, international and charity sectors. Two major public programs that finance and deliver healthcare in Jordan are the Ministry

Corresponding author: Ibrahim Alabbadi
i.abbadi@ju.edu.jo
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of Health (MoH) and Royal Medical Services (RMS). Other smaller public programs include universities-based programs, namely the University of Jordan, and Jordan University of Science and Technology. In addition, several non-governmental organizations and donors own and operate facilities such as the United Nations Relief Works Agency (UNRWA), which provides care mostly to Palestinian refugees and the United Nations High Commissioner for Refugees (UNHCR), which with the support of MoH, provides medical care to Syrian refugees inside camps. Those outside the camps pay out of pocket at the same rate as uninsured Jordanians, which are highly subsidized. Yet, this might account for a considerable burden on them [(3)].

Many rare diseases cause chronic or progressive physical deterioration, disability, or premature death. Usually they start in childhood, creating a huge burden on parents and caregivers. Mostly, rare diseases are thought to be genetic in nature. Although there is increasing demand for therapies for rare diseases, drug companies were not interested in adopting them to develop treatments, and as such became known as orphan diseases. The development of new rare disease therapies has encountered significant obstacles with respect to understanding the incidence and prevalence (epidemiology), patient reported burden of disease, economic cost of the disease and treatment, health technology assessment, and patient access [(4)].

There is no universal agreed on definition of what constitutes a rare" disease. A recent survey of definitions from more than 1,100 organizations worldwide found significant variations, ranging from prevalence thresholds of five to 76 cases per 100,000 population [(5)]. Individual rare diseases affect less than 5 to 7 individuals in 10,000[(6)].Hemophilia is a rare congenital blood disorder that primarily affects males and causes potentially fatal internal bleeding in the brain and the gastrointestinal tract as well as frequent bleeding in joints and soft tissues [(7)] [(8)]. The two forms of the condition are Hemophilia A (Factor VIII deficiency) and Hemophilia B (Factor IX deficiency); Hemophilia A is approximately four times more common than Hemophilia B [(9)].

For individuals with hemophilia, acute bleeding episodes can occur spontaneously and after trauma or surgery. Repeated bleeding in joints may eventually lead to debilitating and painful chronic hemophilic arthropathy, limiting mobility [(8)]. The clinical severity of hemophilia A and B is best correlated with the factors VIII, IX activity level. Patients with severe and milder clinical hemophilia who have factor VIII, IX activity levels below 30-40% of normal and they are at risk for excessive bleeding when undergoing a major surgical procedure. Female carriers of hemophilia A can also be at risk of excessive surgical bleeding. About 10% of female carriers have factor VIII activity below 30%.

Hemophilia is characterized by frequent hemarthrosis, leading to acute/chronic joint pain. Patients with chronic pain, particularly those with both acute/chronic pain, frequently experience psychological issues, functional disability and reduced Health Related Quality of Life (HRQoL) [(10)].

Severe hemophilia patients experience chronic hemophilic joint disease, characterized by chronic inflammation and progressive joint deformity, in one or more major joints by the age of 30. Furthermore, the latter experience significant acute pain during bleed events and chronic pain due to arthropathy, leading to disability and impaired quality of life in more than half of cases [(9)].

The overall weighted prevalence of hemophilia was 3.6 per 100,000 and the prevalence among males was 5.5 per 100,000. The prevalence based on community studies was 2.9 per 100,000 in mainland China, lower than the prevalence worldwide [(11)]. The prevalence of hemophilia in India, Russia, Taiwan and Turkey was 2.27 per 100 000, 5.12 per 100 000, 3.61 per 100 000 and 4.93 per 100 000 respectively [(12)].

Global incidence of hemophilia A is approximately 1

in every 5000 male births; hemophilia B is approximately six times rarer than hemophilia A (13, 14).

Individuals with severe hemophilia (have factor levels less than 1% of that expected in a healthy person) representing approximately one-third of the hemophilia population in Europe [(9)]. Hemophilia affects approximately 20,000 individuals in the United States (more than 80% are of A type) [(8)]. Without prophylactic treatment, patients with severe disease have an average of 20 to 30 episodes per year of spontaneous bleeding or excessive bleeding after minor trauma [(15)].

Joint damage remains a major complication associated with hemophilia and as one of the most debilitating symptoms for persons with severe hemophilia. The presence of chronic synovitis has a significant negative impact on HRQoL for adults with severe hemophilia. Approximately 80% of bleeding events are intra-articular in nature, two-thirds of which are reported in the knees, elbows, and ankles (9, 10, 15, 16). In the absence of effective treatment, either with bypass therapies or through 'training' the body to accept factor concentrate ('immune tolerance induction' or ITI), the presence of an inhibitor can significantly increase bleed frequency and accelerate joint damage [(16)].

Hemophilic arthropathy (HA) is a major complication in patients with hemophilia (PWH), however, studies of age-specific prevalence and severity of HA are very limited in Asian countries. Although severe arthropathy of the six major joints was rare in PWH aged <30 years, it increased rapidly in PWH after 30 years [(17)].

Hemophilia A and B are X-linked diseases that predominantly affect male patients. Patients can develop coagulation factor inhibitors, which exponentially increases the treatment cost. The factor replacements were derived from plasma (48.4%), recombinant concentrates (22.9%), both sources (14.6%), or fresh frozen plasma (14.1%). Factor VIII inhibitors were observed in (29.3%). Most patients who developed inhibitors had severe hemophilia (90.9%), and inhibitors were also common among patients who received recombinant product 32.6%[(18)].

Central venous access devices (CVADs) facilitate repeated or urgent treatments for pediatric hemophilia patients but are associated with complications. Pediatric hemophilia patients with CVADs experienced greater infection rates, healthcare utilization and higher hospitalization costs compared with non-CVAD patients[(14)].

Longer length of Stay (LOS) in hospitals and higher total hospital costs for the CVAD cases were also found[(14)].

TREATMENT OF HEMOPHILIA:

Administering the missing coagulation factors by replacement therapy is the treatment option. In the 1960s, the use of plasma-derived factor concentrates made these disorders manageable and made the first significant impact on life expectancy. After that, recombinant factor concentrates have been introduced that guarantee a high degree of safety. A further important innovation in hemophilia treatment in the last 20 years has been the increasing use of prophylactic therapy rather than on-demand replacement therapy [(19)].

The major risk associated with the use of clotting factor replacement therapy is the development of inhibitors due to production of neutralizing antibodies that inhibit factor uptake leading to poor control of bleeds associated with more mortality and decrease in HRQoL. The formation of inhibitors is multifactorial being associated with both genetic and environmental factors [(20)]; treating patients with inhibitor is a lengthy process with high costly regimens of ITI with large risk uncertain success [(9)].

Inhibitors can be low or high titer based on the maximum titers developed by a patient after repeated exposure to FVIII. A person with high-titer inhibitors is someone with a titer >5 Bethesda units (BU), whereas a low-titer person is someone with <5 BU. The Scientific and Standardization Committee of the International

Thrombosis and Hemostasis Society has recommended that inhibitor titers equal to or greater than 5 BU be considered as high titer. These antibodies, especially in cases of high titer, can modify the pharmacokinetics of replacement therapy, reducing the effectiveness of treatment. In addition, even after increasing the frequency and dose of FVIII, in some patients it is not possible to control bleeding episodes, making necessary the use of alternative therapies, immune tolerance induction (ITI) as an option to eradicate inhibitors, or bypassing agents, either activated prothrombin complex concentrate (aPCC) or activated recombinant factor VII (rFVIIa) [(21)].

Prevention, early diagnosis and treatment of target joints should be an important consideration for clinicians and patients when managing hemophilia [(16)]. Prevention of bleeding through prophylaxis, rather than the on-demand treatment of bleeding events when they occur, is considered the gold standard of treatment for severe hemophilia by trying to maintain factor activity above a trough of 1% baseline factor activity level [(22)].

Economic Aspects of Hemophilia

Target joints are a common complication of severe hemophilia as mentioned above, while factor replacement therapy constitutes the majority of costs in hemophilia, prevention and management of target joints should be an important consideration for managing hemophilia patients[(13)].

Main concerns for hemophilia healthcare are shifting from the pure clinical aspects to the economic considerations of long-term replacement therapy, equity considerations are relevant as well[(23)]. Hemophilia is a condition whose treatment requires a large amount of financial resources associated with the cost of hemostatic factors and care of hemorrhage, the latter being lower in patients on prophylaxis relative to on-demand [(24)].

Cost-of-illness (COI) studies quantify the economic burden of a disease, including direct healthcare and non-healthcare costs and productivity losses. COI studies are useful to inform policymakers about the magnitude of a disease. To correctly support the decision-making process, it is necessary to identify the cost-drivers through COI studies with robust design and standardized methodology. There is a lack of COI studies in the field of rare diseases.

The major cost driver accounting for more than 70-95% of the direct medical costs for treating hemophilia are due to clotting factor usage [(8)] i.e. costs of factor replacement therapy account for the vast majority of the cost burden in severe hemophilia. However, the importance of the indirect impact of hemophilia on the patient and family should not be overlooked [(9)]. On the other hand, it is estimated that 99.8% of the calculated cost corresponds to coagulation factors and bypassing agents. This evidence will allow countries to continue generating policies to offer access to technologies, under the assumption of system sustainability [(21)].

The large observed variability in hemophilia prevalence prevents robust estimation of burden of disease. Establishing prevalence at birth is a milestone toward assessing years of life lost, years of life with disability, and burden of disease [(25)].

Only a small share of new drugs is truly innovative; 85% to 90% of all new health technologies have little or no advantage over existing therapeutic alternatives. Although higher price levels are usually associated with higher investments in R&D, there is still a need to improve access to new technologies and to guarantee that they provide more health benefits than they displace in consequence of their costs[(26)]. Health economic evaluations can be used to inform decision makers in this regard to achieve economic efficiency by maximizing value for money.

OBJECTIVES

The aim of this overview was to:

- Estimate current annual spending on Hemophilia treatment in Jordan.

- Estimate the financial impact of adapting a new medication (Emicizumab) recently used for treating hemophilia patients in Jordan

METHODOLOGY

In order to estimate the economic burden of hemophilia in Jordan, at first literature review showed that the direct medical costs that have to be quantified-if available or if applicable- are of the following items (27, 28):

– **Clotting factor and bypassing agent**, **Healthcare service** (Comprehensive care, Clinician visit including Hematologist, Rheumatologist, Orthopedic surgeon, Infectious disease specialist, Physical therapy, Social worker and Psychology), **Hospitalization, Emergency department**, **Outpatient procedure.**

– **Lab tests** (laboratory, radiological and diagnostic)**,** MRI Ultrasound, Other tests (e.g., bone scan, immunology test) **and other hemophilia-related medication(s)**

The second step was to identify the required items' costs from the actual practice in Jordan. The latter requires expert opinion elicitation in which one to one interview with six consultants, who usually treat hemophilia patients in Jordanian big hospitals (MoH Albashir and Prince Hamza Hospitals, Royal Medical Services Hospitals, Jordan University Hospital and King Abdallah University Hospital) was conducted [29]. Furthermore, a focus group meeting with the same panel of experts was conducted one month later. The latter ended up with a consensus of the expert panel identifying the following required data to be collected:

1. Determine current estimated number of Hemophilia Patients in Jordan (classified in 3 age groups), estimated number of severe patients (average), estimated number of patients with inhibitors, estimated number of patients with inhibitors low titer and high titer and estimated number of patients treated on demand.
2. Identify current treatment on demand and its price obtained from the Joint Procurement Directorate (JPD) (the governmental body responsible for buying medications for the treatment of rare diseases patients in Jordan).
3. Determine current annual estimated number of bleeding episodes, the estimated number of hospital days per bleeding episodes per year (as average), estimated number of inpatient ward days per bleeding episodes and estimated number of Intensive Care Unit (ICU) days per bleeding episode.
4. Estimate total on demand ideal current need as practiced; annual consumption of Recombinant Factor VIIa I.V. (Novoseven® 2 mg) (2019) for estimated age groups with severe hemophilia patients with inhibitors high titer only (as the major cost driver)
5. Calculate total estimated on demand real current annual quantities consumed of Recombinant Factor VIIa I.V. (Novoseven® 2 mg) (2019 tender) for estimated age groups with severe hemophilia patients with inhibitors high titer
6. Estimate real practice scenarios for annual quantities consumed of Emicizumab = Hemlibra® S.C. for the same estimated age groups with severe hemophilia patients with inhibitors high titer
7. Estimate real practice scenarios of annual cost of Emicizumab = Hemlibra® S.C. for estimated age groups with severe hemophilia patients with inhibitors high titer (based on data on item number 6 above) in JODs

RESULTS

Table 1 shows the total current cases of Hemophilia in Jordan including number of hemophilia patients, severe cases number with and without inhibitors and consequently estimated number of annual bleeding episodes, hospital length of stay (days), specific length of stay (days) within inpatient wards and ICU per bleeding episode.

Table 1: Hemophilia in Jordan: current situational analysis [(29)]

Category (annual)	**%**	**JUH**	**MoH**	**KAUH**	**DRMS**	**Total**
Estimated number of Hemophilia Patients	100%	280		50	70	**400**
Estimated number of Hem B	≈ 10%	20		10	10	**40**
Estimated number of Hem A	≈ 90%	260		40	60	**360**
Estimated number of severe patients (average) [A]	60%	140		32	44	**216**
Estimated number of patients with inhibitors (9% of all)	15%	23		4	6	**33**
Estimated number of patients with inhibitors low titer	≈ (1/3)	7-9		1-3	2- 4	**11**
Estimated number of patients with inhibitors high titer	≈ (2/3)	18		2	3	**23**
Estimated number of patients treated on demand	(in case of symptoms or elective surgery) **23**					
Estimated age groups: Severe patients with inhibitors high titer	**23**					
< 5 years	**5** (average weight = 12 kg)					
5 - 15 years	**8** (average weight = 25 kg)					
> 15 years	**10** (average weight = 50 kg)					
Estimated number of patients on prophylaxis	**NONE**					
Current treatment on demand	Novoseven® 2 mg (Recombinant Factor VIIa) **I.V.**					
Estimated number of bleeds annually	12.5 (average of 10-15)					
Estimated number of hospital days/bleed/year (average of 2-3 days)	2.5 X 12.5 = 31.25 **total** hospital days/year due to S.E.					
Estimated number of **inpatient ward** days/bleed	28.125 (90%) **inpatient ward** days/year due to S.E					
Estimated number of **ICU** days / bleed (10%)	3.125 (10% of 31.25)					

Total annual estimated on demand ideal (current **need as practiced)** cost of using of Recombinant Factor VIIa I.V. (Novoseven® 2 mg) i.e., annual consumption if all patients treated (acquisition cost of the drug only for 2019 tender prices obtained from JPD) is 7,939,036 JOD ($11,213,328) for different estimated age groups with severe hemophilia (patients with inhibitors high titer) are shown in Table 2.

Table 2: **Estimated on demand ideal current need as practiced; annual consumption of Novoseven® 2 mg (Recombinant Factor VIIa I.V.) (2019) for estimated age groups with severe hemophilia patients with inhibitors high titer (Tender prices from JPD)**

Estimated age groups: Severe with inhibitors high titer	Number of patients	Average weight (Kg)	Average each dose 90 µg / Kg / Patient in (µg)	Average of each dose/ Patient (vial)	Average of each dose/ Patient i.e. TID/ Bleed (vial)	Average dose/ Patient/Bleed (total of 5) (vial)	Annual consumption/ Patient (aver. of 12.5 bleeds) (vial)	Annual consumption/ number of patients (vial)	Unit tender price (JOD) / vial	Total annual cost (JOD) for total number of patients
< 5 years	5	12	1080	≈ 1	≈ 3	≈ 15	≈ 188	≈ 940	1,281.730	1,204,826
5 – 15 years	8	25	2250	≈ 1	≈ 3	≈ 15	≈ 188	≈ 1504	1,281.730	1,927,722
> 15 years	10	50	4500	≈ 2	≈ 6	≈ 30	≈ 375	≈ 3750	1,281.730	4,806,488
Total annual current cost of using **Novoseven® 2 mg** (acquisition cost of the drug only)										**7,939,036**

However, not all patients were treated in Jordan, and not all treated patients took the required full doses of Recombinant Factor VIIa I.V. (Novoseven® 2 mg). Table 3 shows the real current total annual estimated cost of using Recombinant Factor VIIa I.V. (Novoseven® 2 mg) on demand i.e. real purchased quantities accounting for 2,498,589 JOD ($3,529,080): the medication cost of 2,307,114 JOD ($3,258,635) and inpatient & ICU length of stay cost of 191,475 JOD ($270,445) for different age groups with severe hemophilia (patients with inhibitors high titer).As the new medication, Emicizumab (Hemlibra®) S.C. is available in four dose strengths (30 mg, 60mg, 105mg, 150mg), the possible scenarios of using any of these doses as per the recommended dose of 1.5mg/kg/week or 3mg/kg/2weeks after excluding doses when not applicable or resulted in higher prices or if the full dose was not needed. Table 4 shows the estimated real practice of two scenarios of the annual quantities consumed of Emicizumab (Hemlibra®) S.C:

A. Scenario A: 676 of 30 mg vials and 520 of 60 mg vials

B. Scenario B: 130 of 30 mg vials and 208 of 60 mg vials and 260 of 150 mg.

Table 3: **Estimated on-demand real current annual consumption of Novoseven® 2 mg (Recombinant Factor VIIa I.V.) (2019 tender) for estimated age groups with severe hemophilia patients with inhibitors high titer**

	MoH	**JUH**	**KAUH**	**RMS**	**Total quantity**	**JPD Unit price**	**Total JOD**
JPD tender 2019	**1,010**					**1281.730**	**1,294,547**
Real purchases (+ direct purchase)	**200 Converted to JUH**	**880**	**770**	**800**	-	-	-
For inhibitors ONLY		**700**	**700**	**400**	**1800**	**1281.730**	**2,307,114**
			Unit cost*	**Cost/patient**	**Number of patients**	**Cost/all patients**	
Estimated number of **inpatient ward** days/bleed		28.125	**254**	**7143.75**	**23**	**164306.25**	
Estimated number of **ICU** days / bleed		**3.125**	**378**	**1181.25**	**23**	**27168.75**	
						191475	**2,498,589**

*(37)

In order to calculate the estimated annual cost of using either scenario A or B of Emicizumab (Hemlibra®) S.C; quantities mentioned in Table 4 above are used considering available pharmacy prices i.e. whole sales prices (not tender price of JPD because Emicizumab is not yet a national formulary item) obtained from Jordan Food and Drug Administration (JFDA) website [30]. Results showed that scenario a costs 3,621,469 JOD ($5,115,069) while scenario B costs 3,895,822 JOD ($5,502,573).

As regulated in Jordan; any new medication listed in the Jordan National Drug formulary (so it can be purchased by JPD for public hospitals) lose 5 % of its price immediately. In addition, any new medication participated alone in the JPD tender must not bid more than 15% less than its pharmacy price [31].

Table 4: Estimated real practice scenarios annual consumption of Emicizumab = Hemlibra® S.C. for estimated age groups with severe hemophilia patients with inhibitors high titer (Prices from JFDA website)

Estimated age groups: Severe with inhibitors high titer	**Average weight (Kg)**	**Real practice scenarios Either - OR** **NA=Not applicable or higher price, NN=not needed**									
		(A): 1.5mg/kg/week					**(B):** 3mg/kg/2weeks				
		Dose	**30mg**	**60mg**	**105mg**	**150mg**	**Dose**	**30mg**	**60mg**	**105mg**	**150mg**
< 5 years	12	18mg	≈ 1	NA	NA	NA	36 mg	≈ 1	NA	NA	NA
5 – 15 years	25	37.5 mg	≈ 1	NA	NA	NA	75 mg	NA	≈ 1	NA	NA
> 15 years	50	75mg	NA	≈ 1	NA	NA	150 mg	NA	NA	NA	≈ 1
No. of vials/patient/year							**No. of vials/patient/year**				
< 5 years			**52**	NA	NA	NA		**26**	NA	NA	NA
5 – 15 years			**52**	NA	NA	NA		NA	**26**	NA	NA
> 15 years			NA	**52**	NA	NA		NA	NA	NA	**26**
No. of vials/all patients/year							**No. of vials/all patients/year**				
No. of patients			**30mg**	**60mg**	**NN**	**NN**		**30mg**	**60mg**	**NN**	**150mg**
< 5 years	5		**260**	NA				**130**	NA		NA
5 – 15 years	8		**416**	NA				NA	**208**		NA
> 15 years	10		NA	**520**				NA	NA		**260**

Accordingly, scenario A costs 2,924,336 JOD ($4,130,418) while scenario B costs 3,145,876 JOD ($4,443,327) (Table 5).

Table 5: Estimated real practice scenarios annual cost of Emicizumab = Hemlibra® S.C. for estimated age groups with severe hemophilia patients with inhibitors high titer (based on Table 4 quantities) in JODs

	Scenario A			Scenario B		
Emicizumab dosage form	30 mg	60mg	150mg	30 mg	60mg	150mg
Total vials/year	676	520	0	130	208	260
Hospital unit price	2110.41	4220.83	10552.06	2110.41	4220.83	10552.06
Total cost for each	1,426,637	2,194,832	0	274,353	877,933	2,743,536
Total cost			**3,621,469**	**Total cost**		**3,895,822**
Cost less by 5% (formulary inclusion)	2004.89	4009.79	10024.46	2004.89	4009.79	10024.46
Total cost for each	1,355,305.3	2,085,090	0	260,635.64	834,036	2,606,358.82
Total cost			**3,440,395.32**	**Total cost**		**3,701,030.46**
Maximum allowed tender prices (cost less by 15% of the new cost)	1704.155	3408.32	8520.79	1704.155	3408.32	8520.79
	1,152,010	1,772,327	0	221,540	708,931	2,215,405
Total cost			**2,924,336**	**Total cost**		**3,145,876**

The lower the cost the better the scenario, as scenario A was selected; annual cost of using Emicizumab (Hemlibra®) S.C is 2,924,336 JOD ($4,130,418) for the same number of hemophilia patients treated with current medication; Recombinant Factor VIIa I.V. (Novoseven® 2 mg) that costs 2,498,589 JOD ($3,529,080). The latter means that the financial impact of using Emicizumab S.C. instead of Recombinant Factor VIIa I.V. on the budget of the Jordanian government will be 425,747 JOD ($601,338) annually (without any discount from the whole sale price or what is called pharmacy price).

DISCUSSION

Use of so-called "orphan" drugs to treat rare diseases are poised to represent more than one-fifth of pharmaceutical expenditures by 2022. Worldwide sales of orphan drugs first reached $100 billion in 2015 but are expected to be more than double by 2022 and will represent more than one-fifth of all prescription drug sales by that time. High acquisition cost is the main factor driving the trend in spending on orphan drugs.

Effort to understand whether rare diseases require special considerations on their part and how to adapt traditional methods of health technology assessment and economic evaluation to accommodate these situations is badly needed [32]. Accordingly, patient access to medicines for rare diseases varies across countries even among high income countries such as in Europe [33].

It was estimated that average per-patient annual direct cost of severe hemophilia in some European countries (France, Italy, Spain, Germany and UK) range from €129,365 in the UK up to €313,068 in Germany, approximately 34 to 87 times higher than the mean per-capita health expenditure in these countries [9].

Public populations would support giving priority to a smaller but more severely ill group of patients over a larger group when prioritizing the needs of the few is life-saving, extends life enough to give hope of future improvement, and relieves otherwise intractable symptoms, especially pain (34-35).

There is simply no magic solution to the conundrum of assessing the evidence on clinical effectiveness, economic impact, and value of drugs to treat rare diseases [(5)]. Although it has been ascertained that on demand treatment can the long-term complications, but it does not prevent them, whereas prophylaxis in patients with severe hemophilia from early childhood prevents such complications. Moreover, even if prophylaxis requires one or two infusions per week, it is associated with improved quality of life [(19)]. Given that as hemophilia begins at birth, the illness has an impact on the lives of caregivers [(36)].

CONCLUSION

Although the efficacy and safety profiles of novel treatments (e.g., Emicizumab) warrant long-term clinical studies, the economic advantages of these new compounds might be very substantial both in patients with inhibitors and in those at risk of developing inhibitors [(36)].

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الهيموفيليا في الأردن: معضلة العبء الاقتصادي للأمراض النادرة

إبراهيم العبادي[1*]، عبدالكريم العويدي[2]، أميرة ضاهر[2]، آية بني هاني[3]، عبد الله العويدي[2]

[1] كلية الصيدلة، الجامعة الأردنية، عمان، الأردن.

[2] كلية الطب، الجامعة الأردنية، عمان، الأردن.

[3] الجمعية العالمية للاقتصاد الصيدلاني (ISPOR)، فرع الأردن.

ملخص

الأردن بلد من الشريحة العليا من البلدان متوسطة الدخل ذات الإنفاق العالي على المستحضرات الصيدلانية. واجه تطوير علاجات جديدة للأمراض النادرة (مثل الهيموفيليا) عقبات كبيرة فيما يتعلق بالتكلفة الاقتصادية للمرض والعلاج. هدفت هذه الدراسة لتقدير الإنفاق السنوي الحالي على علاج الهيموفيليا في الأردن والأثر المالي لإستخدام دواء جديد (Emicizumab) استخدم مؤخرا لعلاج مرضى الهيموفيليا في الأردن. **الأساليب:** بناء على مراجعة الأدبيات، تم تحديد التكاليف الطبية المباشرة، وتم استخلاص عناصر التكاليف المطلوبة من الممارسة الفعلية في الأردن من لجنة خبراء، وتم عقد اجتماع لهذه اللجنة مع مجموعة من المختصين بعد شهر واحد من أجل تقدير عدد مرضى الإيموفيليا في الأردن، والتعرف على كميات العلاج حسب الطلب وأسعارها لهؤلاء المرضى. كما تم تحديد جميع التكاليف الطبية ذات الصلة (مثل النزيف، والعدد المقدر لأيام المكوث في المستشفى و/ أو وحدة العناية المركزة لكل حالة نزيف). تم حساب تقدير الاستهلاك السنوي لكميات وتكلفة العلاج الحالي عند الطلب ومقارنته بسيناريوهات إضافة العلاج الجديد (Emicizumab). أظهرت **النتائج** أن الأثر المالي لاستخدام Emicizumab S.C. بدلا من Recombinant Factor VIIa IV على ميزانية الحكومة الأردنية سيكون 425,747 دينار أردني (601,338 دولار) سنويا. **الإستنتاج:** قد تكون المزايا الاقتصادية لعلاج الهيموفيليا الجديد كبيرة جدا للمرضى.

الكلمات الدالة: الهيموفيليا، الأردن، العبء الأقتصادي، 2019.

المؤلف المراسل:

i.abbadi@ju.edu.jo

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