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Original Article

Economic Burden of Multiple Sclerosis Drugs in Iran during 2011-2019

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Abstract

Background: Due to the invariably progressive nature of multiple sclerosis (MS) and the high economic burden of chronic diseases, this study was performed to estimate the economic burden of MS medications in Iran.

Methods: The present research is a descriptive study performed using comprehensive national data of Iran's Health Insurance Organization (IHIO). The timeframe for study was 2011-2019. In order to calculate the economic burden of MS medications, the cost of illness (COI) method based on the prevalence approach was used. In this study, economic burden estimation was performed according to available data on medication costs. Data mining was also used to perform different stages of study.

Results: The number of patients receiving MS medications covered by IHIO has increased from 19,367 in 2011 to 50,642 in 2019. The economic burden of MS medications of patients covered by the IHIO increased from $81 million to $96 million between 2011 and 2019, respectively. Among the 9 medications studied, Interferon accounted for a very high share of costs in all years. The cost per patient receiving medication has also increased from $7,000 in 2011 to $18,000 in 2019.

Conclusion: Calculations of the economic burden of MS medications in Iran showed an upward trend during the 9 years of the study, which due to the increasing number of patients in Iran, the arrival of new medications and also the increase in prices.

Keywords: Multiple sclerosis (MS); Economic burden; Medication costs; Iran

Introduction

Multiple sclerosis (MS) is a chronic myelin-degrading disease of the central nervous system that leads to pathological inflammation, nerve tissue destruction, and makes some changes (1).

The onset and progression of this disease occurs in four stages: relapsing-remitting, secondary progressive, primary progressive, progressive-relapsing. Most patients in the advanced stage of relapsing-remitting MS will also experience the secondary progressive stage. About 50% of patients experience a progression of disability within 10 years of the first attack, and about 90% of patients will experience a progressive form of the disease after 25 years (2).

According to the National MS Association of the United States, about 2.5 million people worldwide have MS, and 200 patients are added each week (3-5). The prevalence of this disease is increasing over time (6). The total number of patients with MS in Iran, like other Middle Eastern and developed countries, has increased (7). The prevalence of this disease was reported to be 33.5-51.9 per 100,000 people (8-10).

The unpredictable course of MS and its variable symptoms along with cognitive impairment, psychiatric disorders, pain and fatigue can lead to negative consequences on daily life, work, family and social disorders (11). Exacerbation of this disease leads to hospitalization of patients and consequently to the disruption of work, social life and family. Even in the early stages of the disease, patients' self-esteem may decline and their individual and professional activities may be limited (12). The economic aspect of this disease also has a wide range of negative consequences in the field of welfare and patients' quality of life (13), all of which lead to high levels of instability, lack of productivity and impose high costs burden on patients, health system and society (5, 7, 14).

In recent years, significant scientific advances have been made in the treatment of MS. But the focus of current therapies is more on reducing attacks and managing them. Various treatment strategies such as medication therapy, complementary therapy and rehabilitation have been used for this disease however the first solution is medication interventions. Over the years, new medications have been approved for the treatment of MS, which, in addition to the effectiveness of these medications, has led to an increase in direct medication costs (15). In addition to the cost of medications, patients with MS use health care services significantly more than other patients. A patient who has recently being diagnosed with the disease will visit the physician an average of eight times a year, which is almost three times more than the average person, which imposes high costs on patients and the health system (16).

Given the limited financial resources in countries and the increasing costs of MS, cost of illness analysis is a useful tool to assess the exchange between the additional costs and potential benefits of disease treatment. These studies describe and estimate the economic burden of a particular disease on a community and present an opportunity to policy makers to prompt actions from an economic perspective and use them for training and awareness in planning and financing (17).

In general, the economic burden of diseases is one of the essential indicators in health systems and their intermittent study is very necessary and important in identifying the economic dimensions of the current situation and monitoring changes and also predicting future trends to use the best strategies. On the same ground, medication costs in the treatment of MS account for a major share of the economic burden (more than 55%) (18, 19). Considering the significant economic burden of MS and the increase in the number of patients in recent years in Iran, as well as the high share of prescribed for MS, it is necessary to examine the use and share of different medications. On the other hand, various changes have been made in the medications used in this disease and new costly medications have been added to treatment protocols over the years, the present study done for the first time in Iran aimed to:

a. Calculate the MS medication costs in Iran over the years from 2011 to 2019.
b. Investigating the trend of changes in the cost of MS medications
c. Investigating out-of-pocket (OOP) and changes of insurance

share of total MS medication costs

Methods

The present study is a retrospective descriptive study conducted on comprehensive national data from 2011 to 2019. This study aimed to investigate the economic burden of MS medications in Iran. For this sake, the cost of illness (COI) method was used based on the prevalence method and the bottom-up method.

The present research has incorporated the data of prescriptions of MS patients of Iran's Health Insurance Organization (IHIO) and the data of medication statistics of the Iran's Food and Drug Administration (FDA).

Due to the lack of access to sufficient data for diagnostic as well as rehabilitation services for all years, in this study only medication cost calculations have been performed in 9-years. IHIO prescription data was used for the research described in this article. IHIO is the largest basic health insurance in Iran, which also covers about 50% of all MS patients in the country. This ratio has been almost the same in different years. For this reason, in the present study, a database of prescription records of this organization has been used, which, considering the high coverage of patients, can provide a relatively accurate estimates of the MS patients in the country.

There was no specific and comprehensive database for MS patients in Iran, the prescriptions of MS patients were analyzed based on other information related to MS medications, radiology information and tests, and finally the prescription records of these patients were extracted and separated. Therefore, at first, the medications usually prescribed for MS patients were extracted based on treatment protocols, instructions and a panel of specialists, and then all prescription records of these medications were extracted from IHIO data. In order to complete the necessary evidences, the FDA's annual pharmaceutical statistics were also used to correct deficiencies in some data. Pharmaceutical statistics is a collection of medication sales information that is prepared by the FDA by summarizing the information submitted by companies and provided to applicants. This statistics has been one of the important sources for pharmaceutical planning in Iran since 1984.

After extracting the specific MS patients' prescriptions, the cost share of each medication and the number of patients receiving medications were determined. Thus, first, the medications received by MS patients, the number of patients receiving medications, the total medications costs, the share of IHIO and the amount of OOP payments of each medication were calculated separately. Then, the costs growth trend, the growth rate of medication costs per capita, the cost burden of expensive medications and their changes in study years were investigated.

For value conversion, the exchange rate of Rial to US Dollar in 2011-2019 was considered to be 10962, 12260, 21253, 26509, 29580, 31386, 34214, 41950 and 42000 Rials, respectively. These values are based on the average official exchange rate in the study years. Accordingly, the effect of annual domestic inflation has been largely removed from the calculations.

All the collected data was refined in Excel 2016 software and entered into Stata 14 software for analysis.

Ethical approval

Present study was approved by ethical committee of the National Institute for Medical Research Development (NIMAD), Tehran, Iran, approval ID: IR.NIMAD.REC.1399.249; approval date: 18.11.2020

Results

Number of Patients and MS Medications Received

Figure 1 shows changes in the number of MS patients covered by the IHIO in study years. This statistic is based on the IHIO prescription data of the patients. Accordingly, the number of patients covered by the IHIO has increased from 13,372 in 2011 to 34,964 in 2019.

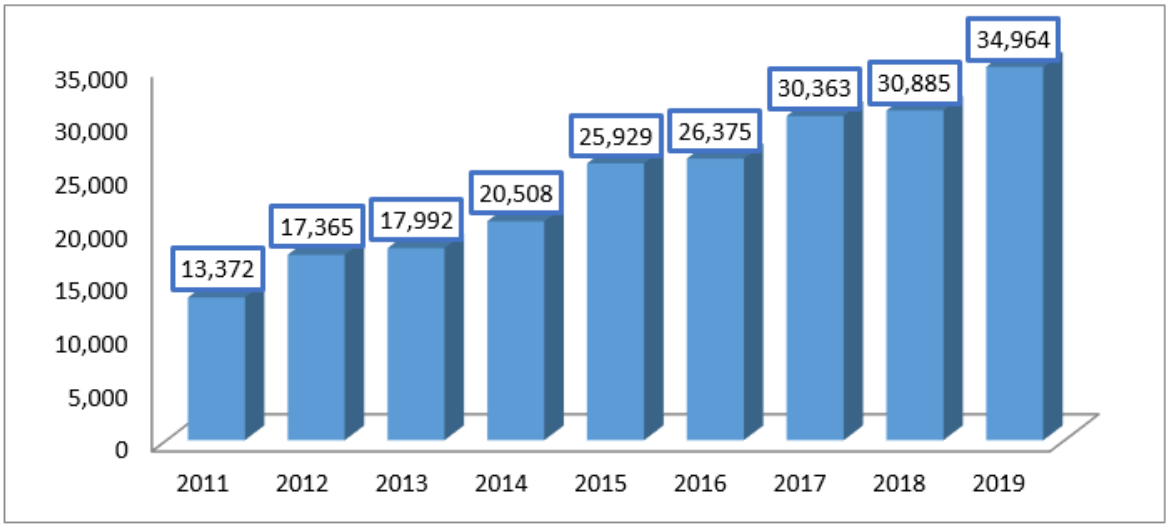

Fig. 1: Number of MS patients covered by the IHIO (2011-2019)

Tables 1-2 and Fig. 2 show the changes in the number of MS medications received between 2011 and 2019 by different MS drugs. Accordingly, the number of MS medications received has increased from 19,367 in 2011 to 50,642 in 2019. Interferon has been the leading drug of MS in Iran in all 9 years, but it has been accompanied by fluctuations over the years. Cyclophosphamide, Mitoxantrone, and Natalizumab were medications with lowest prescription for MS patients. Examining the trend of changes, all medications have an oscillating trend of the number of MS medications received. Significant increase in the number of Interferon received from 2013 to 2014 and 2018 to 2019 is considerable.

Table 1: Changes in the number of MS medications received (2011-2019)

Medication Name	***Generic***	***Year***								
		2011	2012	2013	2014	2015	2016	2017	2018	2019
INTERFERON		12547	14394	12370	23165	22601	16112	14206	16071	21019
GLATIRAMER ACETATE	ACE-	697	2240	3387	1236	1867	1673	1824	2121	1434
DIMETHYL FUMARATE		0	0	0	0	3736	4605	4991	6285	8779
FINGOLIMOD		0	0	652	2534	3085	6439	10071	7352	7333
TERIFLUNOMIDE		0	0	0	0	0	486	490	516	1553
RITUXIMAB		5483	7527	8045	3878	5243	7522	10538	10667	9506
NATALIZUMAB		0	0	596	235	258	683	1120	1082	724
CYCLOPHOSPHAMIDE		232	460	513	481	425	459	565	431	192
MITOXANTRONE		408	529	496	461	339	221	172	209	102
Total		19367	25150	26059	31992	37554	38200	43977	44733	50642

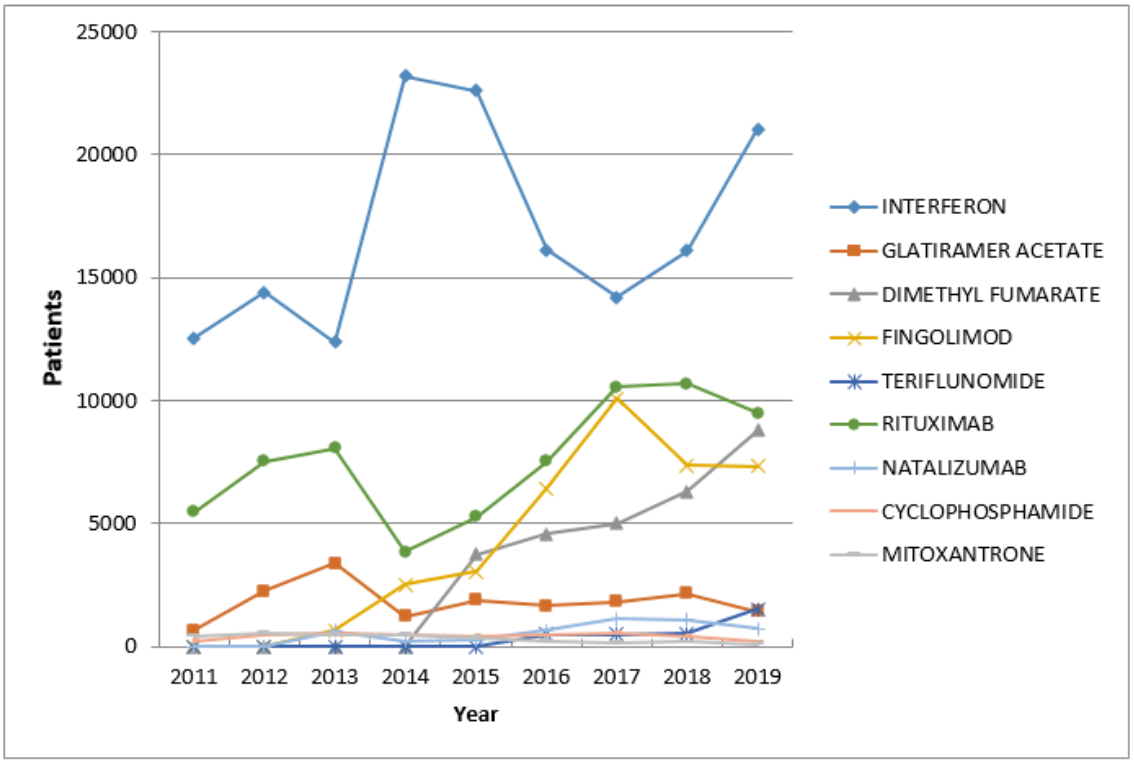

Fig. 2: Changes in the number of patients received MS medications (2011-2019)

Economic burden of MS medications in Iran

In this section, calculations of MS medications economic burden in Iran from 2011 to 2019 are presented. The total cost of patients' medications (based on IHIO prescriptions records), the IHIO cost share, the amount of OOP payments, the total cost per patient and OOP payments per patient were extracted and calculated.

The total cost of MS medications has increased from $81,240,000 in 2011 to $96,149,000 in 2019, part of this increment could be attributed to the rising medication prices and a significant portion due to an increase in patients and increased receiving medications interventions. Of these, $70,792,000 in 2011 and $83,407,000 in 2019 were paid by the IHIO, respectively, and the rest was paid patients' OOP. Patients' OOP payments had increased from $10,447,000 in 2011 to $12,741,000 in 2019, based on the different rate of medication franchises.

Table 2: Details of the total medication costs of MS patients in Iran (2011-2019) (USD)

Medication Generice Name	*Variable*	*Year*								
		2011	2012	2013	2014	2015	2016	2017	2018	2019
INTERFERON	Total Medication Costs (1000$)	77456.0	68587.0	46547.2	43903.7	35174.2	30544.7	25629.9	29536.6	56280.2
	Out of Pocket(1000$)	10069.3	8916.3	6051.1	5707.5	4572.6	3970.8	3331.9	3839.8	7316.4

GLATIRAMER ACE-TATE	IHI Cost share (1000$)	67386.7	59670.7	40496.0	38196.2	30601.6	26573.9	22298.0	25696.8	48963.8
	Total Med-ication Costs (1000$)	96.1	209.6	199.3	161.4	2759.3	3269.5	3613.0	4801.6	4251.2
	Out of Pock-et(1000$)	9.6	21.0	19.9	16.1	275.9	327.0	361.3	480.2	425.1
DIMETHYL FUMARATE	IHI Cost share (1000$)	86.5	188.6	179.3	145.2	2483.4	2942.6	3251.7	4321.4	3826.1
	Total Med-ication Costs (1000$)	0.0	0.0	0.0	0.0	598.5	1167.5	2034.9	3386.6	7546.5
	Out of Pock-et(1000$)	0.0	0.0	0.0	0.0	179.5	350.3	610.5	1016.0	2263.9
FINGOLIMOD	IHI Cost share (1000$)	0.0	0.0	0.0	0.0	418.9	817.3	1424.5	2370.6	5282.5
	Total Med-ication Costs (1000$)	0.0	0.0	3315.8	2767.6	2506.1	6210.0	9226.8	4793.1	7585.4
	Out of Pock-et(1000$)	0.0	0.0	165.8	138.4	125.3	310.5	461.3	239.7	379.3
TERIFLUNOMIDE	IHI Cost share (1000$)	0.0	0.0	3150.0	2629.2	2380.8	5899.5	8765.4	4553.5	7206.2
	Total Med-ication Costs (1000$)	0.0	0.0	0.0	0.0	0.0	438.4	402.6	419.0	1540.8
	Out of Pock-et(1000$)	0.0	0.0	0.0	0.0	0.0	131.5	120.8	125.7	462.2
RITUXIMAB	IHI Cost share (1000$)	0.0	0.0	0.0	0.0	0.0	306.9	281.8	293.3	1078.6
	Total Med-ication Costs (1000$)	3644.3	3833.4	3257.2	3294.0	4484.5	8811.2	12288.7	11742.0	13470.8
	Out of Pock-et(1000$)	364.4	383.3	325.7	329.4	448.4	881.1	1228.9	1174.2	1347.1
NATALIZUMAB	IHI Cost share (1000$)	3279.8	3450.1	2931.5	2964.6	4036.0	7930.1	11059.8	10567.8	12123.7
	Total Med-ication Costs	0.0	0.0	1855.0	1588.7	1442.1	4665.8	7313.6	6326.1	5459.1

	(1000$)									
	Out of Pock-et(1000$)	0.0	0.0	185.5	158.9	144.2	466.6	731.4	632.6	545.9
	IHI Cost share (1000$)	0.0	0.0	1669.5	1429.8	1297.9	4199.3	6582.2	5693.5	4913.1
CYCLOPHOSPHA-MIDE	Total Med-ication Costs (1000$)	12.0	20.0	13.9	13.4	10.9	16.3	20.6	11.5	6.4
	Out of Pock-et(1000$)	1.2	2.0	1.4	1.3	1.1	1.6	2.1	1.1	0.6
	IHI Cost share (1000$)	10.8	18.0	12.5	12.1	9.8	14.7	18.5	10.3	5.7
MITOXANTRONE	Total Med-ication Costs (1000$)	31.8	35.6	25.2	26.5	17.0	13.5	10.1	14.9	8.9
	Out of Pock-et(1000$)	3.2	3.6	2.5	2.6	1.7	1.3	1.0	1.5	0.9
	IHI Cost share (1000$)	28.6	32.0	22.7	23.8	15.3	12.1	9.1	13.4	8.0
Total	Total Med-ication Costs (1000$)	81240.1	72685.6	55213.6	51755.3	46992.4	55137.0	60540.0	61031.4	96149.2
	Out of Pock-et(1000$)	10447.7	9326.2	6752.0	6354.3	5748.9	6440.7	6849.1	7510.7	12741.5
	IHI Cost share (1000$)	70792.4	63359.4	48461.6	45401.0	41243.6	48696.3	53691.0	53520.7	83407.7

Figure 3 shows the trend of changes in the total cost of MS medications (by IHIO share and OOP payment) between 2011 and 2019. The trend of changes in total costs, the share of IHIO and OOP payments during the study years were similar and has been decreasing until 2015 and increasing from 2015 to 2019. These various prescription spending show different trends.

Figure 4 shows the trend of changes in the MS medication costs in Iran between 2011 and 2019. On the same ground, interferon has the highest share in terms of medication costs in all years. Cyclophosphamide has the lowest share in all years except 2017. In return, Rituximab had a regular increase over the study years. However, other medications did not show a regular trend in this regard. Moreover, significant increase in the Interferon costs from 2018 to 2019 is considerable.

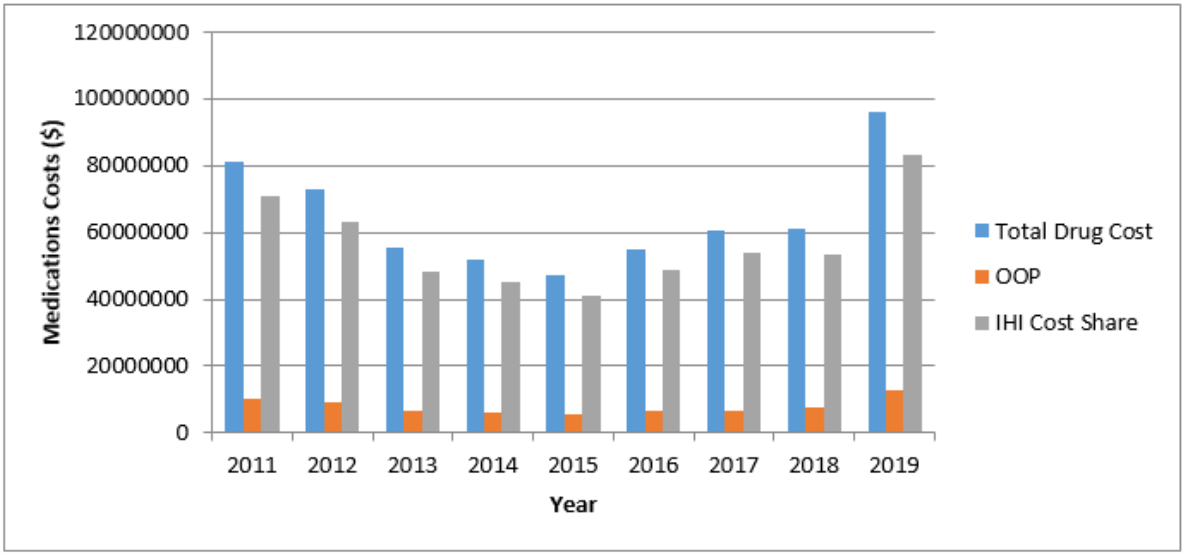

Fig. 3: The trend of changes in the economic burden of all MS medications in Iran (by IHIO and OOP share) between 2011 and 2019

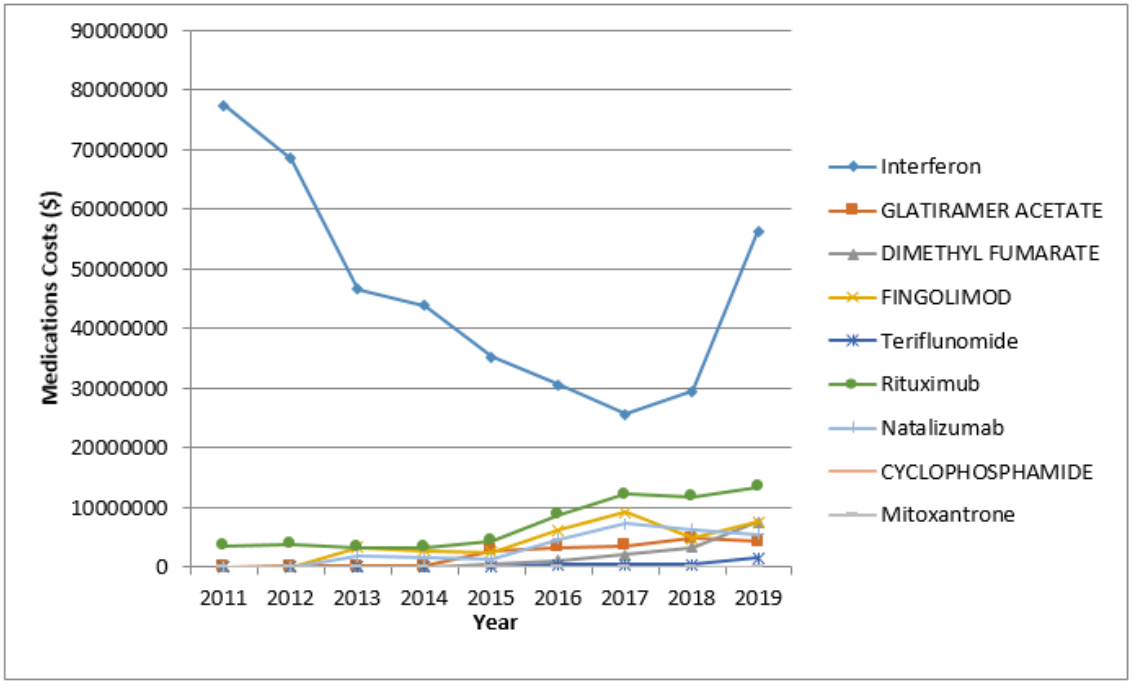

Fig. 4: The trend of changes in the economic burden of all MS medications in Iran (2011-2019)

Table 3 shows the details of the calculations related to the total cost and OOP payments per patient receiving MS medications in Iran between 2011 and 2019. Accordingly, the total cost per patient has increased from $17,605 in 2011 to $17,605 in 2019. OOP payments per patient has also increased from $895 in 2011 to $2,159 in 2019.

Table 3: Total cost and OOP payment per patient receiving MS medications in Iran (2011-2019)

Medication Generice Name	*Variable*	*2011*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019*
INTERFERON	Costs Per Patient ($)	6173.4	4764.9	3762.8	1895.2	1556.3	1895.8	1804.2	1837.8	2677.6
	OOP per Patients ($)	802.5	619.4	489.2	246.4	202.3	246.4	234.5	238.9	348.1
GLATIRAMER ACETATE	Costs Per Patient ($)	137.9	93.6	58.8	130.5	1477.6	1953.8	1980.4	2263.6	2964.6
	OOP per Patients ($)	13.8	9.4	5.9	13.1	147.8	195.4	198.0	226.4	296.5
DIMETHYL FUMARATE	Costs Per Patient ($)	0.0	0.0	0.0	0.0	160.2	253.5	407.7	538.8	859.6
	OOP per Patients ($)	0.0	0.0	0.0	0.0	48.1	76.1	122.3	161.7	257.9
FINGOLIMOD	Costs Per Patient ($)	0.0	0.0	5082.0	1092.2	812.5	964.5	916.1	651.9	1034.4
	OOP per Patients ($)	0.0	0.0	254.1	54.6	40.6	48.2	45.8	32.6	51.7
TERIFLUNOMIDE	Costs Per Patient ($)	664.7	0.0	0.0	0.0	0.0	901.7	822.2	812.6	992.1
	OOP per Patients ($)	66.5	0.0	0.0	0.0	0.0	270.5	246.7	243.8	297.6
RITUXIMAB	Costs Per Patient ($)	664.7	509.3	404.9	849.3	855.3	1171.4	1166.1	1100.8	1417.1
	OOP per Patients ($)	66.5	50.9	40.5	84.9	85.5	117.1	116.6	110.1	141.7
NATALIZUMAB	Costs Per Patient ($)	0.0	43.4	3109.9	6760.6	5591.4	6831.8	6532.9	5849.2	7540.1
	OOP per Patients ($)	0.0	4.3	311.0	676.1	559.1	683.2	653.3	584.9	754.0
CYCLOPHOSPHAMIDE	Costs Per Patient ($)	51.6	67.2	27.0	27.8	25.6	35.6	36.4	26.6	33.2
	OOP per Patients ($)	5.2	6.7	2.7	2.8	2.6	3.6	3.6	2.7	3.3
MITOXANTRONE	Costs Per Patient ($)	78.0	67.2	50.9	57.4	49.9	61.2	58.6	71.3	87.1
	OOP per Patients ($)	7.8	6.7	5.1	5.7	5.0	6.1	5.9	7.1	8.7
TOTAL	Costs Per Patient ($)	7105.5	5478.4	12496.5	10813.2	10528.9	14069.3	13724.7	13152.7	17605.9
	OOP per Patients ($)	895.8	690.8	1108.4	1083.6	1091.0	1646.6	1626.8	1608.1	2159.5

Figure 5 also shows the trend of changes in the total cost and OOP payments of MS medications per recipient patient over the study years. Accordingly, the total cost and OOP payments per patients for MS patients have significantly increased and fluctuated in the three years of 2012, 2015 and 2018.

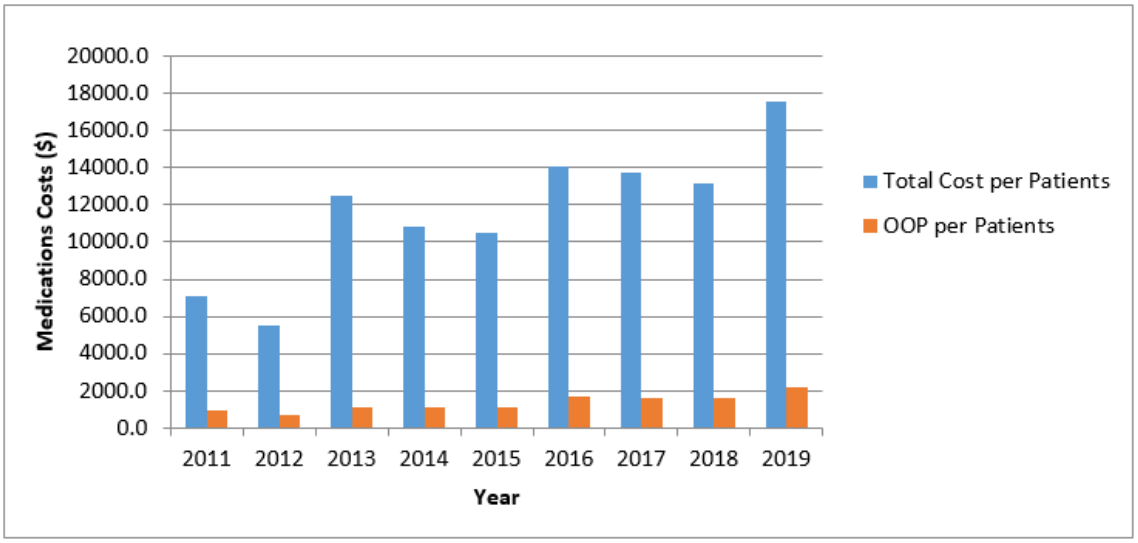

Fig. 5: Changes in the total cost and OOP payments for MS medications per patient (2011-2019)

Figure 6 also depicts the total cost trend per patient in Iran by MS medications, separately. In 2011 and 2012, the largest share of this value was allocated to Interferon. In 2013, Fingolimod, and in 2014-2019 Natalizumab had the largest share in terms of total cost per patient. The trend of changes in most medications generally indicates an increase over the years.

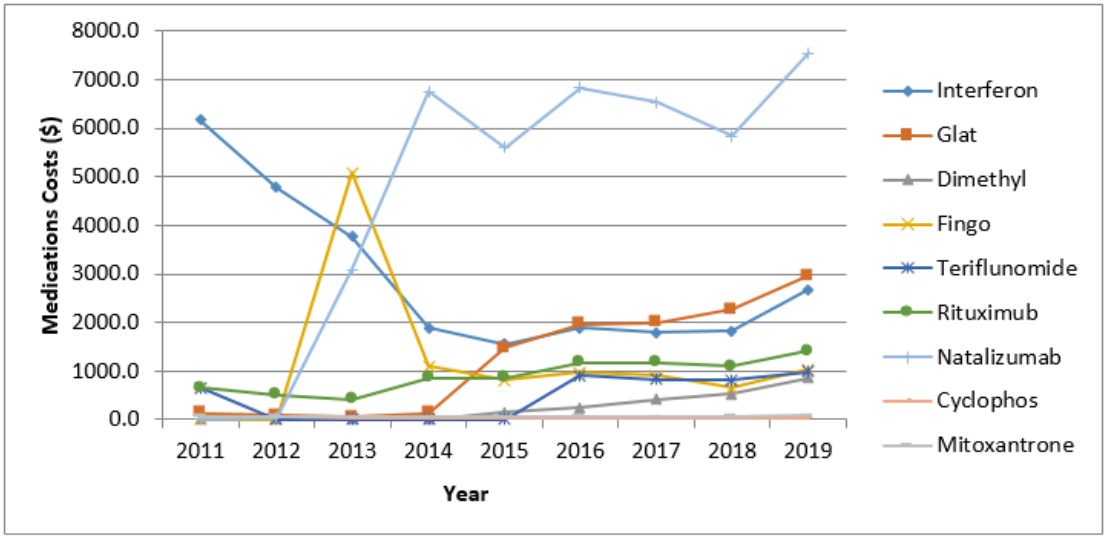

Fig. 6: Share of total medication costsper patient of different MS medications (2011-2019)

Figure 7 shows the share of different medications from the total economic burden of MS medications in 2011 and 2019. As shown in Fig. 7, Interferon owns the largest share; however, has decreased from 95% in 2011 to 58% in 2019, but still accounts for more than half of MS medication costs. In contrast, Mitoxantrone and Cyclophosphamide made up less than one percent of medication costs.

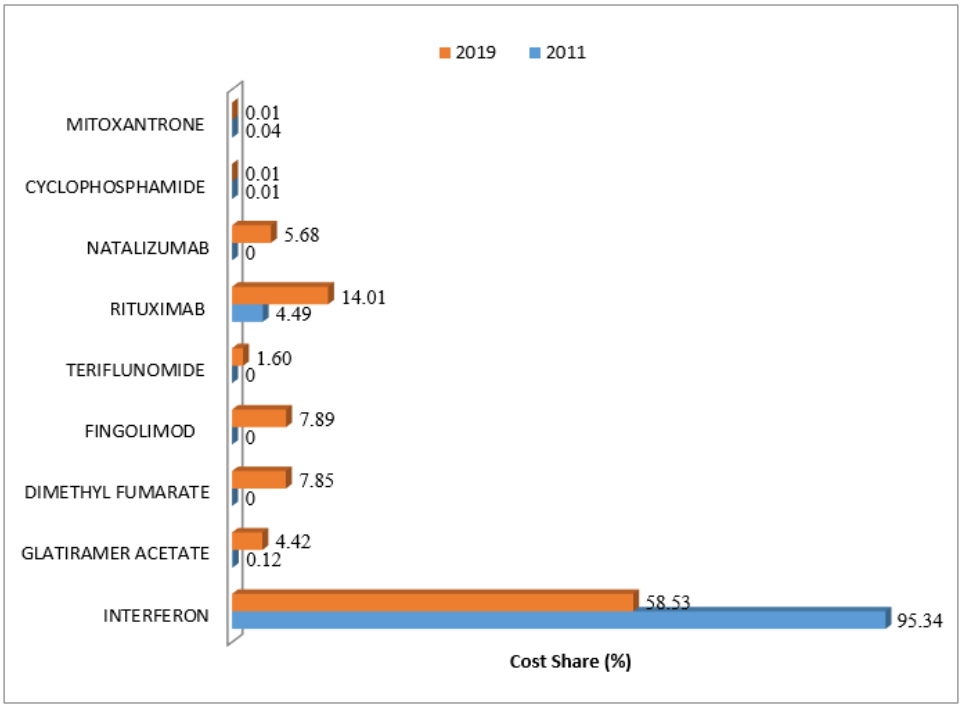

Fig. 7: Comparison the share of different medications in the total economic burden of MS medications (2011-2019)

Discussion

We investigated that the medication costs of MS in Iran using comprehensive national data. According to the findings, the number of MS medications received has increased from 19,000 in 2011 to 50,000 in 2019, revealing more than 150% increase in 9 years. Meanwhile, Interferon has the highest share in all 9 years studied, but it has been accompanied by fluctuations over the years. In return, Cyclophosphamide, Mitoxantrone, and Natalizumab each had the lowest share of the medication received over the years.

The total medication costs of patients covered by IHIO has increased from $81 million in 2011 to $96 million in 2019. These changes show a growth of 18% over a period of 9 years, some of attributed to the increase in medication prices and the import of new drugs into the Iranian market and a significant part is related to the increase in the number of patients receiving medication interventions. Of these, $71 million in 2011 and $83 million in 2019 were the IHIO payment share.

A discretely review of the medications showed that Interferon has the highest share in terms of medication costs in all years, and in return, Cyclophosphamide has the lowest share in terms of cost in all years except 2017. Regular increase in the cost share of Rituximab in study years is noteworthy. However, the other medications did not show a regular trend changes in this regard. Increase in the Interferon costs from 2018 to 2019 is considerable which it because significant increase in the number of Interferon received.

The cost per patient receiving MS medications has also increased from $7,000 in 2011 to $18 in 2019, which due to the increase in the number of patients shows a significant increase (about 2.5 times) in terms of this index over 9 years. The largest share of this index was allocated to Interferon. In 2013, Fingolimod and in 2014-2019, Natalizumab had the largest share in terms of cost per patient. The trend of changes by medications is similar to the overall results showing an increase in the medication costs per patient in most medications. A review of cross-sectional studies also showed that similar to the results of the present study, Interferon had the largest share

of the medication basket of MS patients and this rate has been increasing (15, 20).

The economic burden of MS medications has increased significantly in recent years which could be attributed to the increase in the number of patients and patients receiving medications, as well as new medications and the increase in the number of MS medications and the raised prices of medication. Moreover, because of increasing knowledge of the community about MS the demand for interventions have been increased. In the study, which aimed to examine the increasing cost of MS in several selected countries, reported that the share of medication costs in the economic burden of MS was 55% (18). In Kuwait, 89% of the medical economic burden of MS medical was allocated to medication costs (19).

In general, the incidence of MS is rising in Iran and that the economic burden of MS medications is accordingly significant. The trend of economic burden in this disease is also increasingly predicted all over the world. In Canada the epidemiological situation and economic burden of MS simulated and estimated that by 2031 the total economic burden of MS health care services will reach to $2 billion (21).

The most important limitation of this study was the lack of access to MS-specific prescription data and separated cost data for MS patients in Iran. This problem was largely eliminated by adapting the prescriptions to the graphs, diagnostic tests, etc. and using FDA's annual pharmaceutical statistics in some cases.

Given the changes in medications over the years and the introduction of new medications with different efficacy and economic burden, and predicting the continuation of this trend in the coming years, it seems that estimating the economic burden of MS in the coming years can provide significant evidences to policymakers. On the other hand, with the introduction of new medications, economic evaluation studies and the study of changes in their economic burden can be significant.

Conclusion

Results showed an upward trend in medication costs of the disease during the 9 years of the study, which due to the increasing number of MS patients in Iran and also rising prices, it seems that in the coming years the trend will continue.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interests

The authors have declared that no competing interests exist

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