A Study on the Direct and Indirect Costs of Multiple Sclerosis Based on Expanded Disability Status Scale Score in Khuzestan, Iran

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ABSTRACT

Background: Multiple sclerosis is a common and chronic neurologic disorder. This disorder imposes physical, economic, and psychosocial burden on individuals, their families and society. This study aims to analyze the costs of multiple sclerosis disease based on the severity of disability.

Methods: We performed a cross-sectional cost of illness study. This study was conducted in 332 patients of Khuzestan province of Iran. Data were included: Patient's characteristics, disability status, medical, and nonmedical costs and were gathered by using the questionnaire during 3 months period. Costs analysis was performed in the basis of expanded disability status scale (EDSS). Data were analyzed by using SPSS 18 software.

Results: Mean age of the patients was 33.5 (standard deviation [SD]: 9.1) and 70.5% of patients were female. Mean EDSS score of the patients was 2.2 (SD: 1.6). Most patients (92.1%) had relapsing remitting multiple sclerosis (MS) form of the disease. Costs mean per patients was 8.6 ± 7.9 million Rial. The direct and indirect costs were 93.1% and 6.9% of total costs, respectively. The major cost of the disease belongs to the pharmaceutical treatment (22% of costs). The majority costs (approximately 62%) attributed to EDSS of 6-7 and >7. Furthermore, there was strong significant relationship between cost of illness and disability severity of patients ($P < 0.05$).

Conclusions: Cost mean per MS patients was relatively high. Furthermore, the results showed that cost of disease had positive and significant relationships with EDSS score that is, progression of disability increase costs of patients.

Keywords: Direct cost, expanded disability status, indirect cost, multiple sclerosis

Original Article

INTRODUCTION

Multiple sclerosis is a common, chronic, and crippling neurologic disorder. According to world health organization, around 2.5 million people had damaged by this disease in the worldwide. Some study showed that multiple sclerosis is an

important cause of disability in young adults, after road accidents.[1-3] this disease is common among young people. Multiple sclerosis results in loss of productivity and increasing cost of pharmaceutical treatments and medical services.[4] This disorder imposes physical, economic, and psychosocial burden to individuals, their families, and society.[5] multiple sclerosis (MS) impact on social welfare of patients and families. A study showed that about 53% of multiple sclerosis patients gave up their jobs and this disease decreased the life standard in 37% of patients and their families.[2] Two hundred surveys on the epidemiology of multiple sclerosis were published in Europe recently that some of them were as to burden of multiple sclerosis. According to these studies, total prevalence rate of MS was 83/100,000 with higher rates in Northern Europe and prevalence rates were higher for women for all countries. Over the last two decades, In England and Wales, the prevalence of multiple sclerosis in different areas of these countries was from 84 to 112 MS patients/100,000.[4] Approximately, 350,000 people in the United States were affected by multiple sclerosis and approximately 12,000 new cases were diagnosed each year.[6] In provinces of Iran, the prevalence and incidence of multiple sclerosis is different. For example, risk of this disease in Isfahan province is medium to high. In this province, the overall prevalence of MS was 43.8/100,000.[7] In term of economic, multiple sclerosis imposes high socioeconomic and medical costs and its economic burden is higher than stroke and Alzheimer's.[3,4] In this disease pharmaceutical treatment by new medications is very expensive. Approximately, the total annual economic burden of MS in the United States exceeded $6.8 billion, with a direct and indirect cost of $2.2 million per patient in 1998.[6] In Colombia, multiple sclerosis imposes high costs on the social security system, an amount of more than 75 times of the annual premium cost of health insurance.[8] Therefore, a cost of illness analysis can be helpful for assessment of the economic burden of multiple sclerosis.[9] "cost-of-illness" (COI) analysis is a tool for assessment of costs of diseases. Usually, costs are mainly divided into three broad categories: Direct costs, indirect costs, and intangible costs.[10] Cost of illness studies are increasingly being used for chronic disease that is, including the large proportion of health expenditures.[11] COI isn't a tool for decision making, but it may be useful for educating and informing policy makers.[9] According to the some studies cost of multiple sclerosis is estimated based on the expanded disability status scale (EDSS).[2,12,13] Hence, we analyzed costs of multiple sclerosis based on this valid scale.

METHODS

Study setting and design

We performed a cross-sectional cost of illness study. This study was conducted in MS patients of Khuzestan branch of Iranian multiple sclerosis association. The study was carried out during a 3 months period (July through September 2012).

Study samples

The research population was included 450 patients. We excluded patients under 18 years of age, the patients that died during of study and patients who didn't participate in the study). Finally, data from 332 patients (73.7% of 450 patients) was analyzed. Some of the patients had been already hospitalized in the medical center and hospitals therefore patients were divided into a hospitalized group (100 patients) and a nonhospitalized group (232 patients). In this study, a hospitalized patient was a patient who had been hospitalized for 24 h or more from 1 to 12 months before the period of study. We assessed only patients that had been hospitalized due to multiple sclerosis disease or its complications.

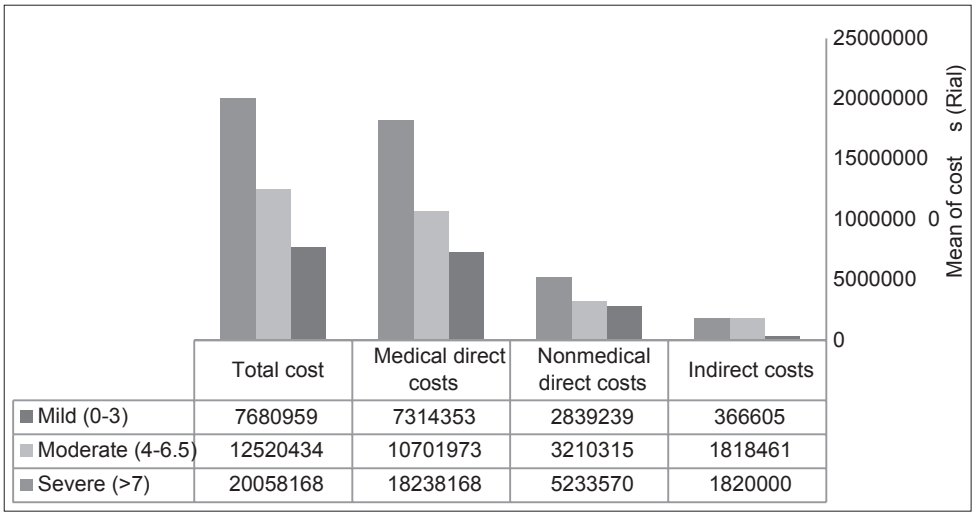
Data gathering and variables

Data were gathered by questionnaires (cost forms) retrospectively. Questionnaires were completed by patients in the basis of a diary list of expenses related to MS. To reduce recall bias, patients were contacted 2 or 3 times/month, and the required recalls were done to complete the forms. The forms were delivered to the MS association at the end of each month by a number of patients and after 3 months by some of them. The forms were completed by patients voluntary. In this study, variables were included: Demographic characteristics of patients, disability status, clinical characteristics of patients, medical direct costs (including hospitalization costs, medical visit, rehabilitation services, diagnosis test, injection, pharmaceutical treatment, transportation, and

aid devices), nonmedical direct cost (including transportation and home care), and indirect cost (including loss of work). Cost analysis of chronic diseases is based on prevalence data. Furthermore, COI studies can be designed either as top-down studies or as bottom-up studies, depending on the database.[14] A top-down approach estimates costs for patients using statistical databases and/or other data registration systems, whereas the bottom-up approach estimate costs from a patient sample and extrapolate this to the population.[10] In this study, we used bottom-up approach for data gathering process. In patients costs were gathered through hospital medical record, hospital bills and other medical documents. Outpatient costs were gathered by patients during 3 months. Finally, data from patients were completed with data of hospital records. We used a human capital approach for estimation of indirect costs. In this approach, indirect cost was calculated based on loss of the productivity attributed to multiple sclerosis disease. We applied the wage/per hour index in each professional/activity sector based on the "list of National Labor Council." Hence, indirect cost was calculated based on the absence from work due to illness. Furthermore, we applied a minimum hourly wage to calculate indirect costs for peoples who did not carried out "productive activities" in the market (e.g. housewives). Price of inpatient and outpatient medical services was calculated by National book of Medical and Diagnosis Tariff. Price of drugs calculated using National Commission of drug pricing. All prices were calculated based on Rial in 2012 and were generalized to the entire year.

Data analysis and statistical methods

Costs analysis was performed based on the severity of disability. Disability level of patients was measured by a neurologist using the EDSS. Grading by this instrument was done on a scale of 0-10, in which the disability rate increases as we get closer to the number 10. Patients were classified into five stages of disability: Stage I (EDSS = 0, the patient is not disabled, but has been diagnosed of a chronic disease), Stage II (EDSS = 1-3, minimally disabled, Stage III (EDSS 3.5-5.5, rather disabled, Stage IV (EDSS = 6-7, patient still capable of walking with aid), and Stage V (EDSS = <7, patient is unable to walk at all).[2] Furthermore, patients were classified into three conditions based on EDSS score (mild = 0-3, moderate = 4-6.5 and sever = <7) [Figure 1].[12] Finally, we analyzed data using SPSS, version 18.0; SPSS Inc., Chicago, Illinois, USA. In the first stage, we reported a descriptive statistic of the variables. The results of the first stage showed that dependent variable (cost) did not distributed normally. Hence, we used nonparametric tests (including Spearman coefficient correlation, Kruskal–Wallis and Mann–Whitney test) for analysis. In this study, significance level for data analysis was determined 0.05.



	Total cost	Medical direct costs	Nonmedical direct costs	Indirect costs
Mild (0-3)	7680959	7314353	2839239	366605
Moderate (4-6.5)	12520434	10701973	3210315	1818461
Severe (>7)	20058168	18238168	5233570	1820000

Figure 1: Costs mean based on severity of disease: Mild (expanded disability status scale [EDSS] = 0-3.5), moderate (EDSS= 4.0- 6.5) and severe disease (EDSS 7<). *Medical direct cost include: Inpatients and outpatients costs; direct nonmedical cost include: Transportation and home car, indirect costs (including loss of work). **Costs were taken into account in Rials in 1391

RESULTS

Data from 332 patients was assessed. The results of this study showed that mean (standard deviation [SD]) age of the patients was 33.5 ± 9.1 years and 75.9% of the people were under 40 of age. Furthermore, the findings showed that most patients (70.5%) were female. In terms of education level, 4.8% of the patients were illiterate, 34% under diploma, and 26.8% had a high school diploma, and 34.3% had an academic degree. Furthermore, 94.3% of the patients were urban. The types of basic health insurance included social security (62.3%), Iranian health insurance (32.8%), armed forces (3.6%) and rural insurance (1.2%). Mean (SD) EDSS of the patients was 2.2 ± 1.6 and median EDSS of patients was 2. Mean of disease duration was 3.3 ± 2.1 years. Clinical forms 92.1% of patients were relapsing remitting (RR) [Table 1]. In nonhospitalized patients group, direct and indirect costs mean were 8 million Rial and 590,000 Rial respectively. Hence, total costs mean per patient was 8.5 million Rial in the period of study. In hospitalized patients group, direct costs mean was 8.3 million Rial and indirect costs mean was 632,000 Rial. Total cost mean for hospitalized patients was 8.9 million Rial. The costs mean per patients was 8.6 ± 7.9 million Rial totally. The cost mean of hospital services in hospitalized patients was 1.1 million Rial. The result of this study showed that multiple sclerosis imposed about 11.48 billion Rial on patients in Khuzestan province annually (equivalent to US $9.36 million). Furthermore, our study showed that significant difference wasn't found between two groups of the patients in term of indirect and direct medical costs mean. According to results of this study patients spent about 46.1% of their income on MS and its complications. The direct costs constituted up to 93.1% of the total costs. Direct costs included: 22% pharmaceutical treatment, 21.1% transport, 11% home care, 10.7% rehabilitation services, 8.8% diagnostic tests, 6% aid devices, and 5.3% injections, respectively. 16.1% of medical direct costs belongs to hospital costs. The results of the current study showed that 85% of the patients had mild disease (EDSS score of 0-3), 10% moderate (EDSS score of 4-6.5) and 5% severe disease (EDSS score of ≤7). Most expenses attributed to moderate and severe stage of disease [Figure 1]. In nonhospitalized group, 31.9% of direct costs attributed to EDSS of ≤7, 27.6% EDSS of 6-7, 14.7% EDSS of 3.5-5.5, 12.9% EDSS of 1-3 and 12.7% EDSS of 0. In hospitalized group, 34.3% of direct costs attributed to EDSS score of ≤7, 30.3% EDSS of 6-7, 15.3% EDSS of 3.5-5.5, 11.4% EDSS of 1-3 and 8.4% EDSS of 0. Totally, most costs (approximately 62%) attributed to EDSS of 6-7 and >7 [Figure 2]. We calculated costs mean per patient based on the EDSS score. The variation of cost units into EDSS stages was different in two patients groups. For example, cost of pharmaceutical treatment was higher than the other cost units in two patients group. Furthermore, the study showed that there was positive and strong significant relationship between EDSS score and costs mean per patients (P = 0.001, coefficient correlation = 0.314), that is, the progression of severity of disease increased costs of the patients [Table 2].

Table 1: Descriptive clinical and demographic characteristics of patients

Variables	Nonhospitalized patients group (n=232)	Hospitalized patients group (n=100)	P value
Mean age (years)	33.8±9	33.2±9.5	0.058
Sex (% female)	72.4	66	0.018
EDSS (median)	2.1 (2)	2.4 (2)	0.001
Mean disease duration (years)	3.1±2.1	3.6±2	0.084
Clinical form of MS (% of RR/SP/PP)*	91.8/3.8/3.4	93/3.5/3.5	-

RR=Relapsing remitting, SP=Secondary progressive, PP=Primary progressive, EDSS=Expanded disability status scale, MS=Multiple sclerosis

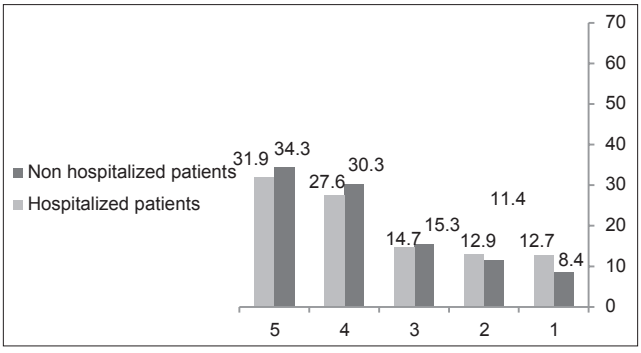


Figure 2: Proportion of costs in the basis of expanded disability status scale (EDSS) among two patients groups (1 = 0 EDSS, 2 = 1-3 EDSS, 3 = 3.5-5.5 EDSS, 4 = 6-7 EDSS, 5 = <7 EDSS)

Table 2: Direct, indirect and total costs mean based on EDSS score (costs were estimated in the period of study) (in Rial)

EDSS	0	1-3	3.5-5.5	6-7	>7	Total cost mean (SD)*	Statistic	Significant
Nonhospitalized patients group (*n*=232)								
Medical visit	211,250	543,491	1,118,076	3,485,833	2,096,666	689,778±1,530,811	14.95	0.002
Rehabilitation**	477,916	634,705	737,692	1,388,333	10,876,666	914,396±4,090,709	6.7	0.082
Diagnosis tests	456,128	752,084	986,807	2,219,466	1,352,800	801,258±1,408,845	14.82	0.002
Injection	403,541	537,244	681,200	797,433	321,980	540,708±609,263	5.48	0.14
Pharmaceutical treatment	2,112,795	1,484,093	1,811,950	316,150	154,500	1,521,282±2,835,997	15.85	0.001
Transportation	2,611,274	2,461,196	1,328,883	3,013,333	427,750	2,311,514±2,301,078	91.08	0.011
Home care	531,625	556,688	1,009,192	2,002,500	1,465,833	665,711±1,042,281	6.12	0.106
Aid devices	884,000	364,294	325,615	3,500,000	0	485,396±2,264,187	1.54	0.673
Direct cost	7,688,531	7,333,798	7,999,418	16,723,050	16,696,196	7,930,047±7,249,307	7.036	0.071
Indirect cost	52,500	413,470	1,171,346	4,083,333	1,700,000	589,245±1,808,133	25.95	0.001
Total cost	7,741,031	7,747,269	9,170,764	20,816,783	18,396,196	8,519,292±7,961,108	11.8	0.008
Hospitalized patients group (*n*=100)								
Hospital costs***	671,732	1,208,198	714,269	721,402	306,559	1,074,720±1,876,001	3.5	0.32
Medical visit	702,000	789,760	582,142	845,000	765,000	758,020±725,789	3.99	0.26
Rehabilitation	577,320	576,682	1,927,542	4,000,000	3,000,000	951,234±1,786,986	20.44	0.001
Diagnosis tests	617,160	664,696	737,428	893,650	982000	688,006±645,945	2.41	0.49
Injection	2,560,000	313,788	190,714	85,000	185,000	281,941±403,120	5.78	0.123
Pharmaceutical treatment	2,611,176	3,246,060	1,256,507	337,275	345,550	2,761,416±3,259,170	7.72	0.053
Transportation	612,000	567,066	1,180,000	1,108,750	1,232,500	690,100±575,097	19.4	0.001
Home care	0	849,333	2,964,285	7,875,000	11,500,000	1,597,000±3,663,702	34.4	0.001
Aid devices	0	272,400	917,857	4,121,250	3,792,500	5735,00±1,235,855	24.57	0.001
Direct cost	5,375,656	7,279,787	9,756,478	19,265,925	21,802,550	8,301,218±6,482,260	14.97	0.002
Indirect cost	0	385,333	950,000	5,250,000	0	632,000±2,609,380	2.91	0.405
Total cost	5,375,656	7,665,120	10,706,478	24,515,925	21,802,550	8,933,218±7,989,607	15.74	0.001
All patients**** (*n*=332)								
Medical visit	295,862.07	618,880	930,500	2,429,500	1,763,750	710,333±1,339,384	19.18	0.001
Rehabilitation	495,055	616,943	1,154,140	2,433,000	8,907,500	925,492±3,554,396	21.08	0.001
Diagnosis tests	483,892	725,332	899,525	1,689,140	1,260,100	767,146±1,229,918	15.51	0.001
Injection	378,103	468,839	509,530	512,460	287,735	462,766±567,271	2.55	0.464
Pharmaceutical treatment	2,198,723	2,023,470	1,617,545	324,600	202,262	1,894,816±3,016,137	22.2	0.001
Transportation	2,266,571	1,881,360	1,276,774	2,251,500	628,937	1,823,136±2,085,478	2.51	0.473
Home care	439,965	646,273	1,693,475	4,351,500	3,974,375	946,220±2,226,184	26.5	0.001
Aid devices	731,586	336,163	532,900	3,748,500	948,125	511,933±2,009,028	14.42	0.002
Direct cost	7,289,760	7,317,264	8,614,389	17,740,200	17,972,785	8,041,845±7,019,436	18.31	0.001

contd...

Table 2: Contd....

EDSS	0	1-3	3.5-5.5	6-7	>7	Total cost mean (SD)*	Statistic	Significant
Indirect cost	43,448	404,857	1,093,875	4,550,000	1,275,000	602,123±2,078,101	24.33	0.001
Total cost	7,333,208	7,722,121	9,708,264	22,290,200	19,247,785	8,643,969±7,953,893	24.04	0.001

*Here total costs mean isn't an arithmetic mean, it is a weighted means in which each quantity to be averaged is assigned a weight (number of patients in each level of disability). Weighted mean usually is a little higher than arithmetic mean. **Rehabilitation services (including physiotherapy, occupational therapy, speech therapy and audiology). ***After the calculation of hospital costs (inpatient cost) for hospitalized patients group (n=100), the average hospital costs were prorated to period of study (a 3 months period). ****To integrate the estimates and reduce the computational error, the hospital costs for hospitalized patients group are not included in direct medical costs. SD=Standard deviation, EDSS=Expanded disability status scale

DISCUSSION

We calculated the direct, indirect and total costs of multiple sclerosis patients based on the EDSS. Furthermore, we assessed disability effect on the cost variations. Many of the studies have been done about Cost analysis of multiple sclerosis. The first large-scale studies on costs of MS were performed in 1995. Studies of cost analysis of multiple sclerosis have been designed based on the deferent categories of costs. According to Battaglia and *et al*. costs of MS is classified in tangible and intangible parts. Tangible costs subsequently are divided into direct and indirect costs.[14] In some study, the basis of costs analysis is direct and indirect costs.[10,15] Furthermore, according to Prescott the patients' costs have been divided into direct medical and nonmedical costs.[6] In the current study, we used mix method of costs taxonomy. The result of our study showed that costs mean per patients was 8.6 million Rial in 3 months, so multiple sclerosis imposed about 11.48 billion Rial on patients in Khuzestan province annually (equivalent to US $9.36 million). A study showed that the costs mean per MS patients was 12879$ in United States annually.[6] In Slovakia total annual costs in 2010 for 6100 dispensed patients with MS were €54.723.592. Indirect costs (€31.728.757) prevailed over direct costs (€22.994.834). The highest part of both costs were €25.207.512 and €12.641.052 for loss productivity due to patients sickness and invalidity pensions and disease-modifying drugs respectively. The average of cost per patient independently of disease severity was €8.971. The proportion of medical direct costs was higher than other costs type. Furthermore, Multiple Sclerosis International Federation reported that cost of the MS patients in Norway, Sweden, UK and Austria were higher than other European countries and proportion of indirect and direct cost was different in between these countries. As in Norway total indirect costs was higher than other costs and in UK and Sweden total direct nonmedical costs were higher. These differences are probably due to the duration of study, methodology of researches, differences in the taxonomy of costs in different studies, differences in the services provided and differences in cost analysis approaches.[16] In this study, we divided patients into hospitalized and nonhospitalized groups. The first, we assumed that the hospital costs impact on nonhospital costs of patients. The second, the large proportion of direct costs mean can be attributed to hospital costs. About first hypothesis we found that prior hospitalization history (due to MS) hadn't impact on the other costs. We didn't found any national or international studies about hospitalization history variable. About second hypothesis, our findings showed that hospital costs were 16.1% of medical direct costs (except surgical services) and inpatient cost mean per patients was 4.2 million Rial (equivalent to US $ 3425). Prescott showed that inpatient costs (hospital services) was 7.8% of total costs of multiple sclerosis patients and imposed 1004$ on the patient annually.[6] In the current study, pharmaceutical treatment costs (22%) accounted for the highest share of the costs. Prescott[6] and Bainbridge[17] showed that pharmaceutical costs of MS were 64.8% and 39.5% of the costs of MS patients respectively. Furthermore, Menzies Research Institute of Tasmania reported that 59% of costs of MS were due to pharmaceutical treatment.[18] Some study show that Clinical and nonclinical factors impact on the costs of illness. The nonclinical factors are including demographics characters, region, type of insurance, and so.[6] One of the most important

clinical factors affecting costs of MS is the severity of disease (or disability) that is, assessed by EDSS scale. In the current study, mean EDSS of the patients was 2.2 and 85% of patients had mild disease (0-3). Kobelt showed that EDSS score is different between countries (respectively, Germany 3.8 (±2.3), The Netherlands 3.9 (±2.2), Switzerland 4.5 (±2.4), and the UK 5.1 (±2).[12] We found that increase of EDSS score raises the costs continuously and most costs (33%) belongs to EDSS of <7 (level 5). Patwardhan *et al*. showed that direct and indirect costs of multiple sclerosis can be increased continuously with progression of EDSS. Hence, costs are positively correlated to score of EDSS.[19] Naci *et al*. found a positive relationship between costs and EDSS score.[20] Some studies such as Orlewska[21] and Tyas *et al*.[22] had also similar results. A study showed that there have significant associations between costs, Quality of life and severity of multiple sclerosis.[23,24] Our study showed that there have differences between cost mean of the disability levels; these differences mainly were seen in medical direct costs. Furthermore, there was a positive relationship between indirect, medical direct and total cost mean with EDSS score. Casado *et al*. found similar results.[2] In our study indirect cost in the stages IV and V was very higher than other Stage (I, II, and III). Perhaps this difference is due to sample size in these levels (IV and V) and it should be noted that the number of patients in each stage can be effective on the variation of cost mean into EDSS stages. However, the results showed that multiple sclerosis imposed relatively high economic burden on patients. In this study, approximately 99% of subjects were covered by Iranian basic health insurance (including social security insurance plan, Iranian health insurance, rural health insurance, and so). However, lack of the comprehensive insurance and benefit package for these patients can be lead to high economic burden of disease. In 2012, most MS drugs weren't covered by basic health insurance plans so patients should be bought the drugs very expensive. Since 2013, 3 items of MS drugs (native production) were covered by basic health insurances in Iran and patients just were paying 10% of costs of these drugs. Cost of illness increase the out of pocket payment by patients. In our country, out-of-pocket payment approximately is high (60% of total health expenditure) that must be decreased to 30% based on the fifth 5-year development planning.[25] The out-of-pocket payments is less than 10% to more than 80% of total national health spending in several countries.[26] However, for improvement of fiscal condition of Iranian MS patients should be created integration between insurance funds, private health sector, and ministry of health. Furthermore, some of the studies showed that geographical condition can be important in term of prevalence and incidence of MS disease as prevalence of disease is higher in a temperate climate. For example, in South Australia prevalence of MS was 75.6/100,000 compared with prevalence of 11/10,000 in Northern Queensland.[27] Hence, it is notable that the results of our study are generalized to the Khuzestan province and it is possible that we will obtain the different results in other areas. In this study, there were limitations. The most important limitations of this study were: The first, data were gathered retrospectively. The next limitation was that the some of the patients didn't participate in this study. The third, clinical visit of patients in order to determine the disability severity was expensive. The forth, existence of intrinsic bias derived from response to the questionnaire (some patient did not provided some information such as income and some patients did not remembered costs). The fifth, in this study intangible cost weren't estimated. The final limitation was that because of difference of monetary value and inflation rate in several countries the international compression of results was difficult.

CONCLUSIONS

According to results of this study, cost mean per MS patients per year was relatively high and a large proportion of costs related to the medical direct costs (especially pharmaceutical treatment costs). Furthermore, the present study showed that progression of disability increase costs of the patients. Finally, this study and other study showed that disability scale is a useful and common tool for cost analysis of multiple sclerosis disease.

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