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Disease Burden of Psoriatic Arthritis Compared to Rheumatoid Arthritis, Hungarian

Experiment

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Abstract

The objectives of this study were to assess the costs of psoriatic arthritis (PsA) in Hungary and to identify key cost drivers among demographic and clinical variables and to compare cost-of-illness of PsA and rheumatoid arthritis (RA). Cross-sectional retrospective survey of 183 consecutive patients from 8 rheumatology centres was conducted. Mean direct medical, direct non medical, indirect and total costs were 1 876, 794, 2 904 and 5 574 euros/patient/year, respectively. Total costs were in significant linear relationship with Health Assessment Questionnaire score and Psoriatic Area Severity Index. Costs of RA were higher in all domains than of PsA. Our study was the first from the Eastern European region that provides cost-of-illness data on PsA. Our study revealed that functional status and severity of skin symptoms was the key cost drivers. The costs of PsA in Hungary were lower than in the high income European countries.

Keywords: Psoriatic arthritis, Rheumatoid arthritis, Cost of illness, Cross-sectional studies, Hungary

Introduction

Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in about 10-30% of the patients with psoriasis. The prevalence in the general population is between 0.1 to 0.3%. The localization of joint inflammation is diverse in PsA, ranging from axial to peripheral disease. Although PsA and rheumatoid arthritis (RA) apparently present similarities and many disease evaluation methods and therapies of PsA were derived from RA, the distinction of the two conditions has been clearly established, both clinically and immunohistologically in the past years. However, there is still a significant disparity between RA and PsA regarding the knowledge on disease related costs and health status of the patients whilst such data are fundamental for health economic analysis. Increasing number of countries, including Hungary, are considering cost-effectiveness - the so called “fourth hurdle” - in licensing requirements and/or reimbursement decisions of new drugs. Registration of highly effective but costly biological drugs for the treatment of arthritis gave an extra impulse to economic evaluations in rheumatology but the majority of the available studies are still from the field of RA [1].

Ackermann et al. [2] conducted a systematic review on the economic burden of PsA. They concluded that there is a dearth of published pharmacoeconomic evaluations in PsA. Javitz et al. [3] described the burden of psoriasis and PsA in the USA on the 1997 basis but their method was not appropriate according to Ackermann’s review. Huscher et al. studied the costs of inflammatory rheumatic diseases in Germany on the 2002 basis but results from an economically developed country are not squarely relevant for all regions of Europe [4]. There are no data on costs of PsA neither from Hungary nor from countries with similar economic status, health care and insurance system (i.e. Poland, Slovakia and Czech Republic).

Therefore, the research question comes up whether disease burden studies of PsA from economically developed countries are applicable in Hungary? What are the key cost drivers? And secondarily, is the disease burden of PsA comparable with RA in our circumstances? The main goal of present study was to collect local data on quality of life and costs of patients with PsA in Hungary and analyze the impact of main disease characteristics on costs. A comparison with costs of RA in Hungary was also conducted to assess the differences from the pharmacoeconomic point of view.

Material and methods

Setting

From December 2007 to March 2008 a cross-sectional questionnaire survey of 183 consecutive patients aged ≥ 18 years with established diagnosis of PsA was conducted in 8 rheumatology outpatient centres based on hospital in Hungary. Data were collected by rheumatologists during routine outpatient visits. Patient informed consent form was signed and the study was authorised by national and local ethical committees.

Assessment

Patients filled in the validated Hungarian version of the Health Assessment Questionnaire (HAQ), EQ-5D and Psoriatic Arthritis Quality of Life Questionnaire (PsAQoL) [5-8]. Interviewing patients and using medical records rheumatologists completed a set of questions. This included demographic data, disease duration, disease activity score (DAS28), psoriasis area severity index (PASI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Present and previous drug use was also assessed: Disease Modifying Antirheumatic Drug (DMARD) therapies, corticosteroids and non-steroid antiinflammatory drugs (NSAID),

systemic and topical therapies for psoriasis, gastroprotective drugs and also the use of medical aids and devices. PsA related imaging, gastroscopy, general practitioner (GP) and specialist visits, admissions to hospital, orthopaedic surgery, spa, physiotherapies, home care and transportation were surveyed. Non-reimbursed health care services, home remodelling and informal care data were also collected. PsA related reduction of working hours, sick leave, early retirement (disability pension) was studied based on the patients' answers.

Cost calculation. Costs were calculated from the perspective of society over a one-year period considering all PsA related direct medical and non-medical costs as well as production losses (indirect costs) of the previous 12 months. Hungarian official price, tariffs and reimbursement lists of 2007 were used. Cost of hospital admissions (including surgery) and outpatient visits was calculated based on reimbursement prices while a true costs calculation was performed for the other elements, including both financing and patients' costs. X-rays, gastroscopy, CT and MR were evaluated on outpatient prices and multiplied with the number of cases. In case of medical aids and devices, prices of the most commonly used assortments were considered for cost calculation. GP and specialist visits were calculated on the basis of mean cost/visit obtained from the official statistical database in 2007. Spa, physiotherapy and formal home care were calculated on the basis of official price lists multiplied by the number of visits. When calculating costs of transportation and travel vouchers we considered the number of occasions and the distance between patients' home and rheumatology centres. Non-reimbursed medical services and PsA related home remodelling costs were based upon patients' answers. The cost of PsA related informal care was calculated using the average hourly net wage in Hungary (2.7 euros/hour) multiplied by the number of hours. The human capital approach (where the cost of employment is considered to reflect an individual's productivity) was used for analysis. The cost of sick leave, part time jobs due to PsA and full

disability were calculated by multiplying the average gross income (996 euros/month in 2007) with the time off work. On the basis of the average exchange rate of 2007 we applied a 250 Hungarian forints 1 euro conversion.

Comparison with RA

A cost-of-illness study with a similar methodology (cross sectional questionnaire survey, covering the same cost matrix) was performed in Hungary, 2004. The survey involved 255 consecutive RA patients in 8 rheumatology centres. Results were reported in detail earlier [9]. Unit-costs based domains were recalculated with prices of 2007 for the comparison. Patient reported amounts (home remodelling, non-reimbursed health care utilizations) were inflated with the cumulative consumer price index 2004-2007, 116%.

Statistical analysis

Comparisons of variables between categories were performed using independent Student's t test or Kurskal-Wallis test, whichever appropriate. Differences in proportions were compared with chi-square tests. Univariate general linear model was used for analysing key cost drivers. The levels of significance were set to 0.05 unless stated otherwise. Data were analysed using the Statistical Package of Social Sciences, version 14.0 (SPSS Inc., Chicago, IL, USA).

Results

Our goal was not only to assess the burden of PsA in Hungary but also to compare with recent data on RA from our country hence results of the present study are displayed in Tables right off with data on RA.

Patients' characteristics

A total of 183 PsA patients were enrolled in the study (Table 1). A slight predominance (57%) of women was observed, but the divergence from the usual 1:1 ratio was not significant ($p=0.054$). Patients were at mean age 50.1 (SD 12.9) years. Eighty one percent of patients were in working-age (<62 years) and 45 patients (25%) received partial or full national work disability pension. Educational level was a degree in 24% of the patients. The difference between the health related quality of life (EQ-5D) and functional ability (HAQ) of males and females was not significant ($p=0.325$ and $p=0.086$).

Costs

Health care utilisation data are presented in Table 2. The annual average total costs per patient were 5 574 (SD 7 551) euros, which were distributable to direct and indirect costs of 2 670 (SD 4 384) and 2 904 (SD 4 899) euros. The most considerable cost domains were the indirect costs (income loss due to work disability, 52%) and the costs of biological treatments (18%). Table 3 presents the mean and median annual costs of all direct and indirect domains. Direct medical, direct non-medical and indirect costs were lower for men than women: mean costs were 1 599, 524, 2 741 vs. 2 082, 995, 3 024 euros (median 530, 0, 0 vs. 817, 8, 0 euros), respectively. Difference was significant in direct non-medical cost ($p=0.005$) and not significant in direct medical and indirect costs ($p=0.063$ and $p=0.601$).

Key cost drivers

Cost drivers were analyzed with univariate general linear model whilst work disability pension and biological therapy were considered as fixed factors. Demographic variables (age, gender, disease duration, age at diagnosis), disease activity (DAS28), functional status (HAQ) and skin symptoms (PASI) were involved in the model. The significance values for

demographic variables and disease activity were less than 0.05, indicating no considerable effects on total costs. Therefore functional status and skin symptoms were included in the final model. HAQ and PASI with the fixed factors of work disability pension and biological therapy were in positive linear relationship with total costs. One point increase of HAQ and PASI resulted in an increase in total costs of 1 153 and 49 euros, respectively ($p < 0.01$). The explanatory power of the model is high with the R square 0.94. (Table 4)

Comparison with RA

Pentek and her colleagues surveyed 255 RA patients in 2004 [9-10]. Comparison with our present results of PsA is presented in Tables 1., 2. and 3. Mean age, rate of women, disease activity (DAS) were significantly higher and functional status (HAQ) was significantly worse in RA. Proportion of patients with at least one GP or rheumatology visit were significantly higher in RA ($p < 0.001$) and also more patients with RA were admitted to hospital than with PsA ($p < 0.001$). Rate of patients using DMARDs was higher in RA, relative ratio of PsA/RA was 58% (95% CI 51-68) and also corticosteroid use was higher in RA. Similarly the proportion of work disabled patients with RA overpassed PsA, relative ratio was 70% (95% CI 18-75) (Figure 1).

Mean total costs were slightly lower in PsA than in RA, the difference was 1 294 euros.

However if patients on biological therapy were excluded from the sample (in order to match with the RA study which did not involved patients on biological treatment) the difference of mean total costs increases up to 2 587 euros. Average annual costs of non-biological DMARDs were 2.5 times higher in PsA than in RA (152 vs. 373 euros). The peak in absolute difference with 1 794 euros was at the indirect costs (work disability pension).

Discussion

Results of a cross-sectional survey on the costs of PsA in Hungary were analyzed in our study and key cost drivers among demographic and clinical variables were identified. Also a comparison with RA was performed.

The average total costs of PsA was 5 574 (SD 7 551) euros/patient/year in Hungary, year 2007. Women's costs were significantly higher at all cost domains. Among direct costs the difference appears in the field of non-medical expenditures, namely use of informal care: women had 2.5 times more hours/week resort to help from family or other caregivers. More women in working age were receiving disability pension (33% vs. 25%) which explains their higher indirect costs (we considered the same average gross income for both genders) however the difference was not significant. Huscher et al.³ (Germany) reported that out of pocket expenses, including domestic help, was considerably higher among women which is in consistence with our results and they found also higher indirect costs among women of working age. Wallenius et al. [11] (Norway) reported also a dissimilarity between women and men (age: 18-45), the proportions of men and women receiving work disability pension were 17% and 33%. These different studies indicate that costs of PsA are higher among women, the same as in Hungary.

Analysis of key cost drivers revealed that physical function (HAQ) and severity of skin symptoms (PASI) have positive significant linear relationship with total costs of PsA whilst work disability and biological therapy were considered as fixed factors. Previously cost-effectiveness models of biologicals assumed linear relationship between functional status (HAQ) and direct costs in PsA based on RA data [12-13]. Huscher et al. [4] confirmed this relation of total costs based on a PsA study and our results pointed out the same with HAQ.

However disease duration and age at diagnosis also significantly correlated with total costs in Germany which was not detectable in our study. As far as we know our research is the first that offers data on skin symptoms as well revealing significant linear relationship between PASI and total costs.

Comparison of disease related costs of PsA and RA in the same country within a close time period is basically advantageous, since the characteristics of the health care system does not alter the results and unit costs can be easily adjusted. Nevertheless, only 3 years passed between the two cost-of-illness surveys in Hungary and we had to face an upside down situation in our analysis. Rate of biologicals was zero in the RA study (2004) whilst 6% in our PsA survey (2007) whilst actually it has become already higher in RA as its regular reimbursement started in 2006. Therefore, we performed a comparison excluding patients on biologicals from the PsA sample (Table 3). In general, costs were lower in PsA than in RA due to a lower consumption of health care resources. Both hospitalisations and out-patient visits were less common the same as the proportion of patients receiving work disability pension was lower in PsA. Costs of non-biological DMARDs were 2.5 times higher in RA due to a more frequent use of DMARDs and a higher share of a quite costly leflunomide. Huscher et al. [4] also reported lower total costs and DMARD costs of PsA than RA but the rate of DMARD use was similar in the two conditions there (84% vs. 90%). [14]

Comparing our results with available data from other countries is challenging due to differences in inclusion criteria and study design. Huscher et al. [4] reported about twofold higher total costs of PsA patients in working age (18-65 years) in Germany (mean 11 075 euros/patient/year in 2002), and the proportion of indirect cost was much higher there (71.5% vs. 52%). Considering only patients in working age (18-62 years) we still find lower total

costs in Hungary (6 254 euros/year/patient, indirect costs: 56 %). Rate of patients receiving disability pension was much lower in Germany among patients in working age (19% vs. 30%) in spite of similar functional status (HAQ<1.2: 67% vs. 69%). Thus the higher indirect costs in Germany were due to the higher average gross income. In Italy, Olivieri et al. [15] assessed the costs of PsA for a shorter time period, reporting mean 3 038 euros/patient/6 months in a study which did not include biological therapy and productivity loss was not considered either. Although half year's costs cannot be directly matched to 1 year, it is impressive that direct costs of 6 months in Italy is higher than of 1 year in Hungary (3 038 vs. 1 681 euros/patient) excluding patients on biological therapy.

One of the limitations of our study is the inclusion of patients whom attended a rheumatology centre. Therefore, conclusions cannot be drawn on all patients with PsA in Hungary. Patients in rheumatology care are probably more severely ill and they are using more intensively health care resources than the average PsA patient.

Our study showed that the economic burden of PsA is considerable in Hungary and revealed that health economic researches of PsA from other European countries cannot be adapted without adjustments. Our findings confirmed results of earlier studies that in general, disease related costs of women are higher and functional status is a good indicator for costs in PsA. In addition, we found that the severity of skin symptoms is determinant as well. Costs of PsA were lower than of RA in our circumstances which is consistent with international findings. Our data provided a baseline to evaluate the economic effect of treatments in PsA in Hungary.

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Table 1 Main clinical characteristics of patients with PsA in comparison with a cost-of-illness survey of RA (2004) in Hungary

General characteristics, mean (SD)	PsA	RA [9, [10]	p
N	183	255	n.a.
Age, year	50.1 (12.9)	55.5 (12.3)	<0.001*
Women, n (%)	105 (57%)	218 (86%)	<0.001*
Disease duration, year	9.2 (9.2)	9.0 (9.3)	0.844
Swollen Joint Count	5.0 (7.2)**	6.5 (5.7)	0.016*
Tender Joint Count	7.7 (8.7)**	9.9 (7.5)	0.011*
ESR (mm/h)	26.8 (22.6)	30.2 (20.0)	0.124
C-reactive protein (mg/l)	15.3 (20.9)	19.0 (27.4)	0.177
Doctor's general health VAS (0-100)	36.9 (24.4)	39.2 (22.9)	0.332
Patient's general health VAS (0-100)	47.9 (26.2)	47.0 (22.8)	0.711
Patient's pain VAS (0-100)	52.0 (24.6)	48.7 (24.0)	0.177
DAS28	4.4 (1.7)	5.1 (1.4)	<0.001*
BASDAI (0-100)	46 (23)	NA	NA
HAQ (0-3)	1.0 (0.7)	1.4 (0.8)	<0.001*
EQ-5D (-0.594-1)	0.47 (0.35)	0.46 (0.33)	0.873
EQ-5D VAS (0-100)	54.7 (20.0)	51.7 (19.8)	0.124
PsAQoL (0-20) - RAQoL (0-30)	7.7 (6.0)	16.2 (8.1)	NA

NA: not applicable

* significant

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Table 2 Health care utilization in the past 12 month of patients with PsA in comparison with a RA cost-of-illness survey (year 2004) in Hungary

	PsA		RA ⁸	
	Rate of patients with at least one occasion (%)	Average frequency in the whole study population	Rate of patients with at least one occasion (%)	Average frequency in the whole study population
Visits				
GP visit	56.3	3.7 (5.7)	78.0	9.0 (6.1)
Any specialist visit	84.7	6.4 (7.8)	96.1	6.7 (6.0)
Rheumatology visit	74.9	3.4 (4.3)	90.6	5.8 (5.5)
Dermatology visit	42.6	1.6 (2.8)	-	-
Admission to hospital	42.1	0.6 (0.9)	62.7	1.1 (1.3)
Admission to hospital with surgery	2.7	0.03 (0.2)	6.7	0.1 (0.2)
Diagnostics				
Joint x-ray	67.2	2.4 (3.3)	73.7	1.6 (1.1)
CT	7.1	0.1 (0.3)	4.7	0.1 (0.3)
MR	5.5	0.1 (0.2)	8.2	0.1 (0.3)
Gastroscopy	8.2	0.1 (0.3)	11.8	1.1 (0.3)
Drugs (present users)				
NSAID	54.1	NA	74.1	NA
Corticosteroid tablets	10.4	NA	47.1	NA
Corticosteroid injections	15.3	NA	21.2	NA

Any DMARD	51.4	NA	87.5	NA
- methotrexate	27.9	NA	44.3	NA
- leflunomide	7.1	NA	27.5	NA
- sulfasalazine	13.1	NA	5.1	NA
- biological	6.0	NA	0.0	NA
Combinations of DMARDs	5.5	NA	13.3	NA
Gastroprotection	24.0	NA	34.9	NA
Retinoids	3.3	NA	-	-
Topical treatments	68.3	NA	-	-
Other health care services				
Spa	12.0	0.1 (0.4)	11.8	0.6 (3.2)
Physiotherapy	19.1	0.5 (1.5)	22.0	1.1 (4.1)
Home care	1.1	0.3 (3.6)	0.4	0.0 (0.1)
Medical aids and devices	29.0	NA	41.6	NA
Not reimbursed services	26.8	NA	10.6	NA
Non-medical cares				
Home remodelling	5.5	NA	9.8	NA
Transportation	18.0	0.94 (4.2)	37.3	2.0 (4.1)
Informal care	37.7	6.7 (19.3)	51.0	10.5 (14.3)
Productivity loss				
Work disability pension	24.6	NA	35.3	NA

Sick leave	22.6	4.9 (18.8)	5.9	14.2 (52.3)
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Table 3 Mean (SD) and median costs of PsA and RA in Hungary (euro/patient/year)

Cost domains	PsA 2007		PsA 2007, patients on biological therapy excluded (n=		RA 2004 ^{§*} , biological therapy was not used (n=255)	
	total sample (n=	183)	172)			
	mean (SD)	median	mean (SD)	median	mean (SD)	median
Outpatient visit	90 (101)	60	88 (103)	55	113 (79)	95
Inpatient treatment	333 (495)	0	323 (459)	0	655 (1 004)	475
Diagnostics	27 (40)	11	27 (41)	11	19 (38)	8
Drugs	1 339 (4 139)	195	338 (500)	186	442 (512)	149
<i>DMARD</i>	<i>123 (406)</i>	<i>0</i>	<i>126 (414)</i>	<i>0</i>	<i>373 (499)</i>	<i>42</i>
<i>Biological</i>	<i>1 008 (4 134)</i>	<i>0</i>	<i>0 (0)</i>	<i>0</i>	<i>0</i>	
<i>Psoriasis</i>	<i>124 (298)</i>	<i>48</i>	<i>127 (306)</i>	<i>48</i>	<i>NA</i>	<i>NA</i>
<i>Other</i>	<i>84 (85)</i>	<i>61</i>	<i>85 (85)</i>	<i>61</i>	<i>69 (86)</i>	<i>63</i>
Devices	11 (26)	0	11 (27)	0	14 (0)	28
Not reimbursed	77 (311)	0	77 (317)	0	23 (99)	0
Non medical cares	794 (1 445)	0	818 (1 477)	0	974 (1 732)	136
Direct costs	2 670	1 061	1 681 (1 720)	983	2 240	1668

	(4 384)				(2 191)	
Sick leave	161 (623)	0	169 (640)	0	92 (630)	0
Work	2 742				4 536	
disability	(4 920)	0	2 431 (4 693)	0	(5 695)	0
pension						
Indirect costs	2 904	0	2 600 (4 674)	0	4 628	0
	(4 899)				(5 661)	
Total costs	5 574	2 134	4 281 (5 386)	1638	6 868	3 932
	(7 551)				(6 196)	

*Costs were recalculated with prices from 2007

Table 4 Univariate general linear model for total costs of PsA, $R^2=0.939$ (n=183)

Model parameter	Estimated effect size; euro/unit	p	95% Confidence interval	Partial Eta squared
Intercept	280	0.296	-248-807	0.007
Slope for HAQ	1 153	0.000	684-1 623	0.130
Slope for PASI	49	0.002	19-79	0.060
On work disability pension (yes/no)	11 523	0.000	10 772-12 275	0.853
On biologic therapy (yes/no)	17 023	0.000	15 687-18 358	0.800

Figure 1 Health care utilization and disease burden, comparison of PsA and RA.