Original article

Indirect and direct costs of treating patients with ankylosing spondylitis in the Brazilian public health system

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ABSTRACT

Introduction: Patients with ankylosing spondylitis require a team approach from multiple professionals, various treatment modalities for continuous periods of time, and can lead to the loss of labour capacity in a young population. So, it is necessary to measure its socio-economic impact.

Objectives: To describe the use of public resources to treat AS in a tertiary hospital after the use of biological medications was approved for treating spondyloarthritis in the Health Public System, establishing approximate values for the direct and indirect costs of treating this illness in Brazil.

Material and methods: 93 patients selected from the ambulatory spondyloarthritis clinic at the Hospital de Clínicas of the Federal University of Paraná between September 2011 and September 2012 had their direct costs indirect treatment costs estimation.

Results: 70 patients (75.28%) were male and 23 (24.72%) female. The mean age was 43.95 years. The disease duration was calculated based on the age of diagnosis and the mean was 8.92 years (standard deviation: 7.32); 63.44% were using anti-tumour necrotic factor drugs. Comparing male and female patients the mean Bath Ankylosing Spondylitis Disease Activity Index was 4.64 and 5.49 while the mean Bath Ankylosing Spondylitis Functional Index was 5.03 and 6.35 respectively.

Conclusions: The Brazilian public health system's spending related to ankylosing spondylitis has increased in recent years. An important part of these costs is due to the introduction of new, more expensive health technologies, as in the case of nuclear magnetic resonance and, mainly, the incorporation of anti-tumour necrotic factor therapy into the therapeutic arsenal. The mean annual direct and indirect cost to the Brazilian public health system to treat a patient with ankylosing spondylitis, according to our findings, is US$ 23,183.56.

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Custos diretos e indiretos do tratamento de pacientes com espondilite anquilosante pelo sistema público de saúde brasileiro

R E S U M O

Palavras-chave:
Espondilite anquilosante
Custos indiretos
Farmacoeconomia
Qualidade de vida
Custos diretos

Introdução: Os pacientes com espondilite anquilosante (EA) exigem uma abordagem de equipe com vários profissionais e várias modalidades de tratamento, continuamente; além disso, a doença pode levar à perda da capacidade de trabalho em uma população jovem, de modo que é necessário medir o seu impacto socioeconômico.

Objetivos: Descrever o uso de recursos públicos para o tratamento da EA em um hospital terciário após o uso dos fármacos biológicos ter sido aprovado para o tratamento das espondiloartrites pelo Sistema Público de Saúde e estabelecer valores aproximados para os custos diretos e indiretos do tratamento dessa doença no Brasil.

Material e métodos: Foram estimados os custos de tratamento diretos e indiretos de 93 pacientes com EA do ambulatório de espondiloartrite do Hospital de Clínicas da Universidade Federal do Paraná, entre setembro de 2011 e setembro 2012.

Resultados: Dos pacientes, 70 (75,28%) eram do sexo masculino e 23 (24,72%) do feminino. A idade média foi de 43,95 anos. A duração da doença foi calculada com base na idade do diagnóstico e a média foi de 8,92 anos (desvio padrão: 7,32); 63,44% dos indivíduos usavam fármacos anti-TNF. Na comparação dos pacientes dos sexos masculino e feminino, a média no Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) foi de 4,64 e 5,49, enquanto a média no Bath Ankylosing Spondylitis Functional Index (BASFI) foi de 5,03 e 6,35, respectivamente.

Conclusões: Os gastos do sistema público de saúde brasileiro relacionados com a espondilite anquilosante aumentaram nos últimos anos. Uma parte importante desses custos deve-se à introdução das novas tecnologias de saúde, mais dispendiosas, como no caso da ressonância nuclear magnética e, principalmente, da incorporação da terapia anti-TNF ao arsenal terapêutico. O custo médio anual direto e indireto do sistema público de saúde brasileiro para tratar de um paciente com espondilite anquilosante, de acordo com os resultados deste estudo, é de US$ 23.183,56.

Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disease, autoimmune in origin, which generally affects the spinal column and can evolve into stiffness and progressive functional limitation of the axial skeleton.[1,2] It is more frequent in young adults aged between 20 and 40 years. There is a greater prevalence in males (3:1), Caucasians, and HLA-B27 positive individuals.[2,3] The HLA-B27 antigen is strongly correlated with the appearance of the disease, and a positive test for this marker is found in 80–98% of cases.[4] It is a progressive disease which, over time, causes the patient's quality of life to deteriorate. In advanced stages, it may lead to complete spinal ankyloses, known as "bamboo spine", and extreme reduction of mobility. Even in the initial stage of the disease, inflammatory lumbar pain may cause significant morbidity in the patient, complicating daily activities and even requiring temporary leave from work duties. Many patients suffer from the progressive loss of their capacity to work, which may result in early retirement, generating additional costs to the public welfare system.[5,6]

The introduction of anti-TNF (anti-tumour necrotic factor) pharmaceuticals to treat AS in 2006 guaranteed patients better quality of life thanks to the efficacy of these medications in lessening symptoms and the progression of the disease. Despite the efficacy and safety these medications provide, their high costs greatly impact health budgets in countries where these drugs were implemented. Various studies of cost effectiveness have been conducted in an attempt to assess differences between the anti-TNF therapies.[7–9]

Because this incapacitating disease requires a team approach from multiple professionals, various treatment modalities for continuous periods of time, and can lead to the loss of labour capacity in a young population, it is necessary to measure its socio-economic impact. International studies of the direct and indirect annual costs of AS have indicated a value of approximately 10 thousand euros per patient.[10,11]

The last Brazilian study intended to demonstrate the direct and indirect costs in AS patients was published in 2010, and demonstrated significant differences between the domestic and international situations. The domestic cost was estimated at U$4597 per patient/year. This value was low in comparison with the findings of international studies that had been published up to that point.[12] However, the Brazilian study was conducted before anti-TNF-alpha medications had been fully introduced into the Brazilian public health system (the Sistema Único de Saúde, or SUS). During the study period, anti-TNF medications were utilised by 13% of AS patients, representing 80% of medication costs.[12]

Table 1 – Clinical and demographic data of ankylosing spondylitis patients treated at HC-UFPR Spondyloarthritis outpatient clinic.

Data	Men (70)	Women (23)	Total
Age (years) mean (SD)	44.55 (10.61)	41.52 (10.70)	43.80 (10.66)
Mean disease time in years (SD)	9.76 (7.22)	6.39 (7.32)	8.92 (7.36)
Ankylosis (%)	45 (64.28)	14 (60.86)	59 (63.44)
Sacroiliitis (%)	63 (90)	19 (82.60)	82 (88.17)
HLA-B27+ (%)	48 (68.57)	19 (82.60)	67 (72)
Mean BASDAI (SD)	4.64 (2.52)	5.49 (2.41)	4.86 (2.49)
Mean BASFI (SD)	5.03 (2.86)	6.35 (2.66)	5.36 (2.84)
Use of anti-TNFα drugs (%)	45 (64.28)	14 (60.86)	59 (63.44)
Mean ASQoL (SD)	12 (5.58)	13 (3.95)	10.57 (5.25)
Education (%)			
<9 years	25.7	43.4	30.1
9–12 years	42.8	26	38.7
>12 years	31.4	30.4	31.1
Individual income (%)			
<1 Salary	23.8	59	31.8
1–3 Salaries	58	31.8	51.6
3–5 Salaries	14.4	9	13
>5 Salaries	4.3	0	3

ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; TNF, tumour necrotic factor.
Data with normal distribution were expressed in mean and standard deviation. Non normal data were expressed in median and 25–75 percentile.
The minimum wage used as reference is U$ 306.40.

The objective of this study was to describe the use of public resources to treat AS in a tertiary hospital after the use of biological medications was approved for treating spondyloarthritis in the SUS, establishing approximate values for the direct and indirect costs of treating this illness in Brazil.

Materials and methods

We describe a transversal study of a sample of 93 patients selected from the outpatient spondyloarthritis clinic at the Universidade Federal do Paraná (UFPR) – Hospital de Clínicas between September 2011 and September 2012. The inclusion criteria were being diagnosed with AS for at least a year according to modified New York criteria, fulfil the ASAS 2009 classification for axial spondyloarthritis and being older than 18 years old. Patients who present malignancies, acute infections and other rheumatologic and autoimmune diseases were excluded from the study.

Before an outpatient clinic visit each patient answered a questionnaire about its demographical and economical status, clinical story, pensions and welfares received, considering the previous twelve months. Disease indexes such as BASFI (Bath Ankylosing Spondylitis Functional Index), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), and ASQoL (Ankylosing Spondylitis Quality of Life) were also assessed at this moment.

The direct costs are defined as the sum of all resources spent to directly treat and manage AS patients.[13] The National Health System provides most of the care without any payment including medical care, medications, laboratory and radiologic exams and physical therapy. Equipment and home adaptations were also classified in direct costs regard its importance in the management of the disease despite being a private spend. Indirect Costs are all the resources spent by the

Brazilian government with welfares, disease pensions and retirement due incapacity resulted from AS.

We performed a descriptive analysis of the direct costs obtained according to the Brazilian health system cost table which applied to the period of 2012.[14] The cost findings were converted from brazilian real into dollar using the exchange rate from the last day of September 2012 (U$ 1 = R$ 2,03), when the study period ended.

The indirect costs estimation took in consideration sick leaves and retirements resulted from the disease. The total amount was calculated based on the national minimum wage for that period, which was U$ 306.40.[15]

The patients were informed about the objective of the study and signed the Free and Informed Consent Agreement. The study was approved by the Ethics Committee of the Universidade Federal do Paraná – Hospital de Clínicas.

Results

Of the 93 patients with ankylosing spondylitis 70 (75.28%) were male and 23 (24.72%) female. The mean age was 43.95 years, and included individuals between 21 and 69 years of age. The duration of the disease was calculated based on the age of diagnosis, and the mean was 8.92 years (standard deviation: 7.32); 63.44% were using anti-TNF drugs. Comparing male and female patients the mean BASDAI was 4.64 and 5.49 while the mean BASFI was 5.03 and 6.35 respectively; 83.4% of the sample received less than three salaries as individual income. Other demographic and clinical data are exposed in Table 1.

The data related to the costs of complementary examinations are summarised in Table 2, and the data pertaining to spending on medications is outlined in Table 3. The total cost with medication is U$ 1.926,429,24, with anti-TNF

Table 2 – Complementary examinations conducted in the last 12 months on patients with AS who were monitored by the HC-UFPR spondyloarthritis outpatient clinic.

Complementary examinations	N° of exams conducted	Unit cost	Total cost	Cost per patient
Hemogram	372	3.36	1253.43	13.477
ESR (sedimentation rate)	372	1.34	500.27	5.37
CRP (C-reactive protein)	372	4.55	1695.07	18.22
Bilirubins	197	0.99	195.05	2.09
Liver transaminases	197	1.98	390.11	4.19
Tuberculin (PPD)	27	0	0	0
anti-HBs	27	9.13	246.72	2.65
HbsAg (Hepatitis B Surface Antigen)	27	9.13	246.72	2.65
anti-HCV	27	9.13	246.72	2.65
X-rays	165	4.92	812.80	8.73
Computer Tomography	24	49.80	1195.27	12.85
Magnetic resonance image of sacroiliac joint	16	132.38	2118.22	22.77
Shoulder ultrasound	4	11.92	47.68	0.51
HLA-B27 test	34	–	–	–
Echocardiogram	1	19.67	19.67	0.21
Analysis of synovial fluid	1	1.82	1.82	0.01
Total	1863		8969.62	96.44

Average price calculated from the most commonly requested images. Values are shown in dollar.

representing 97.96% (1.887,131,43), NSAIDs 0.58% (11.249,84) and DMARDs 1.09% (21.131,2) of this amount.

The direct costs are reported in Table 4 and indirect costs in Table 5.

The total cost for the sample was U$ 2,156,070.83/year, representing U$ 23,183.56 per patient/year.

Discussion

In Brazil, there is a scarcity of studies that evaluate the impact of the costs of treating patients with ankylosing spondylitis. Furthermore, although this was not our objective, we noted that studies of cost effectiveness related to AS are almost non-existent compared to the proportion of studies in European countries and the United States. This is the first study conducted in Brazil that assesses the costs of AS after the full

Table 3 – All drugs prescribed for treatment of ankylosing spondylitis during an one year period.

Medication	Number of patients using the drug	Total cost of medication/year
Adalimumab	28	884,947.41
Infliximab	17	423,234.71
Etanercept	14	578,949.31
Methotrexate	13	974.64
Leflunomide	2	1226.50
Sulfasalazine	30	18,930.06
NSAIDs	70	11,249.84
Prednisone	13	1013.60
Other drugs	30	5903.17
Total		1,926,429.24

Values are shown in dollar. Other drugs include Omeprazole, Folic Acid, Codeine, Cyclobenzaprine and Amitriptyline.

introduction of biological medications by the SUS for treatment of this affliction.

The study sample was mainly composed of men and the mean age was 44 years. The mean disease duration was approximately 9 years, differing from the results found by Torres, which was 16 years.[12]

The mean BASFI functional score was 5.36, and the BASDAI was 4.86, similar values to those found by Torres (BASFI = 5 and BASDAI = 4), suggesting a similar sample with relation to functional state and disease activity. As for quality of life, the mean ASQoL score was 10.57, also higher than the findings by Torres (ASQoL = 8); nevertheless, as this index has not yet been validated in a Brazilian Portuguese version, comparisons may be controversial.

The total number of complementary examinations requested for the group was 1863. The most commonly requested tests were laboratory evaluations, principally hemograms, ESR, CRP, liver enzyme panels and bilirubins, used to assess disease activity and to monitor the side effects of immunosuppressant therapy. The costs spent on imaging accounted for 46.8% of total examination costs, compared with the 56% obtained by Torres. Although this author did not conduct more expensive tests such as computer tomography (CT) and nuclear magnetic resonance (NMR), that study described greater utilisation of examinations such as X-rays and bone density scans.[12]

Only 16 NMRs were ordered, despite the growing importance of this test to the early diagnosis of the disease, principally for diagnosing axial spondyloarthritis according to ASAS classification when no alterations are evident in conventional radiography imaging of the spinal column or the sacroiliac joint.[16] However, the patients selected had had their diagnosis well established for at least one year prior to the study. As both of the facilities where the studies were conducted are very similar (tertiary public university hospitals), we can observe that the utilisation of this test has grown,

Table 4 – Total direct costs related to treatment of ankylosing spondylitis patients during an one year period.			
	Total cost	Percent of direct costs	Total cost per patient
Direct costs			
Anti-TNFα	1,887,131.43	96.21	20,291.74
Other drugs	39,297.80	2.00	422.56
Medical consultations	1832.51	0.09	19.70
Physical therapy	2424.71	0.12	26.07
Complementary examinations	8969.63	0.46	96.45
Adaptations	20,714.28	1.06	222.73
Equipment	1133.99	0.06	12.19
Total	1,961,504.34	100.00	21,091.44
Values are shown in dollar.			

contributing to the increase in the direct costs of diagnosing and treating the disease.

Non-steroidal anti-inflammatories were the most widely used medications in this study; however, the cost of these medications corresponds to approximately 0.6% of the total spending on medications. The second most widely used class of medications was the biologicals, corresponding 63.44% of the sample. The cost of these drugs corresponded to 97.96% of the spending on medications and 87.53% of the total cost of treatment. The larger proportion of spending on biological medications had already been observed in Brazil; in that sample, only 13.33% of the sample used biological medications but these were responsible for 80% of drug spending and 74% of the total cost.[12] Our objective was not to compare the costs of different biological therapies, as this is the subject of a study currently underway at the same facility.

Physical therapy was responsible for a small increase in costs, US$ 26.00 per person, which demonstrates a small degree to which this therapeutic resource is used.

Only 14 patients reported costs related to adapting their residences, representing only 1% of direct costs of the disease. Nevertheless, this number may not correspond to reality, as it depends on the subjects' memories. Costs related to transportation were not obtained due to the degree of difficulty associated with the sample subjects providing this information in retrospect; however, Torres reported in his study that these costs could represent around 2% of direct costs and 1% of total costs.[12]

Indirect costs associated with retirement and sick leave constitute 8.9% of total costs. As the disease primarily affects young people in the productive age ranges, inability to work is one of the factors that contributes to the increase in total costs. Nearly 59% of the sample was retired or on leave from work as a result of the disease, which is similar to the findings by Torres (56%).

In the current study, total annual costs to treat 93 patients with AS reached a total of US$ 2,156,070.83 dollars/year and a mean value of US$ 23,183.56/patient/year, while Torres's study found a total of 4597.00/patient/year. An increase in the cost of treating AS patients in Brazil over the last three years was found, particularly as a result of the addition of anti-TNF agents to the therapeutic arsenal in treating spondyloarthritis.

The direct costs were US$ 1,961,504.34, corresponding to 90.9% of total costs, while indirect costs were US$ 194,566.49, corresponding to only 9.1% of total costs. This data indicates a divergence from the data generated by Torres's study, which found direct costs of 45% and indirect costs of 55%, despite the fact that the total number of retired patients and patients on leave were similar in both studies. The result we obtained was principally due to the higher costs of treatment with anti-TNF agents, which are now used on a larger scale in Brazil.

The introduction of new medications based on the recommendations of the ASAS group and the Brazilian Society of Rheumatology since 2006 have revolutionised the treatment of people with axial spondyloarthritis.[16–19] Patients with AS are prescribed anti-TNF medications after the failure of at least two non-steroidal anti-inflammatories (NSAIDs) over a period of three months, without the need to use disease-modifying antirheumatic drugs (DMARDs) beforehand, according to the Brazilian public health system (SUS) protocol.[20] Consequently, there is an earlier use of these biopharmaceuticals in AS compared with other diseases such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA) with peripheral manifestations, for example, in which it is necessary to demonstrate the therapeutic failure of at least two DMARDs.

In Brazil, three anti-TNF medications are available for treating AS patients in the public health system. In our sample,

Table 5 – Total indirect costs related to treatment of ankylosing spondylitis patients during an one year period based on human capital approach.			
	Number of patients (% of total number)	Total cost	Cost per patient
Retirement due to AS	51 (54.83%)	184,761.57	3622.78
Sick leave due to AS	4 (4.30%)	9804.92	2451.23
Unemployed	8 (8.6%)[a]		
[a] 21.05% of the non-retired patients who were not on sick leave. Values are shown in dollar.			

none of the patients had the financial resources to pay for their treatment themselves, considering the mean individual and household income of each, as well as the fact that they also did not have access to private health plans. Furthermore, during the period this data was being collected, it was rare to find cases of AS patients being treated by the private health care system.

Due to the increase in the incoherent costs of treatment with anti-TNF agents, cost effectiveness studies have been conducted. Studies by Kobelt et al.[8,9] indicate that infliximab is cost-effective and its use is justified by the increase in quality of life and the reduction of the costs of the disease; at the same time, Boonen et al.[10] propose the need to identify the patients in which treatment with infliximab and etanercept will be effective and cost-effective because of the high costs associated with treatment with biologicals. At this present time, there have been no studies of cost-effectiveness in Brazil.

Brazil has few studies about the socio-economic and financial impact of rheumatologic diseases. Due to the large expanse of the country and especially inequalities in accessing diagnostic procedures and therapies, the cost projections should not be generalised.

We also believe that, with regard to the increase in direct costs associated with AS, the overall scene encountered in South America should not differ from the findings in Brazil, as the majority of countries on the continent have incorporated anti-TNF therapy into the treatment of AS patients.

It is important to stress that studies of the impact on quality of life have reinforced the need for more effective participation by other health professionals in the monitoring and treatment of patients with AS, and this also could be responsible for a partial increase in costs.[21,22]

An additional limitation of our study is that although the authors believe that the clinical and epidemiological characteristics of the patient sample are representative of the other patients served by the SUS, our study tracked a sample served at a university hospital located in a large state capital in Brazil, a city where access to more expensive health technologies such as nuclear magnetic resonance imaging has been easier in relation to the challenges faced by patients in other SUS hospitals in more remote locations throughout Brazil.

Conclusions

The Brazilian public health system's spending related to ankylosing spondylitis has increased in recent years. An important part of these costs is due to the introduction of new, more expensive health technologies, as in the case of nuclear magnetic resonance and, principally, the costs resulting from the incorporation of anti-TNF biological therapy into the therapeutic arsenal. The mean annual direct and indirect cost to the Brazilian public health system to treat a patient with ankylosing spondylitis, according to our findings, is US$ 23,183.56.

Conflicts of interest

The authors declare no conflicts of interest.

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