Assessing the functional status and quality of life of patients with rheumatoid arthritis

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ABSTRACT

Objectives: To assess the impact of Rheumatoid Arthritis (RA) on functional working status, and health-related quality of life (HRQL) of patients. **Methods:** This is a descriptive study with 53 patients from a public rheumatology center in Montevideo, Uruguay. A series of instruments were used to assess pain, functional impairment, HRQL, and activity level: P-VAS (Pain Visual Analogue Scale), G-VAS (Global Status Visual Analogue Scale), HAQ (Health Assessment Questionnaire), SF-12 (Medical Outcomes Study Short Form 12), and DAS 28 (Disease Activity Score). Linear regression coeficients, *t* test, and ANOVA were used to investigate the associations among several independent parameters and the HRQL. Correlations between the assessments of general well-being made by physicians and patients were studied using the intraclass correlation coefficients (ICC). **Results:** High levels of disease activity (41.5%, severe activity; 26.5%, low activity or remission), severe pain (60%), and impact on global health status (median G-VAS 40, range: 0-100) were observed. More than 70% of the patients had HAQ rates indicating moderate to severe disability. The SF-12 PCS (Physical component Summary) had mean scores of 31.5 points (range 15.2- 59.5; SD=10.1) while those of the MCS (Mental Component Summary) were 37.9 points (range: 15.7 – 66.4; SD=14.6). One or more years of disease evolution and the level of activity were determining factors of HRQL scores. **Conclusions**: The study showed that RA is associated with higher disease burden, reflected on pain, impact on global health, and functional and working status, as well as the physical and emotional dimensions of the HRQL. The need for changes in the treatment of this psychologically vulnerable group of patients is paramount.

Keywords: rheumatoid arthritis, quality of life, functional status, SF-12, HAQ.

INTRODUCTION

Rheumatoid Arthritis (RA) is a complex disease that generates articular inflammation and structural damage, leading to physical and work-related disabilities, which is associated with elevated social-economic costs. It has been reported that patients with RA stop working 20 years earlier than expected,[1] and their quality of life is extremely compromised. The use of biological agents faces the challenge of reducing the consequences of this disease.

Clinical indicators and questionnaires to assess the functional capacity and quality of life are available for the clinical evaluation of patients with RA and their response to different treatments.[2-4] Health-related quality of life (HRQL) is an evaluation, by the patient, of the impacts of the disease and treatments on different physical, functional, emotional, social, and spiritual dimensions.[5-9]

The objective of the present study was to evaluate the work and functional status, as well as the quality of life of patients with RA to establish strategies and reduce the impact of the disease.

METHODS

Patients

This is a transversal descriptive study of patients with RA, 18 years or older, seen at a specific clinic of the National Rheumatology Institute (INRU, from the Spanish) of the Health Services Administration and hospitalized patients between

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September 2007 and March 2008. Patients included in this study fulfilled ACR classification criteria for RA[10]. Patients with the diagnosis of connective tissue disease and overlapping syndromes were excluded. This study was approved by the institution, and patients signed an informed consent.

Evaluation tools

The following tools were used:

Pain Visual Analogue Scale (P-VAS). This is a unidimmensional scale in which pain intensity receives scores ranging from 0 to 100 mm. Scores lower than 34 indicate "mild pain", from 35 to 67 "moderate pain", and higher than 67 "severe pain".[11]

Global Visual Analogue Scale (G-VAS). A scale from 0 to 100 mm was used to evaluate the perception of the patient of his/her general status in the previous week.[12]

Health Assessment Questionnaire (HAQ). This tool, developed by James F. Fries *et al.*,[13,14] is one of the first self-reports of the functional status (and disabilities), and has become an obligatory tool in clinical assays of RA.[15] The Disability Index (DI) provided is evaluated in eight categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities of daily living. For each category, the patient indicates the degree of difficulty in four possible answers ranging from "without any difficulty=0" to "unable to do=3". It also includes a questionnaire on the use of devices or aids necessary to perform those eight categories. The score for each item is represented by the highest number within each one. The mean score of the eight items represents the final HAQ score.[16]

Medical Outcomes Study Short Form 12 Health Survey (SF-12) version 1. The short form of the Medical Outcome Study SF-36, the SF-12, is the HRQL assessment tool used more often.[18-20] It is composed of 12 items derived from the eight dimensions of the SF-36: Physical functioning (2), Social functioning (1), Role-Physical (2), Role-Emotional (2), Mental Health (2), Vitality (1), Bodily Pain (1), and General Health (1). The answer options compose Likert-type scales that evaluate the severity or frequency. The SF-12 version 1 only provides the scores of the Physical Component Summary (PCS) and Mental Component Summary (MCS). Those summaries constitute the mean scores of the different items. To facilitate the interpretation, those scores are standardized along with the values of the norms of the population, in which 50 (standard deviation of 10) is the mean of the general population. Since norms for the Uruguayan population for SF-36 or SF-12 do not exist, the norms of the Spanish population were used. Documented punctuation algorithms and available software were used to recodify the items and for punctuation scales.[21] The abbreviated version has several advantages, such as: reduction in the answer time and decreased filling burden for patients, while maintaining the psychometric properties and correlation with the values of the punctuation summary of the SF-36.[22] Both instruments have been validated in Uruguay.[23]

Questionnaires were answered privately by each patient in the waiting room, in the case of clinic patients, and on bed, for hospitalized patients.

Sociodemographic data were also recorded. The Graffar index was used to stratify social classes.

Biomedical data were recorded by the attending physician, including disease evolution, extra-articular manifestations, rheumatoid factor (RF), erythrocyte sedimentation rate (ESR) in the previous month, remission-inducing treatment, and use of corticosteroids. A homunculus, in which the physician could indicate swollen and painful joints, as well as a version of the G-VAS for the physician, were included.[12]

The Disease Activity Score 28 (DAS 28)[24] was used to calculate disease activity in a computer software. According to the results obtained, patients with scores lower than 2.6 were considered in remission; between 2.6 and 3.2, low activity; from 3.3 and 5.1, moderate activity; and higher than 5.1, high activity.

Statistical analysis

The association among the different biological and sociodemographic variables, the degree of disability, and the HRQL was investigated through univariate analysis using linear regression coefficients, to compare continuous parameters, and the *t* test and ANOVA (with Schefée comparison), for dichotomic and polytomic categorical parameters, respectively.

The concordance between patient and physician G-VAS was also investigated using the intraclass correlation coefficient (ICC).

In all cases, the level of statistical significance of $P < 0.05$ was established.

RESULTS

Sixty-four patients were enrolled in this study; 11 (17%) were excluded because their questionnaires were incomplete. Fifty-three (83%) patients were included in the analysis. Table 1 shows the sociodemographic characteristics of the study population. Note that the majority of the patients had a low cultural level, were unemployed or had a low-level occupation, and they came from low economic classes. Among them, 66% (n = 35) referred being unemployed because of the disease.

Mean disease duration was 9.8 years (range: 1-31 years; SD = 7.2). Table 1 also shows the clinical characteristics, as well as the treatment at the time of the study. Patients on prednisone were receiving less than 20 mg/day. None of the patients in this study were treated with biological agents.

Table 2 shows the results of the clinical features. A high percentage (60%, n = 32) of the patients had P-VAS equal or greater than 67 mm, i.e., severe pain. An important difference was observed in the mean G-VAS reported by the physicians and patients, with worse evaluation of the general status by the latter. On the other hand, mean ICC was 0.48 (95% CI = 0.24-0.66; $P < 0.000$), which corresponds to a moderate correlation.

The mean DAS 28 was 4.68 (median 4.7; range: 1.74-7.92; SD = 1.79). Table 3 shows the patient distribution according to DAS 28. Only 26.5% (n = 14) of the patients were on remission or showed low disease activity (DAS 28 equal or lower than 3.2), 32% (n = 17) had moderate diseases activity, and 41.5% (n = 22), severe activity.

Functional capacity and quality of life

According to the HAQ, functional analysis (Table 3) showed a mean of 1.56 (range: 0-3; SD = 0.86); 77.3% of the patient had moderate or severe disease.

As for HRQL, the Physical Component Summary (PCS) had a mean value of 31.5 points (range: 5.2 - 59.5; SD = 10.1). Approximately 56.6% (n = 30) of the patients had scores lower than two standard deviations (SD). The mean Mental Component Summary (MCS) was 37.9 (range: 15.7-66.4; SD = 14.6), and 32.2% (n = 17) of the patients had scores lower than 2 SDs. This indicates a severe deterioration of the quality of life in a large proportion of the patients, both in the physical and emotional dimensions.

The association among quality of life and clinical and sociodemographic variables was determined. Simple linear regression showed negative coefficients, which were statistically significant for P-VAS and G-VAS with both components of the SF-12 (Table 4).

ANOVA showed significant differences in mean PCS ($P = 0.001$) and MCS ($P = 0.018$) scores among patients with the disease for one year or more (Table 5). Significant differences were also observed in mean PCS in relation to greater levels of disease activity measured by the DAS 28; the same was not seen in MCS scores (Table 5). Table 5 shows the differences in mean PCS and MCS scores according to the different HAQ groups (mild, moderate, severe), indicating an association

Table 1
Socio-demographic and clinical characteristics of the study population

	n	%
Gender		
Female	47	88.7
Age		
Mean 51.9 years (SD=12)		
Schooling		
Incomplete primary	13	24.5
Complete primary	18	34
Incomplete secondary	8	15.1
Complete secondary	4	7.5
Technical	10	18.9
University	0	0
Working status		
Unemployed	35	66
Non-specialized worker	8	15
Specialized worker	3	5.7
Administrative	1	2
Retired	6	11.3
Social class according to the Graffar scale		
I Upper class	0	0
II Upper middle class	1	1.9
III Middle class	4	7.5
IV Lower middle class	23	43.4
V Lower class	25	47.2
Income of unemployed patients (n = 35)		
Disability pension	10	28.6
Emergency plan	1	2.8
No income	24	68.6
Positive rheumatoid factor	40	75.5
Type of disease onset		
Polyarthritis syndrome	44	84.0
Monoarthritis	5	9.4
Coxofemoral manifestation	5	9.4
Extra-articular manifestations		
Subcutaneous nodes	15	28.3
Sjögren syndrome	6	11.3
Pulmonary involvement	4	7.5
Vasculitis	1	1.9
Patients treated with DMARDs		
Methotrexate	37	69.8
Leflunomide	17	32.1
Hydroxichloroquine	6	11.3
Sulfasalazine	2	3.8
Combined treatment	13	24.5
Patients treated with Prednisone		
	39	74.0

DMARDs: Disease-Modifying Anti-Rheumatic Drugs.

Table 2
Evaluation of the Clinical Parameters of RA Patients

	Mean ± SD (range)
P-VAS mm	68.7 ± 34.6 (0 – 100)
G-VAS (patient) mm	66.4 ± 36 (0-100)
G-VAS (physician) mm	36.5 ± 24.3 (0-90)
ESR mm	35.8 ± 27.4 (7-120)
Swollen joints	3.2 ± 4.9 (0-19)
Painful joints	7.2 ± 9 (0-28)

P-VAS: Pain Visual Analogue Scale; G-VAS: General Status Visual Analogue Scale; ESR: Erythrocyte Sedimentation Rate.

Table 3
Disease Activity, According to DAS 28, and Degree of Disability, According to HAQ (n=53)

	%	n
DAS 28		
Remission (<2.6)	19.0	10
Low Activity (2.6-3.2)	7.5	4
Moderate Activity (>3.2 - 5.1)	32.0	17
Severe Activity (>5.1)	41.5	22
HAQ		
Mild disability (HAQ de 0 a 1)	22.7	12
Moderate disability (HAQ>1 a 2)	39.6	21
Severe disability (HAQ>2 a 3)	37.7	20

DAS: Disease Activity Score; HAQ: Health Assessment Questionnaire.

Table 4
Correlation among Pain, Global Disease Evaluation by the Patient, and Quality of Life

	P-VAS	G-VAS
PSC	Beta - 0.6 P < 0.001	Beta - 0.60 P < 0.001
MSC	Beta - 0.48 P < 0.001	Beta - 0.43 P = 0.001

P-VAS: Pain Visual Analogue Scale; G-VAS: Global Status Visual Analogue Scale; PCS: Physical Component Summary; MCS: Mental Component Summary; Beta: Standardized Linear Regression Coefficient

Table 5
Differences in SF-12 Scores of the Different Clinical Group

		PCS	MCS
Time since the diagnosis	**n**	**Mean ± SD**	**Mean ± SD**
1 year or less	4	46.9 + 10.8	53.9 ± 8.6
> de 1 year	49	30.3 ± 9.0	36.6 ± 14.3
P**		.001	.018
DAS 28			
< 2,6	10	41.3 ± 12.3	46.3 ± 14.3
2,6 – 3,2	4	39.2 ± 12.2	45.2 ± 13.4
> 3,2 – 5,1	17	29.3 ± 6.55	35.4 ± 13.2
> 5,1	22	27.4 ± 7.3	34.7 ± 15.0
P*		0.000	NS
Differences among subgroups *		(< 2.6) and (2.6 – 3.2) > (> 3.2 – 5.1) and (>5.1)	
HAQ			
0-1	13	42.5 ± 11.5	46.7 ± 14.1
> 1 – 2	24	30.9 ± 6.15	36.6 ± 14.9
> 2 – 3	16	23.6 ± (4.1	32.9 ± 12.1
P*		0.000	0.03
Difference among subgroups*			
		0-1 > 2 > 3	0-1 > 2.3

*Scheffé comparisons; the symbol > separates groups with significantly higher scores from those with lower scores; ** t test for independent parameters. Significant P < 0.01; HAQ: Health Assessment Questionnaire; HAQ 0-1 Mild disability; >1 -2 Moderate disability; >2-3 Severe disability; DAS 28: Disease Activity Score; DAS 28: Remission: <2.6; Low activity: 2.6 – 3.2; Moderate activity: >3.2 – 5.1; Very active disease: >5.1; PCS: Physical Component Summary; MCS: Mental Component Summary.

among functional deterioration and the physical and emotional components of the HRQL.

Differences in HAQ, PCS, and MCS regarding gender, age, and cultural level were not observed.

DISCUSSION

Patients with RA were investigated to evaluate the impact of the disease on functional capacity and quality of life in order to improve therapeutical interventions.

The majority of the patients in this study had low socioeconomic level and schooling. More than half of the patients had attended only primary school, often incomplete, and, for this reason, they worked as maids or in construction. Those jobs require an elevated level of manual dexterity and physical strength and, for this reason, they lose their jobs in the first years of the disease, without possibility of being relocated or reinserted in other jobs. This explains the high level of unemployment (66%) of the study population, in which the majority of the patients were of working age. This is in agreement with the findings of Bjork *et al.*[25], who observed a 70% reduction in hand function in women with RA, at the initial stages of the disease, and 50% during evolution, when compared to women without hand pathologies, explaining the high incidence of loss of manual labor.

In this study, clinical indicators of pain, global disease assessment, activity, functionality, and quality of life were useful in quantifying the burden of RA on patient functioning and well-being.

As a rule, patients with RA reported a significant reduction in functional capacity, measured by the HAQ, and in the physical and mental components of quality of life, measured by the PCS and MCS scales of FS-12, when compared to the general population. Comparison with other chronic disorders showed that the impact of RA documented in the present study should be considered clinically significant.[26]

Sixty per cent of our patients reported severe pain, indicating the need for more specific analgesic measures, since this is a disease in which pain management is considered an integral component of remission.

The difference between the impacts on general status (G-VAS) reported by the patient and by the physician is impressive, being significantly greater according to the patients. It is known that psychosocial factors, besides disease related factors, influence the perception of pain and general well-being, indicating the importance of patient-based evaluations to determine the results of the treatment.[27]

Many patients had moderate to elevated activity index, which is impressive since all patients were followed-up only by rheumatologists. This could be linked to the following factors:

1) "Weaknesses" of the activity indicator. Patients with any comorbidity (for example, incapacitating lumbago or fibromyalgia) reported severe pain and great disease repercussion on the general status (G-VAS), with scores close to 100, even in the absence of painful or swollen joints. High scores are obtained when calculating the DAS 28.

2) The treatment of some of those patients might not have been optimal, failing to achieve adequate control of inflammation. We observed that only one fourth of the patients received combined treatment with two or three remission-inducing drugs and none of the patients were on biological agents. This can be explained by the fact that only recently, from January 2009 on, those agents were incorporated in the treatment of patients in governmental health services.

3) Non-compliance with the medical treatment regarding the dose of the drugs, as well as irregular control secondary to problems related with information or health care barriers, such as lack of economic resources to attend medical appointments.

The present study observed higher HAQ scores than those reported by other authors in descriptive studies, which could be explained by the low socio-economic level and schooling, leading to the speculation that those are the main risk factors for disability. This means that lower schooling is related with higher HAQ scores.[27-29] In the present study, we did not observe statistically significant differences in mean HAQ scores according to the cultural level, which is probably due to the homogeneity of the cohort.

It is known that an elevated HAQ at the onset of the disease represents a poor prognostic factor for work disability.[29] A deficient socio-cultural environment would have a higher impact on RA-related disability than factors determined by the disease itself. This occurs because patients have little access to sanitation and, in some occasions, they do not follow medical recommendations properly due to the lack of understanding and lack of knowledge about the disease.[28-30]

Several investigators stated that elevated P-VAS and HAQ scores (especially at the onset of the disease) should be considered alarming signs, and that more aggressive treatments should be instituted to avoid disabilities in future years[27]. Therefore, early combined therapy would represent a protection against disability, keeping the patient at work for a longer time.[27]

An important deterioration in quality of life regarding the health of those patients, reaching both components, but greater in the physical component, was also observed. The scores of the PCS and MCS subscales of the SF-12 of patients with RA in the present study are identical or even worse than those of patients on renal substitutive therapy and Parkinson disease in Uruguay.[23]

Quality of life, represented by both components, physical and mental, of the SF-12, was worse in patients with greater pain, G-VAS, and functional disability. Patients with very active disease reported worse quality of life in its physical component.

This study has limitations that do not allow generalization of the results to the population of RA patients in Uruguay. It involved a small population belonging to only one public center in Montevideo, selected by convenience, and homogenous regarding socio-demographic and schooling characteristics. However, this is the first study of this type in the country and its results represent a good starting point to better understand the impact of the disease in this group of patients, who are especially vulnerable, requiring implementation of more health resources to relieve the high disease burden.

Similarly, it establishes the basis to implement studies with larger populations, with greater variability of biological, socio-economic, and cultural factors, to evaluate the efficacy of therapeutic interventions, not only from the biological perspective, but also including patient evaluation of his/her degree of disability and quality of life. Besides, it is a contribution to the Latin-America rheumatologic community, since this type of study has not yet been undertaken in our continent.

Regarding the functional deterioration and quality of life, with the consequent loss of employment, symptomatic load with severe pain, and elevated levels of disease activity were detected in this population, there are several measures regarding medical assistance, according to international treatment guidelines and considering the resources available in our health system, whose implementation should be considered to reduce the degree of disability generated by RA:

1) Permanent education, maintaining good physician-patient relationship, especially for those patients with low cultural levels, to achieve greater understanding, compliance with the treatment, and clinical control.

2) Application of a minimal set of clinical measurements and self-reported questionnaires (P-VAS, G-VAS, DAS 28, HAq, and SF-12) throughout follow-up and in the control of the treatment to complement medical observation.

3) Those patients with elevated HAQ, P-VAS, G-VAS, and DAS 28 from the onset should undergo more aggressive treatment with combination of remission-inducing drugs that follow international protocols to decrease the incidence of the structural damage and preserve function.

4) An early consultation with the physical therapist for work therapy and advice on joint-preserving actions related with the work of the patient to keep the patient at work as long as possible.

CONCLUSIONS

In the present study, it is patent the huge burden of RA on function and quality of life of patients, generating a high level of unemployment. We stress the importance of the symptomatic control, especially pain. The assessment of the degree of functional impact by physicians and patients do not coincide, indicating the need of the evaluation of the treatment by the patient to improve results. We suggest that an aggressive and global focus on the patient should be from the onset of the disease on to help improve the vital and functional prognosis of our patients.

REFERÊNCIAS

REFERENCES

1. Woolf A, Pfleger B. Burden of mayor musculoskeletal conditions. Bulletin of the World Health Organization 2003; 81(9).
2. Van Riel P, Shumacher H. How does one assess early rheumatoid arthritis in daily clinical practice? Best Pract Res Clin Rheumatol 2001; 15(1):67-76.
3. Pincus T. Advantages and limitations of quantitative measures to assess rheumatoid athritis. Bull NYU Hosp Jt Dis 2006; 64:1-2.
4. Van Riel P, Franse J. DAS 28: a useful instrument to monitor infliximab treatment in patients with rheumatoid arthritis. Arthritis Res Ther 2005; 7:189-90.
5. Aaronson N. Quality of Life Research in Cancer Clinical Trial: A Need for Common Rules and Language. Oncology 1990; 4(5):59-66.
6. Calman K. Definitions and Dimensions of Quality of Life. In: N.K. Aaronson and J.H. Beckmann (eds.). The Quality of Life of Cancer Patients. New York: Raven Press, 1987.
7. Cella D, Tulsky D. Measuring Quality of Life Today: Methodological Aspects. Oncology 1990; 4(5):29-38.
8. Guyatt GH, Feeny DH, Patrick D. Measuring Health-Related Quality of Life. Ann Intern Med 1993; 118(8):622-9.
9. Patrick DL, Erickson P. Health Status and Health Policy: Quality of Life in Health Care Evaluation and Resource Allocation. New York: Oxford University Press, 1993.
10. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS *et al*. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988; 31:315-24.
11. Bird SB, Dickson EW. Clinically significant changes in pain along the visual analog scale. Ann Emerg Med 2001; 38:639-43.
12. Pincus T, Sokka T. Quantitative measures for assessing rheumatoid arthritis in clinical trials and clinical care. Best Pract Res Clin Rheumatol 2003; 17(5):753-81.
13. Fries JF, Spitz P, Kraines G, Holman H. Measurement of Patient Outcome in Arthritis. Arthritis Rheum 1980; 23:137-45.
14. The Health Assessment Questionnaire Manual. Stanford University School of Medicine. Division of Immunology & Rheumatology. Disponible en [http://www.chcr.brown.edu/pcoc/EHAQDESCRSCORINGHAQ372.PDF] (Acesso em 12 de maio de 2008).
15. Ramey DR, Fries JF, Singh G. The Health Assessment Questionnaire. 1995 Status and Review. In B. Spilker Quality of Life and Pharmacoleconomics in Clinical Trials, 2nd ed. Philadelphia, Lippincott-Raven Publishers, 1996.
16. Bruce B, Fries J. The Stanford Health Assessment Questionnaire Dimensions and Practical Applications. Health Qual Life Outcomes 2003; 1:20.
17. Ware JE Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34:220-233.
18. Ware JE, Gandek B, and the IQOLA Project Group. The SF-36 health survey: Development and use in mental health research and the IQOLA Project. Int J Ment Health 1994; 23:49-73.
19. Alonso J, Prieto L, Ferrer M, Vilagut G, Broquetas JM, Roca J *et al*. For the Quality of Life in COPD Study Group: Testing the measurement properties of the Spanish version of the SF-36 Health Survey among male patients with chronic obstructive pulmonary disease. J Clin Epidemiol 1998; 51:1087-94.
20. Gandek B, Ware JE Jr, Aaronson NK, Alonso J, Apolone G, Bjorner J *et al.* Tests of data quality, scaling assumptions, and reliability of the SF-36 in eleven countries: results from the IQOLA project. J Clin Epidemiol 1998; 51:1149-58.
21. BiblioPro. Red IRYSS. IMIM, Barcelona, España. Disponible en [http://iryss.imim.es/iryss/PDFs/Descripcion_SF-12_BiblioPRO.pdf] (Acesso em 6 de março de 2008).

22. Dapueto JJ, Galain AI, Olaizola I, Schwartzmann L. Comparison or the SF-36 and SF-12 in dialysis patients in Uruguay. Disponible en [http://www.isoqol.org/2007mtgabstracts] The QLR Journal. A-60. Abstract #1181.
23. Galain AI, Dapueto JJ, Schwartzmann L. Evaluation of the SF-36 in Various Clinical Settings in Uruguay. 2006 International Society for Quality of Life meeting abstracts [http://www.isoqol.org/2006mtgabstracts]. The QLR Journal. A-68. Abstract #1543.
24. Prevoo MLL, van´t Hof MA, Kuper HH. Modified disease activity scores that include twenty-eigth-joint counts: developmentand validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995; 38:44-8.
25. Bjork M, Thyberg I, Haglund L, Skogh T. Hand function in women and men with early rheumatoid arthritis. A prospective study over three years (The Swedish TIRA project). Scand J Rheumatol 2006; 35:15-9.
26. Kosinski M, Kujawski SC, Martin R, Wanke LA, Buatti MC, Ware JE Jr *et al*. Health related quality of life in early rheumatoid arthritis: impact of disease in treatment response. Am J Manag Care 2002; 8:231-40.
27. Puolakka K, Kautiainen H, Mattonen T. Predictors of productivity loss in early rheumatoid arthritis: a year follow up study. Ann Rheum Dis 2005; 64:130-3.
28. Pincus T. Patient questionnaires and formal education as mores significant prognosis markers than radiographs or laboratory tests for rheumatoid arthritis mortality. Bull NYU Hosp Jt Dis 2007; 65(1):S29-S36.
29. Scott DL, Pugner K, Kaarela K. The links between joint damage and disability in rheumatoid arthritis. Rheumatology 2000; 39:122-32.
30. Helliwell P, O’Hara M, Holdsworth J. A 12-month randomized controlled trial of patient education on radiographic changes and quality of life in early rhematoid arthritis. Rheumatology 1999; 38:303-8.