ORIGINAL ARTICLE

Disease Activity Score on 28 Joints and Polypharmacy Are Independent Predictors for Health-Related Quality of Life Evaluated by INCAVISA in Patients With Rheumatoid Arthritis

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Objective: The aim of this study was to investigate the main factors associated to a diminished health-related quality of life (HRQoL) evaluated by INCAVISA (Health-Related Quality of Life Inventory for Latin American Patients) in patients with rheumatoid arthritis (RA).

Methods: Female, 18 years or older, RA (American College of Rheumatology 1987 criteria and American College of Rheumatology/European League against Rheumatism 2010 criteria) patients who attended the outpatient rheumatology department of the Hospital Civil "Dr. Juan I. Menchaca," Guadalajara, Mexico, matched with healthy controls were included. Patients with any known comorbidities or treatment with antidepressive drugs were excluded. Trained physicians performed the RA clinical evaluation and INCAVISA. All data were analyzed using SPSS 21.0 software (SPSS Inc, Chicago, IL); $P < 0.05$ was considered statistically significant.

Results: Patients with polypharmacy (≥ 3 drugs) had a lower HRQoL by INCAVISA. The number of drugs, total comorbidities, and DAS-28 (Disease Activity Score on 28 Joints) were negatively correlated with total INCAVISA. In multivariate analysis, DAS-28 and polypharmacy were independent predictors for a negative perception of HRQoL evaluated by INCAVISA in RA patients.

Conclusions: Disease activity and disability secondary to RA have a negative impact in the HRQoL. Other factors such as the number of drugs prescribed to these patients have been shown to be important for the negative perception of their HRQoL evaluated by INCAVISA.

Key Words: DAS-28, HRQoL, INCAVISA, polypharmacy, rheumatoid arthritis

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Rheumatoid arthritis (RA) as a chronic inflammatory disease may affect the quality of life (QoL). Current approaches to evaluate QoL in RA do not consider the complete spectrum of health-related QoL (HRQoL), which is defined as "how health conditions affect the patient's physical abilities and their development in emotional and social roles."[1,2] A complete evaluation of HRQoL should include physical abilities and emotional well-being. The clinicians' approach to RA patients' QoL will never be as accurate as the own patient's perceived well-being.[3]

The main causes that reduce QoL in RA patients are pain, disease activity, and disability.[4,5] In other chronic diseases, the presence of comorbidities, polypharmacy, and sociodemographic and psychological factors as perceived by the patient might diminish the QoL.[2,6] Little has been investigated about how these factors may affect the RA patient's perception on HRQoL.

The Inventory of Quality of Life and Health (INCAVISA) is an instrument designed for chronic diseases in the Latin American population to assess HRQoL in their specific biopsychosocial context (Table 1). INCAVISA has been used to evaluate HRQoL in diseases such as cancer, AIDS, hypertension, and diabetes,[7] but has not been used to evaluate HRQoL in RA.

The aim of this study was to investigate the main factors associated to a diminished HRQoL evaluated by INCAVISA in RA patients.

PATIENTS AND METHODS

This was a cross-sectional study of RA patients from the outpatient rheumatology service of the Hospital Civil "Dr. Juan I. Menchaca," Guadalajara, Jalisco, México. Inclusion criteria were as follows: female gender, 18 years or older, who met the 1987 American College of Rheumatology and 2010 American College of Rheumatology/European League against Rheumatism criteria.[8,9] Patients with known chronic comorbidities (diabetes mellitus, hypertension, renal or liver disease, thyroid dysfunction, metabolic syndrome) and patients under treatment with antidepressive pharmacotherapy were excluded. Healthy controls (HCs) matched by age were selected as long as they did not have a familial history of either autoimmune rheumatic diseases or any chronic medical condition.

Clinical Assessment

In order to evaluate the demographic and clinical variables, each patient was asked to fill a structured questionnaire that included duration of illness and treatment history. Rheumatoid arthritis disease activity was measured using Disease Activity Score on 28 Joints (DAS-28).[10] The Health Assessment Questionnaire Disease Index (HAQ-Di) was used.[11] Erythrocyte sedimentation rate (in millimeters per hour) was measured by Wintrobe's

TABLE 1. Evaluated Areas and Scores of INCAVISA

Explored Areas	Questions	Score	Definition
(1) Health and wellness	4	0–20	It refers to the perception of the patient's health status in current general and related to the previous year, as well as evaluated in relation to other people.
(2) Body perception	5	0–25	Deals with the level of satisfaction or pleasure that held about physical appearance and whether it has been modified by the disease.
(3) Physical performance	5	0–25	It refers to the subject's perception on energy and physical capacity it has to perform their daily activities.
(4) Independence	6	0–30	Physical capacity and self-perception to realize their self-care activities from their disease process
(5) Therapeutic adherence	5	0–25	Explores the level of dislike of the person having to undergo medical treatment, including components such as taking medication, attending consultations, and following treatments
(6) Perceived support	4	0–20	Assesses the perceived interpersonal resources to address economic, emotional, and health needs
(7) Cognitive function	7	0–35	Refers to everyday problems facing the person on your memory and concentration
(8) Family	5	0–25	Explores the level at which it is perceived that family members are involved emotionally
(9) Family concerns	4	0–20	It refers to thoughts about changes that might occur in their relationships with significant others in their environment because of the disease process
(10) Self-confidence	4	0–20	Evaluates the subject's self-esteem in relation to his/her environment and the changes that have been following his/her illness
(11) Isolation	4	0–20	Assesses interpersonal resources that the person has to deal with everyday situations
(12) Interaction	5	0–25	Explores feelings about the lack of ownership and lack of meaningful relationships in their environment

method; C-reactive protein and rheumatoid factor were determined by nephelometry. In the HC group, the questionnaire included family history and risk factors for chronic diseases.

Health-Related Quality of Life

The INCAVISA was designed to evaluate the HRQoL in Latin American population with chronic diseases.[12] The instrument has

TABLE 2. Comparison of Selected Characteristics Among HCs and RA Groups

Variable	HCs (n = 24)	RA Without Polypharmacy (n = 30)	RA With Polypharmacy (n = 24)	P
Sociodemographic characteristics				
Age, y	42 ± 10.48	39 ± 11.01	45 ± 9.58	0.11
Marital status: married, n (%)	11 (45.8)	14 (46.7)	16 (80.0)	0.94
High school or less, n (%)	9 (33.3)	19 (63.3)	12 (50)	0.09
Handwork, n (%)	9 (37.50)	23 (76.7)	18 (75)	**0.003**[b,c]
Paid work, n (%)	16 (66.7)	16 (53.3)	8 (33.3)	0.93
Main supplier, n (%)	9 (37.5)	4 (13.3)	3 (12.5)	0.52
Monthly family income, US dollars	444.44 (0–388.88)	222.22 (55.56–666.67)	250 (55.56–444.44)	**0.006**[b,c]
Presence of at least comorbid, n (%)	0	13 (43.3)	16 (76.2)	**<0.001**[a,b,c]
History contraceptive consumption, n (%)	10 (41.7)	9 (30)	4 (16.7)	0.29
Menopause, n (%)	7 (29.2)	9 (30)	9 (37)	0.79
RA characteristics				
Disease duration, y	—	3 ± 5.44	3 ± 9.89	0.35
DAS-28 score, units	—	3.17 ± 1.23	3.26 ± 1.48	0.30
HAQ-Di score, units	—	0.38 ± 0.64	0.81 ± 0.57	0.26
ESR, mm/h	—	16.50 ± 8.21	22.50 ± 21.88	0.09
CRP, mg/L	—	5.13 ± 4.63	4.53 ± 27.86	0.21
RF, IU/mL	—	26.20 ± 49.44	17.10 ± 74.87	0.51

P value is based on the Kruskal-Wallis test and 1-way analysis of variance.

[a]Polypharmacy versus without polypharmacy.

[b]Polypharmacy versus HCs.

[c]Without polypharmacy versus HCs.

CRP indicates C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor.
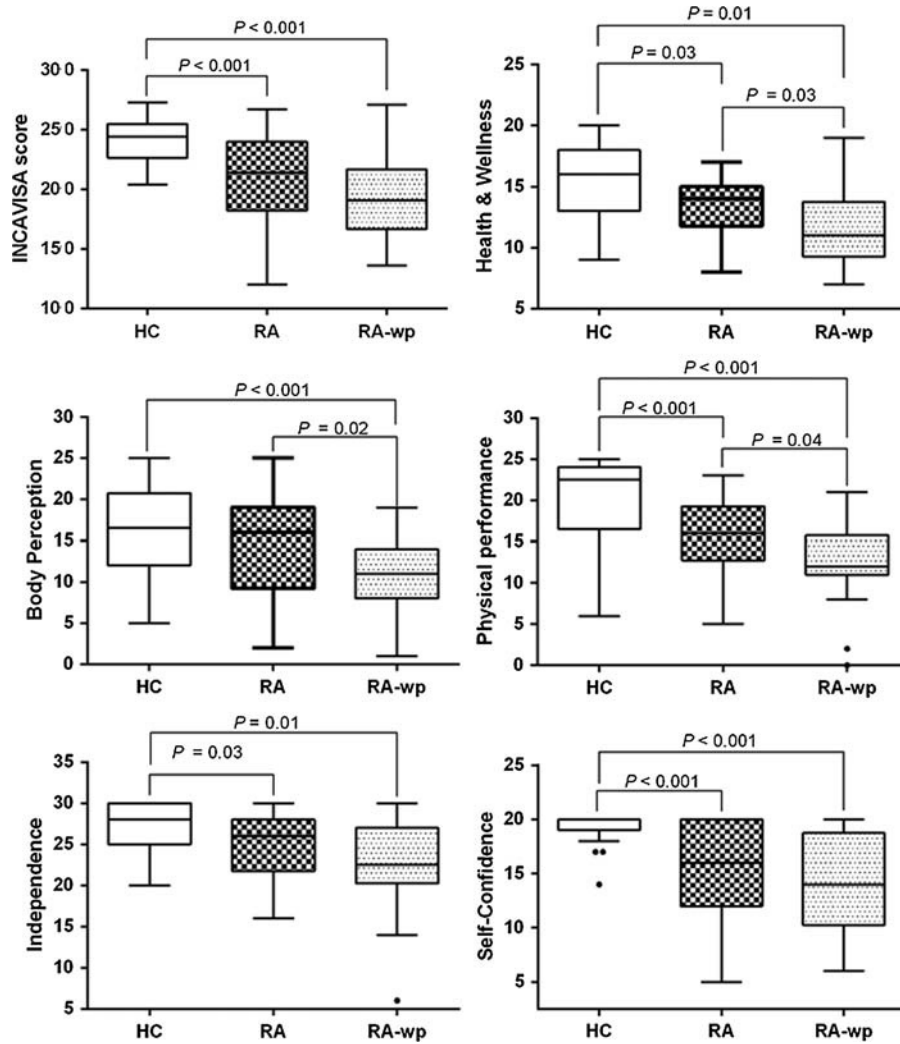
FIGURE 1. Comparison of the different areas evaluated by INCAVISA score in the study groups. RA indicates patients without polypharmacy; RA-wp, patients with polypharmacy. *P* value is based on Mann-Whitney *U* test.

58 items with Likert-scale, multiple-choice format of 6 possible responses, with 3 different ways to answer: (1) colloquial (never to always), (2) percentage (0%–100%), and (3) a continuous line in 12 domains assessing QoL: health and wellness, body perception, physical performance, independence, therapeutic adherence, perceived support, cognitive function, family, family concerns, confidence, isolation, and interaction. The items are adapted for illiterate or with minimal education, so they are easy to understand.

Statistical Analysis

Variables were assessed for normality using the Kolmogorov-Smirnov test; values are presented as mean ± SD, median with ranges, or percentages (%), as appropriate. Comparisons were made using 1-way analysis of variance and Kruskal-Wallis test. Post hoc tests were carried out using the Tukey and Mann-Whitney *U* tests, as applicable. Pearson and Spearman correlation coefficients were also calculated, as appropriate. Subsequently, we performed multiple linear regression analysis (analysis of covariance) to assess contribution to INCAVISA and HAQ-Di scores; we used a stepwise forward selection process. Variables with a $P < 0.2$ in univariate analyses were considered for inclusion in analysis of covariance. A 2-tailed $P < 0.05$ was considered statistically significant for

univariate and multivariate analyses. All data were analyzed using SPSS 21.0 software (SPSS Inc, Chicago, IL), considering a 2-tailed level of $P < 0.05$ to be statistically significant for analysis.

Ethical Approval

The Hospital Civil "Dr. Juan I. Menchaca" institutional review board approved this protocol (with registration no. 1068/10). Written consent was obtained from every study participant. Research was conducted following the Declaration of Helsinki.

RESULTS

In our study, 54 patients and 24 matched HCs were included. Demographic and clinical characteristics of the studied groups are shown in Table 2. Scores on DAS-28 were similar between RA with and without polypharmacy. We found a higher prevalence of manual labor, lower monthly family income (in US dollars), and comorbidities (gastrointestinal symptoms secondary to polypharmacy) in RA patients compared with the HC group.

We observed that 83% of HRQoL areas evaluated by INCAVISA were significantly affected in RA patients; RA patients with polypharmacy had worse INCAVISA scores in the areas of health and wellness ($P = 0.001$), body perception ($P = 0.002$),

TABLE 3. Correlation Coefficients (*r*) Between Areas Assessed by INCAVISA Score and Characteristics of Interest

	INCAVISA Total Score	Health and Wellness	Body Perception	Physical Performance	Independence	Therapeutic Adherence	Perceived Support	Cognitive Function	Family	Family Concerns	Self-confidence	Isolation	Interaction
Monthly income	0.164	−0.056	0.415[a]	0.120	−0.030	0.250	−0.021	−0.049	−0.087	0.292	0.003	0.79	0.366
Total comorbidities	−0.326[a]	−0.567[b]	−0.108	−0.320[a]	−0.212	−0.320[a]	−0.090	−0.217	−0.231	−0.256	−0.148	0.030	−0.178
No. of drugs	−0.350[a]	−0.372[b]	−0.301[a]	−0.410[b]	−0.278[a]	−0.246	−0.128	−0.076	−0.093	−0.273[a]	−0.172	−0.074	−0.174
Disease duration	0.102	−0.103	0.152	−0.120	0.225	0.110	0.121	0.132	0.250	−0.063	0.084	0.301[a]	−0.003
DAS-28 score	−0.394[b]	−0.535[b]	−0.237	−.0239	−0.296[a]	−0.244	0.012	−0.098	−0.381[b]	−0.269	−0.399[b]	−0.256	−0.113
ESR	−0.200	−0.138	−0.130	−0.188	−0.413[b]	−0.259	−0.226	.0137	−0.154	−0.175	−0.215	−0.237	0.109
CRP	−0.223	−0.071	−0.263	−0.306[a]	−0.051	−0.165	0.000	−0.056	0.093	−0.142	−0.098	−0.109	−0.086

[a]$P < 0.05$.
[b]$P < 0.01$.

physical performance ($P < 0.001$), independence ($P = 0.002$), self-confidence ($P < 0.001$) (Fig. 1), therapeutic adherence ($P = 0.05$), family concerns ($P < 0.001$), isolation ($P = 0.01$), and interaction ($P = 0.02$) compared with patients without polypharmacy and HCs (Fig. 1).

The univariate correlation coefficients between areas assessed by INCAVISA and clinical characteristics are shown in Table 3. The number of drugs, total comorbidities, and scores on DAS-28 were negatively correlated with the total INCAVISA score, but with different biopsychosocial areas. The number of drugs prescribed was negatively correlated as follows: physical performance > health and wellness > independence > family concerns. Score on DAS-28 was negatively correlated with the total perception of health and wellness, independence, family involvement, and self-confidence. Total comorbidities were correlated with health and wellness, physical performance, and therapeutic adherence.

The previous results from univariate analysis were included in multivariate analysis (Table 4) to determine their impact on HRQoL assessed by INCAVISA. We found that the predictors for HRQoL were the number of drugs ($P = 0.001$) and type of work (handwork or office job) ($P = 0.006$), among the study group. Meanwhile, exclusively in RA patient¢ predictors for decreased HRQoL were DAS-28 ($P < 0.001$), polypharmacy ($P = 0.006$), and consumption of alcohol ($P = 0.016$).

Instead, HRQoL evaluated by INCAVISA total score showed a highly negative correlation with HAQ-Di score (Fig. 2); therefore, we analyzed most affected HRQoL areas associated to functional disability evaluated by HAQ-Di, and these were health and wellness ($P = 0.004$), therapeutic adherence ($P = 0.017$), and interaction ($P = 0.018$) (Table 4).

DISCUSSION

In the last decades, the relevance of a holistic treatment in RA patients has been shown, favoring QoL during treatment. In patients affected with chronic diseases, the assessment of QoL is a complex endeavor. In order to evaluate the QoL in Latin American population, INCAVISA is a useful tool that offers a better scope for evaluation of biopsychosocial aspects than are not included in other instruments for health-related issues.[11]

Our findings showed that HRQoL evaluated by INCAVISA is lower in RA patients than in the general population, which is consistent with previous studies.[13] This may largely be due to RA being a disease that causes detriment of the biopsychosocial spheres of individuals because of presence of pain and functional disability.[4,5,14,15] However, a poor HRQoL comes not only from RA symptoms, because other factors could be relevant to determine a patient's HRQoL, such as comorbidities, gender, and age.[16]

After multivariate analysis, we found that polypharmacy had a negative impact in HRQoL evaluated by INCAVISA. This finding has not been reported previously in RA patients. Treat-to-target strategy in RA even considers HRQoL and does not include the evaluation of biopsychosocial aspects and the impact of polypharmacy.[17] Patients with polypharmacy had lower scores than did patients without polypharmacy and HCs in the majority of HRQoL areas assessed by INCAVISA. This is consistent with other studies of chronic diseases. Pirio Richardson et al[18] found in patients with epilepsy that individuals with monotherapy had better scores on HRQoL than did individuals with polypharmacy, in different areas such as memory loss, concerns about long-term effects of medication, difficulties in compliance with treatment, difficulties in conducting leisure activities, and perception of health status.

TABLE 4. Multiple Linear Regression Analysis

Model 1, INCAVISA Scores Among the Study Group as a Dependent Variable

Total R^2	0.444	
	β **Coefficient (95% CI)**	***P***
Constant	222.47 (208.64 to 236.37)	<0.001
Drugs (number)	−16.50 (−25.50 to −7.49)	0.001
Work (0 = handwork; 1 = office job)	22.49 (6.73 to 38.26)	0.006

Model 2, INCAVISA Scores Among RA Patients as a Dependent Variable

Total R^2	0.451	
	β **Coefficient (95% CI)**	***P***
Constant	269.78 (241.89 to 291.15)	<0.001
DAS-28	−12.81 (−19.41 to −6.20)	<0.001
Polypharmacy	−26.34 (−42.89 to −10.20)	0.003
Alcohol consumption	−10.47 (−18.85 to −2.09)	0.016

Model 3, HAQ-Di Scores Among RA Patients as a Dependent Variable

Total R^2	0.538	
	β **Coefficient (95% CI)**	***P***
Constant	3.46 (2.54 to 4.38)	<0.001
Health and wellness	−0.09 (−0.15 to −0.03)	0.004
Therapeutic adherence	−0.04 (−0.08 to −0.01)	0.017
Interaction	−0.04 (−0.07 to −0.01)	0.018

β Coefficients are given as value (95% confidence interval [CI]); unit for β coefficient are points for the INCAVISA score. Variables excluded for model 1: age, smoke, drink alcohol, and use of contraceptives; model was adjusted for monthly family income. Variables excluded for model 2: age, smoke, use of contraceptives, work, and number of drugs. Variables excluded for model 3: body perception, physical performance, independence, perceived support, cognitive function, family, family concerns, self-confidence, and isolation. Some of the HCs at the time of the study consumed drugs for conditions that were not chronic degenerative.

Meanwhile, Unsar et al[19] found that in an elderly population HRQoL, depression, perceived social support, and carrying out activities of daily life worsened by consuming a greater number of drugs.[20]

In univariate and multivariate analyses, DAS-28 and polypharmacy or total number of drugs contributed independently to a negative perception of HRQoL in patients with RA, affecting similar areas evaluated by INCAVISA (Table 3). We consider that polypharmacy had a greater impact on HRQoL than disease activity, because of the lack of difference on DAS-28 between our patients with and without polypharmacy (Table 2).

In our study, the most affected areas of HRQoL were health and wellness, body perception, physical performance, independence, self-confidence, adherence, family concerns, isolation, and interaction. Other reports have shown reduction in general health perception, although using other instruments.[21–23]

In our study, HAQ-Di score was negatively correlated with different areas evaluated by INCAVISA (Fig. 2); this means that higher HAQ-Di score not only reflects a lower score in physical function but also a reduced HRQoL in the rest of psychosocial areas. In multivariate analysis, we observed that perception in biopsychosocial areas such as health and wellness, therapeutic adherence, and interaction was predictive of a lower HAQ-Di score, meaning that patients with meaningful relationships and more willingness to follow medical treatment have better physical function, evaluated by HAQ-Di.

While it is true that there are several tools that can be used to assess HRQoL, INCAVISA provides a better overview of HRQoL in patients with chronic diseases, as well as helps us identify those specific areas where special care must be taken and provide patients with a more comprehensive care.

Therefore, we encourage including the assessment of the patient's perceived HRQoL as a fundamental part of the clinical evaluation performed by the rheumatologist. Encouraging the development of interventions that contribute to the patient's holistic well-being is mandatory to identify the biopsychosocial factors that have a negative impact on the patient.[1,24]

One caveat of this study is the cross-sectional nature of the study, all patients being female, and the low sample size. Therefore, we were not able to go further in the analysis to clarify significant contribution of drug combinations or posology that could interfere with the negative perception of HRQoL.
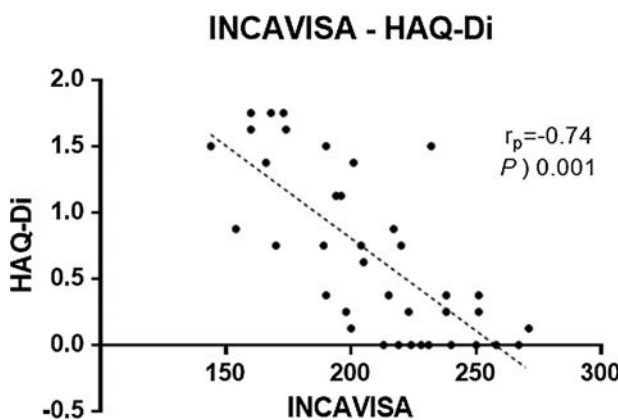

FIGURE 2. Correlation coefficient between INCAVISA and HAQ-Di scores.

The data obtained in this study suggest that it is necessary to combine the clinical evaluations performed by the rheumatologist with assessments of the subjects' perception about their HRQoL by a multidisciplinary team added to the cornerstone of treat-to-target strategy. The negative impact of disease activity and disability in HRQoL in RA patients is well known; however, other factors such as the number of drugs prescribed to these patients contribute to a negative perception of HRQoL. INCAVISA score is a helpful tool for the evaluation of polypharmacy impact in RA patients' HRQoL. Identification of biopsychosocial factors is mandatory to encourage the development of interventions that will greatly contribute to the well-being of patients.

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