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Original Article

Effect of Formal Education Level on Measurement of Rheumatoid Arthritis Disease Activity

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Objective. The aim of this study is to analyze the capacity of three demographic variables - age, sex, and formal education level - as well as disease duration to explain variation in 7 Core Data Set variables and 4 indices used to assess rheumatoid arthritis (RA), in a cohort of Korean patients seen in usual care. **Methods.** All RA Core Data Set measures were collected in usual care of 397 RA patients, including tender/swollen joint counts (TJC, SJC) 28, physician global estimate of status, erythrocyte sedimentation rate, C-reactive protein, and a multidimensional health assessment questionnaire to assess physical function, pain, and patient global estimate of status (PATGL). Four indices were computed: disease activity score with 28 joint count (DAS28), simplified disease activity index (SDAI), clinical disease activity index (CDAI), and routine assessment of patient index data 3 (RAPID3). Descriptive statistics and multivariate generalized linear models were used in data analysis. **Results.** Patients with lower education had higher scores, indicating greater severity, for all 7 Core Data Set measures and 4 indices (significant for TJC, function, pain, PATGL, DAS28, SDAI, CDAI, RAPID3). In a series of regressions that included age, sex, disease duration, and education, formal education level was the only significant variable to explain variation in TJC, pain, PATGL, physician global estimate of status (DOCGL), DAS28, SDAI, CDAI, and RAPID3. **Conclusion.** Significant associations with education were found in Korean RA patients according to most RA Core Data Set measures and 4 indices. Education was more likely than age, sex, or disease duration to explain variation in most measures and indices. **(J Rheum Dis 2015;22:231-237)**

Key Words. Rheumatoid arthritis, Social class, Education

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, inflammatory disease that presents physical, vocational, functional and psycho-socioeconomic problems for patients [1,2]. Measures of clinical activity are potentially confounded by demographic variables, including age, sex and socioeconomic status (SES), as well as duration of disease. SES is recognized to be associated with higher prevalence, greater severity and earlier mortality of many diseases [3-5], including RA [6-11]. The most easily measured SES variable is formal education level, which has been interpreted as a surrogate for patient actions and attitudes that may affect health [12]. One report indicated that education was more likely than age or sex to be associated with clinical status measures in a cohort of United States (US) patients with RA [13].

Associations of socioeconomic factors, particularly education, with disease have been investigated in many previous studies. Education and annual household income were correlated with Short Form-36 health survey (SF-36) scores in patients with systemic lupus erythematosus (SLE) [14]. Low education and health insurance status were associated independently with acute-onset SLE [15], and with work disability [16]. In ankylosing spondylitis, low education was associated significantly

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with higher disease activity [17], and also explained functional limitation [18].

Despite the above and many similar observations concerning the possible importance of SES in assessment of clinical status, a variable describing SES is not included in many clinical research reports. By contrast, age, sex and duration of disease are almost always included as potential confounders of differences between patients in clinical status, treatment responses and outcomes. In this report, we analyze a cohort of Korean patients seen in usual care for possible significance of education, age, sex and duration of disease to explain variation in RA Core Data Set variables [19] and 4 RA disease activity indices.

MATERIALS AND METHODS

Study patients

A total of 397 RA patients seen in a rheumatology outpatient clinic for usual care between May 2012 and November 2012 in Daegu, Republic of Korea, were investigated in a cross-sectional study. Included patients were 18 years of age and older, diagnosed according to 1987 revised American College of Rheumatology (ACR) RA classification criteria [20] or 2010 revised criteria [21], and could provide all target measures and indices by medical record. Patients with psychiatric disease and illiterate patients who could not complete a questionnaire were excluded.

Patients were classified into 3 education categories: <7 years (elementary school, n=76; median age 62.9 years), 7 to 12 years (high school, n=228; median age 55.8 years), and >12 years (college, n=93; median age 42.9 years).

Measures and indices

All patients completed a Korean version of a multidimensional health assessment questionnaire (MDHAQ), translated and validated by Lee et al. [22]. Three of the 7 RA Core Data Set measures are included on the MDHAQ: physical function, pain, and patient global estimate of status (PATGL). Demographic measures also are collected on the MDHAQ: age, sex and education.

Three Core Data Set measures were collected by the physician: tender joint count (TJC), swollen joint count (SJC), and physician global estimate (DOCGL). The physician also estimated year of disease onset to calculate duration of disease. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) were assessed. Body mass index (BMI) was also calculated by the physician.

Four indices derived from the Core Data Set were calculated: disease activity score with 28 joint count (DAS28) formulated by $0.56\times\sqrt{TJC}+0.28\sqrt{SJC}+0.70\ln ESR+0.014$ PATGL [23]; simplified disease activity index (SDAI), formulated by SJC+TJC+PATGL+DOCGL+CRP [24]; clinical disease activity index (CDAI), calculated by SJC+TJC+PATGL+DOCGL [24]; routine assessment of patient index data 3 (RAPID3, an index of only the 3 patient self-report Core Data Set measures found on an MDHAQ: physical function+pain+PATGL) [25].

Statistical analysis

Statistical analyses were performed using SAS version 9.3 TS (SAS Inc., Cary, NC, USA) and Stata 12.1 for Windows (Stata, College Station, TX, USA). The Shapiro-Wilk W test was used to identify normality of distribution in the study population. Quantitative data are presented as median values and interquartile range. Qualitative data are presented as frequency and percentage. Non-parametric Kruskal-Wallis tests were used in comparisons of ACR Core Data Set measures between different education groups. A Poisson distribution was applied to examine differences in 7 Core Data Set measures among education groups, adjusted for age, sex and disease duration. Multivariate generalized linear models (GLM) with a log link were performed. A series of multiple linear regression was performed for each Core Data Set measure and index as a dependent variable, with education, age, sex and disease duration as independent variables. To select significant variable among 4 independent variables, the forward selection method was performed in each multiple regression. No issue was detected regarding collinearity. All tests were 2-sided; a p-value <0.05 is considered to indicate statistical significance.

RESULTS

Among the 397 patients, 89.4% were female (Table 1). Mean disease duration was significantly longer in females, 7.3 years, than in males, 5.5 years (p=0.011). Age and BMI, patient-reported measures, and laboratory measures (ESR, CRP, RF and ACPA) did not differ significantly between males and females. The disease activity indices DAS28 and RAPID3 were slightly higher in males, albeit not statistically significant.

Table 1. Demographic and clinical parameters of study population

Parameter	Female	Male	Total
Number of patients	355 (89.4)	42 (10.6)	397 (100)
Age (yr)	54.8 (46.2～61.7)	60.0 (45.8～64.2)	55.3 (46.2～62.1)
Disease duration (yr)	7.3 (3.2～13.8)	5.5 (2.1～7.8)	6.8 (3.1～13.4)
BMI (kg/m^2)	22.1 (20.2～24.3)	21.8 (20.8～24.1)	22.0 (20.2～24.3)
MDHAQ physical function	1.0 (0.3～2.7)	1.3 (0.7～2.3)	1.0 (0.3～2.7)
MDHAQ pain	4.0 (2.0～6.0)	4.5 (2.5～7.0)	4.0 (2.0～6.5)
PATGL	5.0 (2.5～6.0)	5.0 (3.5～7.0)	5.0 (3.0～6.0)
DOCGL	3.0 (2.0～4.0)	3.0 (2.0～4.0)	3.0 (2.0～4.0)
ESR (mm/h)	25.0 (15.0～42.0)	21.0 (12.0～36.0)	24.0 (15.0～41.0)
CRP (mg/dL)	0.2 (0.1～0.7)	0.3 (0.1～0.9)	0.2 (0.1～0.7)
RF (IU/mL)	39.1 (16.4～85.9)	37.6 (18.4～173.8)	38.6 (16.5～88.7)
ACPA (U/mL)	115.5 (14.5～500.0)	106.5 (50.5～500.0)	107.3 (15.5～500.0)
RAPID3	10.3 (5.7～14.7)	11.0 (7.2～16.0)	10.5 (6.0～14.7)
DAS28	3.5 (2.7～4.5)	3.6 (2.7～4.6)	3.5 (2.7～4.5)

Values are presented as number (%) or median (interquartile range). ACPA: anti-citrullinated protein antibodies, BMI: body mass index, CRP: C-reactive protein, RF: rheumatoid factor, DAS28: disease activity score with 28 joint count, DOCGL: physician global estimate of status, ESR: erythrocyte sedimentation rate, MDHAQ: multidimensional health assessment questionnaire, PATGL: patient global estimate of status, RAPID3: routine assessment of patient index data 3.

Table 2. Rheumatoid arthritis measures and indices according to years of formal education

Measure/index	Formal education			p-value*
	Elementary n=76 (19.1%)	High school n=228 (57.4%)	College n=93 (23.5%)	
Age (yr)	62.9 (0.8)	55.8 (0.6)	42.9 (1.1)	<0.001
Female (%)	93	89	87	0.396†
Disease duration (yr)	7.0 (1.0)	7.6 (0.5)	5.1 (0.7)	0.084
TJC28 (0～28)	2.5 (0.6)	1.0 (0.3)	1.0 (0.4)	0.003
SJC28 (0～28)	0.0 (0.2)	0.0 (0.1)	0.0 (0.2)	0.125
MDHAQ physical function (0～10)	2.0 (0.2)	1.0 (0.1)	1.0 (0.1)	<0.001
MDHAQ pain (0～10)	5.0 (0.3)	4.0 (0.2)	3.5 (0.2)	<0.001
PATGL (0～10)	5.0 (0.3)	5.0 (0.2)	4.5 (0.3)	0.046
DOCGL (0～10)	3.0 (0.2)	2.0 (0.1)	3.0 (0.2)	0.071
ESR (mm/h, normal <30 mm/h)	28.0 (2.5)	23.0 (1.5)	28.0 (2.1)	0.292
CRP (mg/dL, normal ≤0.5 mg/dL)	0.2 (0.1)	0.2 (0.1)	0.3 (0.1)	0.598
RF (IU/mL, normal ≤15 IU/mL)	34.8 (8.7)	40.1 (4.7)	33.5 (6.5)	0.796
ACPA (U/mL, normal ≤17 U/mL)	101.9 (25.3)	100.0 (14.4)	173.2 (22.5)	0.263
DAS28	4.0 (0.1)	3.4 (0.1)	3.3 (0.1)	0.001
SDAI	13.3 (0.9)	9.5 (0.5)	10.5 (0.3)	0.003
CDAI	13.0 (0.9)	9.0 (0.5)	8.5 (0.7)	0.002
RAPID3	12.3 (0.7)	10.0 (0.4)	9.3 (0.6)	<0.001

Values are presented as median (standard error). Elementary school: <7 years, high school: 7～12 years, college: >12 years. ACPA: anti-citrullinated protein antibodies, CDAI: clinical disease activity index, CRP: C-reactive protein, DAS28: disease activity score with 28 joint count, DOCGL: physician global estimate of status, ESR: erythrocyte sedimentation rate, MDHAQ: multidimensional health assessment questionnaire, PATGL: patient global estimate of status, RAPID3: routine assessment of patient index data 3, RF: rheumatoid factor, SDAI: simplified disease activity index, SJC28: 28 swollen joint count, TJC28: 28 tender joint count. *p-value by Kruskal-Wallis test except where otherwise indicated; †Pearson's chi-square test.

Demographic variables, the 7 RA Core Data Set measures, additional laboratory tests, and 4 RA indices were compared according to education (Table 2). Age differed significantly in the three education categories: highest in the low education group and lowest in the college group (elementary=median 62.9 years, high school= 55.8 years, college=42.9 years; $p<0.001$). The highest proportion of female patients was in the low education group. TJC28, pain, physical function, PATGL, and all 4 composite disease activity indices – DAS28, SDAI, CDAI and RAPID3 – differed significantly in the three education groups. Disease duration, SJC28, DOCGL, and laboratory tests did not differ significantly in the 3 education groups.

A multivariate GLM with a log link and a Poisson distribution was applied to examine variation in 7 RA Core Data Set measures according to education, as well as age, sex and disease duration (Table 3). TJC28, pain, physical function, and DOCGL were significantly higher in the low education group, elementary vs. high school and elementary vs. college, after adjusting for age, sex and disease duration. PATGL also was higher in the low education group, although it did not differ significantly in the multivariate GLM. SJC28, ESR, CRP did not differ significantly among education groups, possibly explained on the basis of low values, most in the normal range. No differences were significant between the high school vs. college groups (Table 3). All 4 indices (DAS28, SDAI, CDAI, RAPID3) were significantly higher in the elementary vs.

Table 3. Comparisons of American College of Rheumatology Core Data Set measures among patients grouped according to years of formal education

Dependent variable	Generalized linear model*			Pairwise comparisons					
	F	p-value	R^2	Elementary ~ high school		Elementary school ~ college		High school ~ college	
				Estimate (SE)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value
TJC28	2.40	0.036	0.029	1.6 (0.6)	0.006	1.7 (0.8)	0.021	0.2 (0.5)	0.749
SJC28	0.88	0.495	0.011	0.4 (0.2)	0.103	0.5 (0.3)	0.137	0.1 (0.2)	0.730
MDHAQ physical function	5.26	<0.001	0.063	0.7 (0.2)	0.001	0.8 (0.3)	0.007	0.1 (0.2)	0.766
MDHAQ pain	4.18	0.001	0.050	1.4 (0.4)	<0.001	1.7 (0.5)	<0.001	0.4 (0.3)	0.298
PATGL	1.89	0.095	0.023	0.8 (0.3)	0.022	1.1 (0.4)	0.011	0.4 (0.3)	0.269
DOCGL	2.38	0.038	0.029	0.6 (0.2)	0.008	0.7 (0.3)	0..019	0.1 (0.2)	0.665
ESR	2.70	0.020	0.033	4.8 (3.0)	0.118	4.4 (4.0)	0.276	−0.4 (2.9)	0.896
CRP	0.68	0.641	0.008	−0.1 (0.2)	0.605	0.2 (0.3)	0.466	0.4 (0.2)	0.126

*Performed after adjusting for age, sex and disease duration. CRP: C-reactive protein, DOCGL: physician global estimate of status, ESR: erythrocyte sedimentation rate, F: observed F value, MDHAQ: multidimensional health assessment questionnaire, PATGL: patient global estimate of status, R^2: coefficient of determination, SE: standard error, SJC28: swollen 28 joint count, TJC28: tender 28 joint count.

Table 4. Comparison of composite rheumatoid arthritis indices among patients grouped according to years of formal education

Dependent variable	Generalized linear model*			Pairwise comparisons					
	F	p-value	R^2	Elementary ~ high school		Elementary school ~ college		High school ~ college	
				Estimate (SE)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value
DAS28	3.91	0.001	0.047	0.6 (0.2)	<0.001	0.6 (0.2)	0.005	0.0 (0.2)	0.881
SDAI	2.48	0.031	0.030	3.2 (1.1)	0.003	4.2 (1.4)	0.003	1.1 (1.0)	0.302
CDAI	2.81	0.016	0.034	3.3 (1.0)	0.001	4.0 (1.3)	0.002	0.7 (1.0)	0.463
RAPID3	4.09	0.001	0.049	2.9 (0.8)	<0.001	3.7 (1.1)	<0.001	0.8 (0.8)	0.311

*Performed after adjusting for age, sex and disease duration. CDAI: clinical disease activity index, DAS28: disease activity score with 28 joint count, F: observed F value, R^2: coefficient of determination, RAPID3: routine assessment of patient index data 3, SDAI: simplified disease activity index, SE: standard error.

Table 5. Multiple linear regressions to analyze each American College of Rheumatology Core Data Set measure and 4 composite rheumatoid arthritis indices as dependent variables

Dependent variable	Independent variable: β coefficient (p-value)				R^2
	Age	Sex	Disease duration	Education	
TJC28	0.000 (0.999)	0.475 (0.483)	0.289 (0.292)	−0.130 (0.034)	0.019
SJC28	−0.009 (0.331)	−0.004 (0.989)	0.130 (0.239)	−0.021 (0.430)	0.002
MDHAQ physical function	0.016 (0.097)	0.129 (0.633)	0.012 (0.256)	−0.051 (0.053)	0.043
MDHAQ pain	−0.008 (0.621)	0.559 (0.196)	−0.001 (0.957)	−0.140 (0.001)	0.038
PATGL	−0.017 (0.232)	0.681 (0.091)	0.011 (0.505)	−0.016 (0.007)	0.023
DOCGL	−0.018 (0.048)	0.259 (0.300)	−0.014 (0.163)	−0.072 (0.003)	0.027
ESR	−0.206 (0.109)	1.351 (0.709)	0.504 (0.001)	−0.539 (0.123)	0.004
CRP	−0.010 (0.341)	0.272 (0.346)	0.001 (0.917)	−0.027 (0.326)	0.005
DAS28	−0.010 (0.153)	0.181 (0.363)	0.021 (0.009)	−0.059 (0.002)	0.022
SDAI	−0.054 (0.231)	1.684 (0.184)	0.040 (0.436)	−0.365 (0.003)	0.025
CDAI	−0.044 (0.294)	1.411 (0.233)	0.039 (0.418)	−0.337 (0.003)	0.025
RAPID3	−0.009 (0.798)	1.369 (0.156)	0.022 (0.567)	−0.297 (0.002)	0.038

CDAI: clinical disease activity index, CRP: C-reactive protein, DAS28: disease activity score with 28 joint count, DOCGL: physician global estimate of status, ESR: erythrocyte sedimentation rate, MDHAQ: multidimensional health assessment questionnaire, PATGL: patient global estimate of status, R^2: coefficient of determination, RAPID3: routine assessment of patient index data 3, SDAI: simplified disease activity index, SJC28: 28 swollen joint count, TJC28: 28 tender joint count.

high school and elementary vs. college groups, but not in the high school vs. college groups (Table 4).

A series of multiple linear regression was performed with individual measures and RA indices as the dependent variable, and age, sex, duration of disease, and education as independent variables (Table 5). By forward selection method, education was dominated for dependent variable, and was the only significant variable to explain variation in TJC, pain, PATGL, DOCGL, SDAI, CDAI and RAPID3. Education and disease duration explained variation in DAS28 significantly, and only disease duration explained variation in ESR. None of the 4 independent variables was significant to explain variation in SJC, physical function, or CRP (Table 5).

DISCUSSION

The results of this study extend previous reports [26] that most clinical measures and all RA indices were significantly higher (indicating poorer clinical status) in Korean patients with low education. Furthermore, education was more explanatory of variation in clinical measures than age, sex, disease duration in regression analyses [26]. The proportions of each education group in the US in the 1980s [26] was similar to proportions in Korea in the 2010s (24% completed elementary school, 48% completed high school, 28% had some college education). In one Korean study [27], the prevalence of RA was associated significantly with low education, but not with urban versus rural residence or with household income.

Professional societies have suggested that poorer health among individuals of low socioeconomic status appears based primarily on limited access to medical services [28]. Although limited access may have some explanatory power [29], extensive evidence suggests that variables intrinsic to a patient that may lead to low education and poor health may be explained more by poor lifestyle behaviors such as smoking, poor diet, lack of exercise [30]; environmental factors such as occupation, residence, et al; poor health literacy [31]; and psychological variables associated with poor health status [12].

This study includes several limitations. Unfortunately, possible associations of clinical status with other SES variables such as income and occupation were not included, because those are not included in usual clinical medical history; however, many studies have shown education to be more explanatory of health status than other SES variables [12,32]. Second, illiteracy was a criterion for exclusion from this study, so associations of education and poor health may be even greater than recorded [33]. Third, the study is cross-sectional, and a follow-up longitudinal study could be informative. Fourth, other confounding variables, for example, delay of diagnosis from symptom onset, medication history, were not analyzed.

CONCLUSION

In conclusion, significant associations of low education level with greater disease severity according to most RA Core Data Set measures and 4 indices were seen in 397 RA patients. Education was more likely than age, sex or duration of disease to explain variation in most Core Data Set measures and RA indices.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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