

The Correlation between the Neurological Complications of Rheumatoid Arthritis with the Disease Activity and Functional Impairment (Disability) in Omdurman - Khartoum in 2015

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Abstract

Objectives: To identify the impact and predictors of the neurological complications of rheumatoid arthritis (RA) among Sudanese patients.

Methodology: A case series study of 58 consecutive patients diagnosed as having RA at Omdurman teaching hospital rheumatology clinic was done. Patients have another possible etiology for the neurological manifestations were excluded. The doctors of rheumatology clinic examined the patients and the Clinical Disease Activity Index (CDAI) was calculated. A senior consultant neurologist objectively assessed the neurological complications of RA. The patients were interviewed using the Health Assessment Questionnaire (HAQ) to evaluate the functional impairment. Various statistical tests were used to assess any possible association between various variables obtained.

Results: Almost 60% have neurological signs (pyramidal system signs 43.1%, proximal weakness 8.6%, sensorimotor neuropathy 5.2%, pure sensory neuropathy 1.7%, extrapyramidal/cerebellar 0%). The mean HAQ scores for patients who express neurological signs and those who don't express are 1.34 and 1.40 respectively without significant difference ($P = 0.778$). The association between the neurological complications and disease activity, ESR value, and rheumatoid factor status is not significant ($P = 0.701, 0.515, 0.299$ respectively). There is not only a strong association between the disease activity (CDAI) of RA and functional status (HAQ) of the patient ($P = 0.0, R = 0.56$), but also 30% of variability of the functional impairment can be attributed exclusively to the variability of the disease activity ($R^2 = 0.3$).

Conclusion: The RA activity is the major determinant of disease morbidity. The functional impairment caused by the neurological complications is negligible.

The disease activity, ESR value, and rheumatoid factor status are poor predictors of the neurologic complications.

Keywords: Rheumatoid Arthritis; Neurological Complications; Disease Activity; Functional Impairment (Disability); Sudan

Introduction

Background

Rheumatoid arthritis (RA) is the most common inflammatory joint disease, affecting 1 - 2% of the population worldwide, with women affected two to three times more commonly than men. RA accounts for 22% of all deaths from arthritis and other rheumatic conditions [1]. Persons with RA are two times more likely to die than persons of the same age without RA in the general population [1]. Approximately one third of patients cease work because of the disease within two years of onset, and this prevalence increases thereafter. The total costs of RA in the UK, including indirect costs and work related disability, have been estimated at between £3.8 billion and £4.75 billion per year [2].

The extra-articular manifestations of rheumatoid arthritis affect the skin, the cardiovascular system, the kidneys, the eyes, the gastrointestinal tract, the liver, the nervous system and the blood [3]. The extra-articular manifestations of RA can occur at any age after onset [4]. Extra-articular manifestations are often recognized too late [3]. The occurrence of these systemic manifestations is a major predictor of mortality in patients with RA [4]. Clinical involvement of the nervous system is not uncommon in rheumatoid arthritis [5].

The importance of assessing the functional impairment of patients with rheumatoid arthritis (RA) arise from the fact that RA potentially changes relationships with others, impacting on ability to remain in work, and therefore affecting the finances and independence of the individual and their family [2]. The neurological complication worsens the functional impairment and disability, increase the burden on the patient and economy, and worsen the health quality. Identification of the possible clinical and immunological predictors of the neurological complications will help build the suitable care plan to avoid further functional impairment and improve the quality of life as much as possible [6].

Patients and Methods

A case series study of 58 consecutive patients who were recruited from the rheumatology clinic of Omdurman university hospital was done over almost three months (July, August and September 2015). The hospital is the largest tertiary hospital in Omdurman city. The hospital has many outpatient clinic to provide tertiary care to patients from different parts of Sudan, and Rheumatology clinic is one of these. After obtaining the verbal consent, the data about the age, gender, neurologic symptoms, the most recent ESR value and the rheumatic factor status were documented. The nervous system was assessed objectively, whereas the rheumatoid arthritis disease activity and the functional impairment were assessed using the Clinical Disease Activity Index (CDAI) and the Health Assessment Questionnaire (HAQ) respectively.

Assessment of the neurological manifestation

A senior consultant neurologist was assigned to objectively assess the neurological complications of RA. Patients who have another possible etiology for the neurological manifestations or had a neurological disease before the diagnosis of rheumatoid arthritis were excluded.

Assessment of disease activity

The development of a disease index that adequately reflects the disease activity by both subjective and objective criteria is a complicated task. Fortunately, extensive efforts have been dedicated to the development of multiple instruments that have been validated to follow disease activity in RA patients [7].

Although these clinical assessment tools have limitations, health care providers can use them as measures of disease progression and to assist in planning treatment strategies to modify disease activity and improve the quality of life for the patient [7].

American College of Rheumatology recommend the use of the CDAI for its good reliability, and its excellent validity and responsiveness [8,9]. The CDAI is determined by the summation of the SJC, TJC, patient's global assessment, and the physician's global assessment. Unlike the DAS28 and the SDAI, the CDAI does not include the ESR or CRP. This enables the physician to immediately know the disease activity score and make treatment decisions during the patient encounter. Similar to the SDAI, the CDAI has been reported to perform well in clinical practice [8-10].

Functional impairment (Disability) assessment

Functional impairment (disability) refers to diminished ability to perform activities of daily living, employment and other tasks. Most RA patients show some functional impairment not explained by age alone [11-13].

In the revised WHO classification disability has been replaced by "activity limitation" and handicap by "participation limitation", both of which may be restricted in nature, duration, or quality [14]. Functional impairment is measured using standardized tests for activities of daily living (ADL) like the Health Assessment Questionnaire (HAQ), which is a self-assessment questionnaire developed for the evaluation of ADL and functions. It is practical and can also be completed within a short period of time [15]. The domain of disability is assessed by the eight categories of dressing, arising, eating, walking, hygiene, reach, grip, and common activities. There are four possible responses for the Disability Index questions:

Without ANY difficulty = 0; With significant difficulty = 2; With minor difficulty = 1; UNABLE to do = 3.

The sum of the computed categories scores is then calculated and divided by the number of categories answered. This gives a score in the 0 to 3 range, with 3 being the worse, giving rise to The Standard Disability Index [4].

Statistical analysis

The following tests were used to assess any possible statistical correlation/association according to the corresponding variables:

1. Analysis of Variance (ANOVA).
2. Correlation/Line regression
3. Independent t- test
4. Chi-square test
5. Mann-Whitney test.

Results

Descriptive statistics

Patients were of different age groups, with almost 56% below age 50 years and 44% above it. Females constituted 86% of the sample. Almost 63.8% of patients complained of neurological symptoms (Table 1) whereas 60.3% had neurological signs on examination (Table 1). The CDAI (Table 2) demonstrates that the majority of patients have moderate disease activity (43%) followed by the high and low activity categories (25.6% and 25.9% respectively). Two thirds of patients had positive rheumatoid factor. The mean HAQ score was 1.36. Figure 1 describes the occurrence frequency of the neurologic complications in the different age groups.

Hypothesis testing

The table 3 illustrates the different hypotheses and statistical tests used in the analysis:

Main category and subcategories		Frequency (%)
Sex	Male	13.8%
	Female	86.2%
Age group	< 20	3.4%
	20 - 29	13.8%
	30 - 39	13.8%
	40 - 49	24.1%
	50 - 59	19.0%
	> 60	25.9%
	Neurologic symptoms	No neurological symptoms
Sensory symptoms		22.4%
Muscle weakness		15.5%
ANS symptoms		0.0%
CNS symptoms		1.7%
Cerebellar symptoms		0.0%
Weakness + sensory symptoms		24.1%
CDAI interpretation	Remission	3.4%
	Low activity	25.9%
	Moderate activity	43.1%
	High activity	27.6%
RF status	RF(-ve)	34.7%
	RF(+ve)	65.3%
Neurologic signs	No neurological signs	39.70%
	Combined UMNL and LMNL	29.30%
	Proximal weakness	8.60%
	Lower motor neuron lesion	8.60%
	Upper motor neuron lesion	5.20%
	Sensorimotor neuropathy	5.20%
	Pure sensory signs	1.70%
	Proximal weakness + Sensory neuropathy	1.70%

Table 1: The frequency by percentages of the variables studied.

	Mean	Minimum	Maximum
HAQ score	1.36	0	3
CDAI Score	18.28	1.00	51.00
ESR value	55	6	115

Table 2: The min, max and mean values of the Disease activity index (CDAI), Health assessment questionnaire (HAQ), and the most recent ESR value.

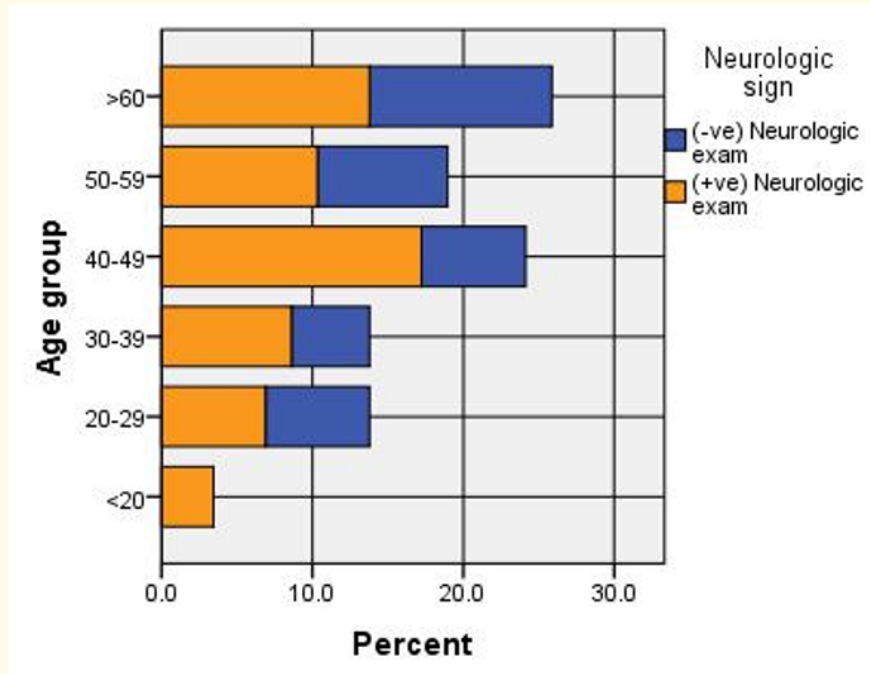


Figure 1: The proportions of abnormal neurologic examination in the different age groups.

The Null Hypothesis	Statistical test	P value	R (R ²)
There is no linear relationship between the disease activity (CDAI) score of rheumatoid arthritis and the (HAQ) score (Figure 1).	ANOVA	0.0	
There is no difference between the mean HAQ score of patients with and without objective neurologic findings.	Correlation/Line regression Independent t-test	0.778	R = 0.56, (R ² = 0.3)
There is no difference between the mean CDAI score of patients with and without objective neurologic findings (Figure 2).	Chi-square test	0.701	
There is no difference between the mean ESR value of patients with and without objective neurologic findings.	Mann-Whitney test	0.515	
There is no association between the neurological manifestations of rheumatoid arthritis and the rheumatic factor status (RF)	Chi-square test	0.299	
There is no association between the neurological manifestations of rheumatoid arthritis and the age group	Chi-square test	0.72	
There is no association between the neurological manifestations of rheumatoid arthritis and the sex	Chi-square test	0.155	

Table 3: The null hypotheses and the used statistical tests.

It can be inferred from the table that there is strong association between the disease activity (CDAI) of rheumatoid arthritis and functional status (HAQ) of the patient ($P = 0.0$, $R = 0.56$), and 30% of the variability of the functional impairment among patients can be attributed to the variability of the disease activity ($R^2 = 0.3$) (Figure 2 and 3).

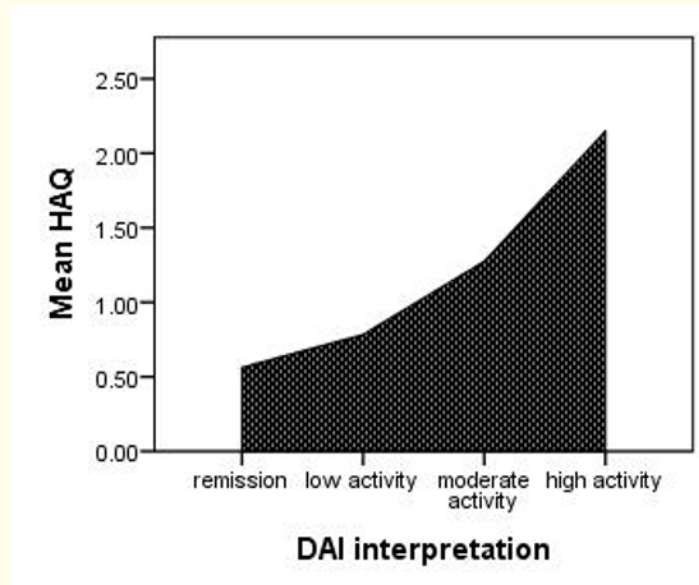


Figure 2: The HAQ for the different CDAI categories.

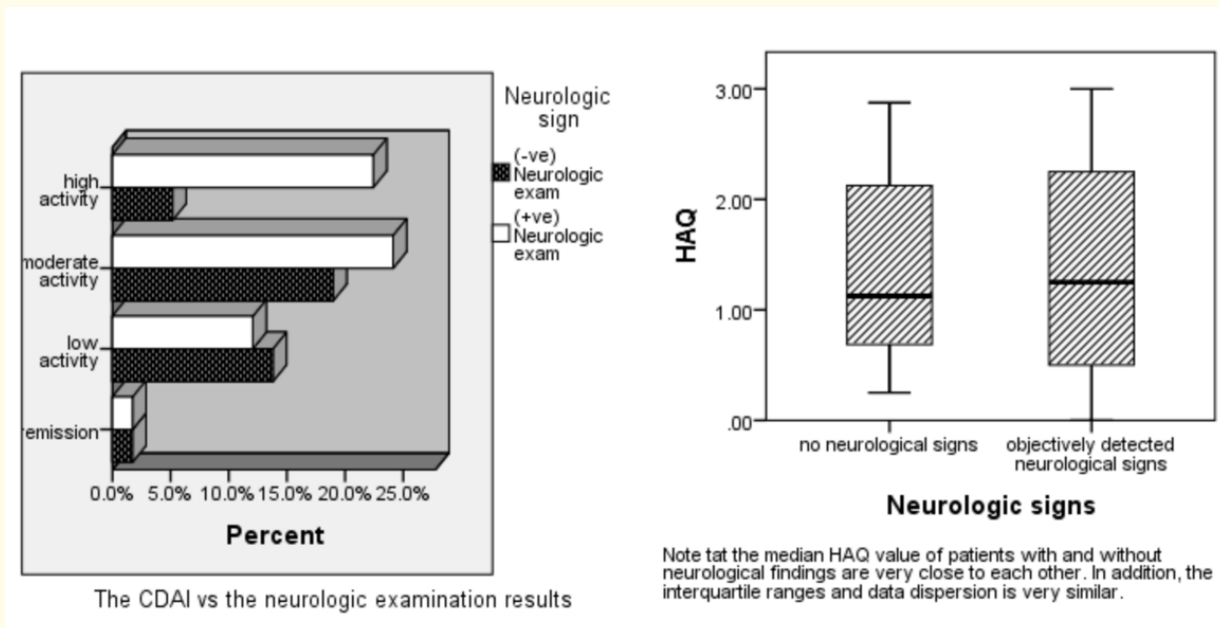


Figure 3: The CDAI and HAQ vs the neurologic examination results.

The mean HAQ scores for patients who expressed neurological signs on examination and those who didn't express were 1.34 and 1.40 respectively. Moreover, There was no significant difference between the mean and median HAQ scores of patients with and without objectively detected neurological manifestations of rheumatoid arthritis (P = 0.778) (Figure 3).

It appears that there is no association between the neurological manifestations of rheumatoid arthritis and neither rheumatoid arthritis disease activity (CDAI) (Figure 3), the ESR value, nor the rheumatic factor status (P = 0.701, 0.515, 0.299 respectively) (Table 4). The age and sex are not associated with the development of the neurologic complications (P = 0.72 and 0.155 respectively). Table 4 demonstrates the mean and frequency of the different variables and subcategories according to the results of the neurologic examination. Figure 1 and table 4 shows the proportions of abnormal neurologic examination in the different age groups.

	Neurologic sign			
	(-ve) Neurologic exam		(+ve) Neurologic exam	
	Column N %	Mean	Column N %	Mean
HAQ score			8	13
DAIS			14.76	20.60
ESR value			51	57
Sex	Male	21.7%		8.6%
	Female	78.3%		91.4%
Age group	< 20	0.0%		5.7%
	20 - 29	17.4%		11.4%
	30 - 39	13.0%		14.3%
	40 - 49	17.4%		28.6%
	50 - 59	21.7%		17.1%
	> 60	30.4%		22.9%
Neurologic symptoms	No neurological symptoms	47.8%		28.6%
	Sensory symptoms	21.7%		22.9%
	Muscle weakness	13.0%		17.1%
	ANS symptoms	0.0%		0.0%
	CNS symptoms	0.0%		2.9%
	Cerebellar symptoms	0.0%		0.0%
	Weakness + sensory symptoms	17.4%		28.6%
DAI interpretation	Remission	4.3%		2.9%
	Low activity	34.8%		20.0%
	Moderate activity	47.8%		40.0%
	High activity	13.0%		37.1%
RF status	RF(-ve)	42.9%		28.6%
	RF(+ve)	57.1%		71.4%

Table 4: The mean and frequency of the different variables vs the neurologic examination.

Discussion

The extra articular manifestations of rheumatoid arthritis and the rheumatoid arthritis burden have been extensively studied. However, the impact of the neurologic complications and their possible predictors haven't been under focus. We studied the impact of the neurologic complications on rheumatoid arthritis patients and tried to deduce the possible predictors of them from the routine follow up and diagnostic tools. In this study we highlight the impairment resulting from the activity and neurologic complications of rheumatoid arthritis, make comparisons where suitable, and try to identify the possible predictors of the neurologic complications of rheumatoid arthritis from the routine examination and basic investigations.

The neurologic complications of rheumatoid arthritis are part of various extra articular manifestations of the disease. The frequencies of the neurologic symptoms and signs in this study are shown in table 1. In comparison to our study that showed detection of sensory symptoms in 22.4% and pure sensory signs in 1.7%, Aneja R., *et al.* a study of 66 patients, revealed that sensory symptoms were present in 9 patients (13.6%). None had motor symptoms. On neurological examination, 16 patients had sensory (24.2%) and 6 (9.09%) had motor abnormalities [3]. In Sakini R. A., *et al.* a study of Iraqi patients, neurological assessment of cases revealed that subjective findings (symptoms) of neuropathy were present in 10% to 37.5% of cases vs 12.5% to 25% of cases with positive objective findings (signs) [16]. This indicates that the frequency of the sensory system involvement in rheumatoid arthritis varies among different populations.

A recent UK study found that significant co-morbidity was present at the outset for a sample of RA patients, which increased with follow-up. The study went on to conclude that, since many of these coexistent Conditions respond to preventative or therapeutic measures, co-morbidity needs earlier detection and management to reduce its impact on people with RA [17]. Turesson., *et al.* showed that age and RF were significant predictors of extra articular manifestations overall, but not specifically of severe extra articular organ manifestations, whereas early disability (measured by estimating the Steinbrocker functional class) was associated with the later development of extra-articular disease [11]. In the same way, Sherifa A. Hamed., *et al.* research revealed that significant association was identified between presence of neuropathy and patients' ages and advanced disease stages [7]. Accordingly, we studied the relationship between the development of neurologic complications of rheumatoid arthritis and the routine parameters used in the diagnosis and follow up of patients with RA. These are: The disease activity, the most recent ESR value, and the rheumatoid factor status at diagnosis. Results show that none of these measures can be used to determine the future possibility of developing neurologic complications of rheumatoid arthritis. This raise the difficulty of early prediction of prognosis regarding the extra-articular and neurologic complications. Nevertheless, other immunologic and clinical parameters can be evaluated to facilitate future expectation of extra-articular and neurologic complications.

Longitudinal data demonstrate a progressive and fairly rapid loss of function among people with rheumatoid arthritis [14]. The greatest decline in function generally occurs within the first two years of disease onset, and after progressing quickly, the rate of functional decline tapers off [14]. Our study revealed a very strong association between the disease activity of rheumatoid arthritis and the functional impairment to the extent that we can purely attribute the impairment in approximately one third of patients exclusively to the advanced disease activity. Moreover, when we compared the functional impairment in patients with and without neurologic complications we discovered that the impact of the neurologic complications is very minor compared to the effect of the disease activity. These results augment the importance of controlling the activity of rheumatoid arthritis. As a result, we encourage doctors to vigorously control the rheumatoid arthritis using the disease modifying agents and lifestyle measures. In addition, an important question is brought to the surface: Does the therapeutic measures of rheumatoid arthritis are adequate enough to control the disease activity and decrease the probability of developing the extra articular manifestations in general; and specifically the neurologic complications? Are there specific therapeutic measures enhance the functional impairment more than the others? Hopefully future researches will give a complete answer.

Conclusion

The frequency of the neurologic complications of rheumatoid arthritis is variable, and the morbidity resulting from uncontrolled rheumatoid arthritis activity is very noticeable compared to the morbidity related to the neurologic complications. The study showed that we

can't simply predict the possibility of developing the neurologic complications from simple measures, but the role of other measures can be investigated. In addition, there is no significant correlation between the neurological Complications of Rheumatoid Arthritis and the disease Activity. On the other hand, the intimate relationship between the morbidity and rheumatoid arthritis activity gives the doctor a chance to significantly improve the life of rheumatoid arthritis patients by extensive control of the disease using the disease modifying agents and supportive measures. In the future, data about the role of the different rheumatoid arthritis therapies in improving the functional status by decreasing the disease activity may alter the preference of treatment choice.

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