

# Achieving comprehensive remission or low disease activity in rheumatoid patients and its impact on workability – Saudi Rheumatoid Arthritis Registry

Hani Almoallim<sup>1-3</sup>

Nahid Janoudi<sup>2</sup>

Fahdah Alokaily<sup>4</sup>

Zeyad Alzahrani<sup>5</sup>

Shereen Alghary<sup>3</sup>

Hanan Alosaimi<sup>3,6</sup>

Suzan Attar<sup>3,7</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Umm Alqura University, Makkah, Saudi Arabia; <sup>2</sup>Department of Medicine, Dr. Soliman Fakeeh Hospital, Jeddah, Saudi Arabia; <sup>3</sup>Alzaidi Chair of Research in Rheumatic Diseases, Umm Alqura University, Makkah, Saudi Arabia; <sup>4</sup>Division of Rheumatology, Department of Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia; <sup>5</sup>Department of Medicine, Faculty of King Saud bin Abdulaziz for Health Sciences, Jeddah, Saudi Arabia; <sup>6</sup>Department of Medicine, King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia; <sup>7</sup>Department of Medicine, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

**Purpose:** Ability to work is an important endpoint in rheumatoid arthritis (RA). It is not clear what outcome measures should be used to guide treatment in order to maximize workability. This study addressed the impact of RA on workability in a Saudi population and examined the correlation between objective measures of disease activity and reduced workability. This will allow better understanding of treatment targets that will translate into improved workability.

**Patients and methods:** Data were collected through a digital patient record keeper: The Rheumatoid Arthritis Saudi Database. Male and female patients,  $\geq 18$  years of age, that met the American College for Rheumatology criteria for diagnosis of RA, were recruited, regardless of treatment. Demographic and disease-specific data were collected. Disease Activity Score-28 (DAS-28) was used to define patients as low (DAS-28  $\leq 3.2$ ) vs high (DAS-28  $> 3.2$ ) disease activity. Health assessment questionnaire (HAQ) score, visual analog scale (VAS) score, and musculoskeletal ultrasound 7 joint score were documented also. The work productivity and activity impairment (WPAI) score was used to measure absenteeism, presenteeism, overall work impairment, and activity impairment. DAS-28 score was correlated with WPAI score and linear regression used to identify the demographic and measures of treatment response that predict improvement in WPAI score.

**Results:** Higher absenteeism and more activity impairment were seen for patients with persistent DAS-28  $> 3.2$  (non-achievers). HAQ and VAS scores correlated with presenteeism, overall work impairment, and activity impairment.

**Conclusion:** Disease activity, as defined by DAS-28 score, correlates with absenteeism and work impairment in a Saudi population. However, on linear regression analysis, HAQ and VAS scores were the only measures predictive of work impairment. These scores should be used to monitor response to treatment regimens that aim to maximize work potential for Saudi individuals.

**Keywords:** rheumatoid arthritis, work impairment, WPAI score, disease activity, HAQ score, VAS score

## Introduction

Rheumatoid Arthritis (RA) is the most common form of inflammatory arthritis<sup>1</sup> with a worldwide prevalence of 0.04%–1.6% in adults, with significant national differences.<sup>2</sup> Patients with RA are often absent from work, decrease their routine work hours, or suffer from job loss, all of which contribute to productivity losses. Many RA patients continue to work despite ongoing active disease during which time they are unable to work at their full potential; “presenteeism”.<sup>3,4</sup> The associated costs are substantial,

Correspondence: Hani Almoallim  
Medical College, Umm Alqura University,  
PO Box 1821, Jeddah 21441,  
Saudi Arabia  
Tel +96 62 665 5000  
Email hani.almoallim@gmail.com

being estimated to account for 32% of the total annual costs per RA patient in Europe, exceeding other cost components, such as medical (21%), drug (14%), non-medical (14%), or informal care costs (19%).<sup>4-6</sup>

Merkesdal et al<sup>7</sup> found that within the first 3 years of RA, there was an average of 82 days of sick leave per person-year and 26% of patients lost work because of RA. In a patient cohort, with a mean duration of RA of 11 months at baseline, Eberhardt et al<sup>8</sup> reported the work disability rate to increase from 28% at baseline to 35% after 5 years. A total of 74.5% of patients reduced working hours by changing working status from full time to part time.

Patient-reported outcomes (PROs) are now recognized as important endpoints in clinical trials in general.<sup>9,10</sup> In RA, patients often cite improvement in health status related to work as an important priority.<sup>11</sup> Improvement in workability is, therefore, an important PRO that should be included as an endpoint in assessment of efficacy of treatment regimens for RA.

The need for objective measurement of disease activity is essential if treatment targets are to be met.<sup>12</sup> However, objective measures that will confidently translate into improved workability still need to be defined.

Furthermore, recent clinical trials have demonstrated that aggressive treatment in early RA leads to positive work-related outcomes. Initial treatment of RA with a combination of disease-modifying anti-rheumatoid drugs (DMARDs), compared with therapy with a single DMARD, significantly reduces the cumulative duration of sick leave and RA-related disability.<sup>13</sup> Similarly, early intervention with a combination of biologic therapy and methotrexate (MTX) significantly improved the employment potential of early RA patients<sup>14-18</sup> and reduced absent workdays.<sup>14,16,17</sup> These studies focused on measuring the impact of combination therapy on job loss, employability, and absent workdays. The consequent impact on overall productivity has yet to be established in Saudi Arabia, as data about workability in Saudi Arabia are minimal. Furthermore, current practice does not have a validated monitoring system to assess the impact of clinical response on work ability.

The aim of this observational cross-sectional study was to determine if clinical response, assessed by Disease Activity Score-28 (DAS-28), correlates with work ability, assessed by Work Productivity and Activity Impairment (WPAI) score, among RA patients in Saudi Arabia.

We believe that an important component of achieving remission/low disease activity (LDA) in RA should be a positive impact on workability measures with an important

therapeutic target in “T2T” being workability and not only disease activity.<sup>19</sup> Our aim is to keep the RA patient an active, working member of Saudi society. This study will define objective measures of disease activity that confidently translate into improved workability. This research was approved by the institutional and review board at Fakeeh hospital.

## Patients and methods

### Data source

The Rheumatoid Arthritis Saudi Database (RASD) is a digital patient record keeper that collates patient data for visits from April 2013 for multiple centers. In this non-interventional, cross-sectional study, data were collected from the RASD for a single center: Dr Suleiman Fakeeh Hospital, Jeddah.

### Data extraction and cohorts

Male and female patients, 18 years old or older, that met the American College of Rheumatology criteria for diagnosis of RA,<sup>20</sup> were included regardless of their treatment.

Demographic data collected included age, race, gender, marital status, educational level, occupation, residence area and number of children. At baseline the following clinical and RA history was collected: tender joint count (TJC), swollen joint count (SJC), pain, stiffness, duration of stiffness, fatigue, extra-articular manifestations of RA, smoking, alcohol consumption, co-morbidities, previous medication (name, dose, duration, reason to stop), current medication (name, dose, duration), previous surgery (RA related, type, site). Joint examination results were used to calculate a DAS-28 score. Vital signs, body mass index (BMI), and laboratory findings (hemoglobin, erythrocyte sedimentation rate, and C-reactive protein) were recorded and WPAI and musculoskeletal ultrasound (MSKUS) 7-joint scores calculated. Patients completed also a health assessment questionnaire (HAQ) and visual analog scale (VAS) allowing scores for each to be calculated.

Follow-up data were collected at routine visits, on average, every 2 months. At follow-up, joint examination results were collected (allowing DAS-28 to be calculated) and WPAI, HAQ, VAS, and change in MSKUS 7-joint scores calculated. Vital signs, BMI, and changes in medication and lab findings were documented.

### Data analysis

The WPAI is a validated tool for measurement of impairment in work ability and activity in RA.<sup>21,22</sup> This study assessed the difference in WPAI scores for the domains assessed (absenteeism, presenteeism, overall work impairment, and

activity impairment) between DAS achievers (patients with DAS-28 $\leq$ 3.2) and DAS non-achievers (patients with DAS-28 $>$ 3.2) and determined if there was any correlation between the following variables and poor work ability:

- DAS remission, DAS LDA, and DAS active disease
- HAQ score
- MSKUS findings
- Therapy (single DMARD, combined DMARD, and biologics)
- Type of work (sedentary and physical)
- Occupation (housewives, working females, and working males)
- Gender (M, F)
- Comorbidities (hypertension, diabetes mellitus, cardiovascular disease, osteoarthritis, and others)
- BMI (underweight, normal, overweight, and obese)
- Adherence (100%, 80%, 60%, and  $<$ 60%)

## Sample size calculation

We estimated the sample size needed to detect differences in WPAI domain scores between groups defined by the presence or absence of LDA (DAS-28  $\leq$ 3.2 versus  $>$ 3.2) by reference to published literature.<sup>3,4,14–17</sup> Based on the reported clinical responses, effect sizes were 0.2146, 0.4067, 0.5430 and 0.5469 for the absenteeism, presenteeism, activity impairment, and overall work Impairment domains, respectively. A total sample of 192 patients (96 per group) was estimated to provide 80% power to detect the effect size corresponding to the difference in presenteeism scores, and greater power to detect the effect sizes corresponding to the overall work impairment and activity impairment domains, with two-tailed  $\alpha=0.05$ .

## Statistical methods

Remission was assessed using the DAS-28, allowing patients to be categorized into patients in remission (DAS-28  $<$ 2.6) or with LDA (DAS-28 between 2.6 and 3.2) vs patients with active disease (DAS-28  $>$ 3.2). Given that data were shown to be non-Gaussian (Kolmogorov–Smirnov test), the Mann–Whitney *U* test was used to compare the distribution of the demographic and disease-related variables listed before between responders (patients with LDA) and non-responders (patients with active disease). The Mann–Whitney *U* test ranks all values and then calculates a mean rank for each group, ascertaining if these mean ranks are significantly different.

Work ability was assessed using the WPAI questionnaire. WPAI scores were calculated as follows:

1. Absenteeism (work time missed) (percent work time missed due to problem:  $Q2/(Q2 + Q4)$ )
2. Presenteeism (impairment at work/reduced on-the-job effectiveness) (percent impairment while working due to problem:  $Q5/10$ )
3. Overall work impairment (percent overall work impairment due to problem:  $Q2/(Q2 + Q4) + [(1 - Q2/(Q2 + Q4)) \times (Q5/10)]$ )
4. Activity impairment (percent activity impairment due to problem:  $Q6/10$ )

Mean WPAI scores were calculated and the association between poor work ability and the demographic and disease-related parameters have been listed before, calculated by Spearman's correlation.

Finally, a multivariate analysis was performed using a linear regression model with WPAI as the dependent variable, with all independent variables included in the model as covariates.

## Results

One hundred ninety-seven consecutive patients with RA treated at Dr Solaiman Fakeeh Hospital, Jeddah, were enrolled into the study (90.2% of Arabic descent), including 50 males (25.4%) and 147 females (74.6%). The median disease duration was 55 months. Additional demographic information is presented in Table 1. Results for WPAI scores are summarized in Table 2. Fifty percent of patients suffered from at least one comorbidity, most commonly hypertension (22.8%) and osteoporosis (18.8%) (Table 3).

**Table 1** Demographic and disease characteristics

| Characteristics                                 | Mean $\pm$ SD   |
|---|-----------------|
| Age (years)                                     | 48 $\pm$ 11.6   |
| Body mass index                                 | 30 $\pm$ 6.1    |
| Disease activity score                          | 2.29 $\pm$ 1.05 |
| Health assessment questionnaire                 | 0.46 $\pm$ 0.28 |
| Rheumatoid arthritis disease duration in months | 55 $\pm$ 61.3   |
| Patient-reported outcomes                       | 30 $\pm$ 10     |

**Table 2** Assessment of WPAI scores

| WPAI scores             | N   | Mean $\pm$ SD      | Min  | SD     | Max  |
|-------------------------|-----|--------------------|------|--------|------|
| Absenteeism             | 56  | 0.049 $\pm$ 0.0751 | 0.00 | 0.0751 | 0.33 |
| Presenteeism            | 56  | 0.281 $\pm$ 0.1328 | 0.05 | 0.1328 | 0.68 |
| Overall work impairment | 56  | 0.308 $\pm$ 0.1456 | 0.06 | 0.1456 | 0.72 |
| Activity impairment     | 196 | 0.356 $\pm$ 0.1350 | 0.08 | 0.1350 | 0.70 |

**Abbreviation:** WPAI, work productivity and activity impairment.

Since the data were non-normal, Mann–Whitney *U* test was conducted to identify significant differences in workability parameters between DAS achievers (patients with DAS-28  $\leq 3.2$ ) and DAS non-achievers (patients with DAS-28  $> 3.2$ ). Higher absenteeism ( $P=0.017$ ) and more activity impairment ( $P<0.001$ ) were seen for DAS non-achievers (Table 4). The mean rank for non-achievers in presenteeism and overall work impairment was higher compared with achievers, although this difference did not achieve statistical significance.

To assess the correlation between all factors and poor work ability, WPAI scores were divided into high and low based on their means and association with demographic and disease-related variables examined. The factors found to be significantly correlated with presenteeism, overall work impairment, and activity impairment were HAQ and VAS scores (Table 5). Multivariate regression model analysis was used to assess the predictive value of WPAI scores by effect of the same demographic and disease-related variables. The model was shown to be a good fit (adjusted  $R^2=0.67$ ). This analysis confirmed HAQ and VAS scores to correlate with workability (Table 6).

## Discussion

Initial studies sought to quantify the costs of disease in terms of early retirement with up to 70% of patients having work impairment by 10 years of disease duration and up to 30% being unable to work.<sup>23</sup> However, these studies documented also

impairment earlier in disease. It is now clear that LDA impacts also on work productivity<sup>24</sup> with significant work impairment appearing as early as the first year of disease.<sup>3,7</sup> Recent studies have emphasized the importance of the impact of RA on ability to work in patients continuing to work, resulting in absenteeism, presenteeism, and impaired work ability.<sup>4,7,25</sup> It has been suggested also that presenteeism may have a significantly greater economic impact than absenteeism.<sup>4,26</sup> Bansback et al<sup>27</sup> studied 150 patients with mean age of onset of 48 years and disease duration of 49 months. This group had mild disease with multidimensional HAQ score of 0.6. Even in this “early disease” cohort, presenteeism, absenteeism, and activity impairment were common. It was suggested that presenteeism was more prevalent in the early years of disease and patients being able to schedule their own work was associated with less presenteeism. The cohort reported here was similarly early in disease with a mean age of 48 years and disease duration of 55 months. Mean HAQ score was 0.46. This study demonstrated a significant difference in absenteeism and activity, but no difference in presenteeism and overall work impairment between DAS achievers and DAS non-achievers. Specific work practices, including cultural differences, may determine the impact of LDA on workability, including presenteeism. Thus, cultural differences between the populations studied may explain these differences.

From a methodological point of view, Breakman-Jansen et al<sup>28</sup> emphasized methodological challenges with such

**Table 3** Comorbidities

| Comorbidities       | N  | %    |
|---------------------|----|------|
| None                | 98 | 49.7 |
| Dyslipidemia        | 26 | 13.2 |
| Osteoporosis        | 37 | 18.8 |
| Osteoarthritis      | 11 | 5.6  |
| Hypertension        | 45 | 22.8 |
| Thyroid disturbance | 16 | 8.1  |
| Allergy             | 8  | 4.1  |
| Diabetes mellitus   | 27 | 13.7 |
| Asthma              | 10 | 5.1  |
| Others              | 2  | 1    |

**Table 5** Correlation of measures of disease activity with work impairment

| WPAI scores             |              | Joint score | HAQ   | VAS   |
|-------------------------|--------------|-------------|-------|-------|
| Presenteeism            | Coefficient  | 0.45        | 0.698 | 0.663 |
|                         | Significance | 0.035       | 0.00  | 0.00  |
| Overall work impairment | Coefficient  | 0.45        | 0.682 | 0.621 |
|                         | Significance | 0.034       | 0.00  | 0.00  |
| Activity impairment     | Coefficient  | 0.515       | 0.517 | 0.652 |
|                         | Significance | 0.014       | 0.014 | 0.00  |

**Abbreviations:** HAQ, health assessment questionnaire; VAS, visual analog score.

**Table 4** Correlation of response to therapy with work impairment

| Work ability            | N   | Achievers           |           | Non-achievers       |           | Significance |
|-------------------------|-----|---------------------|-----------|---------------------|-----------|--------------|
|                         |     | Mean score $\pm$ SD | Mean rank | Mean score $\pm$ SD | Mean rank |              |
| Absenteeism             | 56  | 0.043 $\pm$ 0.073   | 26.96     | 0.104 $\pm$ 0.071   | 44.20     | 0.017        |
| Presenteeism            | 56  | 0.268 $\pm$ 0.123   | 27.28     | 0.405 $\pm$ 0.176   | 40.90     | 0.074        |
| Overall work impairment | 56  | 0.295 $\pm$ 0.137   | 27.31     | 0.435 $\pm$ 0.181   | 40.60     | 0.085        |
| Activity impairment     | 196 | 0.346 $\pm$ 0.133   | 94.37     | 0.470 $\pm$ 0.089   | 148.33    | <0.001       |

**Note:** Achievers had DAS-28 score  $\leq 3.2$  following therapy, whereas non-achievers scored  $> 3.2$ .

**Table 6** Multiple regression analysis of variables correlating with improvement in workability

| Predictors | Absenteeism |       |       | Presenteeism |       |       | Overall work impairment |      |       | Activity impairment |      |       |
|------------|-------------|-------|-------|--------------|-------|-------|-------------------------|------|-------|---------------------|------|-------|
|            | B           | F     | Sig.  | B            | F     | Sig.  | B                       | F    | Sig.  | B                   | F    | Sig.  |
| HAQ        | 0.10        | 6.7   | 0.01  | 0.305        | 26.7  | 0.00  | 0.169                   | 2.39 | 0.02  | 0.16                | 4.3  | 0.00  |
| MSKUS      | 0.041       | 0.95  | 0.33  | 0.07         | 1.1   | 0.2   | -0.7                    | -2.7 | 0.01  | 0.00                | -1.7 | 0.6   |
| BMI        | 0.001       | 0.159 | 0.6   | 0.01         | 0.12  | 0.61  | -0.02                   | -0.6 | 0.5   | 0.001               | 0.4  | 0.6   |
| VAS-GH     | 0.003       | 7.0   | 0.01  | 0.009        | 44.8  | 0.00  | -0.042                  | -2.1 | 0.04  | 0.003               | 3.01 | 0.003 |
| VAFS       | -0.013      | 2.2   | 0.13  | -0.04        | -2.7  | 0.007 | -0.04                   | -2.3 | 0.02  | -0.03               | -4.5 | 0.00  |
| DAS-28     | 0.131       | 0.286 | 0.595 | 0.332        | 0.484 | 0.489 | -0.087                  | 0.02 | 0.885 | 0.255               | 5.52 | 0.131 |

**Abbreviations:** BMI, body mass index; DAS-28, disease activity score-28; HAQ, health assessment questionnaire; MSKUS, musculoskeletal ultrasound; Sig., significance; VAFS, visual analog fatigue scale; VAS-GH, visual analog scale-general health.

studies emphasizing the importance of including a control group and the fact that different tools produce different results. In this study, this problem was avoided as the study compared groups defined by DAS-28 score and a validated tool was used. Chaparro del Moral et al<sup>29</sup> and Zhang et al<sup>21</sup> have similarly shown a correlation between DAS score and work impairment.

With recognition of the impact of RA on workability, even early in disease, and the recognition of the importance of this to patients, the importance of including PRO measuring workability as a primary endpoint in studies of RA treatment is becoming increasingly recognized. This study reinforces this assertion. Patient-reported outcomes have been measured using a variety of tools, including the WPAI-RA score. In the RA-BUILD study, comparing baricitinib to placebo at a mean of ~7 years from symptom onset, only 35%–40% of patients were employed at baseline.<sup>30</sup> Activity and presenteeism were improved for baricitinib vs placebo at week 12 but these differences were not sustained to week 24. No difference was seen for absenteeism. Strand et al reported improvement in PRO following certolizumab pegol treatment<sup>31</sup> and tocilizumab to be superior to MTX or adalimumab monotherapy.<sup>32</sup>

Finally, cultural differences in work practices make it essential that such studies are carried out within the specific cultural groups to which they are applicable,<sup>33</sup> in particular given the potential for differences in work practice to be a determinant of the impact of RA. National differences in work practices will thus influence the impact of RA on workability.

This study emphasizes the importance of including assessments of workability in evaluation of treatments for RA and addresses also the importance of country-specific studies.

Objective disease measures that confidently predict improvement in workability are needed to manage treatment on a day-to-day basis. Strand et al<sup>34</sup> demonstrated

treatment-related improvements in WPAI, which were predicted by age, overall work impairment, disease duration, HAQ-disability index score >0.5, and pain VAS. Our study similarly demonstrated an association between poor work ability and both Joint score and HAQ. Finally, a multivariate regression model correlated the factors significantly associated with presenteeism, overall work impairment, and activity impairment to HAQ score and VAS only. It is of interest that measures of disease activity that are based on “observer” assessment, such as DAS-28 (clinician examining joints) or MSKUS-7 (ultrasound criteria) do not predict workability on linear regression analysis. Whereas outcome measures that rely on patient reporting of health status (HAQ and VAS general health scores) do predict workability (Table 6). This emphasizes the importance of PRO in assessing responses to treatment rather than arbitrary clinical criteria, the correlation of which with functionality may not be clear.

## Conclusion

Disease activity early in disease, as defined by DAS-28 score, correlates with absenteeism and work impairment in a Saudi population. By linear regression analysis, the objective measures found to be predictive of work impairment were HAQ and VAS scores. In attempting to maximize work potential for Saudi individuals, this study, therefore, suggests that improvement in these objective scores should be a focus for treatment regimens aiming to “Treat to Work”, allowing rheumatologists to achieve the important PRO of improved workability.

This study confirmed the WPAI to be a useful tool for measurement of workability and defined disease parameters that can be used to guide treatment that will confidently translate into improved workability.

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## Disclosure

The authors report no conflicts of interest in this work.

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