Journal of Ayurveda and Integrative Medicine 14 (2023) 100689

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: http://elsevier.com/locate/jaim

Original Research Article

# Development and validation of an *ama* instrument for assessing the disease activity on the basis of constitutional features in *Amavata* (Rheumatoid Arthritis)

Preeti Pandey [a], Sanjeev Rastogi [a, *], Able Lawrence [b], Girdhar G. Agrawal [c]

[a] *Ayurveda-Arthritis Treatment and Advanced Research Center (A-ATARC), State Ayurvedic College and Hospital, Lucknow, India*
[b] *Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India*
[c] *Department of Statistics, University of Lucknow, Lucknow, India*

ARTICLE INFO

*Article history:*
Received 3 August 2022
Received in revised form
1 November 2022
Accepted 12 January 2023
Available online xxx

*Keywords:*
Disease activity score
Rheumatoid arthritis
Amavata
Ayurveda

ABSTRACT

*Background:* Rheumatoid Arthritis (RA), having a striking clinical resemblance to *amavata* in traditional Indian medicine (Ayurveda) presents an opportunity to look at disease from two different healthcare perspectives. This differential information may potentially supplement one system with the knowledge of the other for optimal application. This study is the first of its kind, where Ayurvedic concepts of *amavata* have been adopted to enhance the knowledge about RA where optimal care is still beyond the common reach.

*Objective:* The study was conducted to develop and validate a novel *ama* score based upon constitutional features of *ama* as depicted in ayurvedic literature as a disease activity indicator in RA.

*Material and methods:* The study was conducted in two parts comprising development and textual validation of the *ama* assessment instrument (AAI) followed by its clinical testing. AAI comprising ten items, was developed where each item was provided with a range of scores to offer the assessment close to the patient's observations. The score obtained through AAI was clinically and statistically tested on 79 RA/*amavata* patients randomly selected for validity and reliability. The score obtained through AAI was tested for its correlation with the DAS-28 score and ESR.

*Results: Ama* Assessment Instrument could find a slight correlation with acute phase reactant ESR (r-value between ESR and AMA at baseline is 0.287, and at 1st, 2nd, and 3rd follow-up is 0.276, 0.276 and 0.160 respectively) and DAS-28 (The r value between DAS and AMA at baseline is 0.231, and at 1st, 2nd and 3rd follow up is 0.218, 0.201 and 0.247 respectively). It however emerged as an independent disease status marker since it could mark the changes in the study population on a time scale more precisely as compared to DAS -28 or ESR. When the *ama* values at different follow-ups were compared, a significant difference was observed consistent with disease activity marker catching constitutional and GI related domain of the patients. When reducing values of *ama* score were compared to overall improvements as reported by the patients, a similar trend was observed showing that a change in *ama* score is reflective of a change in disease status and the impact of the disease on the patient.

*Conclusion:* This study provided a quantitative measure for the abstract concept of *ama* which could be used to mark the disease activity in *amavata* or RA. The change in *ama* based scores can be used to assess disease status and the intervention related benefits. The observations prompt for the possible inclusion of AAI in RA composite score to make it more dynamic in terms of disease activity identification in RA.


## 1. Introduction

In the management of rheumatoid arthritis (RA), assessment of disease activity plays crucial. The level of disease activity primarily works as a point of reference to predict the course of illness

* Corresponding author.
*E-mail:* rastogisanjeev@rediffmail.com
Peer review under responsibility of Transdisciplinary University, Bangalore.

https://doi.org/10.1016/j.jaim.2023.100689

prospectively. Disease activity score (DAS) on its own or in combination with acute phase reactants like ESR and CRP has also been critically utilized to judge the outcome of any intervention in RA [1]. Knowing the disease activity status in rheumatoid arthritis therefore became the first mandate in the current practice of clinical rheumatology.

Although important, we observe that the DAS score is not always reflective of the clinical conditions or the concerns of the RA patients and similarly is not always a reliable reflector of the outcomes observed after any therapeutic intervention in RA [2]. The reason for this mismatch between observed and actual disease status is that DAS largely relies upon observations made by the physician on the domain areas like joint pain, swelling and tenderness. Tenderness, pain or swelling reported by the patient but not elicitable to the physician, obviously leads to a lower disease activity score. To overcome the limitation of DAS score, the use of composite scores having multiple variables have been proposed. Two commonly utilized indices of this kind in RA are the clinical disease activity index (CDAI) and simplified disease activity index (SDAI) [3].

Rheumatoid arthritis is a systemic disorder, with many extra articular and constitutional features that contribute to the status of the disease. Unfortunately, in the conventional disease activity identification done by the tools currently available, such features remain unnoticed irrespective of their importance from the patient's perspective. Finding this gap, recently some suggestions have been made to include fatigue [4] and sleep [5] as disease activity indicators and outcome assessors in RA. Weight loss during the early and active phase of RA is also a key observation during the high disease activity indicative of poor prognosis [6,7]. Recently, the normalization of appetite and resulting weight gain has beenproposed to be one important outcome measure in selected RA patients [8]. However, these new entrants of disease monitoring are yet to find a place in routine assessment of RA.

On the contrary, the traditional health care system particularly Ayurveda, has a vivid clinical description of *amavata*, a disease entity resembling to inflammatory arthritis including RA and Spondyloarthritis (SpA) gives a great attention to the systemic features besides adhering to the joint related features. This is observed that the patients diagnosed with RA or SpA on the basis of ACR or EULAR criteria, if simultaneously diagnosed as *amavata* based on Ayurveda fundamentals and are treated based on such principles, respond well to the Ayurveda interventions [9]. More importantly, in such cases treated with Ayurveda, systemic features respond well and early. RA patients on Ayurveda interventions report less fatigue, stiffness, lethargy, lack of interest, improved appetite and improved weight [10]. Although, this is yet to be understood that to what extent these systemic features can be correlated to the primary joint pathology in RA, their correction simultaneous to the reduction in joint symptoms after the ayurvedic intervention gives a clue for their possible association in altering the primary pathology and thereby in determining the disease activity status.

From Ayurvedic perspective, *ama* is an important pathogenic produce involved in *amavata*. This is conceptualized as a product of incomplete digestion and metabolism resulting from impaired metabolic fire (*agni*) .*Ama* produced at GIT, tissue or cellular level is proposed to have obliterative properties owing to its stickiness and macromolecular nature. Due to this nature, *ama* can produce features resulting from the obstruction of the conduits. *Ama* can be involved in a disease either as a primary factor like in *amavata* or can secondarily be involved in the disease process because of consequences impairing digestive or metabolic *agni* [11].

*Ama* produces pathognomonic GI related or systemic features depending on the site of its primary production and settlement. Its presumed level and associated features often correlate with disease activity. All treatments involving *ama* are directed towards dissociating of existing *ama* (*ama pachana*) and stopping further production and accumulation of *ama* (*agni deepana*). For this reason, a treatment focusing on *ama* leads to the disappearance of *ama* related features gradually [12].

To ease the understanding of *ama* related pathogenesis in a clinical setting, various features related to *ama* association of *dosha* are described in Ayurvedic texts. *Sama* (features with *ama*) and *nirama* (features without *ama*) examination make one important point of clinical examination in Ayurveda helping to determine the relative availability of *ama* in the body and thus determining the appropriate therapeutic action plan.

The association of *ama* in the body with various *dosha* and *mala* may be identified by clinical features representing their association. Once such association is lost, the clinical features also disappear. It is for this reason; *ama* related features seem to have a high indicator value for *ama* related disease activity. This can also help assess the therapeutic responses by seeing if the features of *ama* are reducing in intensity after the appropriate therapeutic interventions in an *ama* related pathology.

*Amavata* is a classical prototype of *ama* related pathogenesis where *ama* has been involved in the disease process since the beginning. Treatments focusing upon *ama* dissociation and prevention of its further formation are the first line of management of *amavata* besides many other interventions aiming to manage other symptoms. Assessing the relative presence or absence of *ama* in a patient of *amavata* has a huge, predictive and prognostic value by knowing the disease activity. This also has a high value for it being utilized as a patient-related outcome measure (PROM) occurring as a response to any therapeutic intervention. In rheumatoid arthritis (RA) which represents a subpopulation under the umbrella term of *amavata* representing most varieties of inflammatory arthritis, PROM has been of renewed interest as dependable measures to assess the outcome of any intervention. Measuring constitutional features like fatigue, stiffness, sleep, appetite etc. have been prompted recently as important indicators of changes in the pathogenesis ofRA in response to any therapeutic intervention. *Ama* assessment from an ayurvedic perspective therefore presents an opportunity to make a composite measurement of all constitutional features thatare highly sensitive from the patient's perspective and truly reflective of an *ama* related joint pathogenesis. It is presumed that an *ama* assessment may not only find its high applicability in ayurvedic clinical practice related to joint diseases but also its high applicability in modern rheumatology practice by providing a composite tool to measure many constitutional features in one go. Despite its high clinical importance, attempts have not been made to make *ama* assessment among *amavata* patients suitable for its predictive and prognostic value.

Development and validation of an *ama* assessment instrument (AAI) for making a quantitative assessment of *ama* for its use in Ayurveda rheumatology practice therefore is highly desired. Subsequent to its development, this AAI when tested for its clinical reliability and validity against existing disease activity indicators of RA, was found to have a potential to emerge as a high utility index to assess disease activity in RA. This study was done to develop and validate the AAI observations as disease activity indicator and to check its reliability as a disease activity indicator in RA.

## 2. Materials and methods

### 2.1. Study setting

This study was conducted at the PG Department of Kaya Chikitsa, State Ayurvedic College and Hospital, Lucknow (PP, SR) in

collaboration with the Department of Clinical Immunology and Rheumatology, SGPGI, Lucknow (AL) and Department of Statistics, Lucknow University, Lucknow (GGA). The development and initial validation of the AAI were done in this setting. The face and content validity was partly by inviting domain experts outside the primary research institution. The clinical testing of the instrument was done at Ayurveda −Arthritis Treatment and Advanced Research Center (A-ATARC), State Ayurvedic College and Hospital, Lucknow.

### 2.2. Time frame of the study

AAI development began in December 2020 and was completed in June 2021. After the instrument's initial validation, the AAI clinical testig was done from July 2021 to April 2022. The data was subsequently statistically analyzed in June 2022.

### 2.3. Ethical clearance

The study had an ethical clearance issued by Institutional Ethics Committee wide letter no. SAC/IEC/2020/Dated 23.10.2020.

### 2.4. Conduction of the study

The study was conducted in two steps. The first was about developing the *ama* assessment instrument (AAI) for quantitative measurement of *ama* (index test) based on available classical literature. This step involved multiple small steps, from screening the available literature to finalizing tool components after pilot testing. The second step of the study was related to the validation of developed AAI on various parameters and correlating the AAI observations with standard biomarkers or disease activity scores (reference test) in RA both before and after a given intervention for a certain time period. The process utilized in this study for the development and validation of a new tool was tested and proven reliable through earlier studies having their relevance to Ayurveda [13,14].

### 2.5. Development of ama assessment instrument (AAI)

The process utilized for the development of AAI was done by utilizing following steps related to the construction of Instrument-

1. **Domain specification**: This involved the specification of "what" is to be measured in the evaluation.
2. **Scaling:** This involved the conversion of qualitative characteristics in quantitative terms. This was done by identifying the two extremes of responses against a given question and subsequently dividing the range of responses into 10 clearly definable categories.
3. **Item generation**: This involved the specific question formation pertaining to the specific domain area.

### 2.6. Literature survey

To begin the process of development of AAI, nine classical texts (Table 1) of Ayurveda were thoroughly screened for the inscription of *ama* related features. After thoroughly reviewing all texts, 51 signs/symptoms were identified for relevance to *ama* related pathology. These symptoms were subsequently listed to identifycommonly agreed upon by all texts consulted for the process. In this process 27 features were found to be described by almost every text either in a similar language or with partially rephrased language having a similar meaning. From the shortlist, the symptoms pertaining to the joint were eliminated to keep the focus on the constitutional features of *ama*. This exercise has eliminated six joint-related features and finally identified 21 features for their relation to the systemic presentation of *ama*.

**Table 1**
Classical texts of Ayurveda reviewed for AAI development.

| Number | Name of the text book |
|---|---|
| 1. | Charak Samhita |
| 2 | Sushruta Samhita |
| 3 | Astanga Samgraha |
| 4 | Astanga Hridaya |
| 5 | Bhava Prakash |
| 6 | Sharangadhara Samhita |
| 7 | Madhava Nidana |
| 8 | Yoga Ratnakar |
| 9 | Bhisahjya Ratnavali |

### 2.7. Finding the standard ayurvedic terms (SAT)/morbidity code and English equivalents for selected items

The selected 21 items had their standard ayurvedic terminologies (SAT) and morbidity identified with the help of the NAMSTP (National Ayurveda Morbidity Code and Standard Terminology Portal) application developed by Ministry of Ayush, Govt of India [15] (Table 2).

### 2.8. Content validity of the selected items

After making the preliminary selection of items reflective of the clinical presentation of *ama* related systemic pathology, the selected items were further reviewed against a relevance scale of 1−5 showing minimum to maximum relevance by a national cohort of 12 clinical experts of Ayurveda selected based on their experience and expertise in rheumatology. Each expert in the process was provided with a detailed item sheet consisting of all 21 items and was asked to mark the relevance of the individual item in reference to disease activity status of *amavata* on a scale ranging from 1 to 5 representing minimum and maximum relevance respectively.

The relevance identification was made by approaching the experts physically or through email. Responses from ten experts were obtained within the stipulated time whereas two experts could not comply with the time specified for the responses. Based on summated responses of all ten experts, the items having an average score four or higher were selected to frame the final index tool. This process has finally identified ten items agreed upon by all experts for having high relevance as the systemic clinical feature related to *ama* pathology (Tables 2 and 3).

### 2.9. Formatting the questions for practical application of AAI and determining the scores for individual observations

Once clearly identified for their relevance and being selected through a process of consensus of a cohort of experts, selected items were expanded into the question to make them comprehensible by the RA patients when attempted for *ama* examination in individual cases (Table 4). Selected items after formatting of appropriate questions were allocated a range of score from 1 to 10 in order to get a closer opinion from the respondent. For this purpose 1 was considered to be minimum intensity of a specific feature whereas 10 was considered the highest intensity of the same selected feature. Based upon this scoring pattern, 100 had been postulated as the highest and 10 as the lowest ama score in any given case.

**Table 2**
Features suggestive of *ama* status in RA/*amavata* patients and summated score given by the cohort of *amavata* experts.

| S.n. | Specific features | SAT code/morbidity code | Interpretation in English[a] | Summated score by 10 experts | Average score |
|---|---|---|---|---|---|
| 1. | सदन | SAT-D.8547 | With body pain | 45 | 4.5 |
| 2. | पृष्ठकटग्रिह | SAT-D.1894 | Stiffness of the lumber region or lower back | 39 | 3.9 |
| 3. | तृष्णा | EK-2 | Polydipsia | 36 | 3.6 |
| 4. | अरोचक | SAT-D.8171 | Tastelessness | 45 | 4.5 |
| 5. | व्याकुलता | SAT-D.7404 | Restlessness | 37 | 3.7 |
| 6. | आलस्य | SAT-D.914 | laziness | 44 | 4.4 |
| 7. | मूत्राधक्रिय | ACB-9 | Polyurea | 29 | 2.9 |
| 8. | उदर गुरुता | SAT-D.1579 | Heaviness in abdomen | 40 | 4.0 |
| 9. | स्रोतोरोध | SAT-C.159 | Obstructive pathology occurring in channels | 47 | 4.7 |
| 10. | बलभ्रंश | SAT-D.5483 | Diminution of physical strength | 45 | 4.5 |
| 11. | गौरव | SAT-D.8463 | Heaviness of the body | 45 | 4.5 |
| 12. | क्लम | SAT-D.2521 | Exhaustion without exertion | 39 | 3.9 |
| 13. | वायुवबिंध | | | 37 | 3.7 |
| 14. | वेदना | SAT-D.7358 | Pain/sensation | 46 | 4.6 |
| 15. | शोथ | EK-3 | Edema/inflammation | 45 | 4.5 |
| 16. | अंग पीडन | SAT-D.167 | Bodyache | 39 | 3.9 |
| 17. | स्तैमत्रिय | SAT-D.8875 | A sensation of dampness/feeling as if wrapped with wet clothes | 33 | 3.3 |
| 18. | अरत ि | SAT-D.817 | Restlessness/distress | 42 | 4.2 |
| 19. | अतनिद्रा | SAT-D.301 | Excessive sleep | 39 | 3.9 |
| 20. | अशन मे वव्रिदेष | No information available | Disliking of food | 39 | 3.9 |
| 21. | गात्र पाण्डुता | No information available | Pallor/paleness of body | 28 | 2.8 |

[a] The English translation of specific features are in accordance of Standardized Ayurveda Terminology (SAT) & National Ayurveda Morbidity Code described by Ministry of Ayush.

**Table 3**
Finally selected list of clinical features for their relevance in assessing the disease activity status in *amavata*.

| S.n. | Specific features | English interpretation |
|---|---|---|
| 1 | सदन | With body pain |
| 2 | अरोचक | Tastelessness |
| 3 | आलस्य | laziness |
| 4 | उदर गुरुता | Heaviness in abdomen |
| 5 | स्रोतोरोध | Obstructive pathology occurring in channels |
| 6 | बलभ्रंश | Diminution of physical strength |
| 7 | गौरव | Heaviness of the body |
| 8 | वेदना | Pain/sensation |
| 9 | शोथ | Edema/inflammation |
| 10 | अरत ि | Restlessness/distress |

### 2.10. Validity testing of the formatted prototype questionnaire

During the process of AAI development, the prototype questionnaire including all items and their scales of quantitative measurement was taken up for its content and construct validity. For content validity each item in the questionnaire was reviewed by a team of in-house Ayurveda experts (having a minimum standard decided before the start of the study) in *ama* assessment through clinical examination and was evaluated if each of the items had the possibility of predicting the *ama* status in *Amavata* patients.

Construct validity was done through an exploration of each item for their construct and showing if the construct of the item and the scale assigned to measure it quantitatively is able to find the answer it is aiming at.

### 2.11. Pilot testing of the prototype questionnaire

The pilot testing of the prototype AAI was done on 10 RA patients fulfilling the specific inclusion and exclusion criteria for selecting cases for clinical validation of the instrument. The participants of the pilot testing were selected from A-ATARC outpatient clinic on routine OP days. Such patients were given the AAI to obtain a response from them and see if there were any interpretational problems. This pilot testing was done by the lead investigator (PP) of this study. After this exercise, one item and the question framed to evaluate this (Q 2) were found ambiguous. This question was therefore elaborated and expanded in the final questionnaire to give a clear meaning and response selection. The questionnaire approved after pilot testing was subsequently taken up for further clinical validation study of the instrument.

**Table 4**
Formatting of the questions for selected items for assessment of *ama*.

| S.n. | Specific features | English interpretation | Proposed question to be asked for enquiry (Hindi) | English translation for the proposed question to be asked for enquiry |
|---|---|---|---|---|
| 1. | सदन | With body pain | क्या आप इन दनिों थका हुआ सा महसूस करते हैं? | Do you feel excessively tired these days? |
| 2. | अरोचक | Tastelessness | क्या आपको इन दनिों भोजन रुचकिर नही लगता हैं? | Do you feel disliking/tastelessness in your favorite food recently? |
| 3. | आलस्य | Laziness | क्या आप इन दनिों अधकि आलस्य महसूस करते हैं? | Do you feel lazy these days? |
| 4. | उदर गुरुता | Heaviness of abdomen | क्या आपको इन दनिों पेट में भारीपन जैसा महसूस होता हैं? | Do you feel heaviness in your abdomen these days? |
| 5. | स्रोतोरोध | Obstructive pathology occurring in channels | क्या आपको इन दनिों शरीर में जकडन सी महसूस होती हैं? | Do you feel any stiffness in your body/body parts these days? |
| 6. | बलभ्रंश | Diminution of physical strength | क्या आपको इन दनिों अधकि शारीरकि कमजोरी सी महसूस होतो हैं? | Do you feel weakness in these days? |
| 7. | गौरव | Heaviness of the body | क्या आपको इन दनिों शरीर में भारीपन सा महसूस होता हैं? | Do you feel heaviness in your body these days? |
| 8. | वेदना | Pain/sensation | क्या आपको इन दनिों शरीर मे दर्द सा महसूस होता है? | Do you feel pain in your body/body parts these days? |
| 9. | शोथ | Edema/Inflammation | क्या आपको इन दनिों शरीर के कसिी भाग में सूजन सी महसूस होती हैं? | Do you feel any kind of swelling in your body/body parts these days? |
| 10. | अरत ि | Restlessness/Distress | क्या आपको इन दनिों बेचैनी, घबराहट अथवा तनाव सा महसूस होता है? | Do you feel any kind of stress, anxiety or restlessness these days? |

### 2.12. Clinical validation study against existing benchmarks of disease activity parameters in RA

The *ama* assessment instrument was subsequently validated against standard disease activity indicators in RA (*amavata*). These standard disease activity scores and markers comprised ESR and DAS 28 scores. Following were the inclusion criteria of the selection of patients of RA (*amavata*) for the validity testing of the instrument –

1. Age between 20 and 60 years, of either gender
2. Diagnosable as *amavata* as per ayurvedic criteria and RA as per ACR criteria
3. Having the symptoms for not less than 3 months and not more than 5 years
4. Should not have taken any long acting steroids or disease modifying anti rheumatic drugs in past three months which may have modified the status of *ama* related features
5. Should not have taken any NSAID or short acting steroids during past 24 h from the time of actual interrogation.

### 2.13. Exclusion criteria

1. Patients having any other joint pathology besides RA (*amavata*)
2. Patients having *ama* related systemic pathology eg. Obesity, hypothyroidism, diabetes, Hepato-stetosis etc. To rule out such conditions, every prospective participant was screened for Random Blood Sugar, BMI, TSH and Serum Alkaline Phosphatase and only those coming under the strict inclusion and exclusion criteria were taken into the study.

### 2.14. Participant's sample for the clinical validation study

The reliability and validity of the instrument were tested on 79 participants fulfilling the inclusion and exclusion criteria.

Construct and content validity was tested with the help of ~10 domain experts fulfilling predetermined inclusion criteria.

## 3. Results

79 patients duly diagnosed with RA and *amavata* fulfilling the inclusion and exclusion criteria having attended the A-ATARC OPD were enrolled in the study (Fig. 1). The study population included

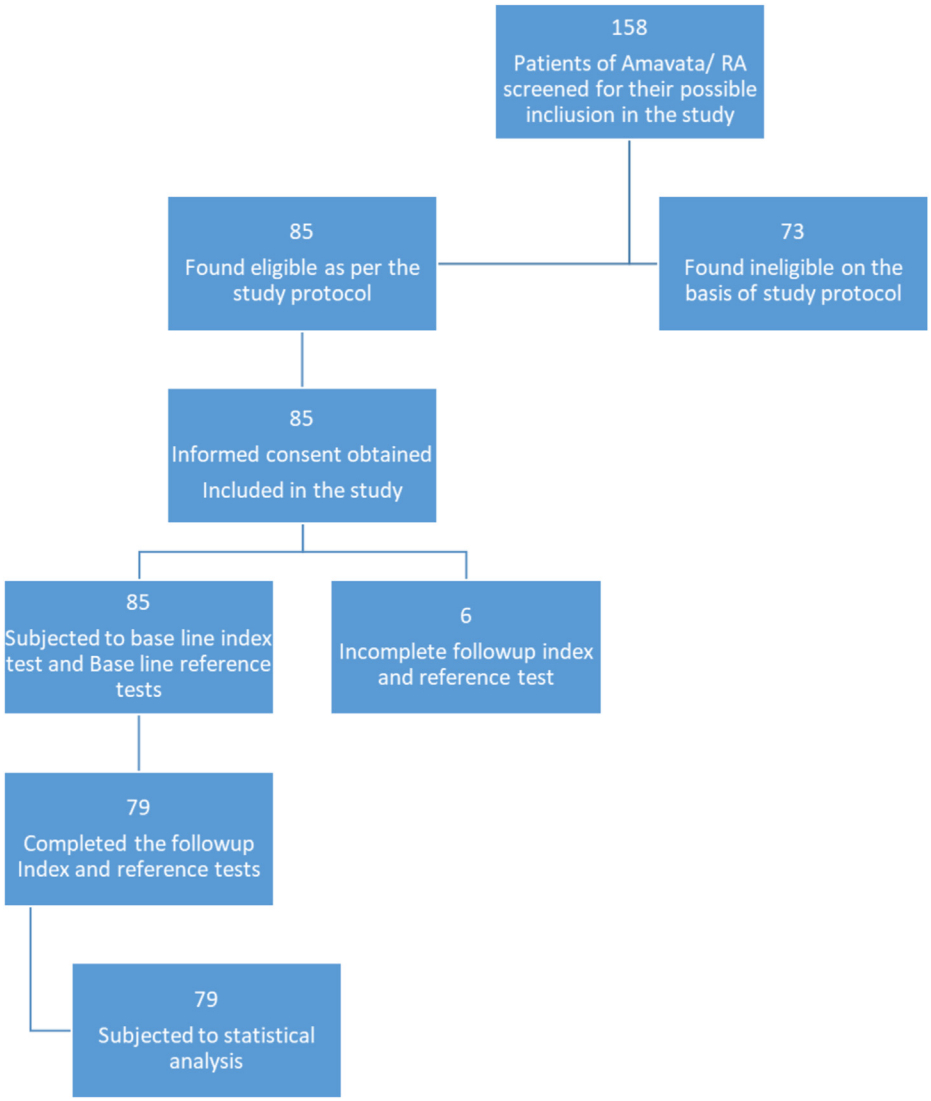


**Fig. 1.** Study flow chart.

14 male (17.72%) and 65 female (82.27%) with mean age of 44.68 years (SD ± 12.68 Years). Mean duration of illness in study population was 3.01 Year.

All study participants were examined at baseline for DAS-28 score, ESR (reference tests) and AMA score (index test). The participants were further examined at follow−ups every month and finally on completion of the study after three months.

*Ama* instrument was tested statistically for reliability using Cronbach's Alpha and Spearman−Brown Coefficient (split half method) (Table 5) and validity using Pearson Correlation and Sig. (2-tailed) (Table 6). Considering Chronbach's Alpha, the reliability of Baseline (0.724) is maximum, whereas minimum for Follow-up 3 (0.689). Similarly, considering split half method, the reliability of Follow-up 3 (0.803) is maximum, whereas minimum for Follow-up 1 (0.750). For the scores computed, the reliabilities obtained are acceptable. Based on the significance value obtained by the Sig. (2 tailed), the sig. (2 tailed) values obtained are less than 0.05, so it can be concluded that the items are valid.

### 3.1. Correlation between ama score and disease activity markers in RA

A Pearson Correlation was obtained at different timelines (baseline, follow-ups and final follow-up) between *Ama* score and DAS score and also ESR. At each of such observations DAS and ESR were found moderately correlated on the basis of r value whereas *Ama* was only slightly related to both DAS and ESR at all 4 observation time points (Table 7).

The r value between DAS and ESR obtained is 0.572 which means the DAS and ESR is moderately correlated. The r value between DAS and AMA obtained is 0.231 which means DAS and AMA are slightly correlated. The r value between ESR and AMA obtained is 0.287 which means ESR and AMA are slightly correlated.

The r value between DAS and ESR obtained is 0.485 which means the DAS and ESR is moderately correlated. The r value between DAS and AMA obtained is 0.218 which means DAS and AMA are slightly correlated. The r value between ESR and AMA obtained is 0.276 which means ESR and AMA are slightly correlated.

The r value between DAS and ESR obtained is 0.400 which means the DAS and ESR is moderately correlated. The r value between DAS and AMA obtained is 0.201 which means DAS and AMA are slightly correlated. The r value between ESR and AMA obtained is 0.276 which means ESR and AMA are slightly correlated.

The r value between DAS and ESR obtained is 0.439 which means the DAS and ESR is moderately correlated. The r value between DAS and AMA obtained is 0.247 which means DAS and AMA are slightly correlated. The r value between ESR and AMA obtained is 0.160 which means ESR and AMA are slightly correlated.

**Table 5**
Reliability testing for *ama* score.

| Reliability | | |
|---|---|---|
| | Cronbach's Alpha | Spearman−Brown coefficient (split half method) |
| Baseline | 0.724 | 0.776 |
| Followup1 | 0.695 | 0.750 |
| Followup2 | 0.695 | 0.782 |
| Followup3 | 0.689 | 0.803 |

**Table 8**
Descriptive statistics of cumulative *ama* scores at various time points.

| | Mean | Std. deviation | N |
|---|---|---|---|
| AMA score (baseline) | 57.15 | 8.476 | 79 |
| AMA score (1st follow up) | 49.39 | 7.155 | 79 |
| AMA score (2nd follow up) | 42.03 | 6.577 | 79 |
| AMA score (3rd follow up) | 34.91 | 5.359 | 79 |

**Table 6**
Validity testing for *ama* score.

| | | *Ama* SCORE_B | *Ama* SCORE_1 | *Ama* SCORE_2 | *Ama* SCORE_3 |
|---|---|---|---|---|---|
| Tiredness | Pearson correlation | 0.751 | 0.636 | 0.675 | 0.740 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Tastelessness | Pearson correlation | 0.461 | 0.384 | 0.528 | 0.579 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Laziness | Pearson correlation | 0.678 | 0.667 | 0.649 | 0.704 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Heaviness in abdomen | Pearson correlation | 0.394 | 0.351 | 0.449 | 0.461 |
| | Sig. (2-tailed) | 0.000 | 0.002 | 0.000 | 0.000 |
| Stiffness in body | Pearson correlation | 0.576 | 0.544 | 0.424 | 0.501 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Diminution of physical strength | Pearson correlation | 0.496 | 0.496 | 0.596 | 0.492 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Heaviness of the body | Pearson correlation | 0.514 | 0.539 | 0.505 | 0.447 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Body pain | Pearson correlation | 0.487 | 0.532 | 0.504 | 0.587 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |
| Swelling in the body/body part | Pearson correlation | 0.447 | 0.477 | 0.427 | 0.237 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.036 |
| Anxiety | Pearson correlation | 0.611 | 0.602 | 0.501 | 0.407 |
| | Sig. (2-tailed) | 0.000 | 0.000 | 0.000 | 0.000 |

**Table 7**
Correlations between DAS, ESR and *ama* score at followup1.

| | | Disease activity score | Erythrocyte sedimentation rate | *Ama* SCORE |
|---|---|---|---|---|
| Disease activity score | Pearson correlation | | 0.485 | 0.218 |
| Erythrocyte sedimentation rate | Pearson correlation | | | 0.276 |

### 3.2. Analyzing ama score for their possibility of being considered as an independent disease variable indicating the disease activity

It the study population mean *Ama* score was found to be 57.15 (SD 8.476) at base line which was subsequently reduced to 49.39 (SD 7.155), 42.03 (SD 6.577) and 34.91 (SD 5.359) at 1st, 2nd and final follow up subsequently (Table 8).

Multivariate tests

| Effect | | Sig. |
|---|---|---|
| factor1 | Hotelling's Trace | <0.001 |

The p-value for AMA obtained is <0.05 which is significant at 5% level of significance; hence there is difference in different levels of AMA.

| Tests of within-subjects effects | | |
|---|---|---|
| Measure: MEASURE_1 | | |
| Source | | Sig. |
| factor1 | Greenhouse–Geisser | <0.001 |

For test of within subjects effects, the p-value obtained is <0.05 for all levels which is significant at 5% level of significance, hence we reject the null hypothesis and conclude that there is significant difference between different levels of AMA.

Table 9 (Supplementary file) makes a pairwise comparison compares the different level of AMA. The p-value <0.05 shows that there is significant difference between means of AMA at different level for the considered pairs.

When a similar descriptive statistics was applied to various levels of DAS scores and ESR and their pair wise comparison was made, a similar trend of reducing values was observed and a similar significance was observed at pair wise comparison of all values in both of these variables (Tables 10–13 in supplementary file and Fig. 2).

The p-value for DAS obtained is <0.05 which is significant at 5% level of significance; hence there is difference in different levels of DAS.

For test of within subjects effects, the p-value obtained is <0.05 for all levels which is significant at 5% level of significance, hence we reject the null hypothesis and conclude that there is significant difference between different levels of DAS.

The p-value for ESR obtained is <0.05 which is significant at 5% level of significance; hence there is difference in different levels of ESR.

For test of within subjects effects, the p-value obtained is <0.05 for all levels which is significant at 5% level of significance, hence we reject the null hypothesis and conclude that there is significant difference between different levels of ESR.

The above table pairwise comparison compares the different level of ESR. The p-value obtained is <0.05 shows that there is significant difference between means of ESR at different level for the considered pairs. The p-value >0.05 shows no significant difference between means of ESR at different level.

## 4. Discussion

Clinical rheumatology faces a dearth of parameters that can precisely reflect the clinical activity of the disease. This seems highly important in conditions like Rheumatoid Arthritis, where high disease activity predicts a bad prognosis warranting urgent actions to arrest the disease progression and joint destruction. Various disease activity parameters currently used for evaluating the clinical staging of RA are either joint-based, defining the joint counts in terms of swelling, tenderness, and stiffness, or the levels of inflammatory markers like ESR and CRP reflecting the underlying inflammatory process in an individual. Scores like DAS which rely heavily upon joint status actually fail to appreciate the systemic features which might be of substantial importance to the patient for the level of discomfort they might pose. Similarly, the inflammatory biomarkers are not specific to RA alone and are obtainable in many conditions other than joint diseases. The level of inflammatory biomarkers can also be misleading for it being a cumulative score for a summated time period. Therefore changes in such scores do not reflect the changes in the clinical status in the case of RA precisely.

Besides being unable to reflect the disease condition through various domain areas precisely, currently utilized RA disease activity indicators also have a poor translational capacity to be considered a dependable outcome reporting measure. Changes in the joint counts in relation to its swelling, pain, and tenderness or even changes in ESR or CRP like inflammatory biomarkers do not necessarily reflect the changes the patient perceives in response to a therapeutic intervention. In RA what is meaningful to a patient may differ much from what is meaningful to a physician in terms of observations.

This delusion about proposing the most appropriate measures to define the disease status and the intervention-related outcome has long been faced in clinical rhematology practice. To overcome this, a composite scoring pattern was proposed, developed, and utilized in clinical trials related to RA [16].

Composite outcome measures have become very popular in assessing RMDs, because of their claim to catch all relevant dimensions of the disease into one convenient measure.

Composite scores are proposed to reflect multidimensionality and heterogeneity in disease pathogenesis, manifestations, and outcome. Multidimensional composites usually include several disease manifestations and outcome dimensions into one index. It is however noticed that multidimensional composites are not free of errors in terms of their use for treat-to-target and window of opportunity like strategies of modern rheumatology. Using multidimensional composites in clinical trials is found to have a different notion when the same is used in clinical practice. Moreover, many aspects of disease impact have not yet been covered in any of the components of the commonly utilized composite scores.

Patients with rheumatoid arthritis are found to differ from controls in their emotion-related personality traits, leading to their increased susceptibility to chronic stress and hypothalamic–pituitary–adrenal axis dysregulation. Such dysregulations make a substantial impact on a patient's well-being and net outcome of a given intervention [17].

Evidence suggests RA is a highly heterogeneous disease with many subtypes characterized by personality, psychiatric and immunological differences. Such complexities associated RA again warrants for a more comprehensive scoring method inclusive of every dimension reflecting the disease activity and outcome status.

Currently used measures of rheumatoid arthritis disease activity are the following: Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, Disease Activity Score (DAS) and Disease Activity Score with 28-Joint Counts (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Patient Activity Score (PAS) and Patient Activity Score-II (PASII), Routine Assessment of Patient Index Data (RAPID), Rheumatoid Arthritis Disease Activity Index (RADAI) and Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5), Chronic Arthritis Systemic

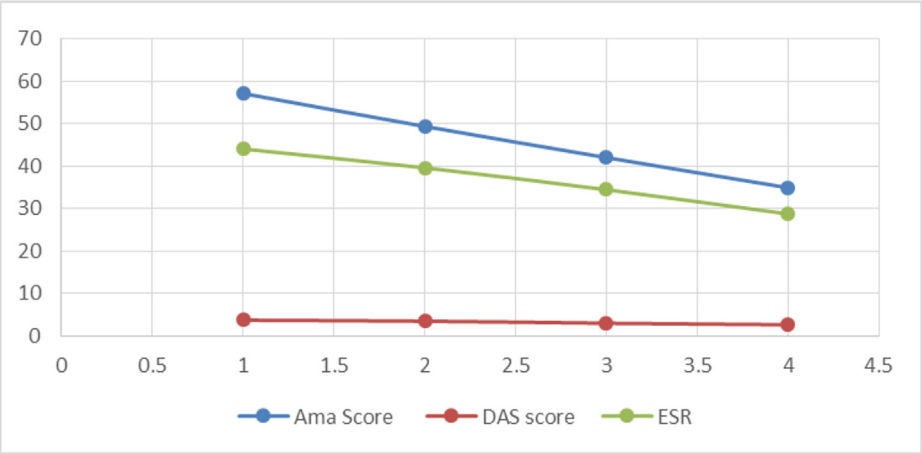


**Fig. 2.** Correlation between *ama* score, DAS score and ESR at various time points.

Index (CASI), Patient-Based Disease Activity Score With ESR (PDAS1) and Patient-Based Disease Activity Score without ESR (PDAS2), and Mean Overall Index for Rheumatoid Arthritis (MOI-RA). We see that despite such a plethora of single and composite indexes, the disease activity in RA and its outcome assessment is still far from being perfect [18].

RA patients are found to have intriguing constitutional features related to general well-being, sleep, energy status, appetite, and GI functioning [19]. This has been observed that such features find little place in the currently used composite score meant for evaluating RA disease activity. Clinical observation on RA patients has revealed that while receiving the Ayurveda treatment, these are the features that are addressed first within 1–3 months before actual improvements in joint related features are observed. This is also observed that during high disease activity, most RA patients report a loss in weight [20] accounting for a loss of appetite and after ayurvedic treatment the improvements in a loss of appetite and weight are reported [8]. Such clinical observations made in ayurveda rheumatology clinics when matched with a near absence of any such parameter or observation in modern rheumatology practice, warrant a serious thought of including these constitutional features in the composite scores meant for a comprehensive clinical evaluation of RA. Finding a parallel to RA in Ayurveda was the first problem to be addressed before any such measure could be developed based on Ayurvedic fundamentals explaining the pathogenesis of RA kind of diseases. A dual diagnosis approach was adopted to overcome this intrigue where the study population was diagnosed simultaneously as having RA and *Amavata* by the standard parameters of diagnosis adopted by both the systems. After finding this parallelism, this was easy to extrapolate the observations made in one context to be inferred in the other.

Subsequent to the establishment of this parallelism, what done was to explore the extra articular and constitutional features in RA which are otherwise the hallmarks of *ama.* A thorough literature search helped extensively identify and determine the most appropriate features reflective of *ama* and check their reliability and validity on established parameters.

After initial textual validation of the instrument which was meant to check the presence and level of *ama* related features in rheumatoid arthritis, its testing as an index test on the sample population was quite rewarding. Although the newly developed *ama* assessment instrument could find only a slight correlation with the reference tests like acute phase reactant ESR and disease activity score based upon 28 joint counts (DAS-28), it stood apart as an independent disease status marker since it was able to mark the changes in the population on a time scale more precisely comparing to DAS -28 or ESR. When the succeeding *ama* values of follow-ups were compared with preceding values, a significant difference was observed, showing it to be a consistent and reliable disease activity marker catching constitutional and GI-related domain of the patients. When reducing values of *ama* score were compared to overall improvements as reported by the patients, a similar trend was observed showing that a change in *ama* score reflects of a change in disease status and the impact of the disease on the patient.

The study however had its limitations. Question framing always has a scope to be refined further, and so is in this study. *Ama* score, the index test used in this study, also needs to be further tested for its sensitivity, specificity and predictive values in reference to RA. Ama, the progenitor of various *ama* induced pathogenesis also prompts the test to be evaluated for *ama* diseases other than *amavata.*

## 5. Conclusion

This study provided a quantifiable measure for the abstract concept of *ama* and helped utilize this percept as a reliable measure to mark the disease activity in *amavata*. This came as a great help in determining the course of ayurvedic therapy based upon *ama* scores reflecting the disease activity status. This *ama* based scoring also came as a help in quantifying the intervention-related benefits in terms of the significance of changes in baseline *ama* score. This study leads to future studies in this area focusing upon the development of *ama* score as a patient-related outcome measure (PROM) in Ayurveda.

## Funding

None.

## CRediT author statement

**Preeti Pandey**: Conceptualization, Methodology, Data Collection; **Sanjeev Rastogi**: Data curation, Writing – Original draft preparation; **Able Lawrence**: Visualization, Review; **Girdhar G Agrawal**: Software, Analysis, Supervision.

## Conflict of interest

We declare no conflict of interest.

## Acknowledgment

Authors wish to acknowledge the kind help of staff of Ayurveda-Arthritis Treatment and Advanced Research Center (A-ATARC), at State Ayurvedic College and Hospital, Lucknow in execution of this study. Help of our colleagues at A-ATARC Dr Neelendra Singh, Dr Nidhi Singh, Dr Ankita Verma, Dr Sumit Kumar, Dr Chinmayi R and Dr Kiran Maurya is also deeply appreciated.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2023.100689.

## References

[1] van Riel PL, Renskers L. The Disease Activity Score (DAS) and the Disease Activity Score using 28 joint counts (DAS28) in the management of rheumatoid arthritis. Clin Exp Rheumatol 2016 Sep-Oct;34(5 Suppl. 101):S40–4. Epub 2016 Oct 18. PMID: 27762189.

[2] Jensen Hansen Inger Marie, Asmussen Andreasen Rikke, van Bui Hansen Mark Nam, Emamifar Amir. The reliability of disease activity score in 28 joints–C-reactive protein might be overestimated in a subgroup of rheumatoid arthritis patients, when the score is solely based on subjective parameters. J Clin Rheumatol March 2017;23(2):102–6. https://doi.org/10.1097/RHU.0000000000000469.

[3] Slama IB, Allali F, Lakhdar T, El Kabbaj S, Medrare L, Ngeuleu A, et al. Reliability and validity of CDAI and SDAI indices in comparison to DAS-28 index in Moroccan patients with rheumatoid arthritis. BMC Musculoskelet Disord 2015;16:268. https://doi.org/10.1186/s12891-015-0718-8. Published 2015 Sep 29.

[4] Pope JE. Management of fatigue in rheumatoid arthritis. RMD Open 2020 May;6(1):e001084. https://doi.org/10.1136/rmdopen-2019-001084. PMID: 32385141; PMCID: PMC7299512.

[5] Coskun Benlidayi I. Sleep impairment: an obstacle to achieve optimal quality of life in rheumatoid arthritis. Rheumatol Int 2018 Dec;38(12):2183–92. https://doi.org/10.1007/s00296-018-4155-5. Epub 2018 Sep 11. PMID: 30206671.

[6] Sparks JA, Chang SC, Nguyen US, Barbhaiya M, Tedeschi SK, Lu B, et al. Weight change during the early rheumatoid arthritis period and risk of subsequent mortality in women with rheumatoid arthritis and matched comparators. Arthritis Rheumatol 2018;70(1):18–29. https://doi.org/10.1002/art.40346.

[7] Baker JF, Billig E, Michaud K, Ibrahim S, Caplan L, Cannon GW, et al. Weight loss, the obesity paradox, and the risk of death in rheumatoid arthritis. Arthritis Rheumatol 2015 Jul;67(7):1711–7. https://doi.org/10.1002/art.39136. PMID: 25940140; PMCID: PMC4826750.

[8] Rastogi S, Pandey P. Scope of specialty practice in Ayurveda: example from practicing Ayurveda rheumatology. J Indian Syst Med 2022;10:77–8.

[9] Krishna KP. The efficacy of Ayurvedic treatment for rheumatoid arthritis: cross-sectional experiential profile of a longitudinal study. Int J Ayurveda Res 2011;2(1):8–13. https://doi.org/10.4103/0974-7788.83177.

[10] Basisht GK, Singh RH, Chandola HM. Management of rheumatoid arthritis (*Aamavata*) using symbiohealth healthcare system. Ayu 2012;33(4):466–74. https://doi.org/10.4103/0974-8520.110513.

[11] Rastogi S. Principles and practice of ayurvedic rheumatology. Delhi: Chaukhambha Sanskrit Pratishthana; 2009.

[12] Rastogi S, Singh RH. Diseases of joints in advances in ayurvedic medicine. Varanasi: Chaukhambha Visvabharati; 2005.

[13] Rastogi S. Development and pilot testing of a prescription quality index for Ayurveda. J Ayurveda Integr Med 2019 Oct-Dec;10(4):277–83. https://doi.org/10.1016/j.jaim.2017.02.008. Epub 2017 Nov 7. PMID: 29122455; PMCID: PMC6938884.

[14] Rastogi S. Development and validation of a prototype Prakriti analysis tool (PPAT): inferences from a pilot study. Ayu 2012;33(2):209–18. https://doi.org/10.4103/0974-8520.105240.

[15] http://namstp.ayush.gov.in/.

[16] Landewé RBM, van der Heijde D. Use of multidimensional composite scores in rheumatology: parsimony versus subtlety. Ann Rheum Dis 2021;80:280–5.

[17] Rosa-Gonçalves D, Bernardes M, Costa L. Quality of life and functional capacity in patients with rheumatoid arthritis – cross-sectional study. Reumatol Clin 2018;14(6):360–6. https://doi.org/10.1016/j.reuma.2017.03.002.

[18] Anderson JK, Zimmerman L, Caplan L, Michaud K. Measures of rheumatoid arthritis disease activity: patient (PtGA) and provider (PrGA) global assessment of disease activity, disease activity score (DAS) and disease activity score with 28-joint counts (DAS28), simplified disease activity index (SDAI), clinical disease activity index (CDAI), patient activity score (PAS) and patient activity score-II (PASII), routine assessment of patient index data (RAPID), rheumatoid arthritis disease activity index (RADAI) and rheumatoid arthritis disease activity index-5 (RADAI-5), chronic arthritis systemic index (CASI), patient-based disease activity score with ESR (PDAS1) and patient-based disease activity score without ESR (PDAS2), and mean overall index for rheumatoid arthritis (MOI-RA). Arthritis Care Res 2011 Nov;63(Suppl. 11):S14–36. https://doi.org/10.1002/acr.20621. PMID: 22588741.

[19] Singh H, Arya S, Talapatra P, Lather K, Mathur R, Singhania A, et al. Assessment of fatigue in rheumatoid arthritis (by functional assessment of chronic illness therapy-fatigue score) and its relation to disease activity and anemia. J Clin Rheumatol 2014;20(2):87–90. https://doi.org/10.1097/RHU.0000000000000073.

[20] Gamal SM, Alkemary AK, Abdo MA, El Dakrony AHM. Low body mass index in long standing rheumatoid arthritis: relation to RA disease activity and functional indices. Reumatismo 2018;70(2):72–7. https://doi.org/10.4081/reumatismo.2018.999. Published 2018 Jul 6.