ASSESSMENT OF AMA PACHANA EFFECT OF AMRUTOTTARAM KASHAYAM IN RHEUMATOID ARTHRITIS

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CERTIFICATE OF THE SUPERVISOR

It is certified that work entitled **Assessment of Ama Pachana effect of Amrutottaram in Rheumatoid Arthritis** is an original research work done by **Dr. Giri. P. V** under my supervision for the degree of Doctor of Philosophy in **Ayurveda** to be awarded by Tilak Maharashtra Vidyapeeth, Pune. To best of my knowledge this thesis:

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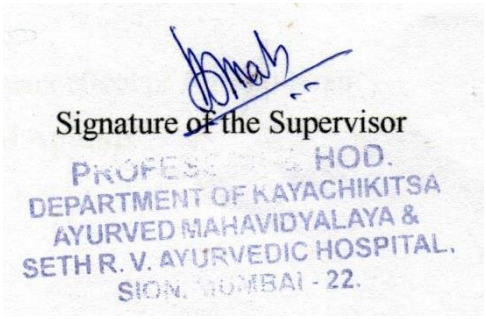

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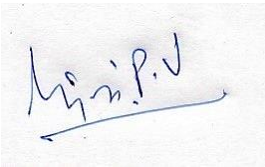
Signature: 

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A B S T R A C T

INTRODUCTION

Rheumatoid Arthritis (RA) is an autoimmune systemic inflammatory disease with clinical presentation of symmetrical polyarthritis. The arthritis affects the small joints of hands first then feet. Later it gradually spreads to larger joints. Distal inter phallangeal joint is usually spared. RA is the major cause of disability.

Burden of RA

RA is widely prevalent throughout the world. As per WHO reports published in 2002, RA is the 31st leading cause of YLDs (Years Lived with Disability) at global level. About 7 million people in India are affected with R A with prevalence of 0 .75%, similar to developed countries. Below the age of 60 the incidence is 4 to 5 times higher. RA is more frequent in females than males. A sample survey study has been conducted in Thaikkattussery ward in Thrissur District, Kerala for chronic illness shows a prevalence of 8.4% for joint disorders with 75% female predominance.

Disease activity and extent of change in Disease activity

In the present study DAS 28 ESR and the DAS-based European League Against Rheumatism (EULAR) response criteria were used to assess the disease activity and response of medication. DAS based EULAR response criteria is useful in assessing the individual response in clinical studies. On the basis of disease activity and extent of change, the patients can be classified as non, moderate or good responders.

Rheumatoid arthritis, Vatasonita

Vathasonitha is a systemic inflammatory disease where both *rakta* **and** *vata* **are vitiated resulting in** *kandu, spurana, nisthoda bheda gourava and supthatha***. Vatasonita is a chronic disease causing deterioration of joint structures resulting deformity and disability such as** *khanjam* **and** *pangu***. Considering the pathophysiology, clinical features and extra articular manifestations in RA, it can be considered as Vatasonita in Ayurveda.**

Ama

The concept of *ama* **can be correlated with the concept of free radicals. Free radicals differ from reactive chemical species that, in the outer orbit they have unpaired electron. They can damage cellular components and evidence suggests their role in RA and in inflammatory diseases. Directly or indirectly the ROS and RNS (Reactive oxygen species and reactive nitrogen species) damages the articular tissue producing inflammation.**

Scope and rationale of the study

The oxidative stress generated in a joint can favor autoimmunity and tissue destructions in RA. The role of anti oxidants becomes significance here. To restrict the disease progression and limiting the deformities Anti oxidants will be of more help.

Finding the relation between *ama* **and free radicals in RA, we can hypothetically conclude that** *Ama pachana* **medicines will of more help in the treatment of RA. The** *Ama pachana* **has to be demonstrated to understand the concept in real sense.**

Dipana pachana dravyas **are having** *Agn***i and** *Vayu* **predominant** *panachamahabhootha* **structure. If the** *Agni* **portion is predominant then it shows** *pachana* **property, if it is** *vayu* **predominant then it shows dipana or secretogogue property.**

In Kerala tradition Amrutottaram kashayam is widely used as *ama pachana* **medicine in RA. It is given in empty stomach. Traditionally it has been used as** *kashaym* **for** *ama pachana* **in RA.** *Amrutottaram kashayam* **contains Phenolic acids such as quinic acid, protocatechuic acid, gallic acid, and chebulic acid were identified in the formulation along with some flavonoids. The constituents possesses antioxidants and anti inflammatory properties. In RA** *Amrutottaram kashayam* **is useful as an antioxidant and anti inflammatory drug. Amrutottaram kashayam contains the following drugs.** *Nagara* **(***Zingiber officinale* Roxb.), *Amrutha* **(***Tinospora cordifolia* **(Willd.) Miers),** *Hareethaki* **(***Terminalia chebula* **Retz).**

The *Ama pachana* **effect of Amrutottaram Kashayam was assessed by pre post test design. The** *Ama* **Assessment Tool was used to assess the** *ama pachana* **effect. This will be of more use to understand the amapahana property. The reverse of** *samyaklanghitha lakshanas* **were used in** *Ama* **Assessment Tool.**

Objectives

The objectives were (1) to assess the severity of ama in Rheumatoid Arthritis and (2) to assess *ama pachana* **effect of Amrutottaram kashayam in RA. The finding of the present study was that Amrutottaram kashayam was effective in RA as an** *ama pachana* **medicine.**

RESEARCH METHODOLOGY

Hypothesis

Null hypothesis

Amrutottaram Kashayam has no *ama pachana* effect in Rheumatoid Arthritis

Alternate hypothesis

Amrutottaram Kashayam has ama pachana effect in Rheumatoid Arthritis

Probability level

Probability level for this study is fixed as p< 0.05

Study Design and setting

Pretest-posttest design study was used in this study in which patients were observed before and after giving Amrutottaram Kashayam for 15 days. The patients fulfilling the criteria were selected from the Kayachikitsa OPD of Vaidyaratnam Ayurveda College, Ollur, Thrissur.

Study population

Patient suffering from Rheumatoid Arthritis in the catchment area of Vaidyaratnam Ayurveda College Hospital, Thaikattussery, Ollur, Thrissur, were considered as study population.

Inclusion criteria

1. **2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis**

Joint distribution	**(0-5)**
1 large joint	**0**
2-10 large joints	**1**
1-3 small joints (large joints not counted)	**2**
4-10 small joints (large joints not counted)	**3**
>10 joints (at least one small joint)	**5**
Serology	**(0-3)**
Negative RF AND negative ACPA	**0**
Low positive RF OR low positive ACPA	**2**
High positive RF OR high positive ACPA	**3**

Symptom duration	**(0-1)**
<6 weeks	**0**
≥6 weeks	**1**
Acute phase reactants	**(0-1)**
Normal CRP AND normal ESR	**0**
Abnormal CRP OR abnormal ESR	**1**

If the score is ≥ 6 = definite RA

2. Age group of **25 – 60**

3. Ama with Kapha predominance

Exclusion criteria

1. **Patients with serum positive ASO titer**
2. **Patients with serum positive Uric acid**
3. **Patients with other systemic complications**
4. **Patients with hypertension and diabetes.**
5. **Age group less than 25 and above 60.**

Sample size

The Sample size has been fixed as 115. And calculated using the formula

$n = \frac{Z^2\ P(1-P)}{d^2}$ **(Prevalence of approximately 0.75 % in India)** [1]

Sampling technique

Purposive sampling technique is used for the sample selection. Patient coming to Kayachikitsa OPD, Vaidyaratnam Ayurveda College Hospital, Thaikattussery, Ollur, Thrissur and fulfilling Criteria for Rheumatoid Arthritis were taken in to study.

Data collection

Data were collected by personal interview including examination, observation, Interview schedule (CRF). It contains the following tools.

Study tools

- **Ama assessment Tool: - 9 item YES/NO Questionnaire.**
- **Visual Analogue Scale: - It is a self administered questionnaire to assess the pain before and after the intervention.**
- **DAS28 score : - is calculated by noting the number of tender joints, swollen joints, activity in the past week (10 to 100 VAS), ESR/CRP**

- **Overall change in Disease activity as per the EULAR Good or Moderate response criteria: - This is calculated by using change in DAS28 score and Present DAS28 score**
- **Prakriti:- Assessed by interviewer assisted TNMC Prakriti 2004 Questionnaire (20). Patients grouped as Vatadhika, Pittadhika and Kaphadhika as per the scores obtained in the different domains.**
- **Hand grip: - This is assessed before and after intervention by using Hand dynamometer.**
- **Range of Motion (ROM) of different joints: - Evaluation of joint range of motion is important in the evaluation of therapeutic approach in patients with RA. ROM in joints measured by using Goniometer.**
- **Blood investigations: - Lab reports for RF, ASO titre, ESR, ACPA (ACCP), Hb%, TC, DC, FBS, PPBS, LFT, Serum Creatinine, Serum Uric acid, CRP, ANA done from accredited lab.**

Procedure

Patients coming to Vaidyaratnam Ayurveda College Hospital OPD fulfilling the 2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis are recruited for the study. Evaluated with study tools.These are evaluated before and after 15th and 30th day of treatment (follow up period).

Procedure	BT 1st Day	AT 15th Day	FU 30th Day
Interview schedule, & Visual analog scale	✓	✓	✓
DAS28	✓	✓	---
TC, DC, ESR, Hb%, LFT, S. Creatinine, CRP	✓	✓	---
Range Of Movements	✓	✓	---
FBS, PPBS, RF (RA), ASO titer, Serum Uric acid, ACPP, ANA,	✓	---	---

Amrutottaram Kashayam

Amrutottaram Kashayachurna was given to 115 patients. Patient is advised to prepare Amrutottaram Kashayam with this *churna*. When the patient feels appetite he is advised to take diet. Diet is restricted to *manda* and *peya* for all patients. Follow up period is fixed as 15 days without medicines. Every patient supplied with 15 packets each packet containing 48 gms of Amrutottaram *kashayachurn*a.

Dose

Amrutottaram Kashayam 96 ml with 6 gms of sugar as single dose is given daily in empty stomach (morning) for 15 days as OP treatment. When the patient feels appetite he can take next diet.

Preparation of medicine

48 gms of churna (supplied as one packet) is taken and 768 ml (16 times) of water is added. The mixture is boiled and reduced to 96 ml (1/ 8^{th}). To take the correct measure of water and kashaya thereafter measure with markings are made familiar with the patients

Statstical analysis

All the data collected are entered into MS Excel master sheet. Statistical tests used for the analysis of data are Paired t test, Independent t test, Wilcoxon Signed Ranks Test, Mann-Whitney U test, FriedmanTest, Mann-Whitney U test, McNemar Testand Cochran's Q test

Ethical considerations

Ethical clearance obtained from Instituitional Ethics Committee. The formulation used in the study is mentioned in the classical text books of Ayurveda and having no known side effects in long term use. Amrutottaram kashayam is widely used among Govt. and Private Institutions and Hospitals in Kerala. Informed consent is obtained from the patient.

ANALYSIS AND INTERPRETATION

The objectives of the study were to assess the severity of *Ama* **and to study the efficacy of** *ama pachana* **effect Amrutottaram Kashayam in patients with Rheumatoid Arthritis by using Ama assessment Tool.**

115 Rheumatoid Arthritis (RA) participants fulfilling the 2010 ACR / EULAR Classification Criteria have been recruited to this study. The participants were recruited from the Kayachikits OPD of Vaidyaratnam Ayurveda College, Ollur, Thrissur, Kerala. They were given Amrutottaram Kashayam for 15 days.

There were total 115 participants recruited for the study. The mean age was 48.40 yrs with SD 8.97 yrs. Among them 25 were males and 90 females (78.3%). Among the 115 participants 80 were Hindus (80%) and 35 were Christians. Of the 5 SES class, half of the participants were from lower middle class (55.7%). There were no participants from Lower class and few from Upper lower class (1.7%).

The mean duration of RA patients participated in the study were 37.39 months with a SD of 17.09 months. The minimum duration was 12 months and maximum duration 120 months. Among the participants 61.7% were using Ayurvedic and Allopathic treatments for RA. Out of 115 RA patients in the study, only 11 (9.6%) patients were having boutonniere deformity. 73 (63.5%) participants of the study had the joint involvement was symmetrical. 72% of the participants were having the Family history of RA.

Most of the participants in this study are using mixed diet (95.7%). The mean BMI of the participants were 25.56 kg/m^2 with SD of 2.61 kg/m^2. Only 7.8% of the participants were lean or normal others (91.2%) are either overweight or obese.

TNMC *prakriti* **assessment tool has been used to find out the prakriti of the participants. It is seen that around half (47.8%) of the participants belongs to** *pittadhika prakriti***.and 30.45 belongs to** *vatadhika prakriti* **and the rest belongs to** *kaphadhika prakriti* **(21.7%). In this study as said above** *pitta* **predominance is seen in females and** *vata* **predominance seen in males.**

The mean RA score as per criteria was 6.53 with SD 0.7413. The minimum score was 6 with maximum score 10. The minimum score in males was 6 and maximum was 7, the maximum score in males was 7 and in female and 10 respectively. Out of 115

participants in the study it is seen that only 5 male (4.3%) participants are addicted to alcohol and smoking.

Blood investigations for diagnosis – ESR, CRP, Anti-CCP, RF and ANA

The mean ESR was 46.13 mm with SD of 16.94 mm. The mean CRP was 6.537 with SD 1.2379. For considering classification criteria (acute phase reactants) the count above 6 was considered as high. 94 (81.7%) participants are having raised CRP (>6 mg/L). The RF was positive (>8 IU/ml) in 41 participants and Anti-CCP was >1 U/ml in 36 participants. Both the RF and Anti-CCP were positive only in 13 participants.

Subjective parameters

Ama **in RA causes the stiffness in** *kapha kaala***. With 15 days of treatment with Amrutottaram kashayam the morning stiffness reduced significantly (0.2957 hrs ± 0.3681), found to be significant irrespctvie of gender (p < 0.001).**

Visual Analogue Scale was used to measure the pain before treatment (BT), after treatment (AT) and after follow up period (FU). There was a statistically significant difference in pain score during these period (p < 0.001).

Das28 score and Change in DAS28 score

91 (79.1%) participants are having High disease activity than the Moderate disease activity group. 77 (67%) participants had change >1.21. p < 0.001, irrespective of gender. Overall change in Disease activity as per the EULAR Good or Moderate response criteria has been calculated and found that the overall moderate response was 70.43%

Ama assessment Tool

Firstly the total score is considered and after that score against each of the questions are discussed. Ama assessment Tool was used to measure the Ama before treatment (BT), after treatment (AT) and after follow up period (FU).

First the total of 9 item score has been considered here. The median score BT, AT and FU was 6 (6-7), 4 (2-4) and 1 (1-2) with Median Rank 2.95, 1.87 and 1.18 respectively. There was a statistically significant difference in score during these period (χ^2 **(2) = 194.644, p < 0.001). The 9 items constipation (*p* = <.0005), Heaviness (*p* = <.0005), loss of taste (p < 0.001), Loss of appetite (p < 0.001), Loss of thirst (*p* = <.001), bad belching**

(p < 0.001), Pain (p < 0.001), Lack of enthusiasm (p < 0.001), Lethargy (p < 0.001) were taken separately and analysed. The symptoms were reduced significantly.

Range of Motion

Range of Motion (ROM) of the participants was assessed before and after treatment by using Goniometer. The mean ROM of knee flexion, shoulder Abduction, shoulder Adduction, shoulder extension, Elbow flexion, forearm pronation, Supination, wrist - radial and ulnar deviation, wrist extension and flexion, thumb MP joint flexion and thumb IP joint flexion was found to be significant, p < 0.001.

Blood investigation parameters

The mean ESR before treatment was 46.130 mm with SD 16.9393 mm and after treatment was 31.217 mm with SD 12.0640 mm. It is seen that the difference in means 14.9130 mm ± 11.7530 mm was found to be significant *p* = <.0005). The change in ESR indicates the effect of Amrutottaram kashayam in reducing thr inflammatory process.

The mean CRP before treatment was 6.537 mm/DL with SD 1.2379 mm/DL and after treatment was 5.730 mm/DL with SD 0.9765 mm/DL. From the data analysis it can be concluded that there was a statistically significant (0.8070 mm/DL ± 0.5281mm/dL) reduction of CRP after the intervention. The change shows the fast and better prognostic outcome. There was no significant change noticed in Haemoglobin (Hb %), Serum Creatinine and Liver Function Test

DISCUSSION AND CONCLUSION

115 Rheumatoid Arthritis (RA) participants have been recruited to study fulfilling the 2010 ACR / EULAR Classification Criteria. They were given Amrutottaram Kashayam for 15 days. During the course of medication the patient was advised to take *mand*a and *peya* only. Follow up period fixed as 15 days without medication. Patients were assessed before and after the intervention as explained in the Methodology.

The minimum RA score was 6 with maximum score 10. The mean ESR was 46.13 mm with SD of 16.94 mm. The mean CRP was 6.537 with SD 1.2379. 94 (81.7%) participants are having raised CRP (>6 mg/L). Anti-CCP and RF were used as serological markers. Only 36 (31.3%) were havimg the Anti-CCP test positive >1 IU/L. Rheumatoid Factor (RF) was positive in 41 (35.7%) participants above >8 IU / ml. Anti nuclear Antibodies (ANA) was positive only in 23.5% of the participants. A negative result does not rule out RA. The prevalence of ANA in healty individuals is 3-15%. A positive ANA indicates the process of auto immunity. The RF was positive (>8 IU/ml) in 41 participants and Anti-CCP was >1 U/ml in 36 participants. Both the RF and Anti-CCP were positive only in 13 participants. 73 (63.5%) participants of the study had the joint involvement was symmetrical. Symmetrical joint distribution is characteristic of RA. Symmetry may not be noticed at the beginning (26). Patients with Hypertension, Type 2 Diabetes Mellitus, Gouty Arthritis, Rheumatic fever were excluded from the study.

The mean age of participants was 48.40 yrs with SD 8.97 yrs having female predominance (78.3%). There were 65 participants in the age group of >49 yrs. below the age of 60 the incidence is 4-5 times higher.

In this study as said above, *pitta* predominance is seen in females and *vata* predominance seen in males. It is seen that around half (47.8%) of the participants belongs to *pittadhika prakriti* and 30.45 belongs to *vatadhika prakriti* and the rest belongs to *kaphadhika prakriti* (21.7). In which *prakriti* the RA is predominant is a debate.

The mean duration of RA was 37.39 months with a SD of 17.09 months. 47.9% of participants are having the disease for the past 36 months and the rest were having the disease more than 36 months. Only 11 (9.6%) patients were having boutonniere deformity and are suffering from RA more than 49 months. 72% of the participants were having the Family history of RA. The family history concept is said to be older one.

The family history is assessed instead of genetic and a part of environmental involvement. In the era of genomics family history has got significance. In RA hereditary factor is estimated as 60% [(28)].

Most of the participants in this study are using mixed diet (95.7%). According to Ayurvedic concept diet has an important role in RA. Poor dietary habits lead to *ama* which in turn becomes a cause for RA. The mean BMI of the participants were 25.56 kg/m^2 with SD of 2.61 kg/m^2. 91.2% of the participants were either overweight or obese. Compared to male female participants are overweight and obese. It is estimated that 2/3rd of the people with RA are overweight or obese.

Among the participants 80 were Hindus (80%) and 35 were Christians. This may be due to the fact that the predominant occupants are Hindus in and around the Vaidyaratnam Ayurveda College, Ollur, Kerala. 55.7% participants were from lower middle class. There were no participants from Lower class and few from Upper lower class (1.7%). 61.7% were using Ayurvedic and Allopathic treatments for RA. It can be concluded that the patients with larger duration of RA are utilizing the OPD of this Institution.

The *Amatwa* has reduced significantly with 15 days medication with Amrutottaram kashayam in RA. The Overall change was statistically significant during the time period. Considering BT-AT and BT-FU it was statistically significant irrespective of gender. (p = <.0005). It can be concluded that Amrutottaram kashayam was effective during the 15 days course of treatment and after the follow up period it was effective. This indicates that the long time medication will be effective for better prognostic outcomes.

Participants relieved of constipation and improvement in appetite was seen during course of study and after follow up period. The *kashayam* was effective in reducing the symptoms bad belching, pain and lack of enthusiasm throughout the period. Significant change in the symptoms; heaviness of body, loss of taste, loss of thirst was noted after treatment and after follow up period. The kashayam was effective in reducing the lethargy during the first 15 days.

The morning stiffness reduced significantly (p = <.0005). The effectiveness was similar in both genders. Morning stiffness is an important tool to assess the severity of RA. It is more linked to functional disability and pain than the disease activity. Ama in RA causes

the stiffness in kapha kaala. Reduction in morning stiffness shows the Ama pachana effect of Amrutottaram kashayam.

Visual Analogue Scale was used to measure the pain before treatment (BT), after treatment (AT) and after follow up period (FU). There was a statistically significant difference in pain score during these period ($p < 0.001$). The effectiveness may be due to the fact that Amrutottaram kashyam is *tridoshghna*. **15 days treatment with Amrutottaram kashyam is effective in reducing the pain is found to be highly significant. Pain reduction is seen while taking the medicine and after follow up period. The Amrutottaram kashayam has similar** *ama pachana* **effect irrespective of gender and age.**

DAS28 score,

91 (79.1%) participants are having High disease activity than the Moderate disease activity group. 84% of the males and 77.8% of the females are having high disease activity score. High disease activity has seen in >49 age group (84.65%) and in Lower middle class. Worse clinical outcomesof RA is seen in low socioeconomic status.

Change in DAS28 score and EULAR Good or Moderate response criteria

77 (67%) participants had change >1.21 ($p < 0.001$) irrespective of gender. The overall response of the Amrutottaram kashayam in reducing the disease activity was analysed. The total of 81 participants out of 115 had Moderate response. Use of Amrutottaram kashayam for 30 days has 70.43% overall moderate response in RA disease activity

Objective parameters

With 15 days of treatment the improvement in Hand grip strength was highly significantly in both hands $p = <.0005$).

ROM of different joint assessed before and after treatment. The overall improvement in ROM of adduction and abduction, extension, flexion of shoulder, elbow flexion, forearm – pronation, supination, wrist - radial and ulnar deviation, wrist extension and flexion, thumb MP joint flexion, thumb IP joint flexion was statistically and clinically significant. With 15 days of treatment with Amrutottaram kashayam the ROM of said joints improved significantly.

Blood investigation parameters

From the data analysis it can be concluded that there was a statistically significant reduction in ESR and CRP after the intervention (*p* = <.0005). Amrutottaram kashayam was very effective in reducing the ESR and CRP. There was no change in Hb% level. No significant change noticed in S. Creatinine and in Liver Function Test. The negligibly small change noticed was within limit and clinically insignificant. Amrutottaram kashayam has no side effects or toxicity.

The Amrutottaram kashayam can be used as an *ama pachana* medicine in RA. This study shows substantial improvement in this disorder. Amrutottaram kashayam contains Phenolic acids such as quinic acid, protocatechuic acid, gallic acid, and chebulic acid were identified in the formulation along with some flavonoids. The constituents possesses antioxidants and anti inflammatory properties. In RA Amrutottaram kashayam is useful as an antioxidant and anti inflammatory drug.

Clinical outcome measured with Ama assessment tool, DAS28 score, EULAR good or moderate response, hand grip strength, ROM of different joints, ESR and CRP were found to be supporting this finding. The medicine was given to patients for 15 days only. RA is chronic auto immune disease and medicine has to be taken for longer period for better outcomes.

Limitations of the study

- **Only Amrutottaram kashayam was used for the study.**
- **The observational period with medicine was 15 days with 15 days follow up period.**
- **The design is pre test post test design.**
- **No tool is available to assess Ama.**

Suggestions

- **Combination of medications with or without ruksha sweda with more observational days can be used for the trial.**
- **Randomized Controlled Trial can be done to compare with DMARDs.**
- **To assess the construct Ama and assess the outcome in Ama perspective, an assessment tool can be developed.**

INTRODUCTION

CHAPTER 1

INTRODUCTION

Rheumatoid Arthritis (RA) is an autoimmune systemic inflammatory disease with clinical presentation of symmetrical polyarthritis. The arthritis affects the small joints of hands first then feet. Later it gradually spreads to larger joints. Distal inter phalangeal joint is usually spared. RA is the major cause of disability [(1)]. As RA is a systemic disease fever, fatigue, weight loss can also accompany with other symptoms. Genetic and environmental factors play important role in immune reactions leading to synovitis and disabilities. The burden of disease leads to emotional and social problems to the sufferings.

Burden of RA

RA is widely prevalent throughout the world. As per WHO reports published in 2002, RA is the 31st leading cause of YLDs (Years Lived with Disability) at global level. This is 0.8% of total global YLDs (The Global burden of Disease 2000-version 2) [(2)].

About 7 million people in India are affected with R A with prevalence of 0 .75%, similar to developed countries [(3)]. Below the age of 60 the incidence is 4 to 5 times higher [(4).] RA is more frequent in females than males. In women 5% increase is seen over the age of 70[(5)].

A sample survey study has been conducted in Thaikkattussery ward in Thrissur District, Kerala for chronic illness (in the study setting area). The total population of this ward was 1066 as per voter's list. Sample size has been calculated and fixed as 323. A prevalence of 8.4% for joint disorders has been identified with 75% female predominance. 50% of these cases were in the age group of 59-69 yrs. Majority of them are from lower and upper lower class (SES as per Kuppuswamy scale) [(6)].

Disease activity and extent of change in Disease activity

RA is a chronic autoimmune disease results in severe disability if untreated or inadequately treated. As there is no cure, the assessment of quality of life of RA patients becomes important. The inflammatory changes cannot be measured by a single variable. For this reason general HRQOL and disease specific validated tools were developed. The

different tools use different domains or Questions for the assessment of quality. The tools assess the patient in different ways. As the goal is same, any convenient tool useful for particular situation can be used. Health Assessment Questionnaire (HAQ), Disability Index , SF-36, RAPID3 (Routine Assessment of Patient Index Data 3), Clinical Disease Activity Index (CDAI) and Disease Activity Score (DAS28) are some validated tools [(7)]. In clinical settings RAPID3 is useful as it can be calculated without any formal joint count.

In the present study DAS28, ESR and the DAS-based European League Against Rheumatism (EULAR) response criteria were used to assess the disease activity and response of medication. DAS-CRP underestimates the disease activity in RA[(8)]. DAS based EULAR response criteria is useful in assessing the individual response in clinical studies. On the basis of disease activity and extent of change, the patients can be classified as non-, moderate or good responders [(9) (10)]

***Ama*, Rheumatoid arthritis, Vatasonita**

Vathasonita is a systemic inflammatory disease where both *rakta* and *vata* are vitiated resulting in *kandu, sphurana, nisthoda bheda gourava and suptata*. Vatasonita is a chronic disease causing deterioration of joint structures resulting deformity and disability such as *khanjam* and *pangu*. Exacerbation and remission is the unique feature of *vata sonita*.

Considering the pathophysiology, clinical features and extra articular manifestations in RA, it can be considered as Vatasonita in Ayurveda. The *raktadushti* consequent v*atakopa*, then the *raktavarana* leads to *srotodushti* and the *doshas* get stagnated in *asthisandhis*. The *thiryaghatatwa* of *doshas* makes the disease chronic and symptoms worsen [(11) (12)]. The hypoactive *agni* in *dhatu* level also has an important role in the manifestation of the disease[(13)].

The digestion and metabolic processes explained can be considered as the functions of different *agnis* working at different levels. In general Digestion and metabolism and specifically neuro endocrinological functions, enzymatic functions etc. can be considered as functions of *agni* [(14)]. Hypoactive *agni* leads to *ama* formation at different levels. The non-articular and constitutional symptoms explained in RA are considered as the

symptoms of *ama*. These may include generalized aching, stiffness, fever, weight loss, and fatigue [15]. These symptoms may appear several months before the RA symptoms appear [16]. This indicates the presence of *Ama* in RA. Contextually it has to be explained that the constitutional and extra articular symptoms or the *amatwa* can be identified in early stages of the disease, in untreated and inadequately treated conditions. *Ama* is considered as an important morbid factor for the causation of RA.

The concept of *ama* can be correlated with the concept of free radicals [17]. Free radicals differ from reactive chemical species that, in the outer orbit they have unpaired electron. They can damage cellular components and evidence suggests their role in RA and in inflammatory diseases. Directly or indirectly the ROS and RNS (Reactive oxygen species and reactive nitrogen species) damages the articular tissue producing inflammation[18].

Scope and rationale of the study

The oxidative stress generated in a joint can favor autoimmunity and tissue destructions in RA. The role of anti oxidants becomes significance here. To restrict the disease progression and limiting the deformities Anti oxidants will be of more help[19].

Finding the relation between *ama* and free radicals in RA, we can hypothetically conclude that *Ama pachana* medicines will of more help in the treatment of RA. The *Ama pachana* has to be demonstrated to understand the concept in real sense.

The drug that digests the *ama* but does not ignite or initiate *agni* is called *Pachana dravya* or Digestive. *Dipana* and *pachana drug*s act on digestive system. *Dipana pachana dravyas* are having *Agn*i and *Vata* predominant *panachamahabhoota* structure. If the Agni portion is predominant then it shows *pachana* property, if it is *vata* predominant then it shows *dipana* or secretogogue property [20].

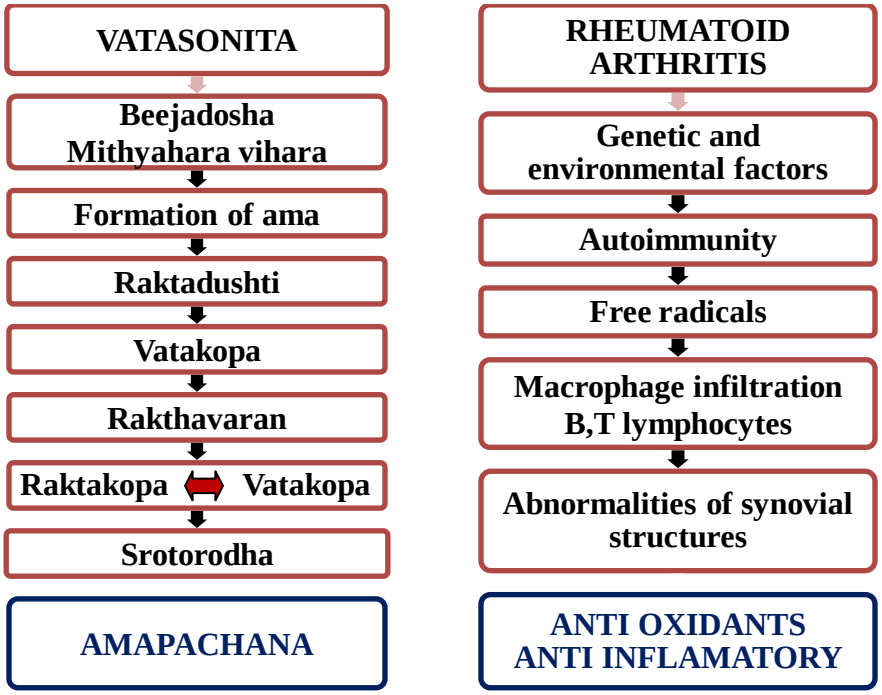
In Kerala tradition, Amrutottaram kashayam [21] is widely used as *ama pachana* medicine in RA. It is given in empty stomach. In text even though mentioned as *siddhamudakam*, traditionally it has been used as *kashaym* for *ama pachana* in RA. *Amrutottaram kashayam* contains Phenolic acids such as quinic acid, protocatechuic acid, gallic acid, and chebulic acid were identified in the formulation along with some flavonoids [22]. The

constituents possess antioxidants and anti-inflammatory properties. In RA *Amrutottaram kashayam* is useful as an antioxidant and anti-inflammatory drug.

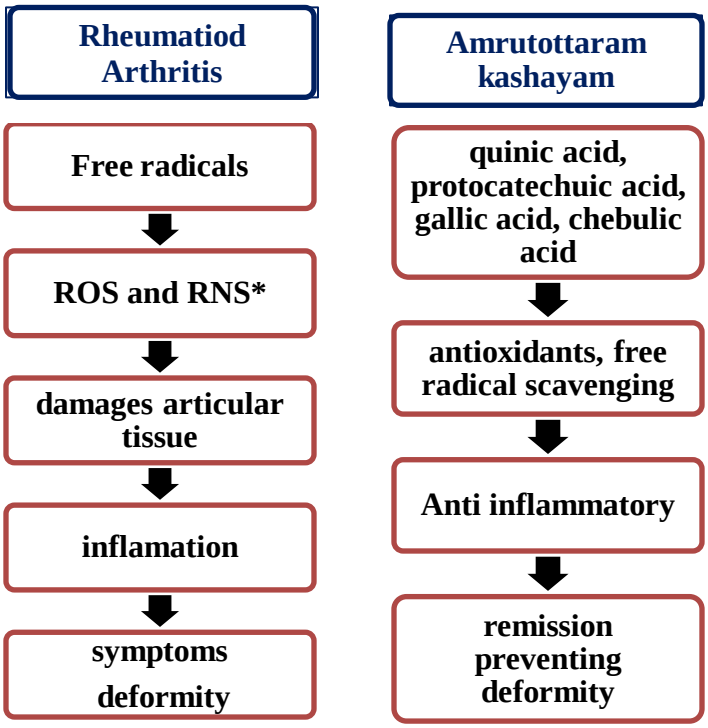
The *Ama pachana* effect of Amrutottaram Kashayam was assessed by pre post test design. The *Ama* Assessment Tool was used to assess the *ama pachana* effect. This will be of more use to understand the *amapahana* property. The reverse of *samyaklanghita lakshanas* were used in *Ama* Assessment Tool [23].

Objectives

The objectives were (1) to assess the severity of ama in Rheumatoid Arthritis and (2) to assess *ama pachana* effect of Amrutottaram kashayam in RA. The finding of the present study was that Amrutottaram kashayam was effective in RA as an *ama pachana* medicine.



Flow chart 1. Comparison of Vatasonita and Rheumatoid Arthritis



*Reactive oxygen species and reactive nitrogen species

Flow chart 2. Role of free radicals (18) and Amrutottaram kashayam (22) in RA

REVIEW OF LITERATURE

CHAPTER 2
REVIEW OF LITERATURE

CONCEPT OF AMA

Introduction

The search for *niramaya* begins form the ancient age. The terminology *Amaya* itself means that 'developed from *ama* [(1)].

The earliest references of Ama appears in Bharadwaja sutra, mentioning that the *Ama* causes *Chittha khsobha Bhaya* [(2)]. The germ theory was developed years after. Before that there was a theory related to Gastro Intestinal tract named as Gastricism. According to this theory all diseases are caused by disturbances in Gastro Intestinal system [(2)]. Healers in Egypt (1500 BC) believed that the ill wind (vata) or the toxic waste of body *whdw, produced* by overeating, drinking of alcohol etc are the causes for the all diseases [(3)]. In Caraka Samhita and Suruta Samhita (400 BC) the definition, aetiology, symptoms, different stages and treatment are clearly described. In Ayurveda, Gastricism has got important role. Vagbhata states that all diseases are caused by *Mandagni* [(4)]. The term *Ama* denotes either a *dravya* (matter) or an abstraction. An abstraction can be understood by observing phenomenon. Ama can be measured or understood by considering it as a construct. The researcher developed abstractions are called constructs [(5)]. That may be reason that acharyas explained the *Ama* through the *lakshanas*.

Importance

Further Acharya Susruta explains the ethical importance of knowledge of *Ama*. Acharya further explains that those vaidyas who are not well versed about the different stages of *Ama* are considered as *Kuvaidyas* (quack). Susrutha foreseen the probability of iatrogenic diastases [(6)]. For better understanding of *Ama*, the concept of *agni* also has to be considered.

Relation with *agni*, definition

The well being of human body definitely depends upon the *agnibala* of that person. So *agni* has to be protected at any cost for the well being [(7)]. The digestion and metabolism

depends on the *agni*. When the *agni* functions properly the digestion and metabolism will be also proper [8].

The functional aspects of *agni* explained in relation to *pitta. Pitta* is considered as *antaragni*. The functions of *pitta* is not only related to digeston and metabolism but also to higer mental faculties and emotional states [9]. The functioning of *pitta* can be tabulated on the basis of etimological derivation and its meaning [10].

Table M 1. Functions of pitta

Etymology	Interpretation	Meaning
Tap santaape	*Tapati ushmanaam ulpadayati iti pittam*	to heat / generate heat
Tap daahe	*Taapayati dahati buktham aahaarajaatam iti pittam*	to burn
Tap iswerye	*Tapyate ashtavidam animaadikam isweryam iti pittam*	accomplishment of eight kind of benefits

The *agni* is having different functions and different chemical structures. The *agni / pitta* generated from one place and functions in another place. In this contest; *kayagni*, *dhatwagn*i and *bhutagn*i are to be considered [11]. In clinical point of view, the relation between *kayagni* and *dhatwagni* is important as the hypo and hyper activity of *kayagni* leads to *vruddhi* and *kshaya* of *dathus* respectively [12]. The functions of *agni* can be explained in general aspect like digestion and special aspect like neuro endocrinilogical functions [13]. Functionally 4 types of *agni* has been explained; *Mandagni, vishamagni, thishnagni and samagni*. From these background knowledge that the *Ama, pakwa* and *pachyamana* terminologies get technical meaning and depth [14]. Susruta clearly states that all the *pakas* in the body are performed by *agni* through *pitta*. No other matter can be termed as *agni* other than *pitta* [15].

In classics the *Ama* has been explained in different standpoints.

As per the definition, the hypoactive *agni* makes the *rasadathu* in *apachit*a condition. As it is not well formed it is not get absorbed. it undergoes putrefaction at the site itself and termed as *ama* [16]. In Madhavanidana, *kayagni* dhourbalya has been mentioned while

explaining the *amavata*. Susruta opines that dhatwagni has an important role in the formation of *Ama* [17].

In health the *doshas* maintain homeostatic balance. The imbalance will lead to ill health [16] . Vagbhata further explains that they get vitiated together resulting in *Ama*. Usually they remain and function normally. Genetic and environmental factors can influence this condition resulting in the formation of *Ama* [18].

Ama combines with *dosha, dhatu* and *mala producing saamadosha, saamadhatu and saamamala.* As a consequence of this, disease develops [19]. Due to unhealthy unhygienic diet acute severe condition called *amavisha* can develop. *Amavisha* is having poor prognostic outcomes. Different terminologies and lakshanas are mentioned according to the *doshadikya* in *ajeerna.* The *ajeerna* - due to *kapha pitta* and *vata* predominance are termed as *Ama, vidagda, and vishtabda* respectively [20].

From these all viewpoint it can be concluded that the condition - *Ama*- can develop at different sites and can precipitate different diseases accordingly. Which means the *Ama* can develop in GI tract, in different parts of the body or in different *dhatus*.

Site of *ama*

Considering the level / site at which the *ama* is involved is useful in identifying and fixing the appropriate medicine for the patient. For explaining this concept *urusthamba* can be taken as an example where the *ama* is in *uru* combines with *sleshma* makes the disease [21]. When combined with *rasa* it affects joints to produce *Amavata*. The similar conditions can be observed in *dushi visha* and in auto immunity also [22]. (*vyadhibala viriditwam, vyadhyulpadaka prathibhadhakatwam*).

Further acharyas explain the *lakshana samucchayas* through which the different conditions of *Ama* can be identified.

The *lakshanasamucchayas* mentioned are *srodhorodha, balabramsa, gourava, anilamudhata, alsya, apakti, nishtiva, malasangha, aruchi, klama* [23]. Each one is a comprehensive approrach to a condition than a symptom. Each one has been dealt below separately.

Body is made up of *srotas* (*srotosamuchaya*). *Srotas* has been explained for easy clinical approach to derive a treatment methodology. All the transport and metabolic exchange and neuro endocrinological transmissions are the functions of srotas. When *kapha* blocks the channels *srotorodh*a develops. Any derangement in aforesaid functions can be considered as *srotorodha* [(24)].

Dalhana explains *bala* as *karmakakaraka shakti* [(25)]. The term *bala* has different meaning according to the context. The *abhyantara prana – ojus* – considered as *bala* [(26).] Three types of *bala* are explained. *Sahaja, kalaja and yukthikruta* [(27)]. When the *bala* acts against the disease or pathogens we say *vyadhikashamatwa* is there [(28)]. *Balbramsa* can be considered as reduced immunity or autoimmunity.

Gourava generally means heaviness; *sirogourava*, *gourava* in *urustamba* are examples. This terminology has more significance even though not much has been mentioned about this. After *udvartana* treatment patients usually say that they feel very light. This indicates the presence of heaviness in particular condition.

Charaka explains the properties of *vayu* as *Vayustandrayantradara:*. *Anilamudata* can be explained as a condition that the person becomes inactive, like to rest all the time [(29)].

Lack of enthusiasm can be considered as *alasya*. *Agnimandya* leads to *apaktki*. *Nishteeva* means excess saliva resulting in spitting. Body considers *ama* as *shalya*. To remove the *shalya* throughout the GI tract mucous secretion initiated. *Malasangha* results from *srotorodha* leads to constipation, absence of sweat, reduced thirst (Neural regulation of thirst hampered). Consequently *aruch*i and *klama* (lassitude) develops.

Ama lakshana in RA can be considered as the constitutional symptoms and the fatigue. There are different approaches for the management of *Ama*. Considering the clinical apporoach is useful for the study.

Ama - treatment principle

Generally for all ama conditions *apatharpana* is indicated. Observing the *doshadikya* conditions three types of approach has been advised. *Langhana, laganapachana* and *sodhana* treatments are indicated for *alpa, madya* and *prabhuta dosha* respectively. This approach is very useful in clinical settings [(30)]. Another approach is based on the

predominant dosha. In *kapadhika* condition (ama) *langhana* is indicated, in *pittadika* condition (*vidagdam*) *vamana* is indicated and in *vatadika* (*vishtabda*) condition *swedana* is indicated. All these are general principles. Comprehensive approach has to be taken according to the site/condition /*doshadikya* [31].

Not only the condition and predominance of *doshas* but also *gati* and extend of spread of dosha are also considered while treating the any disease in *ama* condition. In chronic illness like RA the *doshagati* will be *tiryak* and the *doshas* spread all over the body (*tiryak, sarvadehapravrisrta*). The first approach is *samana, pachana and dipana*. When the *doshas* reach the *kosta*, appropriate *sodhana* can be done [32][33]. The concepts can be tabulated as below;

Table M 2. Ama pachana in RA

RA and Ama		
Chronic Autoimmune Systemic disease	*Dosha* in *Tiryak gati* *Balabramsa* *Sarvadehapravrisrta* *Chirakari Ama*	*samana*, *pachana* and *dipana*

Assessment in a patient

There is no tool available till date to assess or measure the *ama* in a patient. Such a tool is essential to measure the prognostic outcomes of *ama* treatment. A conceptual framework has developed and the project is accepted by Kerala University of Heath Sciences [34].

In the present study, the tool used is based on the *samyak langhita lakshana* - mentioned in Ashtanga Hridaya. Reverse of *samyaklanghithalakshanas* are used to assess the subjective measures. The reverse of *samyaklanghithalakshanas:* Constipation, Heaviness of body, Loss of taste, Loss of appetite, Loss of thirst, Bad belching, Pain (Joint pain), Lack of enthusiasm (*Utsah*), Lethargy (*tandra*) [35].

Aobut the management of ama in RA the following can be concluded.

- In RA, Ama combines with *dosha, dhatu* and *mala* forming toxic *saamadosha, saamadhatu and saama mala* respectively.
- In RA *Ama* extends all over the body and the *gati is tiryak*.
- First line of treatment is *Samana*. When dosha reaches the *kosta sodhana* may be an option.

RHEUMATOID ARTHRITIS

Introduction

Rheumatoid Arthritis is a chronic multisystem disease that affects the joints, connective tissues, muscle, tendons, and fibrous tissue. It causes deformity and functional disability. The peripheral joints are symmetrically affected[37]. The systemic manifestations are haematologic, cardiovascular, pulmonary and neurological.

In India the prevalence rate is 0.7% and worldwide prevalence is 0.8%. The age group more affected is 20-40. RA strikingly increases in females to 5% over the age of 70. In all age groups females are more affected by RA than male and the ratio being 3:1[38][39][40].

The clinical course of Rheumatoid Arthritis is prolonged, with intermittent exacerbations and remissions. The severity of the disease is associated to increased mortality due to increased risk of CVD. In these patients expected life span is reduced (8-15 yrs). Long term outcome can be predicted by functional status of the patient within 1st year of RA. Factors affecting the poor prognosis are [41].

Female gender
Disability at the time of presentation
Involvement of MTP joints
Radiographic changes at the time of presentation of disease
Smoking
Positive RF or Anti-CCP

Pattern of joint involvement

There are different criteria to confirm the diagnosis of RA. The 1987 ACR criteria is useful for when the disease is fully established. The 2010 ACR EULAR criteria will help to diagnose RA in early stage. Still there are practical difficulties in confirming the diagnosis. The pattern of joint involvement can be considered together with or alone to confirm the diagnosis.

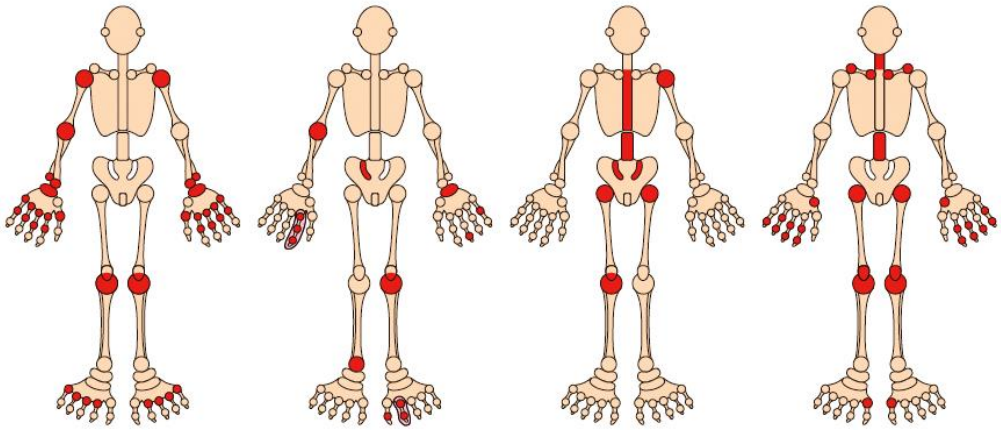


Image 1. Pattern of joint involvement

A. RA, **B.** Psoriatic Arthritis, **C.** Ankylosing spondylitis, **D.** OA

(Courtesy Davidson's Principles and Practice of Medicine)

Genetic considerations, family history

In most of chronic illness the genetic factors play an important role in the occurrence and severity of RA (with HLA-DR4 and HLA-DR1 association). At the same time genetic and environmental factors cannot be separated. In the era of genomics family history has got significance. In RA hereditary factor is estimated as 60% [(42)]. Family history is a proxy for a genetic and a part of environmental involvement [(40) (43)]. In first degree relative of a patient RA is 2-10 times greater than the general population. Due to gene–environment interactions, the estimate of genetic influence may vary in different studies [(44).]

Environmental factors

Environmental factors have an important role in the pathogenesis of RA in addition to genetic factors. One of the most important extrinsic risk factor for the development and severity is smoking. Smoking is a risk related to RF and anti CCP disease [(45)].

Pathophysiology [(40) (46)]

The bone, underlying cartilage and the synovial tissue are affected by RA. The synovial membrane is a thin layer of connective tissue which covers most articular surfaces, tendon sheaths, and bursae [(47)]. It becomes hyperplastic, synoviocytes increases and immune and inflammatory cells infiltrates mainly macrophages, B-lymphocyes, T-lymphocytes etc. cytokinin increases [(48)]. T cell activities leading to abnormalities of

synovial structure [49]. Through the synovial lining tissue, the synovial fluid infiltrates to the joint cavity. The main changes occurs in RA are synovial inflammation, proliferation, bone erosions and thinning of cartilage. Pannus is formed due to longstanding inflammation. Pannus is a thick cellular membrane under the cartilage and bone cartilage. The infiltrate is made up of T cells, B cells, plasma cells, dendritic cells, mast cells, and a few granulocytes [44]. The pannus spreads all over the cartilage eroded and destroyed gradually. Gradually adjacent bone also erodes, leading to fibrous or bony ankylosis. Muscles nearer to those joints may be infiltrated with lymphocytes. Atrophy to adjacent muscles occurs. This may lead to biochemical changes and amplify destruction [41].

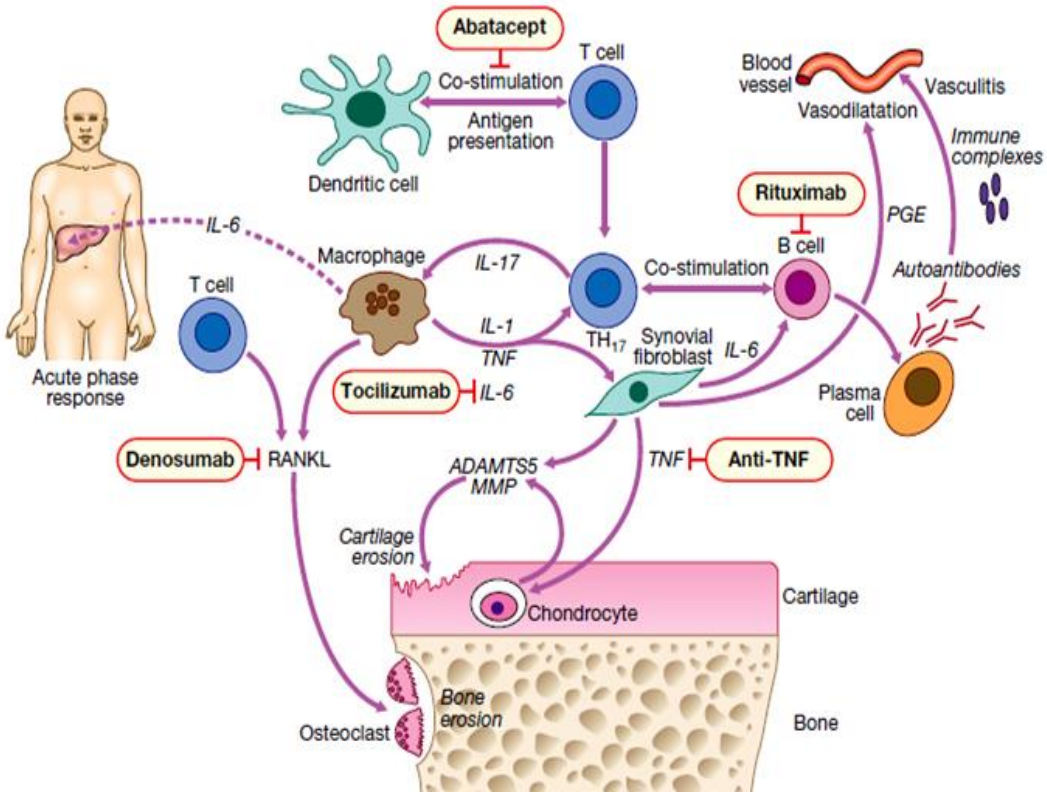


Image 2. Pathophysiology of RA

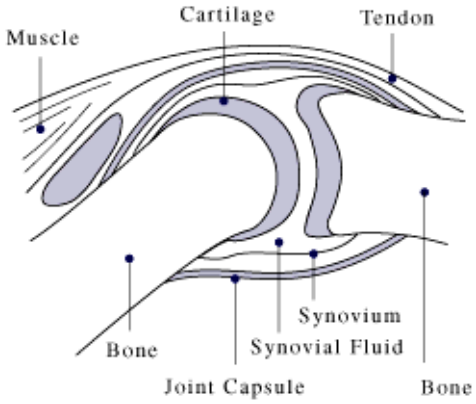


Image 3. Normal joint [50]

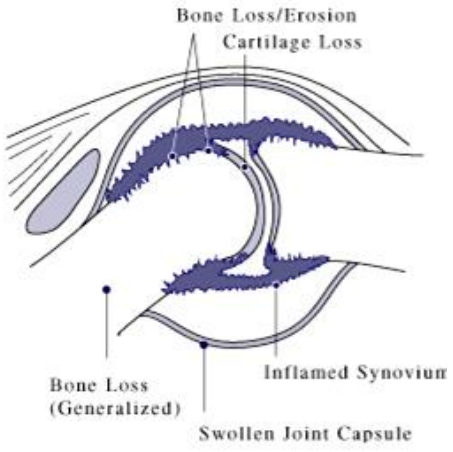


Image 4. Joint affected with RA [50]

Around 20% of patients develop rheumatoid nodules in elbows and fingers. Comparison between patients who started smoking at the onset of disease and who stopped it was studied. Patients who smoked at the onset was more affected by RA nodules than the other group [51].

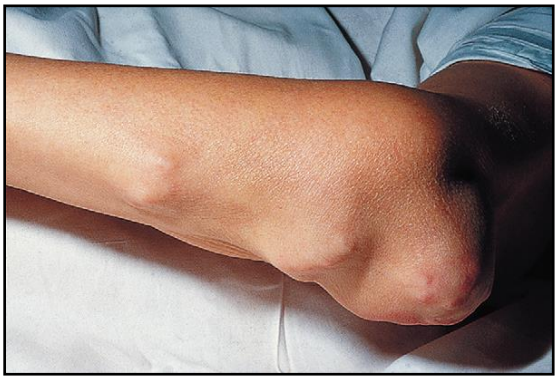


Image 5. Rheumatoid nodules and olecranon bursitis
(Courtesy Davidson's Principles and Practice of Medicine)

The bone marrow is hyperplastic in RA. In chronic RA extra compartmental involvement can be seen as in BM [52]. Bone marrow study in 20 patients with RA revealed eosinophilia in seven [53].

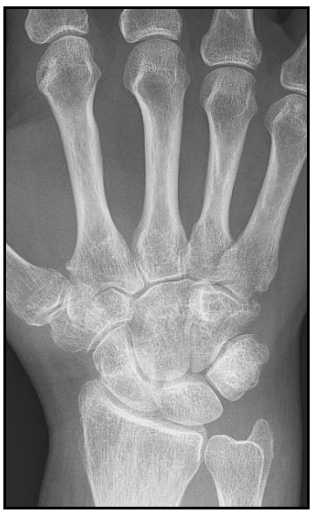


Image 6. X-ray wrist of a woman with RA[50]

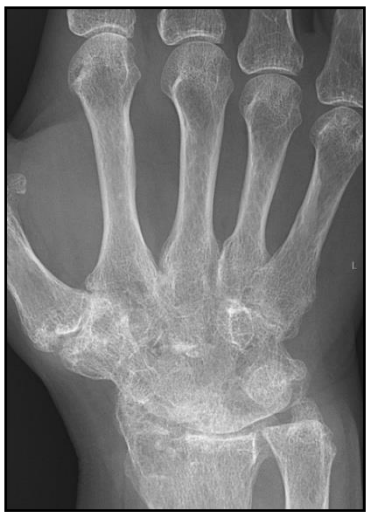


Image 7. Ankylosing fusion after 8 years [50]

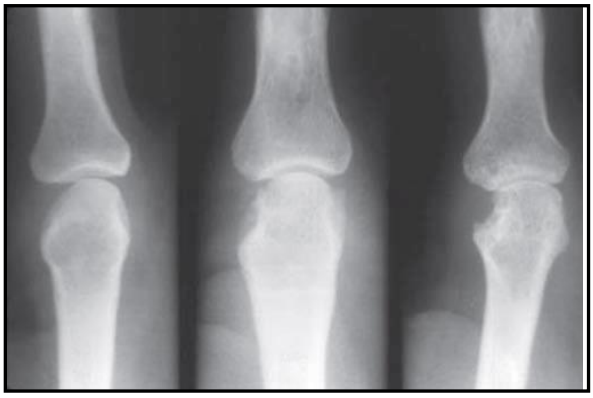


Image 8. X-ray demonstrating progression of erosions on the proximal interphalangeal joint. ***(Courtesy: American College of Rheumatology)***

Clinical features, Diagnosis

Insidious onset

prodromal symptoms [40]

fatigue

weakness

joint stiffness

vague arthralgias, myalgias

Symptoms [40] [44] [46]

- Pain and swelling of joints of hands, wrists and feet- symmetrical involvement of MCP and PIP joints. DIP joint involvement may usually due to coexistent OA.

Usually no shifting of joint arthralgia is seen, continues in the same joint. In rheumatic fever shifting of involvement of joint is seen.

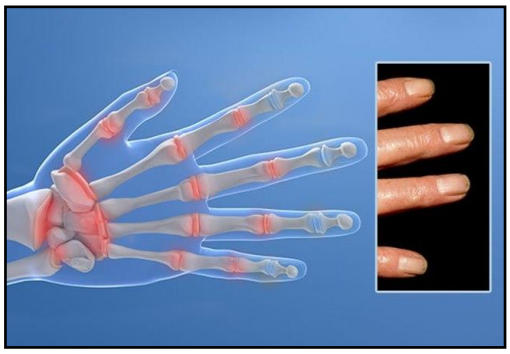


Image 9. Distal Interphalangeal (DIP) joint not affected [54]

- Decreased ROM, reduced grip strength and trigger fingers due to tendon tenosynovitis. Destruction of joints and soft tissue leads to deformities
- Deformities in longstanding uncontrolled diseases - swan neck deformity, the boutonnière deformity, Z deformity of the thumb. These days deformities are less as a result of different treatment modalities. Popliteal cysts in combination with synovitis may occur. Rapture of these cysts may lead to calf pain mimicking DVT.
- Rheumatoid nodules can be seen over the extensor surfaces of the elbows and fingers (20%).
- Compressive myelopathy and neurologic dysfunction can occur due to involvement of C1, C2 cervical spine. The prevalence of C1 C2 involvement is decreasing (10%). RA does not affect Thoracic and lumbar spine. Radiographic changes can be seen in tempero mandibular joint.

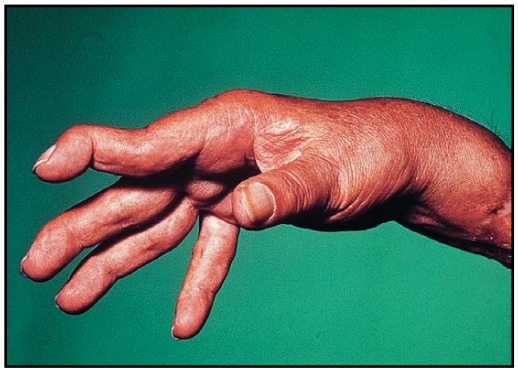


Image 10. Swan neck deformity

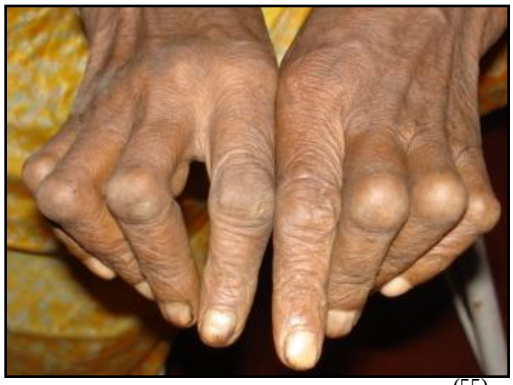


Image 11. Boutonnière deformity [55]

(Courtesy: Davidson's Principles and Practice of Medicine)

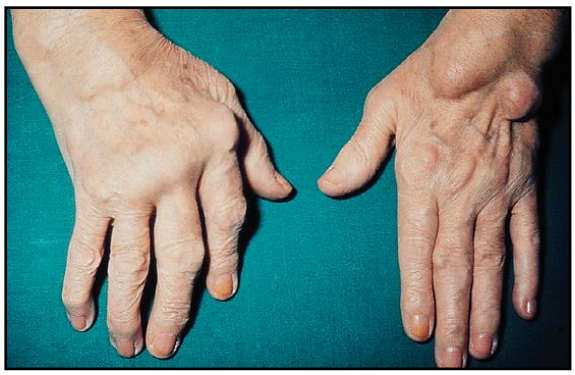


Image 12. Ulnar deviation
(Courtesy: Davidson's Principles and Practice of Medicine)

Extra articular manifestations

Extra articular manifestations (EAM) are more common in males and in patients with RF and/or are HLA-DR4 positive. Systemic manifestations are a major predictor of mortality in RA [(56)]. And the mortality is higher than the RA. The prevalence of these manifestation is approximately 8%-12% [(57)]. EAM may develop even prior to the onset of RA. History of smoking plays important role in systemic manifestations. Most frequently seen extra articular manifestations are subcutaneous nodules, secondary Sjogren's syndrome, pulmonary nodules, and anemia [(44).]

Constitutional

These signs and symptoms: - weight loss, fever, fatigue, malaise, depression, presence of a fever of >38.3°C (101°F) at any time during the clinical course [(44)].

Nodules

Subcutaneous nodules occur in 30–40% patients with positive RF, radiographic changes and highest disease activity. Nodules are firm tender seen adherent to periosteum, tendons, or bursae. Several pulmonary nodule, has been reported with its difficulty in management [(58)]. They develop in areas where repeated trauma or irritation occurs such as theelbow, sacral prominences and the Achilles tendon. Nodules are typically benign, can also occur in pleura, pericardium, and peritoneum. They are associated with infection, ulceration, and gangrene. Usually seen in elbows. The differential diagnosis for RA nodules are; [(54)]

Gouty tophi

Tendon xanthomas

Malignancies

Fibromas

Metastatic lesions

Sjögren's syndrome

The prevalence of secondary Sjogren's syndrome (sSS) in northern India is 5.5%. Old age is associated with the sSS but not with the damaged joint count [59]. It is charecterised by lymphocytic infiltrates into exocrine glands with symptoms keratoconjuctivitis sicca or xerostomia [60].

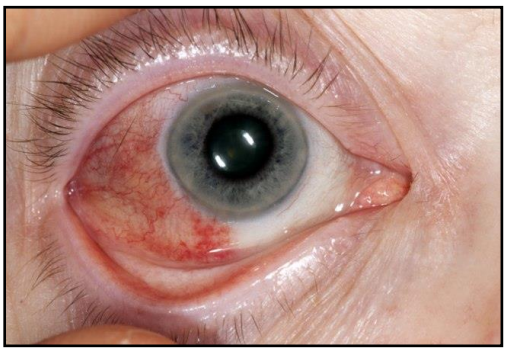


Image 13. Episcleritis in RA (60)

Pulmonary

Pulmonary manifestation of RA can be of different types: pleural effusion, ILD, nodules, drug related disease, infection. Pleural effusion is most common among these. This produces chest pain, dyspnoea, pleural rub. Dry cough with progressive shortness of breath in RA indicates ILD. Diagnosis confirmed by CT scan. ILD in RA indicates poor prognosis [44].

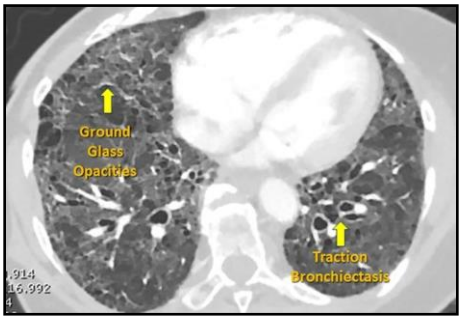


Image 14. Pleural effusion in RA [60]

Cardiac

In RA cardiac involvement are common. EAM features include pericarditis, cardiomyopathy/myocarditis, cardiac amyloidosis, coronary vasculitis, arrythmia and valve diseases. Most common one is pericrditis [61]. Clinical manifestation in less than 10%.

Vasculitis

Vasculitis in RA is very rare (1%), seen in patients with chronic RA and positive RF. Cutaneous signs vary from purpura infarcts etc. Ulcers can occur. Differentiation with venous insufficiency is difficult.

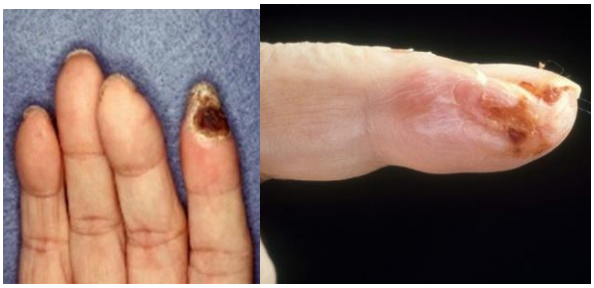


Image 15. Vasculitis [60]

Hematologic

In RA the hematological abnormalities are common. The degree of anemia correlates with the degree of inflammation: the CRP and ESR [62]. In RA patients with high disease activity Hb% is low compared to low disease activity patients. The platelet count and MPV was significantly high in anemic patients [63].

The clinical triad of neutropenia, splenomegaly, and nodular arthritis considered as Felty's syndrome (FS). 1-3% of RA patients likely to get FS and prevalence is 10 per 100,000. The role of genetic is more prominent in FS than in classic RA [64]. Leucopenia can be noted due to drug therapy.

Lymphoma

Compared to general population the risk of getting lymphoma in RA patients is 2 - 4 times. The risk is high if the patient is havinf high disease activity and Felty's syndrome [65].

Diagnostic versus Classification Criteria

Diagnosis intended to determine the cause and nature of the illness in a person, where as the classification intended to create well-defined, relatively homogenous cohorts for clinical research [66].

1987 ACR classification criteria for RA has been revised in 2010 in collaboration with European League Against Rheumatism (EULAR) for early diagnosis. (2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis) [67]. In this classification criteria includes Anti CCP and other markers. Rheumatoid nodules or radiograpphic changes are not considered because these do not occures in early stages of RA.

Joint distribution	**(0-5)**
1 large joint	**0**
2-10 large joints	1
-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
Serology	**(0-3)**
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
Symptom duration	**(0-1)**
<6 weeks	0
≥6 weeks	1
Acute phase reactants	**(0-1)**
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1
≥6 = definite RA	

There are several tools available to measure the disease activity. RAPID3 (Routine Assessment of Patient Index Data 3), Clinical Disease Activity Index (CDAI) and DAS28. Among them DAS28 score is widely used one [68].

How to calculate DAS28

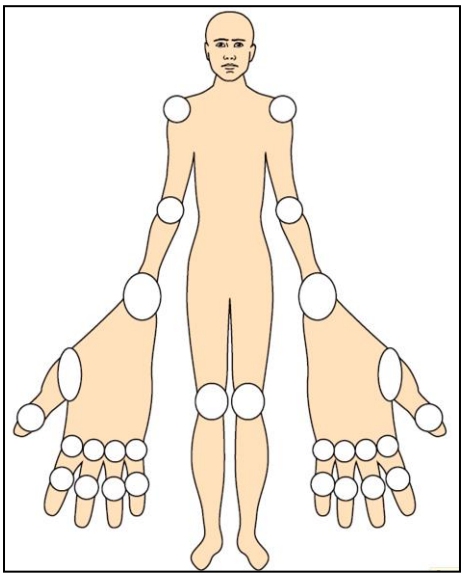


Image 16. Joints count in DAS28
(Courtesy Davidson's Principles and Practice of Medicine)

- Count the number of tender joints
- Count the number of swollen joints
- Measure the ESR
- Ask the patient to rate global activity of arthritis during the
- past week from 0 (no symptoms) to 100 (very severe)
- Enter data into an online calculator1 or work out using a formula

DAS28 = 0.56 × square root (tender joints) + 0.28 × square root (swollen joints) + 0.70 × loge(ESR) + 0.014 (global activity score)

DAS28 with ESR is more reliable than DAS28 with CRP [(69)].

Laboratory features

In the diagnosis of RA the three markers (anti-CCP antibodies, IgM and IgA RF) either alone or together is useful. Disease severity symptoms with the presence these markers are useful for the prognosis [(70)]. RF titres are positive for 80% of RA cases, for other conditions like hepatitis, cirrhosis, sarcoidosis, Sjogren's syndrome, and leprosy also. But negative results do not exclude RA. Serum RF is positive in 5% of healthy population [(44)]. Elevated ESR and CRP, Mild normocytic and normochromic anaemia, mild leucocytosis and hyper gammaglobulinaemia can be also noted in RA.

Anti-CCP assay and RF has similar sensitivity for the diagnosis of RA. Over the course of 3 years it is a better predictor(71). The sensitivity and specificity of anti-CCP for RA were 74.0% and 94.5%, respectively. For RF The sensitivity and specificity were 69.7% and 81.0% respectively [(72)]. Advantage of testing the presence of both anti CCP and RF, is that patients RF positive but anti–CCP negative and vice versa. Anti CCP with most values predicts the worse prognosis [(39)]. Radiographic abnormalities like narrowing of joint space, radial deviation of wrist and ulnar deviation of fingers can be seen in advanced cases [(39)]

Monitoring, investigations

The assessments, blood investigations and radiographs are used

to establish diagnosis

to monitor disease activity

to assess disease damage and

to assess drug safety.

VATASONITA

Introduction

Vatarakta, vatavalasa, adhyaroga and khuda are synonyms of vatasonita [73]. As the name '*vatasonita*' indicates the vitiated *vata* as well as *sonitha* are the two main causative factors involved in this disease. The term *vathavalasa* indicates the *avarana* of *vata* by the vitiated *rakta*. *Adhyaroga* means patients with sedentary life style are afflicted by this disease. *Khuda* means the deformed joints. If we amplify scope of terminologies the definition of vatasonita can be derived [74].

Vatasonita is a disease formed due to the *avarana* by the aggravated *rakta* over the vitiated *vatha*. Vatasonita is a chronic painful condition which mainly affects the joints, later causes deformities and functional damages. Those who live a sedentary life style are more prone to this disease. In this study vatasonitha has been compared to Rheumatoid Arthritis as it is having greater similarities in signs and symptoms [75].

Nidana, *dosha* and *dushya* are the three important factors for the development of a disease (*roga ghatakas*). When they combined together the disease will develop in a person. When they do not combine there will not be any disease at all, when they combine together in a weak form the disease will develop later or the symptoms will be milder [7]. Considering these factors will be more useful to explain *vatasonita* in the present juncture.

Nidanam / Aetiology

Nidanas are the aetiological factors of a disease, can be categorized as *Nija* (endogenous), *Aganthu* (exogenous) and *manasika*. *Beejadosha* (genetic), *prakriti*, *sroto dushti*, *agnivaishmyam*, *am*a, age and gender can be included in *Nija* factors. *Aganthu* factors include *vihara*, *krimi*, *janapadodmsa*, *kaala*, *daisika* and *vadyakritha*. Willful negligence from what he himself knows to be harmful and unhealthy [2]. The *beeja dosha* (genetic factor) has important role in in the formation of *Vatasonita*. The important endogenous factor *ama* has been dealt first in this chapter.

Considering the above factors the *nidana* can be discussed under *Ahar*a (diet) and *Vihara* (habits), excluding the non modifiable factors like genetic factors, *prakriti*, age and gender. In case of *vatasonita*, vitiation of *rakta* occurs first and later followed by vitiation of *vata*.

Ahara* that causes *rakta prakopa

Vidahi anna, *virudhanna* are said to be type of food that causes vitiation of blood [(76)]. Caraka opines that excessive intake of sweet foods, *athibhojana*, excessive intake of *lavana*, *sneha*, *ushna* and uncooked food, intake of petrified or dry meat or excessive intake of *kulattha*, *masa*, *nispava*, leafy vegetables, etc., meat and sugar-cane , excessive intake of curd, *aranala*, *sauvira*, *sukta*, buttermilk, alcohol and wine, intake of mutually contradictory food, intake of food before the previous food is digested can cause the *raktaprakopa* [(8)]. Susruta includes unhealthy food intake by *sukumara* and taking in foods opposite of the seasons [(77)].

Related comparison of *ahara nidana* for *rakta prakopa*

Ahara hetu	**Vagbhata**	**Caraka**	**Susrutha**
Vidhahyannam	+	+	-
viruddhannam	+	+	-
Asrikpradushannam	+	-	-
Klinna- sushkaanupa and ambujamamsa	-	+	-
Pinyaka	-	+	-
Mulaka	-	+	-
Kulatha, masa,nispava,sakadi,palala,ikshu	-	+	-
Dadhi,aranala,sauvira,sukta,takra,sura,asava	-	+	-
Adyasana		+	
mithyaharam	-	-	+
Rituasatmyabhoganam	-	-	+

Vihara* that causes *rakta prakopa

Awkward sleeping habits, *nisijagara*, improper sexual activities has been mentioned as *raktaprakopaja* viharas in Ashtanga Hridaya [(76)]. Day time sleep, *nisijagara*, emotional disturbances like anger, trauma to joints, avoidance of proper *sodhanakarma*, not following the *pathyas* after *sodhana karma* were described by Caraka [(8)].

According to Susruthasamhitha, *viharanidana* for *raktaprakopa* of vatasonita are indulgence in unhealthy activities by tender physique persons, who are greatly troubled by diseases, long walk,women, drinking wine and physical activities, who indulge in activities opposite of the seasons and accustomed ones, improper administration of oleation and other therapies, abstinence from copulation, and obese persons [(77)].

Related comparison of *vihara nidana* for *rakta prakopa*

Vihara hetu	Vagbhata	Caraka	Susrutha
Vidhiheenaswapnam	+	+	+
VidhiheenaPrajagaram	+	+	+
Vidhiheenamaidhuna	+	-	-
Achankramanaseelm	+	-	-
Krodha	-	+	-
Abhighata	+	+	-
Asuddhi	+	+	-
Rituasatmyavihara	-	-	+
Snehadivibhrama	-	-	+
avyavaya	-	-	+
Sthula	-	-	+

Ahara* that causes *vata prakopa

Vagbhata explains the *vatakopa nidana* in *sarvaroganidana*. *alpahara* with *tiktoshna rooksha*, taking it after the usual time are mentioned as *vataprokopa nidanas* [(78).] Caraka says that, excessive intake of *ruksha*, *katu*, *tikta* and ingredients, *alpamatra* or abstinence from food are mentioned as *aharanidanas* for *vataprakopa* in vatasonita. According to

Susrutha vegetables which are *usna*, *theeshna amla kshara* are considered as the *aharanidanas* for *vataprakopa* in vatasonita.

Related comparison of *ahara nidanas* for *vata prakopa*

Ahara hetu	**Vaghbhata**	**Caraka**	**Susrutha**
Tiktha-usna-kashya rasa ahara	+	+	usna
Rookshaahara	+	+	-
Alpaahara	+	+	-
Pramithabhoganam	+		-
abhoganam	-	+	-
Teekshna-amlakshara-sakadibhoganam	-	-	+

Vihara* that causes *vata prakopa

Vega udeerana and *dharana* (initiation and suppression of urges), *niisi jagara*, *uccha bhashana* (speaking in high pitch), excess physical activities and *sodhana athiyoga* can cause *vataprakopa* in vatasonita[(78)]. Caraka opines that tough type of travel like horse riding, excessive exercises like swimming for log time and exercises in hot season, *vegadharana*, can be considered as *vihara nidana* for *vataprakopa* in *vatasonita* [(79)]. In Susrutha samhitha horse riding camel riding ad tough exercises are considered for *viharanidana* for *vataprakopa* in vatasonita.

Related comparison of *vihara* that causes *vata prakopa*

Vihara hetu	**Vagbhata**	**Caraka**	**Susrutha**
Vega udheerna dharana	+	+	-
Nisajaagaram	+	-	-
Atyuchabhashana	+	-	-
Kriyaatiyoga	+	-	-
Bhi	+	-	-
Soka	+	-	-
atichintha	+	-	-

Ativyayama	+	-	-
Atimaidhuna	+	+	-
Greeshmaritu	+	-	-
End of day, night and food	+	-	-
Riding over horses, camels , or vehicles drawn by them	-	+	+
Ambukrida	-	+	-
swimming	-	+	-
jumping	-	+	-
Long walk in hot season	-	+	-

These are the different aspect of aetiological factors for vatasonita. The Nidana part of roga ghataka has been discussed. The roga ghtakas to be considered next are dosa and dushya:

Dosha *vatapradhana dosha*	
Vata	*vyanavata*
Pitta	*pachaka pitta*
Kapha	*sleshakakapha*
Dushya	
Uthanavatasonita	*rakta, rasa, mamsa*
Gambeeravatasonita	*rakta rasa. mamsa, meda, asthi, majja*
Other Ghatakas	
Upadhatu	*Sira, kandara, sandhi,snayu, twak.*
Mala	
Sareerika mala	*mutra, purisha*
Dhatumala	*kapha, sweda, pitta*
Agni	*jadaragni, dhatwagni predominantly Raktagni*
Agnidushti	*mandagni*
Srotas	*vatavaha, rasavaha, raktavaha initially later all dhatuvahasrotas*
Srotodushti	*sangam*
Adhisthana	*janu, janga, uru, kati, amsa, dhamani, hastha, padangasandhi*
Svabhava	*asukari*
Rogamarga	*madhyama.*

Samprapthi

Samprapthi vighattana is considered as *chikitsa*. *Vighattana* means hewing in pieces or separation. Interfering in to the disease forming situation may be considered as *chikitsa*. For developing treatment principles and to understand the mode of action of drugs it is important to understand the *samprapthi* or aetio pathogenesis of a disease. In most of chronic illness the genetic factors play an important role. At the same time genetic and environmental factors cannot be separated [(42)].

Acharya Vagbhata, Caaraka and Susrutha explain the *samprapthi* of *vatasonita* in similar fashion. Due to *apthyahara vihara rakta* get vitiated. Due to this vitiation *vata* also get aggravated and the path is obstructed by the already vitiated rakta (*avarana*). The obstructed *vata* vitiates the *rakta* again. The *athislashnadhi* symptoms are produced aftermath of this [(80).] The explanation is similar in carakasamhita [(81)] and in Susruthasamhitha also [(82)].

Flow chart 3. Aetio pathogenesis of Vatasonita

Classification of vatasonita

Depending upon nature of disease

Vatasonita affects all *dhatus* and *sandhis*. When affects *twak* and *mamsa* it is termed as *Utthana vatasonita*. Gradually it will affect the other *dhatus* and *sandhis* – it is termed as *gambhira vatasonita* [(83)].

Depending upon predominance of *doshas*

1. *Vatadhika*
2. *Raktadhika*
3. *Pittadhika*
4. *Kaphadhika*
5. *Vataraktadhika*
6. *Vatapittadhika*
7. *Vatakaphadhika*
8. *Raktapittadhika*
9. *Raktakaphadhika*
10. *Pitta kaphadhika*
11. *Tridoshaja*
12. *Vatatha pitta kaphadhika*

Purvaroopa

While describing the *purvaroopas*, Vagbhata says '*Kushta samam';* similar to *kushta*. Skin becomes very shiny or rough, over sweating or no sweat, burning sensation, itching, severe hot annoying pain, uricaria, ulcerations, *harsha* are explained in Ashtanga hridaya (84). As per Caraka, prodrominal symptoms of vatasonita include *athisweda*, *asweda*, etc as similar to Ashtanga hridaya. *Sandishaidilya*, *alasyam and gurutwam* has been additionaly explained [(85).] In Susruthasamhitha, heaviness of the body and burning sensation has been additionally explained [(86).]

Vagbhata and susrutha opines that vatasonita is first manifested in the lower limb and or upper limbs and later spreads to all other parts of the body. According to caraka the signs and symptoms first developed in the joints of the fingers of hands and feet and

spreads to all other joints of the body. From the symptomatological approach of the disease it can be concluded that vatasonita affects the *nadis*, *twak*, *muscles* and joints.

***Purvaroopa* mentioned by different acharyas**

Poorvarupas	**Vagbhata**	**Caraka**	**Susrutha**
Atislashnakharasparsa	+	-	-
Atisweda	+	+	+
Asweda	+	+	-
Daha	+	-	+
Kandu	+	+	-
Swapa	+	+	+
Thoda	+	+	+
Kodonnathi	+	-	-
Shrama	+	-	-
Vranananamadhikamsoolam	+	-	-
Shigrotpathichirasthithi	+	-	-
Roodhanamapirookshathwam	+	-	-
Nimittaealpaeapikopanam	+	-	-
Karshnyam	+	+	-
Kshatatiruk	-	+	-
Sandhishaithilya	-	+	-
Alasyam	-	+	-
Sadanam	+	+	-
Pidakodgama	-	+	-
Sphuranam	+	+	-
Bheda	+	+	-
Gurutwam	-	+	+
Supti	+	+	+
Sandhishurukbhutwabhutwa pranashyati	+	+	-
Vaivarnyam	+	+	+
Mandalotpati	-	+	-

Lakshanas

In vatasonita pain and swelling is first seen in smaller joints of the feet and then spreads to entire like the poison of rat bite. Site of *uthanavatasonita* is in *twak* and *mamsa* and in course time it spreads to all *dhatus* leads to *gambheera* vatasoniota [(83)] because of the *soushmya* and *sara* properties of *vata* and *rakta*. *Saraguna* and *dravaguna* makes the *doshas* enter in to joints and gets obstructed by the *vakratwa* [(87)].

Signs and symptoms of *uthana* and *gambheera* by caraka and vagbhata

Lakshanas	**Vagbhata**	**Caraka**
kandu	+	+
twak tamrasyavalohita	+	+
ayama	+	+
daha	+	+
osha	+	
ruk	-	+
thoda	-	+
sphurana	-	+
Shavathu	+	+
Grathitam	+	
Paki	+	+
Cutting pain in joints	+	+
vakrata	+	+
Khangam and pangu	+	+
sthambham	-	+
kadhinam	-	+
Antarbrishamartiman	-	+
twakshyavata	-	+
daha	-	+
Thoda	-	+
sphurana	-	+

Comparison of the *lakshanas* of vatasonita

Vatadhika vata sonitha

Lakshanas	**Vagbhata**	**Caraka**	**Susrutha**
Sirayama	-	+	-
Soola	-	+	-
Sphurana	+	+	-
Todam	+	+	+
Karshya	+	+	-
Rooksha	+	+	-
Syavatha	+	+	-
Vridhihani	+	+	-
Sandhisankocha	+	+	-
Angagraha	+	+	-
Athiruk	+	+	-
Aakunchanam	-	+	-
Sthambhanam	-	+	-
Seethe dwesha	+	+	-
Seethe anupasaya	+	-	-
Supti	+	-	-
Vepathu	+	-	-
Sparshaasahishnutham	-	-	+
Bhedam	-	-	+
Prasosham	-	-	+
Swapam	-	-	+

Raktadhika vatasonita

Lakshanas	**Vagbhata**	**Charaka**	**Susrutha**
Bhrisharuk	+	+	-
Todam	+	+	-
Tamravarnam	+	+	-
Chimichimayana	+	+	-
No relief from snigha and *rukshaprayoga*	+	+	-
Kandu	+	+	-
Kleda	+	-	+
Atidaham	+	-	+
Atiusna	-	-	+
Raga	-	-	+
Mridusopha	-	-	+

Pittadhika vatasonita

Lakshanas	**Vagbhata**	**Charaka**	**Susrutha**
Vidaham	+	+	-
Vedana	-	+	-
Moorcha	-	+	-
Sweda	+	+	-
Trishna	+	+	-
Mada	-	+	-
Bhrama	-	+	-
Raga	+	+	+
Paka	-	+	-
Sosha	-	+	-
Sparshakshamatwa	+	-	+
Sammoham	+	-	+
Ruk	+	-	+
Bhrisoshnatha	+	-	+
Daha	-	-	-
Mrudushopha	-	-	-

Kaphadhika vatasonita

Lakshanas	Vagbhata	Charaka	Susrutha
Sthaimithya	+	+	-
Gouravam	+	+	-
Sneha	+	+	-
Supti	+	+	-
Mandharuk	+	+	-
Seethalatwa	+	-	+
Kandu	-	-	+
Peena(Shoola)	-	-	+
Stabhatha	-	-	+

Prognosis

Prognosis of all disease depends on the nature of *upadravas*, chronicity, and the healthy combination of *padachatustaya*. In vatasonita, the *sadyasadyata* has been explained by Vagbhata and Caraka in a similar manner [(88) (89)].

Sadhyam (curable)

- Recent onset
- Duration less than 1 year
- Involvement of one dosha
- No *upadravas*

Yapyam (palliable)

- Duration about 2 years
- 2 *doshas* involved
- No *upadravas*

Asadhyam (incurable)

- Chronic
- All three *doshas* involved
- *Upadravas* present

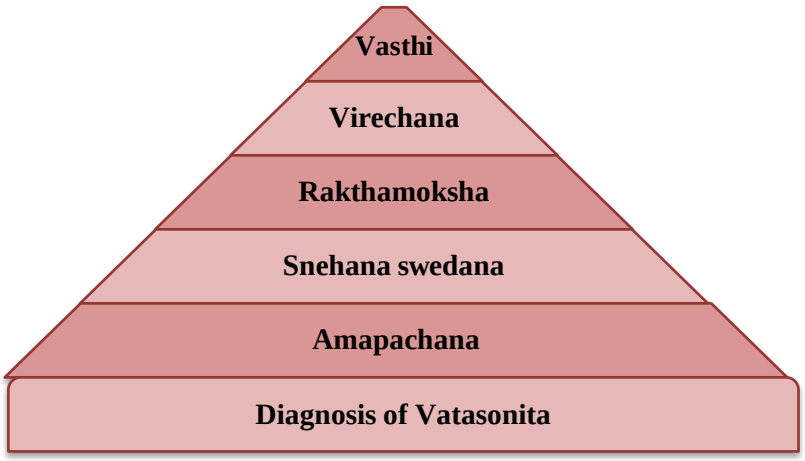
Complications of vatasonita

Caraka opines that if vatasonita is accompanied by sleeplessness, unconsciousness, fainting, intoxication, giddiness, mental fatigue, trembling, breathlessness, muscles cramp, stiffness of the head, pain, thirst, fever, hiccup, pricking pain, deformities of

fingers and toes, pustular eruptions, burning sensation, affliction of vital parts. then it becomes asadya [89]. Acharya Susrutha has added the following as complications:

- Cracked feet
- Fissures up to knees
- Broken skin
- Fluid exudation
- Loss of strength and muscles

Management



Flow chart 4. Management principle of Vatasonita

To explain the rationality of acharya's treatment methodology in vatasonita, understanding the basic concepts becomes essential. Considering this selection of *sodhana* and *samana* becomes critical.

Vagbhata explains the indication of *sodhana* and *samana*. In a chronoc illness (*chirakari roga*) the *dosha gati* is *tiryak*. In that condition *samana* is indicated. While using *samana* the *dosha* moves towards *koshta*. When *dushta dosha* reaches it can be eliminated by appropriate *sodhana karmas* [90]. At any cost immediate *sodhana* is contraindicated. After assessing the *dehabala* and *agnibala*, *vaidya* can proceed for *sodhana*.

Applying this concept and considering the important aetiological factor *ama*, as a first step *samana* is advised. After *ama pachana* naturally doshas will be led to koshta. At that time *sodhana* is advised. It has to be noted that the management strategy depends on the presence of *ama*. The *poorvakarmas* (*sneha swedas*) are performed to make the *doshas*

utklishta samuthklishta and opening the *srotomukas*, so that the vitiated *doshas* will come to *koshta*. In the presence of *ama, snehana* is contra indicated. Then *ruksha sweda* alone is enough to bring back the doshas to koshta.

In vatasonita as the *rakta dushti* is so high that the *rakta dhatu* has to be removed. That is why Vagbhata advises the *raktamoksha* after proper *snehana karma*. It should not be performed at a stretch as it will vitiate *vata* [91]. If *rakta moksha* is contraindicated then *virechana* is advised [92]. Vagbhata opines that *Vasthi karma* is of prime importance in vatasoinita. To eliminate the vitiated *doshas* and *malas ksheeravasthi* instead of *virechana* is advised [93].

Abhyanga, *pariksheka*, *lepa*, *avagaha* and *upanaha* is adviseed for *Uthana* variety of vatasonitha and for *gambheera vatasonita*, *snehapana*, *virechana* and *asthapana* are advised [94].

Below listed are the different karmas and medications preffered in Kerala for the management of vatasonita. The medicines in different combinations used according to the condition of the patient.

Sweda

- Rukshasweda with appropriate churnas (whole body)
- Dhanyamla dhara (whole body)
- Patrapotala after ama pachana for vata samana
- Upanahaswedam (Ekanga)

Parisheka or dhara

- Dasamula ksheeram
- Tailams
- Dhanyamla
- Karaskarasrithaksheera
- Dasamoolasrithaksheera
- Pindatailam

Vasthi

- Ksheeravasthi
- Vaiswanaram churnam vasthi

Kashayas

- Amrutottaram kashayam
- Rasnerandadi kashayam
- Maharasnadi kashayam
- Manjishtadi kashayam
- Rasnasaptakam kashayam
- Gulguluthikthakam kashyam
- Kokilaksham kashayam

Gulika

- Yogarajaguggulu
- Mahayogarajaguggulu
- Kaisoraguggulu
- Gokshuraguggulu
- Amrithaguggulu
- Nava guggulu

Ghruta

- Gulguluthikthakamghritham
- Karaskara ghruta
- Indukantham ghruta
- Guluchy ghruta

Arishtas

- Amritarishtam
- Balarishtam
- Punarnavarishtam
- Ayaskrithi
- Dasamoolaristam
- Aswagandharishtam

Asavas

- Lohasavam
- Punarnavasavam

Choornam

- Shaddharanam
- Gulgulupanchapalam
- Vaiswanaram
- Vacachoornam

Tailam (internal)

- Ksheerabala tailam
- Dhanwantharam tailam
- Madhuyashtyadi tailam
- Karaskaratailа tailam
- Gandharvaerandam
- Satahwadi tailam
- Dasapakabalatailam

Tailam (external)

- Maduyashtyadi tailam
- Pinda tailam
- Mahapindatailam
- Kottamchukkadi tailam

Lepam

- Jadamayadi lepam
- Kottam chukkadi lepam
- Ellumnisadi lepam
- Gruthadhoomadi lepam
- Thaila lepam
- Erandabejjadi lepam
- Duthuradi lepam

Pichu (Ekanga) With appropriate taila

DRUG REVIEW

In the present study the formulation used for Ama pachana purpose is the Amrutottaram kashayam [95]. It contains the following drugs.

Nagara	*Zingiber officinale* Roxb.
Amrutha	*Tinospora cordifolia* (Willd.)Miers
Hareethaki	*Terminalia chebula* Retz

SUNDI [96]

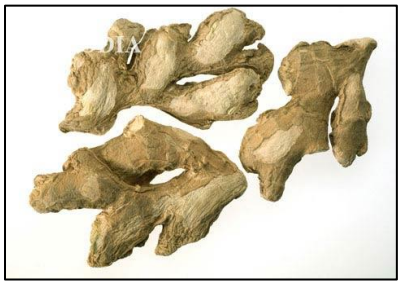


Image 17. Ginger root

Botanical name	*Zingiber officinale Roxb*.
Family	Zinglberaceae
Sanskrit name	Ausadha, Nagara, Visva, Visvabhesaja, Visva,
English name	Ginger root, Ginger
Hindi name	Sonth
Malayalam name	Chukku

Description

Rhizome, laterally compressed bearing short, ovate, oblique, flattish, , branches on upper side each having at its apex a depressed scar, pieces about 5-15 cm long, 1.5-6.5 cm wide (usually 3-4 cm) and 1-1.5 cm thick, externally buff coloured showing longitudinal striations and occasional loose fibres, fracture short, smooth, transverse surface exhibiting narrow cortex (about one-third of radius), a well-marked endodermis and a wide stele showing numerous scattered fibro-vascular bundles and yellow secreting cells, odour agreeable and aromatic, taste, agreeable and pungent.

Part used	Rhizome
Properties	
Rasa	Katu
Guna	Laghu, Snigdha
Virya	Usna
Vipaka	Madhura
Karma	Anulomana, Dipana, Pacana, Vatakaphapaha
Constituents	Essential oil, gingerol, zingiberol, shogaol, resinous matter and starch.
Important formulations	Trikau, Vaisvanara Curna, Amrutottaram kwatha
Therapeutic uses	Agnimandya, Svasa, Adhmana, Amavata, Pandu
Dose	1-2 g of the drug in powder form

GUDUCHI [97]

Image 18. Amritaleaves and dried stems

Botanical name	Tinospora cordifolia (Willd.)Miers.
Family	Menispermaceae
Sanskrit name	Amritavalli, Amrita, Madhuparni, Guducuka, Chinnobhava
Hindi name	Giloe, Gurcha
Malayalam name	Chittamrutu
Tamil name	Seendal, Seendil kodi

Distribution

A perennial climber found throughout Tropical India, drugcollected during summer preferably in the month of May, drug is used in fresh form also.

Description

Drug occurs in pieces of varying thickness ranging from 0.6-5 cm in diameter, young stems green with smooth surfaces and swelling at nodes, older ones show a light brown surface marked with warty protuberances due to circular lenticels; transversely smoothened surface shows a radial structure with conspicuous medullary rays traversing porous tissues, taste bitter.

Parts used	Stem, leaf, aerial roots.
Properties	
Rasa	Tikta, Kasaya
Guna	Laghu
Virya	Usna
Vipaka	Madhura
Karma	Dipana, Rasayana, Jwaraghna
Constituents	Tinosporin, tinosporidine, cordifolide, and alkaloids
Important formulations	Amritarishta, Amrutottara kwatha, Guduchi Sattva
Therapeutic uses	Jwara, Kusta, Pandu, Prameha, Vatarakta, Kamala
Dose	3-6 g of the drug in powder form. 20-30 g of the drug for decoction

HARITAKI [98]

Image 19. Myrobalan Fruit

Botanical name	*Terminalia chebula* Retz.
Family	Combretaceae
Sanskrit name	Abhaya, Kayastha, Siva, Pathya, Vijaya

English name	Myrobalan
Hindi name	Harre, Harad, Harar
Malayalam name	Katukka

Distribution

A moderate sized or large tree found throughout India, chiefly indeciduous forests and areas of light rainfall, but occasionally also in slightly moist forests.

Description

Intact fruit yellowish-brown, ovoid, 20-35 mm long, 13-25 mm wide, wrinkled and ribbed longitudinally, pericarp fibrous, 3-4 mm thick, non-adherent to the seed, taste, astringent.

Parts used `	Fruit rind.
Properties	
Rasa	Madhura, Amla, Katu, Tikta, Kasaya
Guna	Laghu, Ruksa
Virya	Usna
Vipaka	Madhura
Karma	Caksusya, Dipana, Hridya, Medhya, Rasayana, Anulomana[137]
Constituents	Tannins, anthraquinones, Chebulinic acid and polyphenolic compounds.
Important formulations	Triphala Curna, Abhayarista, Agastya Haritaki Rasayana, Amrutottaram kwatha, shaddharanam choornam.
Therapeutic uses	Sotha, Arsa, Aruci, Hridroga, Kasa, Pandu, Prameha,
Dose	3-6 g of the drug in powder form

Preparation of medicine (99)

48 gms of churna (supplied as one packet) is taken and 768 ml (16 times) of water is added. The mixture is boiled and reduced to 96 ml (1/ 8^{th}). To take the correct measure of water and kashaya thereafter measure with markings are made familiar with the patients.

Dose [100]

Amrutottaram Kashayam 96 ml with 6 gms of sugar as single dose is given daily in empty stomach (morning) for 15 days as OP treatment. When the patient feels appetite he can take next diet.

Amrutottaram Kashayam

Liquid Chromatography Coupled with Electro Spray Ionization Mass Spectrometry of the Amrutottaram kashaya led to the structural identification of separated compounds. Phenolic acids such as quinic acid, protocatechuic acid, gallic acid, and chebulic acid were identified in the formulation along with some flavonoids [101].

Quinic acid [102]**:** Quinic acid is an astringent and used in influenza [103].

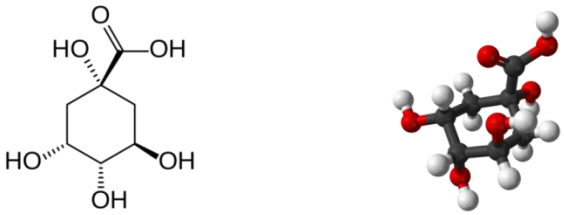


Image 20. Structure and model of Quinic acid

Protocatechuic acid (PCA) [104]**:** Protocatechuic acid (PCA) is an anti inflammatory, anti microbial and anti oxidant. It can be used along with other antibiotics against resistant pathogens [105].

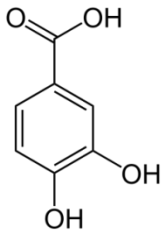


Image 21. Structure of Protocatechuic acid

Gallic acid [106]**:** Gallic acid is a natural antioxidant and cardio protective [107]

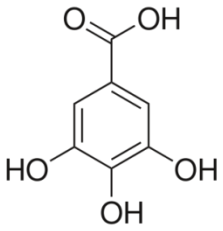


Image 22. Structure of Gallic acid

Chebulic acid [108]**:** Chebulic acid were identified in the formulation along with some flavonoids [101]. It is ans antifungal, antibacterial agent. Improves skin complexion, Hepato protective [109]

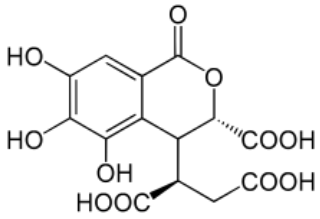


Image 23. Structure of Chebulic acid

RESEARCH METHODOLOGY

CHAPTER 3

RESEARCH METHODOLOGY

Hypothesis

Null hypothesis

Amrutottaram Kashayam has no *ama pachana* effect in Rheumatoid Arthritis

Alternate hypothesis

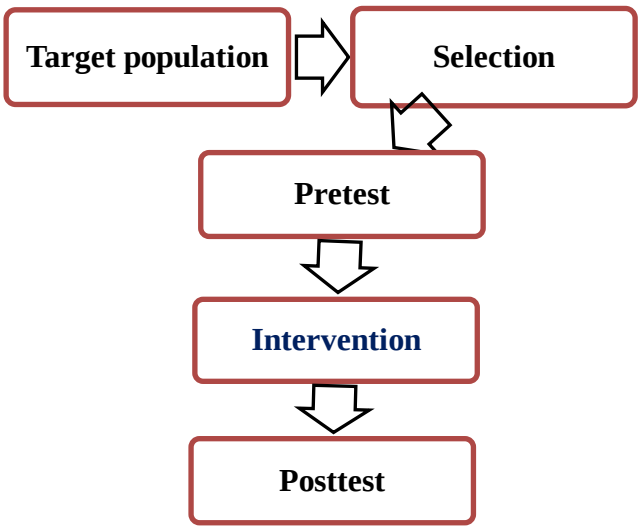
Amrutottaram Kashayam has *ama pachana* effect in Rheumatoid Arthritis

Probability level

Probability level for this study is fixed as $p < 0.05$

Study Design and setting

Pretest-posttest design study was used in this study in which patients were observed before and after giving Amrutottaram Kashayam [21] for 15 days. This study design only looks at one group of individuals who receive the intervention, which is called the treatment group. The pre-post test design allows making inferences on the effect of intervention by looking at the difference in the pre-test and post-test results. The patients fulfilling the criteria were selected from the Kayachikitsa OPD of Vaidyaratnam Ayurveda College, Ollur, Thrissur.



Flow chart 5. Pretest-posttest design

Study population

Patient suffering from Rheumatoid Arthritis in the catchment area of Vaidyaratnam Ayurveda College Hospital, Thaikattussery, Ollur, Thrissur, were considered as study population.

Inclusion criteria [87]

1. **2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis**

Joint distribution	**(0-5)**
1 large joint	**0**
2-10 large joints	1
-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
Serology	**(0-3)**
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
Symptom duration	**(0-1)**
<6 weeks	0
≥6 weeks	1
Acute phase reactants	**(0-1)**
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1
≥6 = definite RA	

2. **Age group of** 25 – 60

3. **Ama with Kapha predominance**

Exclusion criteria

1. Patients with serum positive ASO titer
2. Patients with serum positive Uric acid
3. Patients with other systemic complications
4. Patients with hypertension and diabetes.
5. Age group less than 25 and above 60.

Sample size (126) (3)

The Sample size has been fixed as 115. And calculated using the formula

$n = \frac{Z^2\ P(1-P)}{d^2}$ (Prevalence of approximately 0.75 % in India) **(1)**

Where

n = required sample size

Z = confidence level at 95% (standard value of 1.96)

P = estimated prevalence (0.75%)

d = margin of error at 8% (0.08)

Sampling technique

Consecutive sampling technique is used for the sample selection. Patient coming to Kayachikitsa OPD, Vaidyaratnam Ayurveda College Hospital, Thaikattussery, Ollur, Thrissur and fulfilling the 2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis were taken in to study.

Data collection

Data were collected by personal interview including examination, observation, Interview schedule (CRF)Annexure I, Ama Assessment Tool Annexure II, DAS28 score Annexure V, EULAR Good or Moderate response criteria (127) (128), Visual Analog Scale Annexure III, TNKC Prakriti assessment tool AnnexureVIII (129), lab investigation. Laboratory reports were collected for RF, ASO titre, ESR, ACPA (ACCP), Hb%, TC, DC, FBS, PPBS, LFT, Serum Creatinine, Serum Uric acid, CRP, ANA were also recorded.

Table M 3. Schedule of data collection

Procedure	Before treatment 1st Day	After treatment 15th Day	After follow up 30th Day
Interview schedule, & Visual analog scale	✓	✓	✓
DAS28	✓		✓
TC, DC, ESR, Hb%, LFT, S. Creatinine, CRP	✓	✓	---
Range Of Motion	✓	✓	---
FBS, PPBS, RF (RA), ASO titer, Serum Uric acid, Anti-CCP, ANA,	✓	---	---

Study tools

In this study Ama assessment tool, DAS28 score, Visual analog scale and Laboratory reports were used as main tools. Interview schedule in relation to Rheumatoid arthritis mainly consists of the following

- **Ama assessment Tool** Annexure II, X **:** - 9 item YES/NO Questionnaire. This questionnaire administered by Researcher to collect information
- **Visual Analogue Scale** Annexure III**:** - It is a self-administered questionnaire to assess the pain before and after the intervention. 1 to 10 continuous scales with gradual increase in intensity of colour is used. Patient is asked to touch the number or coloured area according to the intensity of pain.
- **DAS28 score** Annexure V (127) (128) **:** - is calculated by noting the number of tender joints, swollen joints, activity in the past week (10 to 100 VAS), ESR/CRP
- **Overall change in Disease activity as per the EULAR Good or Moderate response criteria:** - This is calculated by using change in DAS28 score and Present DAS28 score (127) (128)

Table M 4. EULAR Good or Moderate response

Present DAS28 score	DAS28 improvement over time points		
	>1.21	0.6 - 1.20	<=0.60
Low disease activity 2.6 - 3.2	Good response	Moderate response	No response
Moderate disease activity 3.2 - 5.1	Moderate response	Moderate response	No response
High disease activity >5.1	Moderate response	No response	No response

- **Prakriti** AnnexureVIII **:-** Assessed by interviewer assisted TNMC Prakriti 2004 Questionnaire [129]**.** Patients grouped as Vatadhika, Pittadhika and Kaphadhika as per the scores obtained in the different domains.

Hand grip: - This is assessed before and after intervention by using Hand dynamometer. The Hand grip was measured using Hand dynamometer. This specifically focuses on hand [130]. The decrease in grip strength can be easily measured by portable dynamometers. It is used as a strong indicator of functional disability in RA patients [131].

Image 24. Hand dynamometer

- **Range Of Motion (ROM) of different joints** [Annexure IV]**: -** Evaluation of joint range of motion is important in the evaluation of therapeutic approach in patients with RA**.** ROM in joints measured by using Goniometer [(132)].

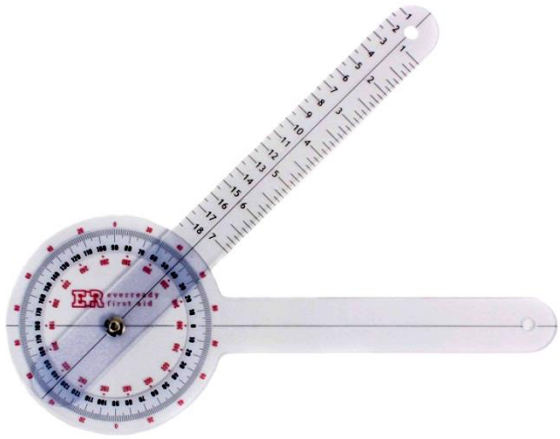


Image 25. Goniometer

- **Blood investigations:-** Lab reports of the blood samples from accredited labs

Procedure

Patients coming to Vaidyaratnam Ayurveda College Hospital OPD fulfilling the 2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis are recruited for the study. Socioeconomic Status has been assessed by Kuppuswamy Socio Economic Status scale.[(133)]. Ama assessment Tool, DAS28 score, Visual Analog Scale, and questionnaire are used to assess Ama and other parameters. These are evaluated before treatment, after 15th and 30th day of treatment (follow up period).

Amrutottaram Kashayachurna was given to 115 patients. Patient is advised to prepare Amrutottaram Kashayam with this churna. When the patient feels appetite he is advised to take diet. Diet is restricted to manda and peya [(134)] for all patients. Follow up period is fixed as 15 days without medicines. Every patient supplied with 15 packets each packet containing 48 gms of Amrutottaram Kashayachurna [Annexure IX].

Dose [Annexure IX (117)]

Explained in Chapter 2, page 43 and in patient information Annexure IX

Preparation of medicine Annexure IX (116)

Explained in Chapter 2, page 42 and in patient information Annexure IX

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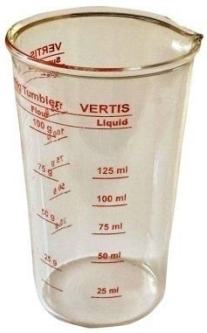


Image 26. 125 ml measure glass **Image 27. 500 ml measure**

STATISTICAL ANALYSIS

Statistical analysis has been conducted and reported under the following headings.

I. **Socio demographic and other characteristics**
II. **Assessment of Blood investigation parameters for exclusion and diagnosis**
III. **Analysis of Subjective parameter**
IV. **Analysis of Objective parameters**
V. **Analysis of blood investigation parameters**

Scoring for modified Kuppuswamy's socio-economic status scale, revised for 2016 (133)

Education		Family income per month	
Profession or honors Intermediate or post-high	7	≥ 42,876	12
Graduate or postgraduate	6	21,438 - 42,875	10
School diploma	5	16,078 - 21,437	6
High school certificate	4	10719 - 16,077	4
Middle school certificate	3	6,431-10,718	3
Primary school certificate	2	02,165 - 06,430	2
Illiterate	1	≤2164	1
Occupation		**Socioeconomic class**	
Profession	10	Upper class	26-29
Semi professional	6	Upper middle class	16-25
Clerical, shop owner, farmer	5	Lower middle class	11-15
Skilled worker	4	Upper lower class	5-10
Semiskilled worker	3	Lower class	<5
Unskilled worker	2		
Unemployed	1		

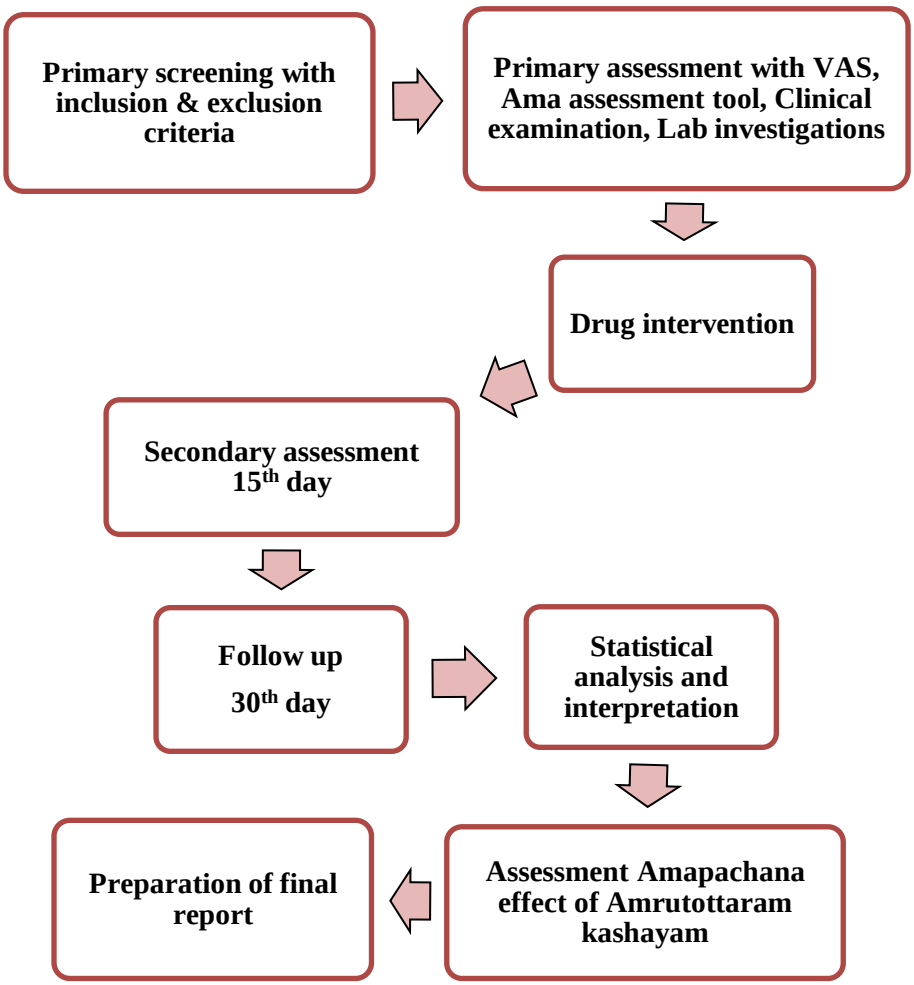
All the data collected are entered into MS Excel master sheet. Statistical tests used for the analysis of data: -

Table M 5. Statistical tests used

Parameters	BT-AT, AT-FU, BT-FU	Comparison between groups	Repeated measures
Morning stiffness	Paired t test	Independent t test	-----
Visual Analogue Scale	Wilcoxon Signed Ranks Test	Mann-Whitney U test	Friedman Test
DAS28,change in DAS28 With Gender & SES	-----	Custom table	-----
Overall Total Ama Assessment tool Score	Wilcoxon Signed Ranks Test	Mann-Whitney U test	Friedman Test
Ama Assessment tool Score Each 9 items	McNemar Test	-----	Cochran's Q test
Hand grip ROM	Paired t test	-----	-----
ESR, CRP, Hb%, S. Creatinine, LFT	Paired t test	-----	-----

ETHICAL CONSIDERATIONS Annexure VII

Ethical clearance obtained from Institutional Ethics Committee. The formulation used in the study is mentioned in the classical text books of Ayurveda and having no known side effects in long term use. Amrutottaram kashayam is widely used among Govt. and Private Institutions and Hospitals in Kerala. Informed consent is obtained from the patient.



Flow chart 6. Methodology

ANALYSIS AND INTERPRETATION

CHAPTER 4

ANALYSIS AND INTERPRETATION

At Vaidyaratnam Ayurveda College Hospital OPD setting Amrutottatam kashayam was given to 115 Rheumatoid Arthritis Patients fulfilling the 2010 ACR / EULAR Classification Criteria. The participants were evaluated for Lab investigations, tools mentioned in the Methodology chapter, before treatment, on 15th day of treatment and on 30th day of treatment.

Statistical analysis reported in five headings as explained in Chapter 3

I. Socio demographic and other characteristics

Table 1. Age – descriptive

Total number	115
Minimum	29.0
Maximum	60.0
Mean	48.40
Std. Deviation	8.9725
Std. Error	0.8367

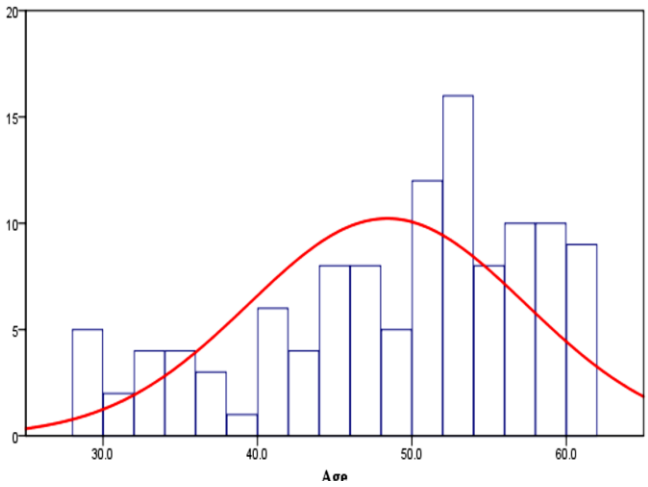


Figure 1. Histogram - Age distribution

Table 2. Distribution according to Age group

Age group	N	Percent
29-39	19	16.5
39-49	31	27.0
50-60	65	56.5
Total	115	100.0

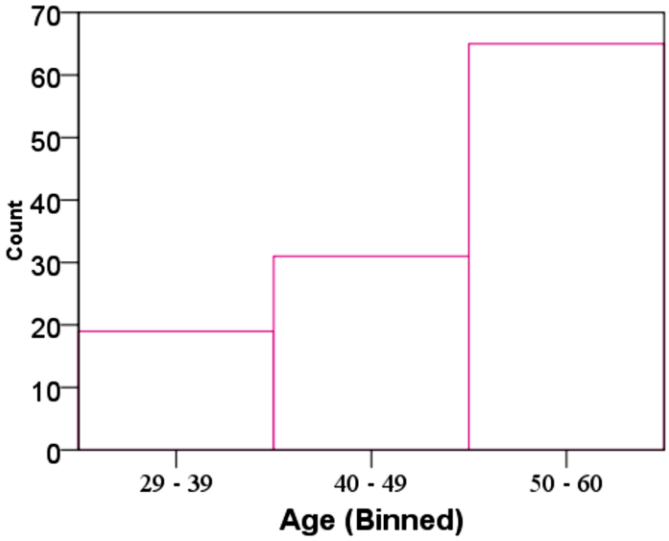


Figure 2. Distribution according to Age group

Table 3. Age – Gender wise distribution

Gender	N	Percent	Minimum Age	Maximum Age	Mean Age	SD	SE
Male	25	21.7	29	60	47.720	9.302	1.860
Female	90	78.3	29	60	48.589	8.922	0.940
Total	115	100.0					

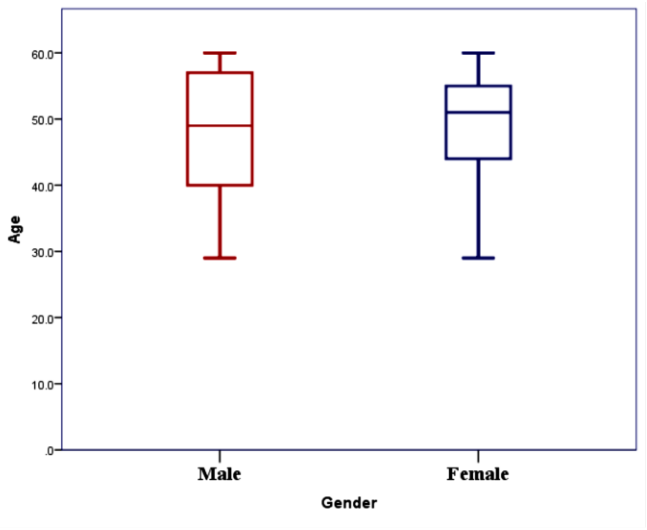


Figure 3. Age – Gender wise distribution

There were total 115 participants recruited for the study. The mean age was 48.40 yrs with SD 8.97 yrs. Among them 25 were males and 90 females (78.3%). The mean age in male was 47.7 yrs with SD 9.30 yrs and in female was 48.59 with SD 8.92 yrs. The participants have been grouped in to 3 according to age. There were 19 participants in the age group of 29-39 yrs, 31 in 39-49 yrs and 65 in > 49 yrs. Most of the epidemiological studies show that RA is more frequent in females than males [(5)]. Below the age of 60 the incidence is 4 to 5 times higher. The age limit for this study was 60 yrs [(4)]. 56.5% of the participants are from the age group of > 49. (Table 1, 2, 3, Figure 1, 2, 3)

Table 4. Distribution according to Religion

Religion	Frequency	Percent
Hindu	80	69.6
Christian	35	30.4
Total	115	100.0

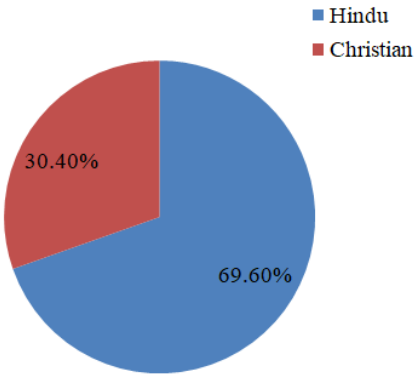


Figure 4.Distribution according to Religion

Among the 115 participants 80 were Hindus (80%) and 35 were Christians. This may be due to the fact that the predominant occupants are Hindus in and around the Vaidyaratnam Ayurveda College, Ollur, Kerala. (Table 4, Figure 4)

Table 5. Distribution according to Socioeconomic Status (Kuppuswamy Socio Economic Status scale)

SES class	Frequency	Percent
Upper lower class	2	1.7
Lower middle class	64	55.7
Upper middle class	43	37.4
Upper class	6	5.2
Total	115	100.0

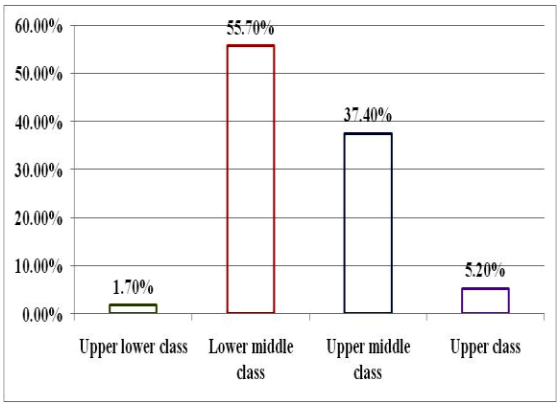


Figure 5. Distribution according to Socioeconomic Status

The 115 participants were grouped according to Socioeconomic status viz. Lower class, Upper lower class, Lower middle class, Upper middle class and Upper class [133]. The grouping has been done on the basis of their Education, Occupation, and Family income per month. Separate scoring has been done for each of these three domains. The entire three scores were added together to get the total score. Of the 5 Socio Economic class half of the participants were from lower middle class (55.7%). There were no participants from Lower class and few from Upper lower class (1.7%). From Upper middle class and Upper class the percentage of participants were 37.4% and 5.2% respectively. In general population people from low SES are likely to smoke and having high BMI etc. They are prone to chronic illness [135]. There are no studies to show the relation between SES and RA. (Table 5, Figure 5)

Table 6. Distribution according to duration of RA

Total number	115
Mean	37.391
Median	40
25th percentile	24
50th percentile	40
75th percentile	48

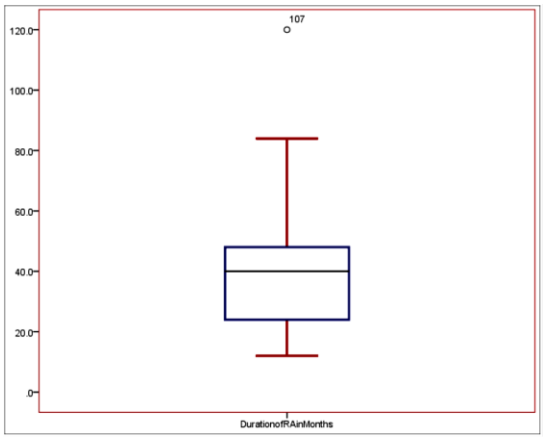


Figure 6. Distribution according to duration of RA

Table 7. Distribution according to duration of RA - grouped

Duration in Months	N	Percent
<= 24	44	38.3
25 - 36	11	9.6
37 - 48	44	38.3
>49	16	13.9

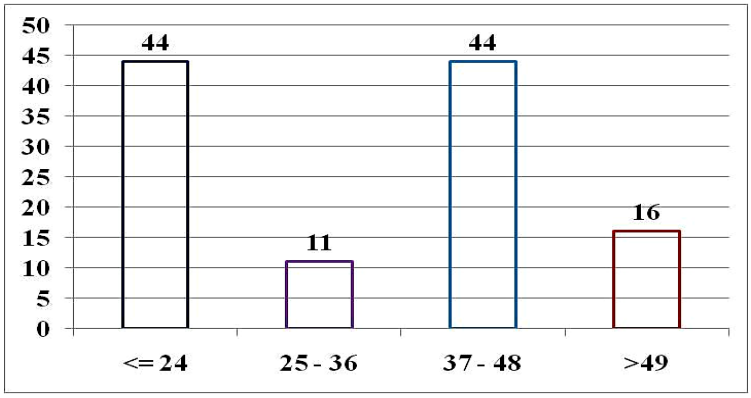


Figure 7. Distribution according to duration of RA - grouped

The mean duration of RA patients participated in the study were 37.391months with a SD of 17.09 months. The minimum duration was 12 months and maximum duration 120 months. When grouped according to duration of RA, 47.9% of participants are having the disease for the past 36 months and the rest were having the disease more than 36 months. (Table 7, figure 7)

Table 8. Distribution according to Treatment history

Treatment history	N	Percent
Ayurvedic & Allopathic treatment	71	61.7
Ayurvedic treatment	21	18.3
Other treatments	23	20.0
Total	115	100.0

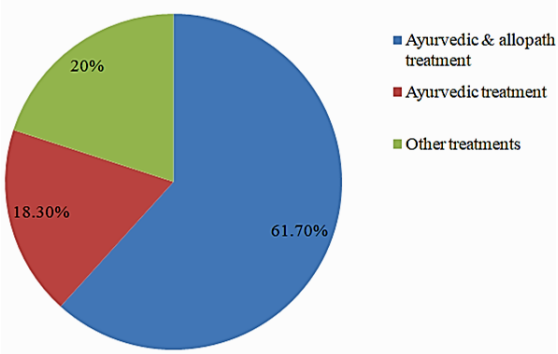


Figure 8. Distribution according to Treatment history

Among the participants 61.7% were using Ayurvedic and Allopathic treatments for RA. 18.3% of the participants were taking only Ayurvedic treatment for RA. 20% were taking other treatments for RA. (Table 8, Figure 8)

Table 9. Distribution according to Family history of Rheumatoid Arthritis

F/H	Frequency	Percent
H/o RA	83	72.2
No H/o RA	32	27.8
Total	115	100.0

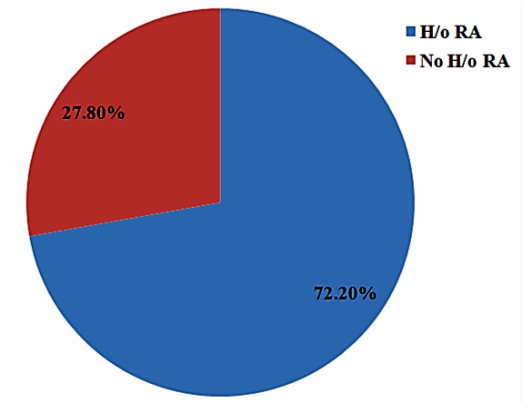


Figure 9. Distribution according to Family history of RA

72.2% of the participants were having the Family history of RA. The family history concept is said to be older one. The Family history is a proxy for a genetic and a part of environmental involvement[63]. (Table 9, Figure 9)

Table 10. Distribution according to Diet

Diet	Frequency	Percent
Vegetarian diet	5	4.3
Mixed diet	110	95.7
Total	115	100.0

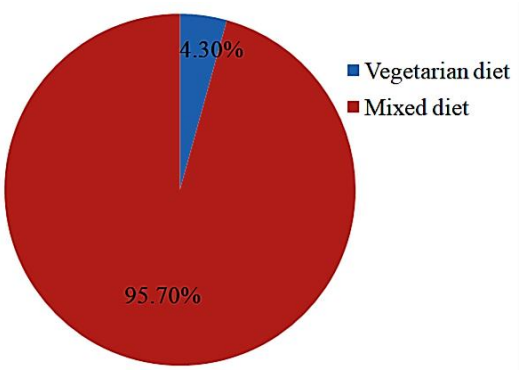


Figure 10. Distribution according to Diet

Most of the participants in this study are using mixed diet (95.7%). Environmental factors and diet has an important role in developing the disease but there is no such study to show that Non vegetarian diet has an association with RA. According to Ayurvedic concept diet has an important role in RA. (Table 10, Figure 10)

Table 11. BMI – descriptive

Total number	115
Minimum	18.77
Maximum	36.68
Mean	25.56
Std. Deviation	2.61
Std. Error	0.24407

Table 12. Distribution according to BMI

BMI	Frequency	Percent
Normal or lean	9	7.8
overweight	39	33.9
obese	67	58.3
Total	115	100.0

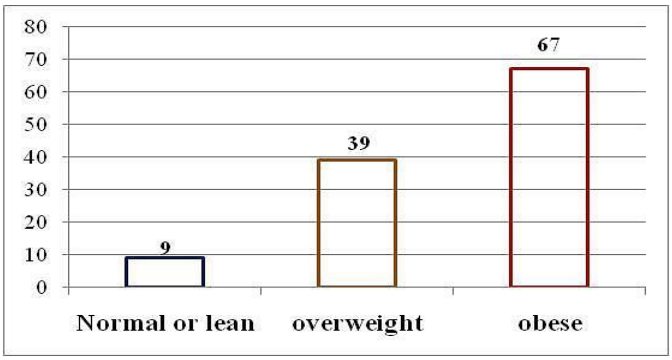


Figure 11. Distribution according to BMI

Table 13. BMI – Gender wise distribution

BMI	Gender	N	Percent
Normal or lean	**Female**	9	100.0
overweight	**Male**	8	20.5
	Female	31	79.5
	Total	39	100.0
obese	**Male**	17	25.4
	Female	50	74.6
	Total	67	100.0

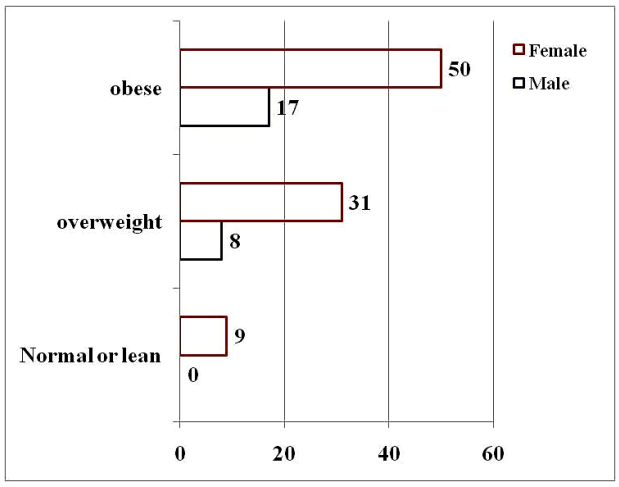


Figure 12. BMI – Gender wise distribution

The mean BMI of the participants were 25.56 kg/m^2 with SD of 2.61 kg/m^2. Only 7.8% of the participants were lean or normal others (91.2%) are either overweight or obese. Compared to male, female participants are overweight and obese. (Table 11, 12, 13 Figure 11, 12)

Table 14. Distribution according to Prakriti

Prakriti	N	Percent
Vatadhika	35	30.4
Pittadhika	55	47.8
Kaphadhika	25	21.7
Total	115	100.0

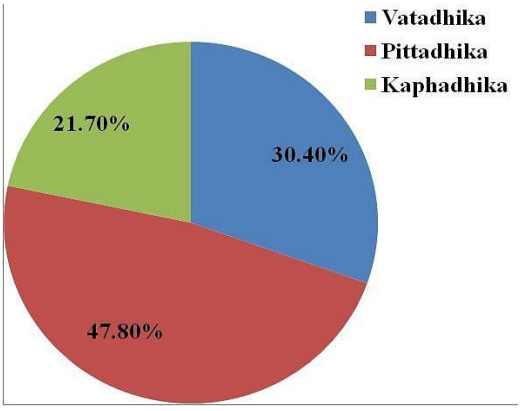


Figure 13. Distribution according to Prakriti

Table 15. Prakriti – gender wise distribution

Gender	Prakriti	N	Percent
Male	Vatadhika	10	40.0
	Pittadhika	9	36.0
	Kaphadhika	6	24.0
Female	Vatadhika	25	27.8
	Pittadhika	46	51.1
	Kaphadhika	19	21.1

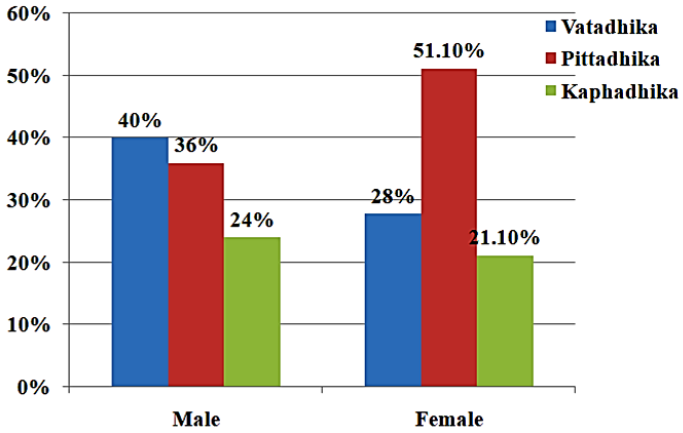


Figure 14. Prakriti – gender wise distribution

TNMC prakriti assessment tool has been used to find out the prakriti of the participants. It is seen that around half (47.8%) of the participants belongs to pittadhika prakriti and 30.45 belongs to vatadhika prakriti and the rest belongs to kaphadhika prakriti (21.7%). Females are having more predominance in pittadhika prakriti with 51.1%. (Table 14, 15 Figure 13, 14)

Table 16. RA score – descriptive

N	Mean RA score	SD	Minimum RA score	Maximum RA score	25th	50th	75th
115	6.530	0.7413	6.0	10.0	6.000	6.000	7.00

Table 17. RA score – Gender wise distribution

Gender	N	Percent	Minimum RA score	Maximum RA score	Mean RA score	SD	SE
Male	25	21.7	6	7.0	6.480	0.509	0.102
Female	90	78.3	6	10.0	6.544	0.795	0.083
Total	115	100.0					

RA score has been calculated by 2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis. The mean score was 6.53 with SD 0.7413. The minimum score was 6 with maximum score10. In males and females the minimum score is 6 and maximum score is 7 and 10 respectively. No intensity has been explained by score calculation. This is only a classification criteria. (Table 16, 17)

Table 18. Distribution according to addiction-gender wise distribution

Addiction	Frequency	Percent	Male	Female
No addiction	110	95.7	20	90
Alcohol, smoking	5	4.3	5	0
Total	115	100.0	35	90

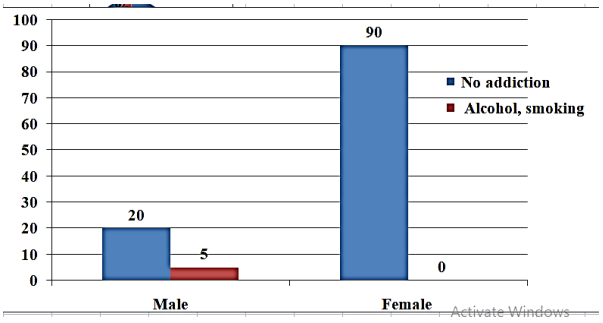


Figure 15. Addiction – gender wise distribution

Out of 115 participants in the study it is seen that only 5 male (4.3%) participants are addicted to alcohol and smoking. Smoking has strong association with RA. (Table 18, Figure 15)

Table 19. Deformity

Deformity	N	Percent	Duration of RA in months			
			<= 24	25 - 36	37 - 48	>49
No deformity	104	90.4	44	11	44	5
Deformity	11	9.6	0	0	0	11
Total	115	100.0				

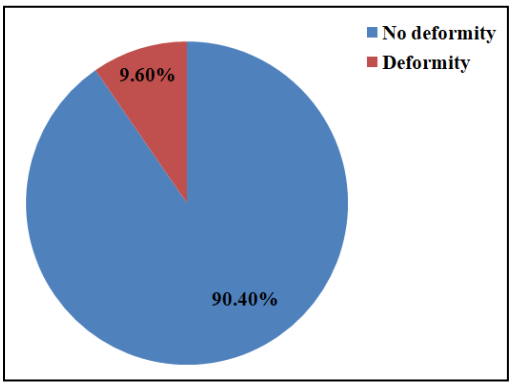


Figure 16. Deformity

Out of 115 RA patients in the study, only 11 (9.6%) patients were having deformity. It is seen that the patients with deformity are suffering from RA > 49 months. (Table 19, Figure 16)

Table 20. Symmetry

Symmetry	Frequency	Percent
No symmetry	42	36.5
symmetrical	73	63.5
Total	115	100.0

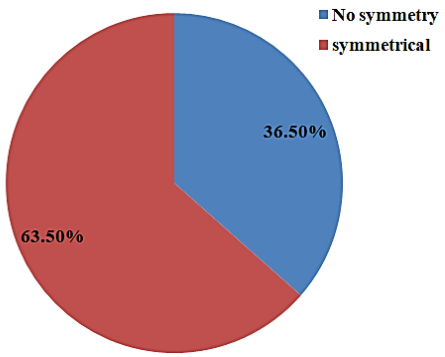


Figure 17. Symmetry

73 (63.5%) participants of the study had the joint involvement was symmetrical. Usually in RA joint distribution is symmetrical (Table 20, Figure 17).

II. Blood investigation parameters for exclusion and diagnosis

Table 21. Blood pressure

BP	Minimum	Maximum	Mean	Std. Deviation
Systolic	110.0	130.0	124.348	6.8172
Diastolic	70.0	86.0	79.887	4.8209

Table 22. Blood investigation for exclusion of related conditions

	Minimum	Maximum	Mean	Std. Deviation	Std. Error
FBS	60.0	110.0	95.843	13.9872	1.3043
PPBS	90.0	135.0	120.148	12.0053	1.1195
Uric acid	2.81	5.800	4.2857	0.75613	0.0705
ASO	15.0	180.0	117.339	44.7090	4.1691

In the present study patients with Hypertension, Type 2 Diabetes Mellitus, Gouty Arthritis, Rheumatic fever were excluded from the study. The mean Systolic BP was 124.35 mm of Hg with SD 6.82 and the mean Diastolic BP was79.89 mm of Hg with SD 4.82 mm of Hg. The Blood pressure was within normal limits. (Table 21)

The mean FBS (95.84 mg% ±13.99 mg %) and PPBS (120.15 mg% ±12.005 mg %) was also within normal limits. The mean Uric acid of the participants was 4.28 mg% with SD of 0.756. The mean ASO titer was 117.34 IU/ml with SD of 44.71 IU/ml. By doing these blood investigations it is seen that participants in this study were not having Diabetes Mellitus, Gouty Arthritis or Rheumatic fever (Table 22).

Table 23. Blood investigations for diagnosis - Erythrocyte Sedimentation Rate

Total number	115
Minimum	18
Maximum	85
Mean	46.13
Std. Deviation	16.9393

Table 24. Gender wise distribution of Erythrocyte Sedimentation Rate

Gender	N	Minimum	Maximum	Mean	SD	SE
Male	25	18.0	85.0	48.480	3.5422	17.7109
Female	90	18.0	85.0	45.478	1.7669	16.7622

115 patients recruited to this study after fulfillig the 2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis For classification the above tabled blood investigation were done. The mean ESR was 46.13 mm with SD of 16.94 mm. Taking the genderwise consideration the mean was 48.48 mm ± 3.54 mm and 45.48 mm ± 1.77 mm in males and females respectively. (Table 23, 24).

Table 25. C-Reactive protein (CRP), Antibodies to Cyclic Citrullinated Peptides (Anti-CCP), Rheumatoid Factor (RF), Antinuclear Antibodies (ANA)

Blood investigation	Group	Frequency	Percent
C-Reactive protein (CRP)	<6	21	18.3
	>6	94	81.7
Antibodies to Cyclic Citrullinated Peptides (Anti-CCP)	<1	79	68.7
	>1	36	31.3
Rheumatoid Factor (RF)	<8	74	64.3
	>8	41	35.7
Antinuclear Antibodies (ANA)	<1	88	76.5
	>1	27	23.5

Table 25A. **Rheumatoid Factor (RF) & Anti-CCP**

		ACCP	
		<1	**> 1**
RF	**< 8.0**	51	23
	>8	28	13

In this study 94 (81.7%) participants are having raised CRP (>6 mg/L). Out of 115 participaqnts only 36 (31.3%) were havimg the test positive. Rheumatoid Factor (RF) was positive in 41 (35.7%) participants. Antinuclear Antibodies (ANA) was positive only in 23.5% of the participants. A negative result does not rule out RA. The RF was positive >8 IU/ml in 41 participants and Anti-CCP was >1 U/ml in 36 participants. Both the RF and Anti-CCP were positive only in 13 participants. (Table 25, 25A)

II. Analysis of Subjective parameters

Table 26. Morning stiffness before and after treatment

Morning stiffness	Mean	N	Std. Deviation	Std. Error
Before treatment	2.909	115	0.9746	0.0909
After treatment	2.613	115	0.8247	0.0769

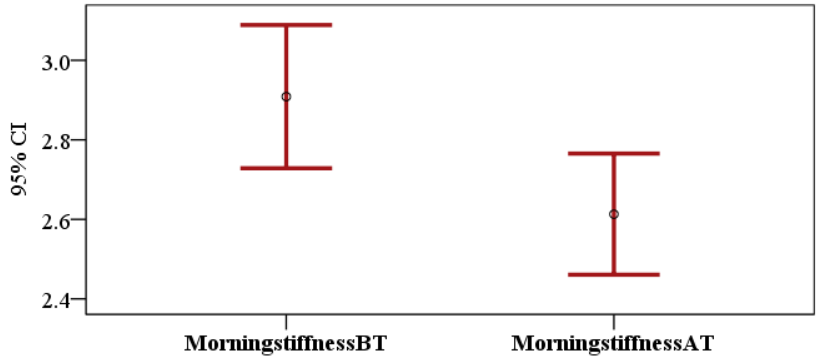


Figure 18. Morning stiffness before and after treatment (Error Bar)

Table 27. Morning stiffness - paired sample t test for comparing means between before and after treatment

Morning stiffness	Paired Differences					t	df	Sig.
				95% CI difference				
	Mean	SD	SE	Lower	Upper			
AT - BT	0.2957	0.3681	0.0343	0.2277	0.3637	8.613	114	.000

The mean Morning stiffness before treatment was 2.909 hrs with SD 0.97 hrs and after treatment was 2.613hrs with SD 0.8247 hrs. Paired t test has been conducted to find out the significance. It is seen that the difference in means 0.2957 hrs ± 0.3681 hrs was found to be significant p < 0.001. (t (114) = 8.613, *p* <.001). With 15 days of treatment the morning stiffness reduced 30 minutes). (Table 26, 27, Figure 18)

Table 28. Morning stiffness - independent t test for comparing means between genders

28A. Gender group statistics

Gender	N	Mean	SD	SE. Mean
Male	25	0.2200	0.25331	0.05066
Female	90	0.3167	0.39270	0.04139

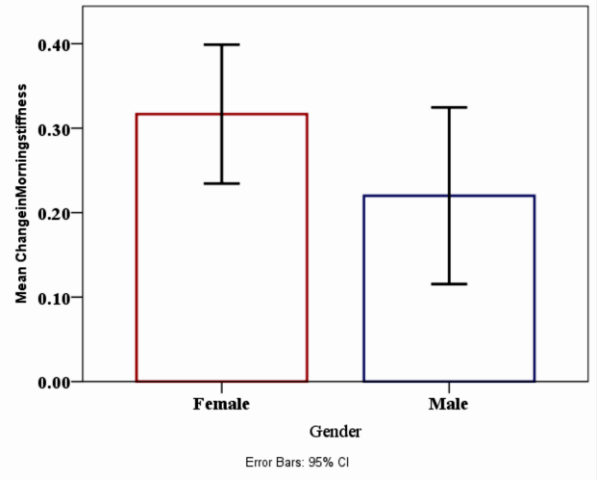


Figure 18A. Morning stiffness Gender group (Error Bar)

28B. Independent t test

t	df	Sig. (2-tailed)	Mean Difference	SE Difference	95% CI of the Difference Lower	upper
1.163	113	0.247	0.09667	0.08309	-0.06796	0.2612

Independent t test has been conducted to find out the mean differences of morning stiffness in males and females. Test results and error bar shows that the difference seen is not significant. The mean hrs of morning stiffness in males and in females was 0.220 hrs ± 0.2533hrs and 0.3167 hrs ± 0.39270 hrs respectively. (t (113) = 1.163, p = 0.247). The effectiveness was similar in both genders. (Table 28A, 28B, Figure 17)

Table 29. Visual Analogue Scale - before treatment, after treatment and after follow up period

VAS	N	Mean	SD	Minimum	Maximum	Percentiles 25th	50th	75th
BT	115	6.983	0.8684	5.0	9.0	7.000	7.000	7.000
AT	115	4.565	1.8550	2.0	9.0	3.000	4.000	6.000
FU	115	6.217	1.0155	4.0	8.0	6.000	6.000	7.000

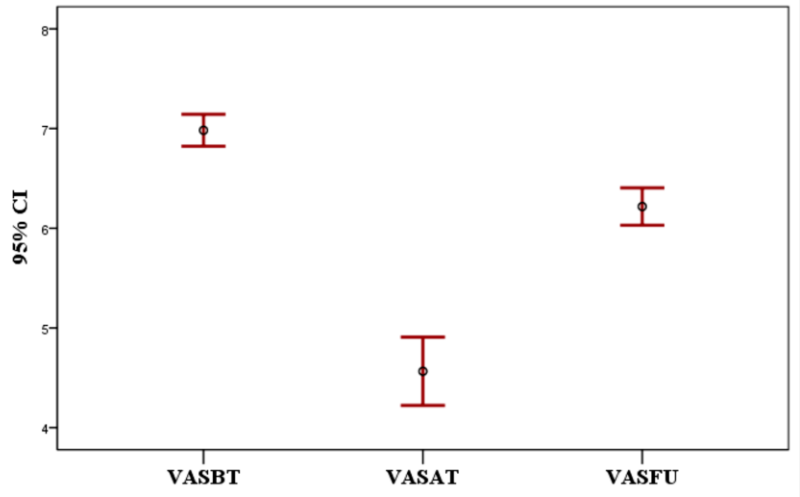


Figure 19. Visual Analogue Scale - before treatment, after treatment and after follow up period

Table 30. Overall differences between related medians of Visual Analogue Scale -- before treatment, after treatment and after follow up period – Friedman Test

Table 30A. Mean rank

Treatment	Mean Rank
BT	2.76
AT	1.32
FU	1.92

Table 30B. Friedman Test

N	Chi-Square	df	Asymp. Sig.
115	139.786	2	.000

Table 31. Paired differences between related means of Visual Analogue Scale before treatment, after treatment and after follow up period using Wilcoxon Signed Ranks Test

Table 31A. Mean Rank

Treatment	Ranks	N	Mean Rank	Sum of Ranks
BT-AT	Negative Ranks	89	45.00	4005.00
	Positive Ranks	0	.00	.00
	Ties	26		
AT-FU	Negative Ranks	85	43.00	3655.00
	Positive Ranks	0	.00	.00
	Ties	30		
BT-FU	Negative Ranks	21	19.00	399.00
	Positive Ranks	88	63.59	5596.00
	Ties	6		

Table 31B. Wilcoxon Signed Ranks Test

Total score	Z	Asymp. Sig. (2-tailed)
BT-AT	-8.353	.000
AT-FU	-9.070	.000
BT-FU	-7.940	.000

Visual Analogue Scale was used to measure the pain before treatment (BT), after treatment (AT) and after follow up period (FU). The median score BT, AT and FU was 7, 4 and 6 with Median Rank 2.76, 1.32 and 1.92 respectively. Friedman Test conducted to find out the significance in 3 different pain scores taken in intervals. There was a statistically significant difference in pain score during these period (χ^2 (2) = 139.786, p < 0.001). Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $p < 0.017$. There was statistically significant reduction in pain score between BT and AT (Z=-8.353, p <

0.001), pain score between AT and FU (Z=-9.070, p < 0.001) & between BT and FU (Z=-7.940, p < 0.001)

In other words considering pain score between BT and AT out of 115 participants 89 participants had a lower score and 26 had no change in pain after treatment. While considering the pain score between AT and FU, 85 participants had a lower score and 30 had no change in pain score.

The change in pain score between BT and FU only 21 had lower score than the time of entry in to study and 88 participants had a higher score. The change is significant but on this study's perceptive it is not, more participants had higher pain score. Overall effectiveness of Amrutottaram kashyam in reducing the pain is significant. (Table 29,30A, 30B, 31A, 31B, Figure 17 error bar)

Table 32. Visual Analogue Scale - Mann-Whitney U test for comparing Mean ranks between Genders

Table 32A. Mean ranks

Gender	N	Mean Rank	Sum of Ranks
Male	25	55.90	1397.50
Female	90	58.58	5272.50

Table 32B. Mann-Whitney U test

N	Mann-Whitney U	Z	Asymp. Sig.
115	1072.50	-0.372	.710

Considering pain score difference in gender it can be concluded that the pain score in female group was high (mean rank 58.58) than the male group. **Mann-Whitney U** test was conducted to find out the significance and found that it was not significant (U = 1072.50, p = .710). (Table 32A, 32B)

Table 33. Overall differences between related medians of Visual Analogue Scale in different age group – Kruskal-Wallis Test

Table 33A. Mean Rank

Age group	Frequency	Mean Rank
29 - 39	19	46.18
39- 49	31	60.40
>49	65	60.31
Total	115	

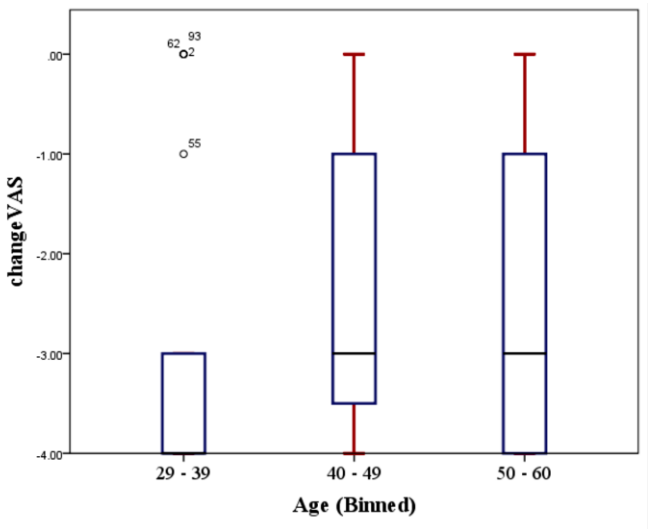


Figure 19A. Overall differences of Visual Analogue Scale in different age group

Table 33B. Kruskal-Wallis Test

Chi-Square	df	Asymp. Sig
3.117	2	0.210

To find out the overall differences between related medians of Visual Analogue Scale after treatment (AT) in different age group, Kruskal-Wallis Test was conducted. The test was not significant (χ^2 (2) = 3.117, p = 0.210). (Table 33A, 33B Figure 18A). Amrutottaram kashayam was equally effective in all age group

Table 34. DAS28 score before treatment and gender wise distribution

DAS28 score	N	Percent	Male	Female
Moderate disease activity 3.2-5.1	24	20.9	4 **16%**	20 **22.2%**
High disease activity >5.1	91	79.1	21 **84%**	70 **77.8%**
Total	115	100	25 **100%**	90 **100%**

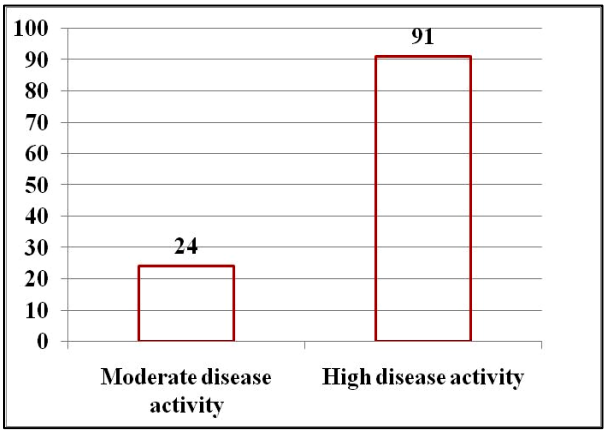


Figure 20A. DAS28 score before treatment

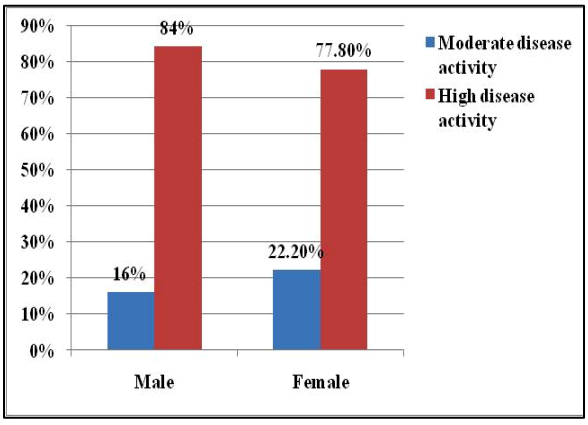


Figure 20B. Gender wise Das28 score before treatment

Table 35. Age group wise distribution of DAS28 score before treatment

Age group	DAS28	N	Percent
29 - 39	Moderate Disease Activity	7	36.8
	High Disease Activity	12	63.2
	Total	19	100.0
39 - 49	Moderate Disease Activity	7	22.6
	High Disease Activity	24	77.4
	Total	31	100.0
>49	Moderate Disease Activity	10	15.4
	High Disease Activity	55	84.6
	Total	65	100.0

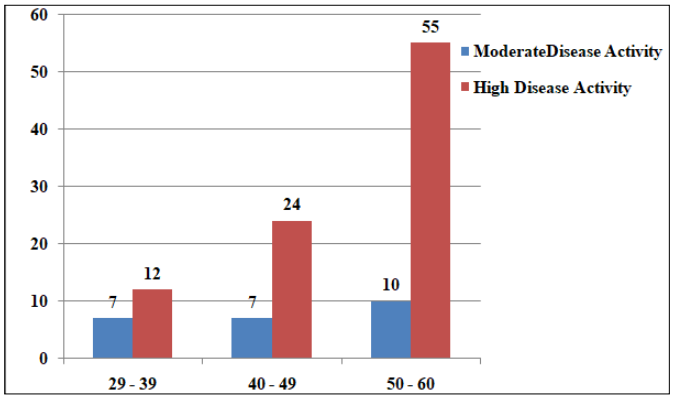


Figure 21. Age group wise distribution of DAS28 score before treatment

Das28 score is used to assess the disease activity of RA patients. It considers the pain and swelling of 28 joints, overall well-being and ESR/CRP. It is grouped in to four; People with DAS score <= 2.6 (Disease remission), 2.6 to 3.2 (Low disease activity), 3.2 to 5.1 (Moderate disease activity) and >5.1 (High disease activity). From the table it can be seen that 91 (79.1%) participants are having High disease activity than the Moderate disease activity group. 84% of the males and 77.8% of the females are having high disease activity score. Considering the age group wise distribution of DAS28 score it can be seen that in the > 49 age group 84.65 of the participants are having High disease activity. The higher the age the higher the disease activity. (Table 34, 35 Figure 19, 20, 21)

Table 36. Das28 score before treatment and socioeconomic status

SES	Disease remission	Low Disease Activity	Moderate Disease Activity	High Disease Activity
Lower class	0	0	0	0
Upper lower class	0	0	0	2
Lower middle class	0	0	11	53
Upper middle class	0	0	11	32
Upper class	0	0	2	4

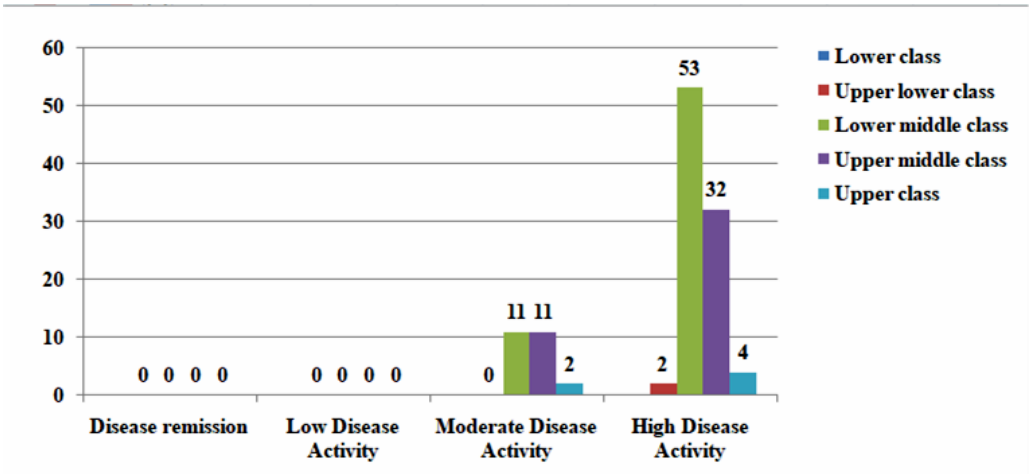


Figure 22. Das28 score before treatment and socioeconomic status

Considering the SES and DAS28 score the High disease activity is seen in Lower middle class. Environmental factors have an important role in chronic illness. Out of 64 lower middle class people 53 (82.81%) are having High disease activity. (Table 36, Figure 22)

Table 37. Change in DAS28 score after treatment

Change in DAS28 score	Observed N	Percent	Expected N	Residual
<=0.60	0	0	57.5	-19.5
0.6 - 1.20	38	33.0	57.5	19.5
>1.21	77	67.0		
Total	115	100.0		

Table 37A. Pearson's chi-square goodness-of-fit test

Chi-Square	df	Asymp. Sig
13.226	1	.000

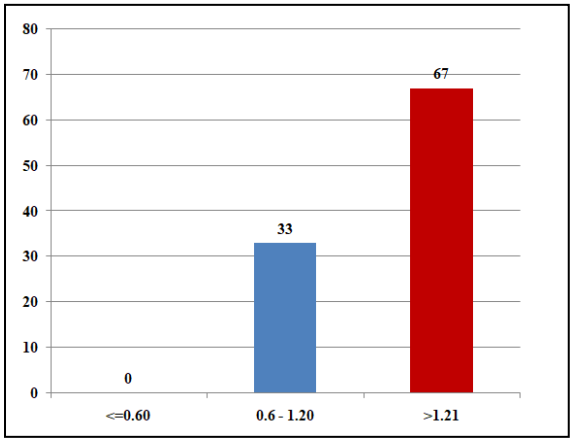


Figure 23. Change in DAS28 score after treatment

Table 38. Change in DAS28 score after treatment - Gender wise distribution

Change in DAS28 score	Male	Female
<=0.60	0	0
0.6 - 1.20	11 44%	27 30%
>1.21	14 56%	63 70%
Total	25	90

Table 38A. Chi-Square test

Chi-Square	df	Asymp. Sig
1.733	1	0.231

As per the EULAR Good or Moderate response criteria Overall change in Disease activity is grouped in to three. DAS28 taken at two different time points are considered for the change in activity score. The change in score has been grouped as; <= 0.60, 0.6 - 1.20, and >1.21. From the table it can be seen that 77 (67%) participants had change >1.21. To find out whether the distribution seen is significant Pearson's chi-square goodness-of-fit test for one sample has been conducted. It is concluded that the difference seen was significant, $p < .001$. (χ^2 (1) = 13.226 $p < .001$). In males 56% were had >1.21 change, and in females 70% had >1.21 change. But the change noticed was not statistically significant, $p = 1.733$. (χ^2 (1) = 1.733, $p = 0.231$. (Table 37, 37A, 38, 38A Figure 23)

Table 39. Change in DAS28 score after treatment in different Age group

Age group	Change in DAS28 score		
	<0.60	**0.6-1.20**	**>1.21**
29 - 39	0	4	15
39 - 49	0	15	16
>49	0	19	46

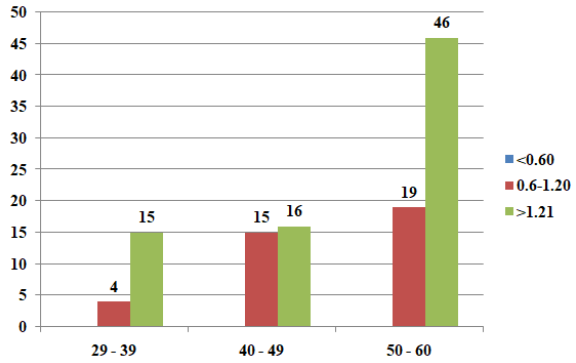


Figure 24. Change in DAS28 score after treatment and Age group

Table 40. Change in DAS28 score after treatment and socioeconomic status

SES	Change in DAS28 score		
	<0.60	**0.6-1.20**	**>1.21**
Lower class	0	0	0
Upper lower class	0	1	1
Lower middle class	0	20	44
Upper middle class	0	14	29
Upper class	0	3	3

Out of 65 participants in the > 49 age group 46 participants had a DAS28 change of >1.21. Considering the change of DAS28 and SES 44 from Lower middle class and 29 from Upper middle class had change of > 1. (Table 39, 40 Figure 24)

Table 41. Change in Disease activity as per the EULAR response criteria (127) (5)

Present DAS28 score	DAS28 improvement over time points		
	>1.21	0.6 - 1.20	<=0.60
Low disease activity 2.6-3.2	Good Response	Moderate response	No response
Moderate disease activity 3.2–5.1	Moderate response 20	Moderate response 4	No response 0
High disease activity >5.1	Moderate response 57	No response 34	No response 0

From this table (Table 41) the overall response of the Amrutottaram kashayam in reducing the disease activity can be analysed. On the left hand side of the table DAS score at the time of entering the study has been considered (Three rows - Present DAS28 score). While on the top right side of the table difference in score between before and after treatment is considered (Three columns - DAS28 improvement over time points). The resultant 9 boxes represent different responses namely Good or Moderate and No response. From the table the following can be concluded. Patients with Moderate disease activity 24 were had Moderate response and patients with High disease activity 57 had Moderate response. The total of 81 participants out of 115 had Moderate response. The overall moderate response is 70.43%.

Overall Good response = 0

Overall Moderate response = 20+4+57=81/115 = 70.43%

No response = 29.57%

Table 42. Ama assessment Tool – Total score before treatment, after treatment and after follow up period

Total score	N	Percentiles 25th	50th (Median)	75th
BT	115	6.000	6.000	7.000
AT	115	2.000	4.000	4.000
FU	115	1.000	1.000	2.000

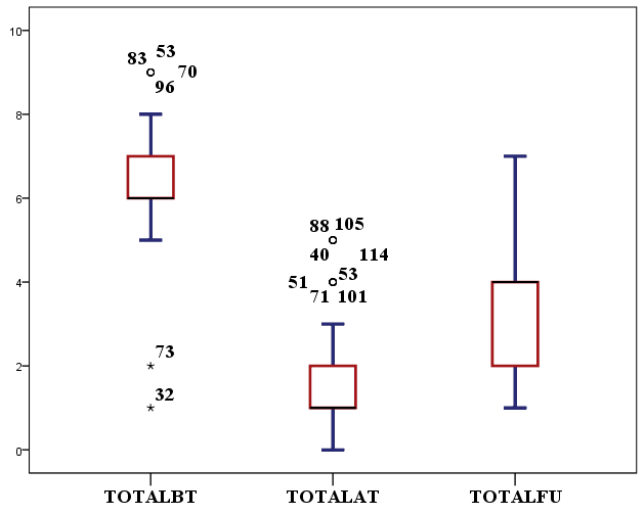


Figure 25. Ama assessment Tool – Total score before treatment, after treatment and after follow up period

Table 43. Overall differences between related medians of *Ama* assessment Tool - Total score before treatment, after treatment and after follow up period – Friedman Test.

Table 43A. Mean Rank

Treatment	Mean Rank
BT	2.95
AT	1.87
FU	1.18

Table 43B. Friedman Test

N	Chi-Square	df	Asymp. Sig.
115	194.644	2	.000

Table 44. Paired differences between related medians of *Ama* assessment Tool – Total score before treatment, after treatment and after follow up period using Wilcoxon Signed Ranks Test.

Table 44A. Mean Rank

Treatment	Ranks		N	Mean Rank	Sum of Ranks
BT-AT	Negative Ranks	AT < BT	113	58.00	6554.00
	Positive Ranks	AT > BT	1	1.00	1.00
	Ties	AT = BT	1		
BT-FU	Negative Ranks	FU < BT	108	55.48	5992.00
	Positive Ranks	FU > BT	2	56.50	113.00
	Ties	FU = BT	5		
AT-FU	Negative Ranks	FU < AT	8	15.63	125.00
	Positive Ranks	FU > AT	85	49.95	4246.00
	Ties	FU = AT	22		

Table 44B. Wilcoxon Signed Ranks Test

Total score	Z	Asymp. Sig. (2-tailed)
BT-AT	-9.329	.000
BT- FU	-8.822	.000
AT-FU	-8.003	.000

Ama assessment Tool was used to measure the Ama before treatment (BT), after treatment (AT) and after follow up period (FU). First the total of 9 item score has been considered here. The median score BT, AT and FU was 6 (6-7), 4 (2-4) and 1 (1-2) with Median Rank 2.95, 1.87 and 1.18 respectively. Friedman Test conducted to find out the significance in 3 different scores taken in intervals. There was a statistically significant difference in score during these period (χ^2 (2) = 194.644, $p < 0.001$). Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $p < 0.017$. There was statistically significant reduction in scores between BT and AT (Z=-9.329, $p < 0.001$), between AT and FU (Z=-8.822, $p < 0.001$) & between BT and FU (Z=-8.003, $p < 0.001$)

In other words considering Ama score between BT and AT out of 115 participants 113 participants had a lower score, 1 had no change and 1 had higher sore after treatment. While considering the Ama score between BT and FU, 108 participants had a lower score, 5 had no change in Ama score 2had higher score.

The change in Ama score between AT and FU only 8 had lower score than the time of entry in to study and 85 participants had a higher score and 22 had no change after the follow up period.. The change is significant but on this study's perceptive it is not, more participants had higher Ama score. Overall effectiveness of Amrutottaram kashyam in reducing the Ama is significant. (Table 42,43A, 43B, 44A, 44B Figure 25 box plot)

Table 45. Ama assessment tool – Total score - Mann-Whitney U test for comparing Mean ranks between Genders

Table 45A. Mean ranks

Gender	N	Mean Rank	Sum of Ranks
Male	25	51.74	1293.50
Female	90	59.74	5376.50

Table 45B. Mann-Whitney U test

N	Mann-Whitney U	Z	Asymp. Sig.
115	968.50	-1.091	0.275

Considering total ama score difference in gender, it can be concluded that the Ama score in female group was high (mean rank 59.74) than the male group. **Mann-Whitney U** test was conducted to find out the significance and found that it was not significant (U = 968.50, p = 0.275). (Table 45A, 45B)

Table 46. Ama assessment Tool - Constipation before treatment, after treatment and after follow up period

Constipation	No	Yes
Before Treatment	18	97
After Treatment	111	4
Follow up	66	49

Table 47. Overall differences between Constipation before treatment, after treatment and after follow up period of Ama assessment Tool –– Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	133.794	2	.000

Table 48. Paired differences between Constipation before treatment, after treatment and after follow up period using McNemar Test

Table 48A. Constipation before treatment - after treatment

Before treatment	After treatment	
	No	Yes
No	18	0
Yes	93	4

Table 48B. Constipation after treatment - follow up

After treatment	Follow up	
	No	Yes
No	62	49
Yes	4	0

Table 48C.Constipation before treatment - follow up

Before treatment	Follow up	
	No	Yes
No	18	0
Yes	48	49

Table 48D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	91.011	36.528	46.021
Asymp. Sig.	.000	.000	.000

As said the *Ama* assessment tool contains 9 questions. The first one is Constipation. Out of 115 participants, before treatment (BT) 97 participants had constipation, after treatment (At) only 4 had constipation and after follow up period (FU) 49 had constipation. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of constipation over time, χ^2 (2) = 133.794, $p < 0.001$ (Table 46, 47). An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of constipation. There was statistically significant difference in proportions between BT and AT ($p < 0.001$), between AT and FU ($p < .001$) & between BT and FU ($p < 0.001$)

BT and AT: before treatment 97 had constipation and after treatment 93 relieved from constipation and 4 continued to have constipation. 18 participants had no change at all. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment only 4 were having constipation, after follow up period 49 had constipation 66 had no change. The difference in proportion found to be highly significant ($p < 0.001$).

BT and FU: before treatment 97 had constipation and after follow up period 48 had no constipation 18 participants had no change. The difference in proportion found to be highly significant ($p < 0.001$). (Table 46, 47, 48A, 48B, 48C, 48D)

Table 49. Ama assessment Tool - Heaviness before treatment, after treatment and after follow up period

Heaviness	No	Yes
Before Treatment	16	99
After Treatment	89	26
Follow up	88	27

Table 50. Overall differences between Heaviness before treatment, after treatment and after follow up period of Ama assessment Tool –- Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	136.545	2	.000

Table 51. Paired differences between Heaviness before treatment, after treatment and after follow up period using McNemar Test

Table 51A. Heaviness Before treatment- After treatment

Before treatment	After treatment	
	No	Yes
No	16	0
Yes	73	26

Table 51B. Heaviness After treatment - Follow up

After treatment	Follow up	
	No	Yes
No	84	5
Yes	4	22

Table 51C. Heaviness Before treatment - Follow up

Before treatment	Follow up	
	No	Yes
No	16	0
Yes	72	27

Table 51D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	71.014		70.014
Asymp. Sig.	.000		.000
Exact Sig. (2-tailed)		1.000	

The second question of *Ama* assessment tool is Heaviness. Out of 115 participants, before treatment (BT) 99 participants had Heaviness, after treatment (AT) only 26 had Heaviness and after follow up period (FU) 27 had Heaviness. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Heaviness over time, χ^2 (2) = 136.545, $p < 0.001$. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of Heaviness. There was statistically significant difference in proportions between BT and AT ($p < 0.001$),) & between BT and FU ($p = <$ .0005). But between AT and FU it was not significant ($p = 1.00$)

BT and AT: before treatment 99 had Heaviness and after treatment 89 relieved from Heaviness and 26 continued to have Heaviness. 16 participants had no change at all. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment only 26 were having Heaviness, after follow up period 27 had Heaviness 84 had no change. The difference in proportion found to be not significant.

BT and FU: before treatment 99 had Heaviness and after follow up period 16 had no Heaviness 27 participants had heaviness. The difference in proportion found to be highly significant ($p < 0.001$). (Table 49, 50, 51A, 51B, 51C, 51D)

Table 52. Ama assessment Tool – Loss of taste before treatment, after treatment and after follow up period

Loss of taste	No	Yes
Before Treatment	39	72
After Treatment	92	19
Follow up	92	19

Table 53. Overall differences between Loss of taste before treatment, after treatment and after follow up period of Ama assessment Tool –- Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	96.862	2	.000

Table 54. Paired differences between Loss of taste before treatment, after treatment and after follow up period using McNemar Test

Table 54A Loss of taste Before treatment- After treatment

Before treatment	After treatment	
	No	Yes
No	43	0
Yes	53	19

Table 54B. Loss of taste after treatment - follow up

After treatment	Follow up	
	No	Yes
No	87	5
Yes	5	14

Table 54C. Loss of taste before treatment - follow up

Before treatment	Follow up	
	No	Yes
No	39	0
Yes	53	19

Table 54D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	51.019		51.019
Asymp. Sig.	.000		.000
Exact Sig. (2-tailed)		1.000	

The third question of *Ama* assessment tool is loss of taste. Out of 115 participants, before treatment (BT) 72 participants had loss of taste, after treatment (AT) only 19 had loss of taste and after follow up period (FU) 19 had loss of taste. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of loss of taste over time χ^2 (2) = 96.862, $p < 0.001$. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of loss of taste. There was statistically significant difference in proportions between BT and AT ($p < 0.001$) & between BT and FU ($p < 0.001$). But between AT and FU it was not significant ($p = 1.00$).

BT and AT: before treatment 72 had loss of taste and after treatment 53relieved of symptom and 19 continued to have loss of taste. 43 participants had no change at all. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment only 19 were having loss of taste, after follow up period these 19 participants continued to be having loss of taste and 87 had no change. The difference in proportion found to be not significant ($p = 1.00$).

BT and FU: before treatment 72 had loss of taste and after follow up period 19 had loss of taste, 39 participants had no change. The difference in proportion found to be highly significant ($p < 0.001$). (Table 52, 53, 54A, 54B, 54C, 54D)

Table 55. Ama assessment Tool – Loss of appetite before treatment, after treatment and after follow up period

Loss of appetite	No	Yes
Before Treatment	31	84
After Treatment	115	0
Follow up	79	36

Table 56. Overall differences between Loss of appetite before treatment, after treatment and after follow up period of Ama assessment Tool -– Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	126.857	2	.000

Table. 57. Paired differences between Loss of appetite before treatment, after treatment and after follow up period using McNemar Test.

Table 57A Loss of appetite Before treatment- After treatment

Before treatment	After treatment	
	No	Yes
No	31	0
Yes	84	0

Table 57B. Loss of appetite after treatment - follow up

After treatment	Follow up	
	No	Yes
No	79	36
Yes	0	0

Table 57C. Loss of appetite before treatment - follow up

Before treatment	Follow up	
	No	Yes
No	31	0
Yes	48	36

Table 57D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	82.012	46.021	34.028
Asymp. Sig.	.000	.000	.000

The fourth question of Ama assessment tool is Loss of appetite. Out of 115 participants, before treatment (BT) 84 participants had Loss of appetite, after treatment (AT) no one had Loss of appetite and after follow up period (FU) 36 had Loss of appetite. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Loss of appetite over time χ^2 (2) = 126.857, $p < 0.001$. An

exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom ($p < 0.001$). There was statistically significant difference in proportions between BT and AT ($p < 0.001$), between AT and FU ($p < 0.001$) & between BT and FU ($p < 0.001$).

BT and AT: before treatment 84 had Loss of appetite and after treatment and relieved of this symptom. 31 participants had no change after the treatment. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment No one had Loss of appetite, after follow up period these 36 participants had Loss of appetite and 79 had no change. The difference in proportion found to be highly significant ($p < 0.001$).

BT and FU: before treatment 84 had Loss of appetite and after follow up period 36 had Loss of appetite, 31 participants had no change. The difference in proportion found to be highly significant ($p = < .0005$). (Table 55, 56, 57A, 57B, 57C, 57D)

Table 58. Ama assessment Tool – loss of thirst before treatment, after treatment and after follow up period

Loss of thirst	No	Yes
Before Treatment	80	35
After Treatment	92	23
Follow up	89	26

Table 59. Overall differences between loss of thirst before treatment, after treatment and after follow up period of Ama assessment Tool –– Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	14.625	2	.001

Table 60. Paired differences - Loss of thirst BT, AT & after FU - McNemar Test

Table 60A. Loss of thirst before treatment- after treatment

Before treatment	After treatment	
	No	Yes
No	80	0
Yes	12	23

Table 60B. Loss of thirst after treatment - follow up

After treatment	Follow up	
	No	Yes
No	87	5
Yes	2	21

Table 60C. Loss of thirst before treatment - follow up

Before treatment	Follow up	
	No	Yes
No	78	2
Yes	11	24

Table 60D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Asymp. Sig.	0.000	0.453	0.022

The fifth question of Ama assessment tool is Loss of thirst. Out of 115 participants, before treatment (BT) 35 participants had Loss of thirst, after treatment (AT) 23 had Loss of thirst and after follow up period (FU) 26 had Loss of appetite. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Loss of thirst over time, χ^2 (2) = 14.625, p = .001. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom. There was statistically significant difference in proportions between BT and AT ($p < 0.001$), between AT and FU it was not significant (p = .453. Between BT and FU it was significant). (p = .022).

BT and AT: before treatment 35 had Loss of thirst and after treatment 23 had the symptom. 80 participants had no change after the treatment. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment 23 had Loss of thirst, after follow up period these 26 participants had Loss of thirst and 87 had no change. The difference in proportion found to be not significant ($p = 0.453$).

BT and FU: before treatment 35 had Loss of thirst and after follow up period 26 had Loss of thirst, 78 participants had no change. The difference in proportion found to be highly significant ($p = 0.022$). (Table 58, 59, 60A, 57B, 60C, 60D)

Table 61. Ama assessment Tool – bad belching before treatment, after treatment and after follow up period

Bad belching	No	Yes
Before Treatment	68	47
After Treatment	99	16
Follow up	65	50

Table 62. Overall differences between Bad belching before treatment, after treatment and after follow up period of Ama assessment Tool -– Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	39.370	2	.000

Table 63. Paired differences between Bad belching before treatment, after treatment and after follow up period using McNemar Test

Table 63A Bad belching Before treatment - After treatment

Before treatment	After treatment	
	No	Yes
No	68	0
Yes	31	16

Table 63B. Bad belching After treatment - Follow up

After treatment	Follow up	
	No	Yes
No	57	42
Yes	8	8

Table 63C. Bad belching before treatment-follow up

Before treatment	Follow up	
	No	Yes
No	53	15
Yes	12	35

Table 63D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	29.032	21.780	0.148
Asymp. Sig.	0.000	0.000	0.700

The sixth question of Ama assessment tool is bad belching. Out of 115 participants, before treatment (BT) 47 participants had bad belching, after treatment (AT) 16 had bad belching and after follow up period (FU) 50 had bad belching. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Bad belching over time, χ^2 (2) = 39.370, p < 0.001. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom. There was statistically significant difference in proportions between BT and AT (p < 0.001), between AT and FU it was not clinically significant (p < 0.001). Between BT and FU it was not significant). (p = 0.700).

BT and AT: before treatment 47 had bad belching and after treatment 16 had the symptom. 68 participants had no change after the treatment. The difference in proportion found to be highly significant (p < 0.001).

AT and FU: after treatment 16 had bad belching, after follow up period these 50 participants had bad belching and 87 had no change. The difference in proportion found to be statistically significant. But clinically not significant because after the follow up period number of participants having Bad belching increased considerably (p < 0.001).

BT and FU: before treatment 47 had bad belching and after follow up period 50 had bad belching, 53 participants had no change. The difference in proportion found to be not significant (p = 0.700). No notable change had occurred after the follow up period. (Table 61, 62, 63A, 63B, 63C, 63D)

Table 64. Ama assessment Tool – pain before treatment, after treatment and after follow up period

Pain	No	Yes
Before Treatment	0	115
After Treatment	81	34
Follow up	33	82

Table 65. Overall differences between Pain before treatment, after treatment and after follow up period of Ama assessment Tool –- Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	117.106	2	.000

Table 66. Paired differences between Pain before treatment, after treatment and after follow up period using McNemar Test

Table 66A Pain Before treatment - after treatment

Before treatment	After treatment	
	No	Yes
No	0	0
Yes	81	34

Table 66B. Pain after treatment- follow up

After treatment	Follow up	
	No	Yes
No	29	52
Yes	4	30

Table 66C. Pain before treatment- Follow up

Before treatment	Follow up	
	No	Yes
No	0	0
Yes	33	82

Table 66D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	79.012	31.030	39.446
Asymp. Sig.	.000	.000	.000

The seventh question of Ama assessment tool is Pain. Out of 115 participants, before treatment (BT) all of the participants had Pain, after treatment (AT) 34 had Pain and after follow up period (FU) 82 had Pain. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Pain over time, χ^2 (2) = 117.106, $p < 0.001$. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom. There was statistically significant difference in proportions between BT and AT ($p < 0.001$), between AT and FU ($p < 0.001$). Between BT and FU ($p < 0.001$).

BT and AT: before treatment all of the 115 participants had Pain and after treatment 34 had the pain. The difference in proportion found to be highly significant ($p < 0.001$).

AT and FU: after treatment 34 had Pain, after follow up period these 82 participants had Pain and 29 had no change. The difference in proportion found to be statistically significant. But clinically not significant because after the follow up period number of participants having Pain increased considerably ($p < 0.001$).

BT and FU: before treatment all of the 115 participants had Pain and after follow up period 82 had Pain, 33 participants had no pain. The difference in proportion found to be statistically significant. But clinically not significant because after the follow up period number of participants having Pain increased considerably ($p < 0.001$). (Table 64, 65, 66A, 66B, 66C, 66D)

Table 67. Ama assessment Tool – Lack of enthusiasm before treatment, after treatment and after follow up period

Lack of enthusiasm	No	Yes
Before Treatment	24	91
After Treatment	75	40
Follow up	84	31

Table 68. Overall differences between Lack of enthusiasm before treatment, after treatment and after follow up period of Ama assessment Tool –- Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	78.525	2	.000

Table 69. Paired differences between Lack of enthusiasm before treatment, after treatment and after follow up period using McNemar Test

Table 69A Lack of enthusiasm before treatment- after treatment

Before treatment	After treatment	
	No	Yes
No	19	5
Yes	56	35

Table 69B. Lack of enthusiasm after treatment- follow up

After treatment	Follow up	
	No	Yes
No	60	15
Yes	24	16

Table 69C. Before treatment - follow up

Before treatment	Follow up	
	No	Yes
No	24	0
Yes	60	31

Table 69D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	40.984	58.017	1.641
Asymp. Sig.	.000	.000	0.200

The eighth question of Ama assessment tool is Lack of enthusiasm. Out of 115 participants, before treatment (BT) 91 participants had Lack of enthusiasm, after treatment (AT) 40 had Lack of enthusiasm and after follow up period (FU) 31 had Lack of enthusiasm. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Lack of enthusiasm over time, χ^2 (2) = 78.525, p < 0.001. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom. There was statistically significant difference in proportions between BT and AT (*p* = <. 0005), between AT and FU (p < 0.001). Between BT and FU it was not significant). (*p* = .200).

BT and AT: before treatment 91 had Lack of enthusiasm and after treatment 40 had the symptom. 19 participants had no change after the treatment. The difference in proportion found to be highly significant (p < 0.001).

AT and FU: after treatment 40 had Lack of enthusiasm, after follow up period 31 participants had the symptom and 60 had no change. The difference in proportion found to be statistically significant. But clinically not significant because after the follow up period number of participants having Lack of enthusiasm increased considerably (p < 0.001).

BT and FU: before treatment 91 had Lack of enthusiasm and after follow up period 31 had Lack of enthusiasm, 24 participants had no change. The difference in proportion found to be not significant (*p* = .200). No notable change had occurred after the follow up period. (Table 67, 68, 69A, 69B, 69C, 69D)

Table 70. Ama assessment Tool – Lethargy before treatment, after treatment and after follow up period

Lethargy	No	Yes
Before Treatment	18	97
After Treatment	69	46
Follow up	44	71

Table 71. Overall differences between Lethargy before treatment, after treatment and after follow up period of Ama assessment Tool –- Cochran's Q test

N	Cochran's Q	df	Asymp. Sig.
115	60.969	2	.000

Table 72. Paired differences between Lethargy before treatment, after treatment and after follow up period using McNemar Test

Table 72A. Lethargy Before treatment- After treatment

Before treatment	After treatment	
	No	Yes
No	18	0
Yes	51	46

Table 72B. Lethargy After treatment- Follow up

After treatment	Follow up	
	No	Yes
No	31	38
Yes	13	33

Table 72C. Lethargy Before treatment - Follow up

Before treatment	Follow up	
	No	Yes
No	18	0
Yes	26	71

Table 72D. McNemar Test

	BT - AT	AT - FU	BT - FU
N	115	115	115
Chi-Square	49.020	24.038	11.294
Asymp. Sig.	.000	.000	.001

The ninth question of Ama assessment tool is Lethargy. Out of 115 participants, before treatment (BT) 97 participants had Lethargy, after treatment (AT) 46 had Lethargy and after follow up period (FU) 71 Lethargy. Cochran's *Q* test determined that there was a statistically significant difference in the proportion of participants who relieved of Lethargy over time, χ^2 (2) = 60.969, p < 0.001. An exact McNemar's test determined that there was a statistically significant difference in the proportion of participants who relieved of the symptom. There was statistically significant difference in proportions between BT and AT (p < 0.001), between AT and FU (p < 0.001) & between BT and FU (*p* =. 001).

BT and AT: before treatment 97 had Lethargy and after treatment 46 had the symptom. 18 participants had no change after the treatment. The difference in proportion found to be highly significant (p < 0.001).

AT and FU: after treatment 46 had Lethargy, after follow up period 71 participants had the symptom and 31 had no change. The difference in proportion found to be statistically significant. But clinically not significant because after the follow up period number of participants having Lethargy increased considerably (p < 0.001).

BT and FU: before treatment 97 had Lethargy and after follow up period 71 had Lethargy, 18 participants had no change. The difference in proportion found to be significant (*p* = 0.001). No notable change had occurred after the follow up period. (Table 70, 71, 72A, 72B, 72C, 72D)

III. Analysis of Objective parameters

Table 73. Handgrip - before and after treatment

Handgrip		Mean	N	Std. Deviation	Std. Error
Left	**BT**	6.304	115	5.3446	0.4984
	AT	8.852	115	4.0959	0.3819
Right	**BT**	8.174	115	4.6041	.4293
	AT	10.174	115	3.9984	.3729

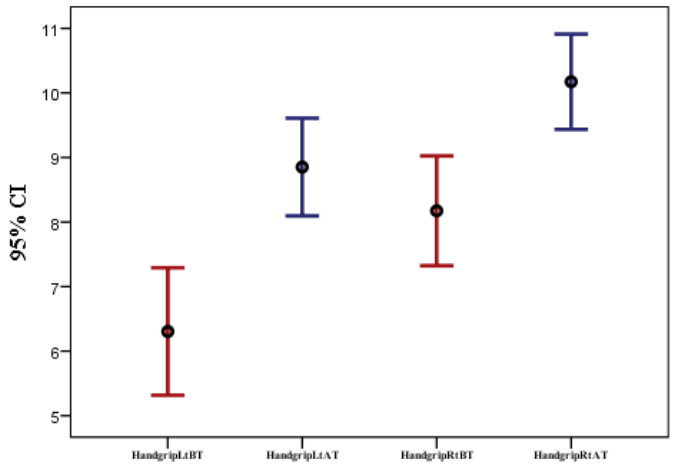


Figure 26. Handgrip - before and after treatment

Table 74. Handgrip - paired sample t test for comparing means between before and after treatment

	Paired Differences							
				95% CI difference				
Handgrip	**Mean**	**SD**	**SE**	**Lower**	**Upper**	**t**	**df**	**Sig.**
Left	-2.5478	1.9612	0.1829	-2.9101	-2.1855	-13.931	114	.000
Right	-2.0000	1.9194	.1790	-2.3546	-1.6454	-11.174	114	.000

The mean Hand grip before treatment in left hand was 6.304 with SD 5.3446 and after treatment were 8.852 with SD 4.0959. Paired t test has been conducted to find out the significance. It is seen that the difference in means -2.5478 ± 1.9612 was found to be significant $p < 0.001$. ($t(114) = -13.931$, $p < 0.001$). With 15 days of treatment the Hand grip improved significantly.

The mean Hand grip before treatment in right hand was 8.174 with SD 4.6041 and after treatment were 10.174 with SD 3.9984. Paired t test has been conducted to find out the significance. It is seen that the difference in means -2.00 ± 1.9194 was found to be significant $p < 0.001$. ($t(114) = -11.174$, $p < 0.001$). With 15 days of treatment the Hand grip improved significantly. (Table 73, 74)

Table 75. Range of Motion of knee flexion - before treatment and after treatment (measured in degrees)

Side	ROM knee flexion	Mean	Std. Deviation	Std. Error
Left	Before treatment	107.522	14.7994	1.3801
	After treatment	134.696	10.2016	0.9513
Right	Before treatment	127.043	23.3949	2.1816
	After treatment	140.348	11.4079	1.0638

Table 76. Range of Motion of knee flexion - paired sample t test for comparing means between before and after treatment

knee flexion BT-AT	Paired Differences					t	df	Sig.
				95% CI difference				
	Mean	SD	SE	Lower	Upper			
Left	27.1739	6.9815	0.6510	28.4636	25.8842	41.740	114	.000
Right	13.3043	12.8399	1.1973	15.6762	10.9325	11.112	114	.000

Range of Motion (ROM) of the participants was assessed by using Goniometer. The mean ROM of knee flexion (Lt. Side) before treatment was 107.522^0 with SD 14.799^0 and after treatment were 134.696^0 with SD 10.2016^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $27.1739^0 \pm 6.9815^0$ was found to be significant $p < 0.001$. ($t(114) = 41.740$, $p < 0.001$). With 15 days of treatment the ROM in Lt. knee flexion improved significantly. The mean ROM of knee flexion (Rt. Side) before treatment was 127.043^0 with SD 23.3949^0 and after treatment were 140.348^0 with SD 11.4079. Paired t test has been conducted to find out the significance. It is seen that the difference in means $13.3043^0 \pm 12.8399^0$ was found to be significant $p < 0.001$. ($t(114) = 11.112$, $p < 0.001$). With 15 days of treatment the ROM in Rt. knee flexion improved significantly. (Table 75, 76)

Table 77. Range of Motion of shoulder Abduction and Adduction - before treatment and after treatment (measured in degrees)

Motion	Side	Treatment	Mean	Std. Deviation	Std. Error
Shoulder Abduction	Left	Before treatment	144.957	5.6776	0.5294
		After treatment	145.304	5.0126	0.4674
	Right	Before treatment	129.565	10.4622	0.9756
		After treatment	139.130	6.5648	0.6122
Shoulder Adduction	Left	Before treatment	26.522	2.3107	0.2155
		After treatment	26.522	2.3200	0.2155
	Right	Before treatment	28.461	3.3826	0.3154
		After treatment	29.748	0.7591	.0000

Table 78. Range of Motion of shoulder Abduction and Adduction - paired sample t test for comparing means between before and after treatment

ROM	BT-AT	Paired Differences					t	df	Sig.
					95% CI difference				
		Mean	SD	SE	Lower	Upper			
Abduction	Left	0.3478	1.8403	0.1716	0.6878	0.0079	2.027	114	.045
	Right	9.5652	5.5237	0.5151	10.5856	8.5448	18.570	114	.000
Adduction	Left	1.3043	3.3826	0.3154	1.9292	0.6795	4.135	114	.000
	Right	-.2870	3.3659	.3139	-1.9087	-.6652	-4.100	114	.000

The mean ROM of shoulder Abduction (Lt. Side) before treatment was 144.957^0 with SD 5.6776^0 and after treatment were 145.304^0 with SD 5.0126^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $0.3478^0 \pm 1.8403^0$ was found to be significant $p = .045$. ($t(114) = 2.2027$, $p = .045$). (Table 77, 78)

The mean ROM of shoulder Abduction (Rt. Side) before treatment was 129.565^0 with SD 10.4622^0 and after treatment were 139.130^0 with SD 6.5648^0. Paired t test has been

conducted to find out the significance. It is seen that the difference in means 5.5237^0 ± 18.57^0 was found to be significant $p < 0.001$. ($t(114) = 18.570$, $p < 0.001$) (Table 78).

The mean ROM of shoulder Adduction (Lt. Side) before treatment was 26.522^0 with SD 2.3107^0 and after treatment were 26.522^0 with SD 2.32^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means 1.3043^0 ±3.3826^0 was found to be significant $p < 0.001$. ($t(114) = 4.135$, $p < 0.001$). (Table 77, 78)

The mean ROM of shoulder Adduction (Rt. Side) before treatment was 28.461 with SD 3.3826 and after treatment were 29.748^0 with SD 0.7591^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $-.287^0$ ± -3.3659^0 was found to be significant $p < 0.001$. ($t(114) = -4.100$, $p < 0.001$). With 15 days of treatment the ROM in Rt. shoulder Adduction improved significantly. (Table 77, 78)

The overall improvement in adduction and abduction of shoulder movement was seen to be statistically and clinically significant after the treatment.

Table 79. Range of Motion of shoulder extension and flexion - before treatment and after treatment (measured in degrees)

Motion	Side	Treatment	Mean	SD	SE
Shoulder Extension	**Left**	Before treatment	33.333	7.4865	0.7012
		After treatment	36.053	7.1480	0.6695
	Right	Before treatment	45.826	7.1307	0.6649
		After treatment	47.130	4.5432	0.4237
Shoulder Flexion	**Left**	Before treatment	122.348	13.0673	1.2185
		After treatment	138.957	6.0152	0.5609
	Right	Before treatment	124.261	13.4138	1.2508
		After treatment	138.957	6.0152	0.5609

Table 80. Range of Motion of shoulder extension and flexion - paired sample t test for comparing means between before and after treatment

ROM		Paired Differences							
					95% CI difference				
	BT-AT	Mean	SD	SE	Lower	Upper	t	df	Sig.
Extension	Left	2.7193	3.6519	0.3420	3.3969	2.0417	7.950	114	.000
	Right	1.3043	3.3826	0.3154	1.9292	0.6795	4.135	114	.000
Flexion	Left	16.6087	8.6994	0.8112	18.2157	15.0017	20.474	114	.000
	Right	14.6957	10.006	0.9331	16.5441	12.8472	15.749	114	.000

The mean ROM of shoulder extension (Lt. Side) before treatment was 33.333^0 with SD 7.4865^0 and after treatment were 36.053^0 with SD 7.148^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $2.7193^0 \pm 3.6519^0$ was found to be significant $p < 0.001$. ($t(114) = 7.950$, $p < 0.001$). (Table 79, 80)

The mean ROM of shoulder extension (Rt. Side) before treatment was 45.826 with SD 7.1307^0 and after treatment were 47.13^0 with SD 4.5432^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $1.3043^0 \pm 3.3826^0$ was found to be significant $p < 0.001$. ($t(114) = 4.135$, $p < 0.001$). (Table 79, 80)

The mean ROM of shoulder flexion (Lt. Side) before treatment was 122.348^0 with SD 13.0673^0 and after treatment were 138.957^0 with SD 6.0152^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $16.6087^0 \pm 8.6994^0$ was found to be significant $p < 0.001$. ($t(114) = 20.474$, $p < 0.001$).

The mean ROM of shoulder flexion (Rt. Side) before treatment was 124.261^0 with SD 13.4138^0 and after treatment were 138.957^0 with SD 6.0152^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $14.6957^0 \pm 10.0063^0$ was found to be significant $p < 0.001$. ($t(114) = 15.749$, $p < 0.001$). With 15 days of treatment the ROM in Rt. shoulder Adduction improved significantly (Table 79, 80). The overall improvement in flexion of shoulder movement was seen to be statistically and clinically significant after the treatment.

Table 81. Range of Motion of elbow - before treatment and after treatment (measured in degrees)

Table 81A. Elbow flexion – mean scoring

Motion	Side	Treatment	Mean	Std. Deviation	Std. Error
Elbow Flexion	Left	Before treatment	116.435	10.1904	0.9503
		After treatment	136.304	4.3472	0.4054
	Right	Before treatment	118.478	9.1569	0.8539
		After treatment	135.391	5.0065	0.4669

Table 81B. Elbow flexion paired t test

ROM	BT-AT	Paired Differences					t	df	Sig.
					95% CI difference				
		Mean	SD	SE	Lower	Upper			
Flexion	Left	-19.8696	11.1501	1.0398	-21.9293	-17.8098	-19.110	114	.000
	Right	-16.9130	11.7835	1.0988	-19.0898	-14.7363	-15.392	114	.000

Table 81C. Elbow extension Wilcoxon Signed Ranks Test

BT-AT	Ranks	N	Mean Rank	Sum of Ranks
Lt. Elbow Extension	Negative Ranks	33	17.00	561.00
	Positive Ranks	0	.00	.00
	Ties	82		
Rt. Elbow Extension	Negative Ranks	8	4.50	36.00
	Positive Ranks	0	.00	.00
	Ties	107		

Table 81D. Wilcoxon Signed Ranks Test

Total score BT-AT	Z	Asymp. Sig. (2-tailed)
Lt. Elbow Extension	-5.533	.000
Rt. Elbow Extension	-2.828	.005

The mean ROM of Elbow flexion (Lt. Side) before treatment was 116.435^0 with SD 10.1904^0 and after treatment were 136.304^0 with SD 4.3472^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $-19.8696^0 \pm 11.1501^0$ was found to be significant $p < 0.001$. ($t(114) = -19.110$, $p < 0.001$). (Table 81A, 81B)

The mean ROM of s Elbow flexion (Rt. Side) before treatment was 118.478^0 with SD 9.1569^0 and after treatment were 135.391^0 with SD 5.0065^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $-16.913^0 \pm 11.7835^0$ was found to be significant $p < 0.001$. ($t(114) = -15.392$, $p < 0.001$). (Table 81A, 81B)

The improvement after the intervention in the ROM of Elbow flexion was clinically significant

Normal range of Extension of elbow is zero. Only few people had mild flexion deformity. As more participants (82) are having zero range, to analyse the data Wilcoxon signed-rank tests was conducted. There was statistically significant reduction in ROM of elbow extension (Lt.) between BT and AT ($Z=--5.533$, $p < 0.001$ and in ROM of elbow extension (Rt.) between BT and AT ($Z=-2.828$, $p < 0.001$) (Table 81C, 81D).

In other words considering elbow extension (Lt.), out of 115 participants 33 had a lower score and 82 had no change in they have zero score before and after treatment. In ROM of elbow extension (Rt.), out of 115 participants 8 had a lower score and 107^0 had zero score before and after treatment. (Table 81C, 81D)

Table 82. Range of Motion of forearm - before treatment and after treatment (measured in degrees)

Forearm	Side	Treatment	Mean	SD	SE
Pronation	Left	Before treatment	75.043	6.6720	0.6222
		After treatment	76.957	4.6214	0.4310
	Right	Before treatment	67.652	12.7960	1.1932
		After treatment	76.522	4.7836	0.4461
Supination	Left	Before treatment	76.957	4.6214	0.4310
		After treatment	78.174	3.8804	0.3618
	Right	Before treatment	72.435	8.7451	0.8155
		After treatment	76.522	4.7836	0.4461

Table 83. Range of Motion of forearm - paired sample t test for comparing means between before and after treatment

ROM		Paired Differences							
					95% CI difference				
	BT-AT	Mean	SD	SE	Lower	Upper	t	df	Sig.
Pronation	Left	1.9130	5.9080	0.5509	3.0044	0.8217	3.472	114	.001
	Right	8.8696	11.680	1.0892	11.0273	6.7119	8.143	114	.000
Supination	Left	1.2174	3.2842	0.3062	1.8241	0.6107	3.975	114	.000
	Right	4.0870	6.9957	0.6524	5.3793	2.7947	6.265	114	.000

The mean ROM of forearm pronation (Lt. Side) before treatment was 75.043^0 with SD 6.672^0 and after treatment were 76.957^0 with SD 4.6214^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $1.913^0 \pm 5.908^0$ was found to be significant $p = .001$. ($t(114) = 3.472$, $p = <.001$). (Table 82, 83)

The mean ROM of forearm pronation (Rt. Side) before treatment was 67.652^0 with SD 12.796^0 and after treatment were 76.522^0 with SD 4.7836^0. Paired t test has been

conducted to find out the significance. It is seen that the difference in means $8.8696^0 \pm 11.68^0$ was found to be significant $p < 0.001$. ($t(114) = 8.143$, $p < 0.001$). (Table 82, 83)

The mean ROM of forearm supination (Lt. Side) before treatment was 76.957^0 with SD 4.6214^0 and after treatment were 78.174 with SD 3.8804. Paired t test has been conducted to find out the significance. It is seen that the difference in means $1.2174^0 \pm 3.2842^0$ was found to be significant $p < 0.001$. ($t(114) = 3.975$, $p < 0.001$). (Table 82, 83)

The mean ROM of forearm supination (Rt. Side) before treatment was 72.435^0 with SD 8.7451^0 and after treatment were 76.522^0 with SD 4.7836^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $4.087^0 \pm 6.9957^0$ was found to be significant $p < 0.001$. ($t(114) = 6.265$, $p < 0.001$). With 15 days of treatment the ROM in Rt. shoulder Adduction improved significantly. (Table 82, 83)

The overall improvement in pronation and supination of forearm was found to be statistically and clinically significant after the treatment. The average motion comes around 5^0 only. As it is related to pronation and supination it is clinically significant.

Table 84. Range of Motion of wrist - radial and ulnar deviation - before treatment and after treatment (measured in degrees)

Wrist	Side	Treatment	Mean	SD	SE
Radial deviation	**Left**	Before treatment	8.609	2.2505	0.2099
		After treatment	18.261	2.3918	0.2230
	Right	Before treatment	10.000	.0000	.0000
		After treatment	18.261	2.3918	0.2230
Ulnar deviation	**Left**	Before treatment	11.261	4.4349	0.4136
		After treatment	22.652	5.3114	0.4953
	Right	Before treatment	14.043	3.4346	0.3203
		After treatment	22.652	5.3114	0.4953

Table 85. Range of Motion of wrist - radial and ulnar deviation - paired sample t test for comparing means between before and after treatment

ROM		Paired Differences					t	df	Sig.
					95% CI difference				
	BT-AT	Mean	SD	SE	Lower	Upper			
Radial	Left	9.6522	1.2776	.1191	9.8882	9.4162	81.016	114	.000
	Right	8.2609	2.3918	0.2230	8.7027	7.8190	37.038	114	.000
Ulnar	Left	11.3913	3.4760	0.3241	12.0334	10.7492	35.144	114	.000
	Right	8.6087	2.2505	0.2099	9.0244	8.1930	41.021	114	.000

The mean ROM of wrist radial rotation (Lt. Side) before treatment was 8.609^0 with SD 2.2505^0 and after treatment were 18.261^0 with SD 2.3918^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $9.6522^0 \pm 1.2776^0$ was found to be significant $p < 0.001$). ($t(114) = 81.016$, $p < 0.001$).

The mean ROM of wrist radial rotation (Rt. Side) before treatment was 10.0^0 with SD 00^0 and after treatment were 18.261^0 with SD 2.3918^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $8.2609^0 \pm 2.3918^0$ was found to be significant $p < 0.001$. ($t(114) = 37.038$, $p < 0.001$). (Table 84, 85)

The mean ROM of wrist ulnar deviation (Lt. Side) before treatment was 11.261^0 with SD 4.4349^0 and after treatment were 22.652^0 with SD 5.3114^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $11.3913^0 \pm 3.476^0$ was found to be significant $p < 0.001$. ($t(114) = 35.144$, *$p < 0.001$*).

The mean ROM of wrist ulnar deviation (Rt. Side) before treatment was 14.043^0 with SD 3.4346^0 and after treatment were 22.652^0 with SD 5.3114^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $8.6087^0 \pm 2.2505^0$ was found to be significant $p < 0.001$. ($t(114) = 41.021$, $p < 0.001$). With 15 days of treatment the ROM in Rt. shoulder Adduction improved significantly. (Table 84, 85)

The overall improvement in radial and ulnar deviation of wrist was found to be statistically and clinically significant after the treatment (8^0 to 11^0)

Table 86. Range of Motion of wrist extension and flexion - before treatment and after treatment (measured in degrees)

Wrist	Side	Treatment	Mean	SD	SE
Extension	Left	Before treatment	34.957	6.8022	0.6343
		After treatment	53.565	8.9041	0.8303
	Right	Before treatment	31.391	2.2505	0.2099
		After treatment	53.870	2.1006	0.1959
Flexion	Left	Before treatment	37.739	3.2608	0.3041
		After treatment	57.739	3.2608	0.3041
	Right	Before treatment	32.783	4.5010	0.4197
		After treatment	52.478	2.5108	0.2341

Table 87. Range of Motion of wrist extension and flexion - paired sample t test for comparing means between before and after treatment

ROM		Paired Differences							
					95% CI difference				
	BT-AT	Mean	SD	SE	Lower	Upper	t	df	Sig.
Extension	Left	18.6087	2.2505	0.2099	19.0244	18.1930	88.671	114	.000
	Right	22.4783	2.5108	0.2341	22.9421	22.0144	96.004	114	.000
Flexi	Right	19.6957	6.3621	0.5933	20.8709	18.5204	33.198	114	.000

The mean ROM of wrist extension (Lt. Side) before treatment was 34.957^0 with SD 6.8022^0 and after treatment were 53.565^0 with SD 8.9041^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $18.6087^0 \pm 2.2505^0$ was found to be significant $p < 0.001$). ($t(114) = 88.671$, $p < 0.001$). (Table 86, 87)

The mean ROM of wrist extension (Rt. Side) before treatment was 31.391^0 with SD 2.2505^0 and after treatment were 53.87^0 with SD 2.1006^0. Paired t test has been

conducted to find out the significance. It is seen that the difference in means $22.4783^0 \pm 2.5108^0$ was found to be significant $p < 0.001$. ($t(114) = 96.004$, $p < 0.001$). (Table 86, 87)

The mean ROM of wrist flexion (Lt. Side) before treatment was 37.739^0 with SD 3.2608^0 and after treatment were 57.739^0 with SD 3.2608^0. Even though the mean is having difference, the SD and the SE were same as there is no change before and after the intervention. (Table 86, 87)

The mean ROM of wrist flexion (Rt. Side) before treatment was 32.783^0 with SD 4.501^0 and after treatment were 52.478^0 with SD 2.5108^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $19.6957^0 \pm 6.3621^0$ was found to be significant $p < 0.001$. ($t(114) = 33.198$, $p < 0.001$). With 15 days of treatment the ROM in Rt. shoulder Adduction improved significantly. (Table 86, 87)

The overall improvement in extension and flexion of wrist was found to be statistically and clinically significant after the treatment (18^0 to 22^0)

Table 88. Range of Motion of thumb MP joint flexion - before treatment and after treatment (measured in degrees)

Thumb MP	Side	Treatment	Mean	SD	S E
Flexion	Left	Before treatment	31.304	15.0159	1.4002
		After treatment	43.739	8.9306	0.8328
	Right	Before treatment	31.304	15.0159	1.4002
		After treatment	46.522	8.4856	0.7913

Table 89. Range of Motion of thumb MP joint flexion - paired sample t test for comparing means between before and after treatment

ROM	BT-AT	Paired Differences Mean	SD	SE	95% CI difference Lower	Upper	t	df	Sig.
Flexion	Left	12.4348	7.0824	0.6604	13.7431	11.1265	18.828	114	.000
	Right	15.2174	7.0522	0.6576	16.5201	13.9147	23.140	114	.000

The mean ROM of thumb MP joint flexion (Lt. Side) before treatment was 31.304^0 with SD 15.0159^0 and after treatment were 43.739^0 with SD 8.9306^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $12.4348^0 \pm 7.0824^0$ was found to be significant, $p < 0.001$. ($t(114) = 18.828$, $p < 0.001$). (Table 88, 89)

The mean ROM of thumb MP joint flexion (Rt. Side) before treatment was 31.304^0 with SD 15.0159^0 and after treatment were 46.522^0 with SD 8.4856^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $15.2174^0 \pm 7.0522^0$ was found to be significant $p < 0.001$. ($t(114) = 23.140$, $p < 0.001$). With 15 days of treatment the MP joint flexion improved significantly (12^0 to 15^0). (Table 88, 89)

Table 90. Range of Motion of thumb IP joint flexion - before treatment and after treatment (measured in degrees)

Thumb IP	Side	Treatment	Mean	Std. Deviation	Std. Error
Flexion	Left	Before treatment	52.217	10.5588	0.9846
		After treatment	73.565	4.3812	0.4086
	Right	Before treatment	47.174	5.5855	0.5208
		After treatment	73.565	4.3812	0.4086

Table 91. Range of Motion of thumb IP joint flexion - paired sample t test for comparing means between before and after treatment

ROM		Paired Differences							
					95% CI difference				
	BT-AT	Mean	SD	SE	Lower	Upper	t	df	Sig.
Flexion	Left	21.3478	10.5822	0.9868	23.3027	19.3930	21.633	114	.000
	Right	26.3913	8.6234	0.8041	27.9843	-24.7983	32.819	114	.000

The mean ROM of thumb IP joint flexion (Lt. Side) before treatment was 52.217^0 with SD 10.5588^0 and after treatment were 73.565^0 with SD 4.3812^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $21.3478^0 \pm 10.5822^0$ was found to be significant, $p < 0.001$. ($t(114) = 21.633$, $p < 0.001$). (Table 90, 91)

The mean ROM of thumb IP joint flexion (Rt. Side) before treatment was 47.174^0 with SD 5.5855^0 and after treatment were 73.565^0 with SD 4.3812^0. Paired t test has been conducted to find out the significance. It is seen that the difference in means $26.3913^0 \pm 8.6234^0$ was found to be significant $p < 0.001$. ($t(114) = 32.819$, $p < 0.001$). With 15 days of treatment the IP joint flexion improved significantly (21^0 to 26^0). (Table 90, 91)

IV. Analysis of blood investigation parameters

Table 92. Erythrocyte Sedimentation Rate -- before treatment and after treatment (measured in mm)

ESR	Mean	Std. Deviation	Std. Error
Before treatment	46.130	16.9393	1.5796
After treatment	31.217	12.0640	1.1250

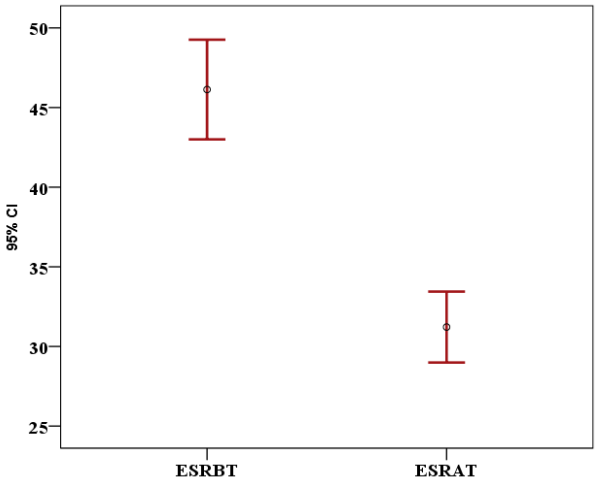


Figure 27. Erythrocyte Sedimentation Rate -- before treatment and after treatment

Table 93. Erythrocyte Sedimentation Rate (ESR) - paired sample t test for comparing means between before and after treatment (measured in mm/ 1 hr)

	Paired Differences							
				95% CI difference				
ESR	**Mean**	**SD**	**SE**	**Lower**	**Upper**	**t**	**df**	**Sig.**
BT-AT	14.913	11.7530	1.0960	12.7419	17.0842	13.607	114	.000

The mean ESR before treatment was 46.130 mm with SD 16.9393 mm and after treatment was 31.217 mm with SD 12.0640 mm. Paired t test has been conducted to find out the significance. It is seen that the difference in means 14.9130 mm ± 11.7530 mm was found to be significant $p < 0.001$). ($t(114) = 13.607$, $p < 0.001$) (Table 92, 93 Figure 26).

ESR in this study used in several situations. It is used as a part of classification criteria, used in DAS28 as overall measure for disease activity and used to assess the change in inflammatory process of RA. From the data analysis it can be concluded that there was a statistically significant (14.9130 mm ± 11.7530 mm) reduction of ESR after the intervention

Table 94. C-Reactive protein (CRP) -- before treatment and after treatment (measured in mm/dL)

CRP	Minimum	Maximum	Mean	SD	SE
Before treatment	1.0	8.0	6.537	1.2379	0.1154
After treatment	1.0	7.0	5.730	0.9765	0.0911

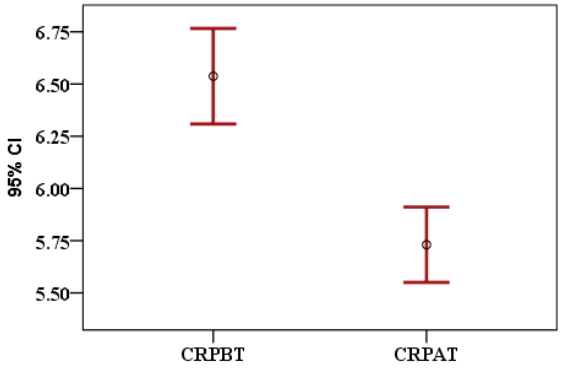


Figure 28. C-Reactive protein (CRP) -- before treatment and after treatment

Table 95. C-Reactive protein (CRP) - paired sample t test for comparing means between before and after treatment

	Paired Differences							
				95% CI difference				
CRP	Mean	SD	SE	Lower	Upper	t	df	Sig.
BT-AT	0.8070	0.5281	0.0492	0.7094	0.9045	16.386	114	.000

The mean CRP before treatment was 6.537 mm/dL with SD 1.2379 mm/dL and after treatment was 5.730 mm/dL with SD 0.9765 mm/dL. Paired t test has been conducted to find out the significance. It is seen that the difference in means 0.8070 mm/dL ± 0.5281 mm/dL was found to be significant $p < 0.001$). ($t(114) = 16.386$, $p < 0.001$). (Table 94, 95 Figure 27)

CRP in this study used in several situations. It is used as a part of classification criteria, used in DAS28 as overall measure for disease activity and used to assess the change in inflammatory process of RA. CRP increases before ESR raises and falls before ESR. From the data analysis it can be concluded that there was a statistically significant reduction of CRP after the intervention (0.8070 mm/dL ± 0.5281mm/dL).

Table 96. Haemoglobin (Hb %) - before treatment and after treatment (measured in gm/dL)

Hb%	Mean	Std. Deviation	Std. Error
Before treatment	12.519	1.0085	.0940
After treatment	12.523	1.0083	.0940

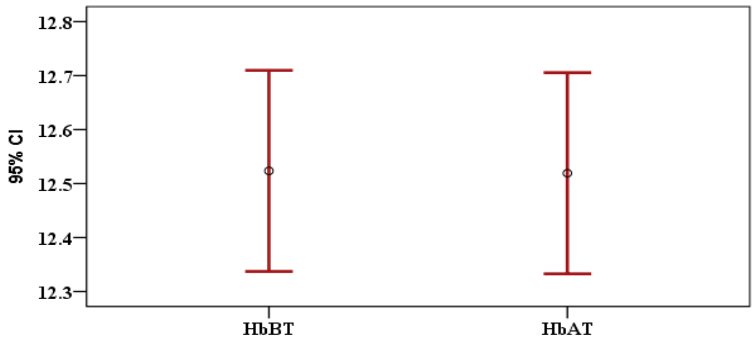


Figure 29. Haemoglobin (Hb %) - before treatment and after treatment

Table 97. Haemoglobin (Hb %) - paired sample t test for comparing means between before and after treatment

	Paired Differences							
				95% CI difference				
Hb%	Mean	SD	SE	Lower	Upper	t	df	Sig.
BT-AT	0.0043	0.0244	0.0023	-0.0002	0.0089	1.912	114	0.058

The mean Hb% before treatment was 12.519 mm/dL with SD 1.0085 mm/dL and after treatment was 12.523 mm/dL with SD 1.0083 mm/dL. Paired t test has been conducted to find out the significance. There was negligibly small increase in Hb% seen in means 0.0043 mm/DL ± 0.0244 mm/dL and was found to be not significant $p < 0.001$). ($t(114) = 1.912$, $p < 0.001$). (Table 96, 97 Figures 28)

Table 98. Serum Creatinine - before treatment and after treatment (measured in mg/dL)

Serum Creatinine	Mean	SD
Before treatment	0.8739	0.12468
After treatment	0.8739	0.12468

The mean Serum Creatinine before treatment was 0.8739mg/dL with SD 0.12468mg/dL. After the intervention it continued to be the same. There was no change in S. Creatinine level after intervention. (Table 98)

Table 99. Liver Function Test - before treatment and after treatment

LFT	Tmt.	Mean	SD	SE	Measurement unit
Alkaline phosphatase	**BT**	85.061	16.0248	1.4943	IU/L
	AT	83.600	17.6450	1.6454	
Bilurubin	**BT**	0.7010	0.2386	0.0222	mg/dL
	AT	0.7056	0.2310	0.0215	
Protein	**BT**	6.973	0.5670	0.0529	mg/dL
	AT	6.952	0.5562	0.0519	
Albumin	**BT**	4.017	0.3250	0.0303	gm/dL
	AT	4.009	0.3230	0.0301	
Globulin	**BT**	3.182	0.5345	0.0498	gm/dL
	AT	3.176	0.5334	0.0497	
SGOT	**BT**	24.870	6.8230	0.6362	IU/L
	AT	24.957	6.8112	0.6352	
SGPT	**BT**	28.696	6.0902	0.5679	IU/L
	AT	28.730	6.1120	0.5699	

Table 100. Liver Function Test - paired sample t test for comparing means between before and after treatment

	Paired Differences					t	df	Sig.
	Mean	SD	SE	95% CI difference Lower	Upper			
Alkal.phos **BT-AT**	1.4609	7.133	0.6652	0.1432	2.7786	2.196	114	.030
Bilurubin **BT-AT**	-0.004	0.0161	.00151	-.00769	-0.0017	-3.111	114	.002
Protein **BT-AT**	0.020	0.0767	.0071	.0067	0.0350	2.919	114	.004
Albumin **BT-AT**	0.0078	0.0498	.0046	-.0014	0.0170	1.685	114	.095
Globulin **BT-AT**	0.0061	0.0305	.0028	.0005	0.0117	2.143	114	.034
SGOT **BT-AT**	-0.087	0.5055	.0471	-.1803	0.0064	-1.845	114	.068
SGPT **BT-AT**	-0.034	0.1840	.0172	-.0688	-0.0008	-2.027	114	.045

Table 99 shows the means of different blood investigation done for the participants before and after the intervention to find out the drug toxicity if any. Table 100 shows the difference in means with significance of these blood investigations. Of the blood report listed Alkal.phos, S.Bilurubin, S.Protein, S.Globulin and SGPT showed significant negligible change which was within limit also. While the S. Albumin and the S. SGOT also showed changes and was not significant.

DISCUSSION AND CONCLUSION

CHAPTER 5

DISCUSSION AND CONCLUSION

The objectives of the study were to assess the severity of *Ama* and to study the efficacy of *ama pachana* effect Amrutottaram Kashayam in patients with Rheumatoid Arthritis by using Ama assessment Tool. The study setting was Kayachikitsa OPD of Vaidyaratnam Ayurveda College, Ollur, Thrissur, Kerala.

Amrutottaram Kashayam was given to 115 patients for 15 days. During the course of medication the patient was advised to take *Manda* and *peya* only. Follow up period fixed as 15 days without medication. Patients were assessed before and after the intervention as explained in the Methodology. Patients with Diabetes Mellitus, Gouty Arthritis and Rheumatic fever were excluded from the study.

The mean age of the participants was 48.40 with SD 8.97. 78.3 % of the participants were female and 56.5% of the participants belong to the age group of > 49. Below the age of 60 the incidence is 4-5 times higher [(4)]. 55.7 percent of the participants are from lower middle class.

In males 40% are from *Vatadhika prakriti*. In which prakriti the RA is predominant is a debate. In this study *pitta* predominance is seen in females and *vata* predominance seen in males. Around fifty percentage of the participants belongs to *pittadhika prakriti* and thirty percentage belongs to *vatadhika prakriti*.

The mean duration of RA was 37.39 months with a SD of 17.09. 47.9% patients were having duration of more than 3 yrs. All the 11 deformity noticed was of Boutonniere deformity [(136)]. Symmetrical joint distribution was noticed in 63.5% of the participants. Symmetry may not be noticed at the beginning[(137)]. Long standing increase in CRP can cause deformity [(136)].

61.7% were using Ayurvedic and Allopathic treatments for RA. Patients with larger duration of RA are utilizing the OPD of this Institution. All of them are under Ayurvedic medicine before this intervention.

It has to be noted that those who were having DAS28 score 6 and above are taken in to study. The minimum and maximum level was extreme in females but the mean with SD is similar in both groups.

Environmental factors have an important role in Rheumatoid Arthritis. In this study the female predominance was noted and smoking and use of alcohol was not noticed. 95.7% of the participants were having mixed diet. Poor dietary habits lead to *Ama* which in turn becomes a cause for RA. It is estimated that 2/3rd of the people with RA are overweight or obese[138]. In the lean category there were 9 female participants and in the overweight category 79.5% were females and only 20.5% were males. In obese category 74.6% were females and 25.4% were males. It can be concluded that in the present study females are having more BMI than males.

Reduction in ESR and CRP were seen after the intervention ($p < 0.001$). Amrutottaram kashayam was very effective in reducing the ESR and CRP. The mean CRP was 6.537 with SD 1.2379. For considering classification criteria (acute phase reactants) the CRP count above 6 was considered as high. 94 (81.7%) participants are having raised CRP (>6 mg/L). In this study ESR and CRP were used for diagnosis and also to assess the prognosis outcome.

Anti-CCP and RF are used as serological markers. Rheumatoid Factor (RF) was positive in 41 (35.7%) participants. Rheumatoid Factor (RF) above > 8 IU/ml, considered as positive. ANA used to find out the autoimmune process in the body. A positive ANA indicates the process of auto immunity [139]. In this study ANA was positive in 23.5% of paticipants. The prevalence of ANA in healty individuals is 3-15%.

Morning stiffness is an important tool to assess the severity of RA. It is more concerned with functional disability and pain than the disease activity [140]. With 15 days of treatment with Amrutottaram kashayam the morning stiffness reduced significantly ($p < 0.001$). The effectiveness was similar in both genders. *Ama* in RA causes the stiffness in *kapha kaala*. Reduction in morning stiffness shows the *Ama pachana* effect of Amrutottaram kashayam.

There was a statistically significant difference in pain score during this period ($p < 0.001$). BT and FU period more participants had higher pain score. *Ruk* is caused by

the vitiated *vata dosha*. RA is *pitta* predominant disease. The effectiveness may be due to the fact that Amrutottaram kashyam is *tridoshghna*. 15 days treatment with Amrutottaram kashyam is effective in reducing the pain is found to be highly significant. Pain reduction is seen while taking the medicine and after follow up period. While the effect compared to BT after the follow up period was insignificant. In both gender the effect of Amrutottaram kashyam in reducing the pain is found to be similar. In all age groups the medicine has same effect. The Amrutottaram kashayam has similar *ama pachana* effect irrespective of gender and age.

Table M6. The *ama pachana* effect of Amrutottaram kashayam using the ama grading tool can be tabulated as below

No.	Symptoms	Significance during different time period		
		BT-AT	AT-FU	BT-FU
1	Overall change	✓	x	✓
2	Constipation	✓	✓	✓
3	Loss of appetite	✓	✓	✓
4	Bad belching	✓	✓	x
5	Pain	✓	✓	x
6	Lack of enthusiasm	✓	✓	x
7	Heaviness of body	✓	x	✓
8	Loss of taste	✓	x	✓
9	Loss of thirst	✓	x	✓
10	Lethargy	✓	x	x

The *Amatwa in* RA has reduced significantly in 15 days of medication with Amrutottaram kashayam. The Overall change was statistically significant during the time period. Considering BT-AT and BT-FU it was statistically significant irrespective of

gender ($p < 0.001$). It was not effective during the period AT-FU. It can be concluded that Amrutottaram kashayam was effective during the 15 days course of treatment and after the follow up period it was effective. This indicates that the long time medication will be effective for better prognostic outcomes.

Participants relieved of constipation and improvement in appetite was seen during course of study and after follow up period. The *kashayam* was effective in reducing the symptoms bad belching, pain and lack of enthusiasm throughout the period. Significant change in the symptoms heaviness of body, loss of taste, loss of thirst was noted after treatment and after follow up period. In between it was not significant. The *kashayam* was effective in reducing the lethargy during the first 15 days.

After 15 days of treatment significant improvement in hand grip was noticed. ROM of different joint assessed before and after treatment. The overall improvement in ROM of adduction and abduction, extension, flexion of shoulder, elbow flexion, forearm – pronation, supination, wrist - radial and ulnar deviation, wrist extension and flexion, thumb MP joint flexion, thumb IP joint flexion was statistically and clinically significant.

There was no change in Hb% level. No significant change noticed in S. Creatinine and in Liver Function Test. Amrutottaram kashayam has no side effects or toxicity.

The Amrutottaram kashayam can be used as an ama pachana medicine in RA. The ingredients possesses antioxidants and anti-inflammatory properties. In RA Amrutottaram kashayam is useful as an antioxidant and anti-inflammatory drug.

High disease activity was seen in most of the participants with predominance in > 49 age group [(135)]. DAS 28 is a comprehensive index to asses the disease activity of RA patient. It is extensively validated for clinical trials in combination with EULAR response criteria [(141)].

Table M7. Overall change in Disease activity as per the EULAR Good or Moderate response criteria (127) (5)

Present DAS28 score	DAS28 improvement over time points		
	>1.21	0.6 - 1.20	<=0.60
Low disease activity 2.6 - 3.2	Good Response ---	Moderate response ---	No Response ---
Moderate disease activity 3.2 - 5.1	Moderate Response 20	Moderate Response 4	No Response 0
High disease activity >5.1	Moderate Response 57	No Response 34	No Response 0

The change in score has been grouped as; <=0.60, 0.6 - 1.20, and >1.21. In this study 77 (67%) participants had change >1.21 ($p < 0.001$) irrespective of gender. Use of Amrutottaram kashayam for 15 days has 70.43% overall moderate response in RA disease activity.

Clinical outcome measured with Ama assessment tool, DAS28 score, EULAR good or moderate response, hand grip strength, ROM of different joints, ESR and CRP were found to be supporting this finding. The medicine was given to patients for 15 days only. RA is chronic auto immune disease and medicine has to be taken for longer period for better outcomes.

Limitations of the study

- Only Amrutottaram kashayam was used for the study.
- The observational period with medicine was 15 days with 15 days follow up period.
- The design is pre test post test design.
- No tool is available to assess Ama.

Suggestions

- Combination of medications with or without *ruksha sweda* with more observational days can be used for the trial.
- Randomized Controlled Trial can be done to compare with DMARDs.
- To assess the construct Ama and to assess the outcome in Ama perspective, an assessment tool can be developed.

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ANNEXURES

Annexure I

ASSESSMENT OF AMA PACHANA EFFECT OF AMRUTOTTARAM KASHAYAM IN RHEUMATOID ARTHRITIS

CASE REPORT FORM I – SCREENING

1. Code No. (of clinical trial) ☐☐☐☐☐☐
2. Name of the subject: _____
3. S.No. of the subject: _____
4. Gender Male (1) ☐ Female (0) ☐
5. Date of Birth: ☐☐ ☐☐ ☐☐ Age (in yrs.) ☐☐
6. Address: _____

CRITERIA FOR INCLUSION

2010 ACR / EULAR Classification Criteria for Rheumatoid Arthritis

JOINT DISTRIBUTION	**(0-5)**
1 large joint	**0**
2-10 large joints	**1**
1-3 small joints (large joints not counted)	**2**
4-10 small joints (large joints not counted)	**3**
>10 joints (at least one small joint)	**5**
SEROLOGY	**(0-3)**
Negative RF AND negative ACPA	**0**
Low positive RF OR low positive ACPA	**2**
High positive RF OR high positive ACPA	**3**
SYMPTOM DURATION	**(0-1)**
<6 weeks	**0**
≥6 weeks	**1**
ACUTE PHASE REACTANTS	**(0-1)**
Normal CRP AND normal ESR	**0**
Abnormal CRP OR abnormal ESR	**1**

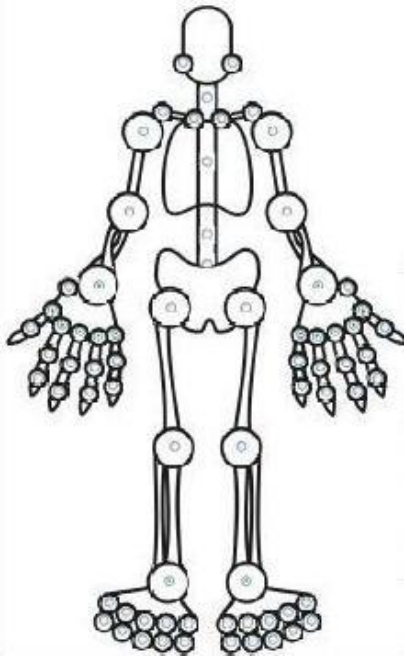
If the score is **≥6 = definite RA** **Patient's score** ☐

CRITERIA FOR EXCLUSION	Yes	No
1. Patients with serum positive ASO titer	☐	☐
2. Patients with serum positive Uric acid	☐	☐
3. Patients with other systemic complications	☐	☐
4. Patients with hypertension and diabetes	☐	☐
5. Age group less than 25 and above 60	☐	☐

1. **If inclusion criteria score is ≥6 and 1 to 5 are 'No' then the participant is eligible for the study.**

Date:_____ Signature of the Investigator

Joint distribution
(Darken the joint)



ASSESSMENT OF AMA PACHANA EFFECT OF AMRUTOTTARAM KASHAYAM IN RHEUMATOID ARTHRITIS

CASE REPORT FORM II – HISTORY

1. Code No. (of clinical trial) ☐☐☐☐☐
2. Centre:
3. Name of the subject:
4. S.No. of the subject:
5. Gender ☐ Male ☐ Female
6. Date of Birth: ☐☐ ☐☐ ☐☐ Age (in yrs.) ☐☐
7. Address:
8. Place: ☐ Urban ☐ Rural
9. **Socio economic Status (Kuppuswamy Socio Economic Status scale)**

Education

Profession or honors	**7**	Graduate or postgraduate	**6**
Intermediate or post-high school diploma	**5**	High school certificate	**4**
Middle school certificate	**3**	Primary school certificate	**2**
Illiterate	**1**		

Occupation

Profession	**10**	Semi professional	**6**
Clerical, shop owner, farmer	**5**	Skilled worker	**4**
Semiskilled worker	**3**	Unskilled worker	**2**
Unemployed	**1**		

Family income per month

≥ 42,876	**12**	21,438-42,875	**10**
16,078-21,437	**6**	10719-16,077	**4**
6,431-10,718	**3**	2,165-6,430	**2**
≤2164	**1**		

Socioeconomic class

1) Upper class	**26-29**	**2)** Upper middle class	**16-25**
3) Lower middle class	**11-15**	**4)** Upper lower class	**5-10**
5) Lower class	**<5**		

Score ☐ **SES** ☐

Religion: **1** Hindu **2** Muslim **3** Christian **4.** Sikh **5.** Parsi

10. **Treatment history** **Yes** 1 **No** 0

Modern medicine/homeo/unani/mixed/naturopathy/others 2

Ayurveda medicines if taken specify: 3

Prognosis after these treatments 4

11. **History of presenting complaints**

12. **History of previous illness**

13. **Family history**

14. **Personal history**

Appetite	1) more	2) reduced	3) normal
Bowel	1) satisfactory	2) constipated	3) irregular
Diet	1) vegetarian	2) non vegetarian	3) mixed
Sleep	1] more	2] less	3] sound

15. **Addictions**

Alcohol consumption	yes	NO	……/day
Smoking	yes	NO	……/day
Tea/coffee	yes	NO	……/day
Carbonated drinks	yes	no	……/day

Other addictions if any

16. **Menstrual and obstetric history**
17. **Physical examination**

Temperature	Respiratory rate	
Weight	Blood pressure	Pulse

Systemic examination

Examination of Locomotor system

General examination

Joints

Inspection	**Present (1)**	**Absent (0)**	**Duration (in days)**
18. 1 Deformity	☐	☐	☐
2 Symmetry.	☐	☐	☐
3 Oedema.	☐	☐	☐
4 Redness.	☐	☐	☐

19. **Palpation.**

1 Tenderness	☐	☐	☐
2 Swelling	☐	☐	☐
3 Temperature.	☐	☐	☐
4 Crepitus	☐	☐	☐

20. **Range of movements**. (Separate sheet Attached)

Shoulder	Abduction-adduction, Flexion-Extension
Elbow	Extension, Flexion
Forearm	Pronation, Supination
Wrist	Radial = Ulnar, Extension-Flexion
Thumb	MP joint flexion, IP joint flexion
Knee	Flexion

21. Others Yes ☐ No ☐

If Yes specify:

22. **Personal History:**

23. Diet: Vegetarian ☐ Non-veg ☐

24. Presence of anxiety No ☐ Yes ☐

25. Constipation No ☐ Yes ☐

Addiction

26. Smoking No ☐ Yes ☐

If yes specify: (a) Quantity [packs]: _____ (b) Total Duration in year's_____

27. Tobacco No ☐ Yes ☐

If yes specify: (a) Quantity: _____ (b) Total Duration in years_____

28. Alcohol No ☐ Yes ☐

If yes specify: (a) Quantity (in ml/day):_____ (b) Total Duration in years_____

29. Any other(specify)_____

Physical Examination

30. Built: lean medium heavy

31. Height (cm) _____

32. Weight _____kg Pulse _____/min

33. Blood Pressure (in sitting position)

Systolic _____mm of Hg

Diastolic _____mm of Hg

34. Body temperature _____ ^{o} Fh

35. Respiration rate _____ /min

Systemic examination

	Absent (0)	Present (1)
36. CVS	☐	☐
If abnormal, details _____		
_____		
37. CNS	☐	☐
If abnormal, details _____		
_____		
38. Digestive system	☐	☐
If abnormal, details _____		
_____		
39. Uro-Genital system	☐	☐
If abnormal, details _____		
_____		
40. Respiratory system	☐	☐
If abnormal, details _____		

Dasa vidha pareeksha

Dooshyam	Desam
Balam	Kalam
Analam	Prakruthy
Vaya	Satwam
Satmyam	Aaharam

Ashtasthana pareeksha

Nadi	Muthra	Mala	Jihwa	Sabdha
Sparsha	Drik	Akrity		

Subjective Assessments related to Rheumatoid Arthritis

GALS screening test

1. Do you have any stiffness or pain in your back
   or any muscles or joints? Yes/No
2. Can you dress yourself without any problem? Yes/No
3. Can you walk up and down stairs without problem? Yes/No

	Appearance	Movement
Gait		
Arms		
Legs		
Spine		

1. Duration of morning stiffness ……hrs
2. Number of joint affected
   Small joints…… Large Joints……
3. Swelling present in number of joints
   Small joints…… Large Joints……
4. Pain present in number of joints
   Small joints…… Large Joints……

Item	Before	After
1		
2		
3		
4		
5		

5. Power of muscles

In Upper limb Triceps **L**……**R**…… biceps **L**……**R**……

In lower limb quadriceps femoris **L**…..**R**….. hamstring muscles **L** …**R**

Gastrocnemius **L**……**R**…… soleus **L** …**R**

Hand grip using Hand dynamometer in kg

BT_____ AT____

muscles	Before		After			
	Left	Right	Left	Right		
Triceps						
biceps						
quadriceps femoris						
hamstring muscles						
Gastrocnemius						
soleus					Before	After
Hand grip						

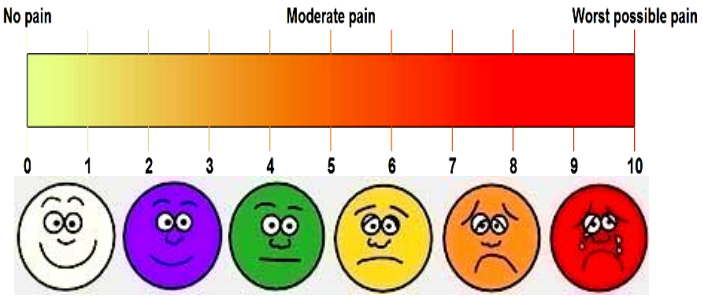
Annexure II

AMA ASSESSMENT TOOL

No.	Symptoms	BT	AT 15th day	FU 30th day
1	Constipation			
2	Heaviness of body			
3	Loss of taste			
4	Loss of appetite			
5	Loss of thirst			
6	Bad belching			
7	Pain (Joint pain)			
8	Lack of enthusiasm (Utsah)			
9	Lethargy (tandra)			
	Total			

Annexure III

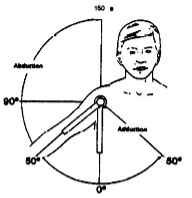
VISUAL ANALOGUE SCALE

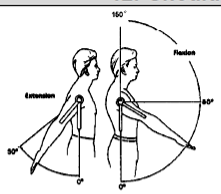


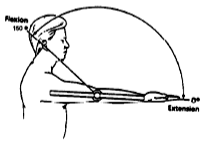
Before	After

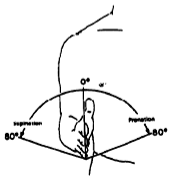
Annexure IV

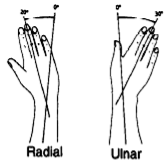
RANGE OF JOINT MOVEMENT

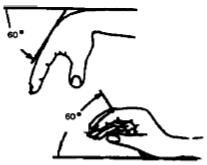
11. Shoulder (Abduction – Adduction)		
	Left	
	Abduction 150^{O}	Adduction 30^{O}
	Degrees	Degrees
	Right	
	Abduction 150^{O}	Adduction 30^{O}
	Degrees	Degrees

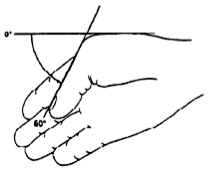
12. Shoulder (Flexion – Extension)		
	Left	
	Extension 50^{O}	Flexion 150^{O}
	Degrees	Degrees
	Right	
	Extension 50^{O}	Flexion 150^{O}
	Degrees	Degrees

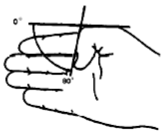
13. Elbow		
	Left	
	Extension 0^{O}	Flexion 150^{O}
	Degrees	Degrees
	Right	
	Extension 0^{O}	Flexion 150^{O}
	Degrees	Degrees

14. Forearm (Pronation – Supination)		
	Left	
	Pronation 80^{O}	Supination 80^{O}
	Degrees	Degrees
	Right	
	Pronation 80^{O}	Supination 80^{O}
	Degrees	Degrees

	Left	
	Radial 20^{O}	Ulnar 30^{O}
	Degrees	Degrees
	Right	
	Radial 20^{O}	Ulnar 30^{O}
	Degrees	Degrees

	Left	
	Extension 60^{O}	Flexion 60^{O}
	Degrees	Degrees
	Right	
	Extension 60^{O}	Flexion 60^{O}
	Degrees	Degrees

19. Thumb (MP Joint)		
	Left	Right
	Flexion 60^{O}	Flexion 60^{O}
	Degrees	Degrees

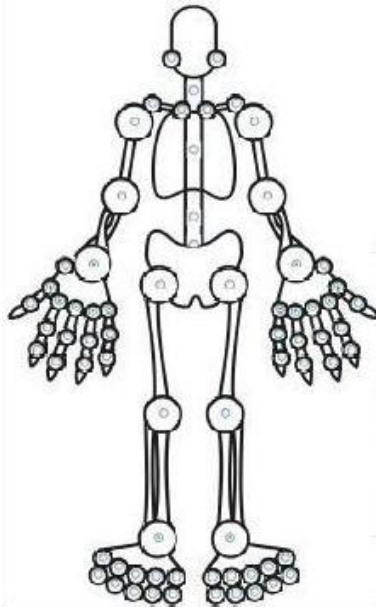
20. Thumb (IP Joint)		
	Left	Right
	Flexion 80^{O}	Flexion 80^{O}
	Degrees	Degrees

10. Knee (flexion)		
	Left 150^{O}	Right 150^{O}
	Degrees	Degrees
		

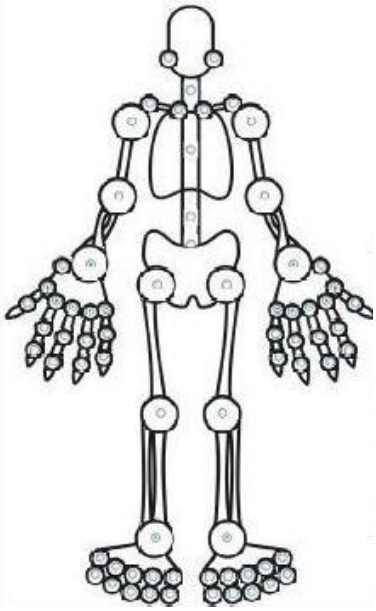
Annexure V

DAS28 form

Swollen



Tender



		Left		Right	
		Swollen	**Tender**	**Swollen**	**Tender**
Shoulder					
Elbow					
Wrist					
MCP	1				
	2				
	3				
	4				
	5				
PIP	1				
	2				
	3				
	4				
	5				
Knee					
Subtotal					
Total		Swollen		Tender	

How active was your arthritis during the past week?

(Please mark the degree of activity on the scale below by placing a vertical line |)

Not active at all **Extremely active**

0 10

Swollen Joint Count (0-28)	
Tender Joint Count (0-28)	
ESR	
VAS disease activity (0-100mm)	

DAS28 = 0.56*√(t28) + 0.28*√(sw28) + 0.70*Ln(ESR) + 0.014*VAS

Annexure VI

VAIDYARATNAM AYURVEDA COLLEGE, OLLUR,TRISSUR

Name of the investigator Dr. P.V.Giri

Address Professor**,** Dpt. of Kayachikitsa
Vaidyaratnam Ayurveda College, Ollur, Thrissur.

INFORMED CONSENT

I, the undersigned do hereby give my full consent to participate in the clinical trial after understanding the objectives and nature of the study as described below, which as explained and understood by me in my own language.

This research titled "Assessment of Ama Pachana effect of Amrutottaram Kashayam in Rheumatoid Arthritis" is done as a part of PhD research in Ayurveda by the investigator under the guidance of Dr.T Nitin Madhav Kamat, Hon. Professor, Ayurved Mahavidyalaya, Sion, Mumbai.

The study helps to know the efficacy of Amrutottaram kwatha in Rheumatoid Arthritis. There is no expense on the part of the participant, nor will any remuneration paid.

1 The information collected will be strictly confidential. The result will not be analyzed or presented in a way that can lead to identification of any individual.
2 The participation is voluntary and the subject is free to refuse to take part in this study or withdraw from the study at any time.
3 The signature of the person in this form indicates that he/she has understood to his/her satisfaction the information regarding participation in this research project and agree to undergo the specific clinical investigation/laboratory investigations.

Signature of the investigator Signature of the patient

Place

Date

Annexure VII

വൈദ്യരത്നം ആയുർവേദ കോളേജ് ഒല്ലൂർ, തൃശൂർ

സമ്മതപത്രം

താഴെ ഒപ്പിട്ടിരിക്കുന്ന ഞാൻ സർവ്വാത്മനാ "റുമാറ്റോയിഡ് ആർത്രൈറ്റിസ് (വാതരക്തം) എന്ന രോഗത്തിൽ നടത്തുന്ന ഗവേഷണത്തിൽ പങ്കെടുക്കാൻ സന്നദ്ധനാണ്. റുമാറ്റോയിഡ് ആർത്രൈറ്റിസിന് (വാതരക്തം) അമൃതാദ്യതരം കഷായം ഉപയോഗിക്കുന്നതിന്റെ ഫലസിദ്ധി" എന്ന വിഷയത്തിലെ ഗവേഷണത്തിന്റെ ഉദ്ദേശശുദ്ധി ഞാൻ മനസ്സിലാക്കുന്നു. പി.എച്ച്.ഡി. ഗവേഷണത്തിന്റെ ഭാഗമായ ഡോ. നിതിൻ മാധവ കമ്മത്ത്, ഓണററി പ്രൊഫസർ, കായചികിത്സ വിഭാഗം, സിയോൺ മുംബൈ എന്ന ഗൈഡിന്റെ മേൽനോട്ടത്തിൽ ഗവേഷകൻ നടത്തുന്ന ഗവേഷണമാണ്.

1. ഈ ഗവേഷണം റുമാറ്റോയിഡ് ആർത്രൈറ്റിസ് (വാതരക്തം) തക്കതായ ചികിത്സ യഥാകാലം നടത്തി റുമാറ്റോയിഡ് ആർത്രൈറ്റിസ് (വാതരക്തം) എത്രത്തോളം നിയന്ത്രിക്കുന്നു എന്ന് പരിശോധിക്കുന്നതിന് സഹായിക്കുന്നു.

2. ഗവേഷണത്തിൽ പങ്കെടുക്കുന്നത് കൊണ്ടുള്ള ഗുണങ്ങൾ രോഗത്തിന് ശമനവും ഗവേഷണത്തിന്റെ ഫലമായി ഉണ്ടാകുന്ന കണ്ടെത്തലുകൾ സമൂഹത്തിന് ഭാവിയിൽ പ്രയോജനപ്പെടുന്നു എന്നുമാണ്.

3. ഇതിൽ ഉപയോഗിക്കുന്ന മരുന്നുകൾ കാലങ്ങളായി ഉപയോഗിച്ച് ഇതിന്റെ ഫലപ്രാപ്തിയെ സംബന്ധിച്ച് വ്യക്തത ലഭിച്ചിട്ടുണ്ട്. ഏതെങ്കിലും തരത്തിലുള്ള പ്രതികൂലഫലങ്ങൾ ഉണ്ടായാൽ തക്കതായ പ്രതിവിധി ഉറപ്പുവരുത്തുന്നതിന് ഡോക്ടർ ബാധ്യസ്ഥനാണ്.

4. ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നവർക്ക് യാതൊരുവിധ ചെലവുകളും വരുന്നതല്ല. കൂടാതെ അവർക്ക് പ്രതിഫലം ലഭിക്കുന്നതല്ല.

5. ഈ രോഗാവസ്ഥയെകുറിച്ച് മനസ്സിലാക്കുന്നതിന് വേണ്ടി ലബോറട്ടറി പരിശോധനകൾ ആവശ്യമാണ് എന്നും അതിന്റെ പരിശോധനഫലം ഉത്തരവാദപ്പെട്ട സ്ഥാപനത്തിൽ നിന്നും ലഭിക്കുന്നതാണെന്നും എനിക്കറിയാവുന്നതാണ്.

6. സ്വമനസ്സാലെ ഈ പഠനത്തിന് പങ്കെടുക്കണം. അതുപോലെ ഏതു സമയത്തും ഈ പഠനത്തിൽ നിന്ന് വിട്ടുനിൽക്കാനുള്ള സ്വാതന്ത്ര്യവുമുണ്ട്.

7. ചികിത്സക്കിടയിൽ എനിക്ക് എന്തെങ്കിലും ബുദ്ധിമുട്ടുണ്ടാകുന്ന പക്ഷം ആരെയാണ് ബന്ധപ്പെടേണ്ടതെന്നും ഡോക്ടർ എനിക്ക് പറഞ്ഞുതന്നിട്ടുണ്ട്.

8. ശേഖരിക്കുന്ന വിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുന്നതാണ് വ്യക്തികളെ തിരിച്ചറിയുന്ന വിധത്തിൽ മാറ്റാരുടെയും മുമ്പിൽ പ്രദർശിപ്പിക്കുന്നതുമല്ല എന്നതും എനിക്കറിയാവുന്നതാണ്.

9. ഈ സമ്മതപത്രത്തിലെ ഒപ്പുകൊണ്ട് മനസ്സിലാക്കേണ്ടത്, പൂർണ്ണസംതൃപ്തിയോടെ ഈ ഗവേഷണത്തിനും അതിനുള്ള പ്രത്യേക പരിശോധനകളിൽ പങ്കെടുപ്പിക്കാനുമുള്ള പരിപൂർണ്ണ സമ്മതമാണ്.

ഗവേഷകന്റെ ഒപ്പ് : ഒപ്പ്

Annexure VIII

TNMC Prakriti 2004 Questionnaire

Date: **Prakriti**

Name: _____Age: Sex: Birth date:_____Actual birthplace: _____Place of intra-uterine life

Height: _____ cms. Weight: _____kg. Body Mass Index: _____ Occupation: _____

Address:

	Vata	*Pitta*	*Kapha*
Total points			

No.	Character	*Vata*	*Pitta*	*Kapha*
1.	Body frame	Lean long	Medium	Large, plump, fleshy, fatty
2.	Body Mass Index	< 19	19-25	> 25
	Speech			
3.	Speed	Fast	Fast	Slow
4.	Clarity	Diffuse words	Clear	Clear
5.	Character	Easily deviates from the topic, more talkative	Impressive speaker	Less talkative, likes to be reserved
	Eyes			
6.	Colour- Sclera	Blackish	Reddish, brown	Milky white Edges- reddish
	Lips			
7.	Character	Cracked, shapeless	Smooth, soft, thin	Smooth, glossy, Proportionate
8.	Colour	Blackish	Reddish	Pinkish
	Nails			
9.	Character	Small, Cracking, breaking, rough, easily break	Small, smooth &flat	Big, smooth, glossy
10.	Colour	Blackish	Reddish	Pinkish
	Hair			
11.	Texture	Rough & Dry	Soft & Delicate	Soft & Shiny
12.	Colour	Black	Gray/ Brown	Black
13.	Thickness	Less	Medium	More
	Skin			
14.	Character	Cracking, rough	Soft, oily, with moles, pimples, freckles	Smooth, glossy
15.	Colour	Blackish tinge	Yellowish tinge	Fair, pinkish
16.	Temperature	Cold	Warm	Cold
17.	**Body odor**	Absent	Present	Absent
	Appetite			
18.	Frequency of eating Quantity at meal	More	More	Less
19.	Habit	Less	More	More
20.	If meal is skipped/ meal timings are	Irregular	Profound	Not much
21.	changed/ style of food is changed	Constipation	Headache/vomiting	Nothing special
22.	**Thirst**	Irregular	More	Less
	Stool			
23.	Habit	Irregular	Regular	Regular
24.	Consistency	Hard	Semi-solid	Well-formed
25.	Colour	Blackish	Yellowish	Yellowish

	Sleep			
26.	Character	Interrupted, less	Uninterrupted, less	Sound, profound
27.	Duration	6 hours	6-8 hours	8 hours or more than 8 hours
28.	**Excitement**	Quickly, cools down quickly	Quickly, does not cool down quickly	Rarely
29.	**Working style**	Quickly	Medium	Slowly
30.	**Other movements**	Fast, unnecessary	Fast, precise	Slow steady

31.	**Strength**	Less, feel exhausted after doing some work	Medium, moderately gets tired	Good, do not feel tired
32.	**Style of tackling problem**	Worrying continuously without expressing	Losing self control, becoming angry/ irritated	With cool and stable mind
33.	**Control on desires**	Hardly, doesn't work hard for the same	Cannot, work hard, achieve it	Can control easily
34.	**Concentration on work**	Lack of concentration	Can concentrate on thing of interest	Can easily concentrate
	Cognition Process			
35.	Grasping	Quick, poor	Quick, good	Delayed
36.	Store	Poor	Average	Good
37.	Memory	Less	Average	Good

Annexure IX

റുമാറ്റോയിഡ് ആർത്രൈറ്റിസിൽ ആയുർവേദ മരുന്നായ അമൃതൊത്തരം കഷായം ഉപയോഗിക്കുന്നതിനെക്കുറിച്ചുള്ള ലഘുലേഖ

- സന്ധിരോഗങ്ങളിൽ സാധാരണയായി കണ്ടുവരുന്ന രോഗമാണ് റുമാറ്റോയിഡ് ആർത്രൈറ്റിസ് അഥവാ ആർ എ. പ്രതിരോധ വ്യവസ്ഥ (ശരീരത്തിന്റെ പ്രതിരോധ സംവിധാനം) ശരിയായി പ്രവർത്തിക്കുന്നില്ലെങ്കിൽ ഇത് സംഭവിക്കുന്നു.
- ആർ എ കൈകളിലും കാലുളിലും വേദനയും ഉണ്ടാക്കുന്നു. വിശപ്പില്ലായ്മ, മടി, ക്ഷീണം, ഉറക്കകുറവ് ഇവയൊക്കെയും ഇതിന്റെ ലക്ഷണമാണ്
- ആർഎയുടെ ആദ്യകാല ചികിത്സ മെച്ചപ്പെട്ട ദീർഘകാല ഫലങ്ങൾ നൽകുന്നു.
- ചെറിയതോതില് ഉള്ള വ്യായാമങ്ങൾ പേശികളുടെ ശക്തി വർദ്ധിപ്പിക്കും. ഇത് നിങ്ങളുടെ മൊത്തം ആരോഗ്യം, മെച്ചപ്പെടുത്തും. ഇത് ഡോക്ടറുടെ ഉപദേശപ്രകാരം മാത്രം ചെയ്യുക.
- ആർഎ എന്ന രോഗത്തിൻറെ ആദ്യകാല ചികിത്സ ലഭിക്കുന്നവർ കൂടുതൽ വേഗത്തിൽ കൂടുതൽ സജീവമായ ഒരു ജീവിതം നയിക്കാൻ കൂടുതൽ സാധ്യതയുണ്ടെന്ന് പഠനങ്ങൾ കാണിക്കുന്നു.
- ഇത് ഒരു തുടർചികിത്സ വേണ്ട ഒരു രോഗമാണ്.
- ഒരു വാതരോഗ വിദഗ്ദ്ധന്റെ സഹായം ലഭിക്കുന്നത് പ്രധാനമാണ്. അനാവശ്യമായ ടെസ്റ്റിംഗ് ഇല്ലാതെ കൃത്യമായ രോഗനിർണയം ലഭിക്കുന്നത് പ്രധാനമാണ്. നിങ്ങളുടെ രോഗത്തിനു മികച്ച ഒരു ചികിത്സ പ്ലാൻ കണ്ടെത്താൻ ഒരു വാതരോഗ വിദഗ്ദ്ധൻ സഹായിക്കും.
- ആയുർവേദ മരുന്നായ അമൃതൊത്തരം കഷായം ഉപയോഗിക്കുന്നത് രോഗലക്ഷണങ്ങള് കുറയാന് ഏറെ സഹായിക്കും. മറ്റു പാർശ്വഫലങ്ങള് ഒന്നും തന്നെ ഇല്ല.

കഷായം ഉണ്ടാക്കുന്ന വിധം

- ചെറിയ പാക്കറ്റില് ഉള്ള മരുന്ന് (48 ഗ്രാം), 768 ml വെള്ളത്തില് കഷായം വച്ച് 96 ml ആക്കി വറ്റിക്കുക. 6 ഗ്രാം പഞ്ചസാര ചേർത്ത് രാവിലെ (ആഹാരത്തിന് മുന്പ്) കഴിക്കുക.
- നിങ്ങളെ കാണിച്ചു തന്നതുപോലുള്ള അളവുപത്രങ്ങള് ഉപയോഗിക്കുക

Annexure X

AMA ASSESSMENT QUESTIONNAIRE

No.	Symptoms		
1	Do you suffer from constipation?	YES	NO
2	Do you suffer from heaviness of body?	YES	NO
3	Do you suffer from loss of taste?	YES	NO
4	Do you suffer from loss of appetite?	YES	NO
5	Do you suffer from loss of thirst?	YES	NO
6	Do you suffer from bad belching?	YES	NO
7	Do you suffer from pain?	YES	NO
8	Do you feel lack of enthusiasm?	YES	NO
9	Do you suffer from lethargy?	YES	NO

Annexure XI

SUBJECTIVE PARAMETERS OF PATIENTS

ID	Initials	Age	Gender	Morning stiff BT	Morning stiff AT	VAS BT	VAS AT	VAS FU	constipation BT	constipation AT	constipation FU	heaviness BT	heaviness AT	heaviness FU	Loss of taste BT	Loss of taste AT	Loss of taste FU	loss of appetite BT	loss of appetite BT	loss of appetite FU	loss of thirst BT	loss of thirst AT	loss of thirst FU	bad belching BT	bad belching AT	bad belching FU	pain BT	pain AT	pain FU	enthusiasm BT	enthusiasm AT	enthusiasm FU	letharg BT	letharg AT	letharg FU	TOTAL BT
1	c	60	2	3	3	8	8	8	0	0	0	1	0	0	1	0	0	1	0	0	1	1	0	0	0	0	1	1	1	1	0	1	1	1	1	**7**
2	v	57	2	8	6	8	4	7	0	0	0	1	0	0	1	0	0	1	0	0	1	1	0	0	0	0	1	0	1	1	1	0	1	0	0	**7**
3	a	56	2	3	3	7	4	6	0	0	0	1	0	0	0	0	0	0	0	0	1	1	1	1	0	0	1	0	1	1	1	0	1	0	0	**6**
4	y	50	2	2	1	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	1	1	1	1	0	0	1	0	1	1	0	0	1	1	0	**9**
5	a	40	2	6	5	8	8	8	1	0	0	1	0	0	1	0	0	1	0	1	1	1	1	0	0	0	1	1	1	0	0	0	1	0	0	**7**
6	b	44	2	4	3	6	3	5	1	0	0	1	0	0	0	0		1	0	0	1	1	1	0	0	0	1	0	0	1	1	1	0	0	0	**6**
7	l	40	2	3	3	5	2	4	1	0	0	1	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	0	0	1	0	0	1	1	1	**9**
8	t	29	2	3	3	7	3	6	1	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	1	0	0	1	0	0	1	1	0	**6**
9	g	46	2	3	3	6	3	5	0	0	0	1	0	0	1	0	0	1	0	0	1	1	1	0	0	0	1	0	1	1	1	1	1	0	1	**1**
10	b	60	2	7	6	9	9	8	0	0	0	1	1	1	1	0	0	1	0	0	0	0	1	0	0	0	1	1	0	1	1	1	0	0	0	**5**
11	v	50	2	3	3	7	3	7	1	1	0	1	1	0	1	0	0	1	0	1	0	0	1	0	0	0	1	0	1	1	1	1	1	1	1	**7**
12	b	59	2	4	3	8	4	7	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	1	**5**
13	b	52	2	2	2	7	7	7	1	0	1	1	0	0	0	0	0	0	0	0	1	1	1	1	0	1	1	1	1	1	0	0	1	0	1	**7**
14	a	54	2	4	3	7	4	5	1	0	0	1	0	0	1	0	0	1	0	0	1	1	1	0	0	0	1	0	1	1	0	1	1	1	1	**8**
15	l	48	2	4	4	5	2	4	0	0	0	1	0	0	1	0	0	1	0	0	1	1	1	0	0	1	1	0	0	1	1	0	1	0	0	**7**
16	v	57	1	3	3	7	3	6	1	0	0	0	0	0	1	0	0	1	0	0	1	1	1	0	0	0	1	0	1	1	0	1	1	1	1	**7**
17	d	48	2	3	3	6	3	6	1	0	1	1	0	0	0	0	0	0	0	0	1	1	1	1	0	1	1	0	1	1	0	0	1	1	1	**7**
18	v	58	2	3	3	9	6	8	1	0	1	1	0	0	1	0	1	1	0	1	1	1	1	0	0	0	1	0	0	1	1	0	1	0	1	**8**
19		57	2	3	3	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	1	1	1	1	0	1	1	1	1	1	0	0	1	0	1	**2**
20	y	29	2	3	3	8	4	8	1	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	1	1	0	1	1	0	0	1	1	0	**6**
21	a	60	2	4	3	7	4	6	1	0	1	1	0	0	1	0	0	1	0	1	1	1	1	0	0	0	1	0	0	0	1	0	0	0	0	**6**
22	b	52	2	3	3	7	4	6	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	**6**
23	l	52	2	3	2	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0	1	0	1	**6**
24	t	59	2	4	4	7	4	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	1	**6**
25	g	60	2	3	2	7	6	7	1	0	1	1	1	1	0	0	0	1	0	1	0	0	0	1	1	0	1	1	1	1	0	0	1	1	1	**7**
26	b	57	2	2	2	6	6	5	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	**7**
27	v	36	2	4	3	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	1	0	1	0	1	1	0	0	1	1	0	**8**
28	b	59	2	3	3	6	3	5	1	0	0	1	0	0	1	0	0	1	0	1	0	0	0	1	1	0	1	1	1	0	0	0	1	0	0	**7**
29	b	58	2	2	2	9	9	8	1	0	0	1	0	0	0	0		1	0	0	0	0	0	1	1	0	1	0	0	1	1	1	0	0	0	**6**

ID	Initials	Age	Gender	Morning stiff BT	Morning stiff AT	VAS BT	VAS AT	VAS FU	constipation BT	constipation AT	constipation FU	heaviness BT	heaviness AT	heaviness FU	Loss of taste BT	Loss of taste AT	Loss of taste FU	loss of appetite BT	loss of appetite BT	loss of appetite FU	loss of thirst BT	loss of thirst AT	loss of thirst FU	bad belching BT	bad belching AT	bad belching FU	pain BT	pain AT	pain FU	enthusiasm BT	enthusiasm AT	enthusiasm FU	letharg BT	letharg AT	letharg FU	TOTAL BT
30	a	36	2	3	2	7	3	7	1	0	0	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	0	0	1	0	0	1	1	1	**9**
31	l	47	2	3	3	8	4	7	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	1	1	0	0	1	0	0	1	1	0	**6**
32	v	55	2	3	3	7	7	7	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	1	0	1	0	1	1	1	1	1	0	1	**8**
33	d	59	2	3	2	7	4	5	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0	1	1	0	1	1	0	1	1	1	0	0	0	**6**
34	v	52	1	3	3	5	2	4	1	1	0	1	1	0	1	0	0	1	0	1	0	0	0	1	1	0	1	0	1	1	1	1	1	1	1	**8**
35	l	40	2	4	3	7	3	6	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	1	1	0	1	0	1	0	0	0	1	0	1	**6**
36	t	36	1	3	3	6	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	0	0	1	0	1	**6**
37	g	49	1	3	3	9	6	8	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
38	b	54	2	4	4	7	3	6	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
39	v	50	2	3	3	8	4	8	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
40	b	50	1	2	2	7	4	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	0	1	**6**
41	b	45	2	4	3	7	4	6	1	0	1	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0	1	0	0	1	1	0	1	0	1	**7**
42	a	46	1	3	3	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
43	l	55	2	2	2	7	4	6	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	1	1	0	**5**
44	v	52	1	2	2	7	6	7	1	0	1	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	**5**
45	l	50	2	3	3	6	6	5	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	**6**
46	t	55	2	2	2	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0	1	0	1	**6**
47	g	44	2	4	4	7	4	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	1	**6**
48	b	51	2	3	3	7	6	7	1	0	1	1	1	1	0	0	0	1	0	1	0	0	0	0	0	0	1	1	1	1	0	0	1	1	1	**6**
49	v	30	2	2	2	6	6	5	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	**7**
50	b	50	1	4	4	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
51	b	40	1	3	3	6	3	5	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
52	a	38	1	2	2	9	9	8	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
53	l	45	2	2	2	7	3	7	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0	1	0	1	**6**
54	v	48	1	3	3	7	4	6	1	0	1	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0	1	0	0	1	1	0	1	0	1	**7**
55	v	59	1	3	3	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
56	b	56	2	2	2	7	4	6	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	1	1	0	**5**
57	b	54	2	4	4	7	6	7	1	0	1	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	**5**
58	a	48	1	3	3	6	6	5	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	**6**

ID	Initials	Age	Gender	Morning stiff BT	Morning stiff AT	VAS BT	VAS AT	VAS FU	constipation BT	constipation AT	constipation FU	heaviness BT	heaviness AT	heaviness FU	Loss of taste BT	Loss of taste AT	Loss of taste FU	loss of appetite BT	loss of appetite BT	loss of appetite FU	loss of thirst BT	loss of thirst AT	loss of thirst FU	bad belching BT	bad belching AT	bad belching FU	pain BT	pain AT	pain FU	enthusiasm BT	enthusiasm AT	enthusiasm FU	letharg BT	letharg AT	letharg FU	TOTAL BT
59	l	32	1	2	2	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0	1	0	1	**6**
60	v	60	1	3	2	7	4	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	1	**6**
61		54	2	3	3	7	6	7	1	0	1	1	1	1	0	0	0	1	0	1	0	0	0	0	0	0	1	1	1	1	0	0	1	1	1	**6**
62	v	50	2	3	3	6	6	5	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	**7**
63	b	44	2	2	2	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	1	1	0	0	1	1	0	**8**
64	b	32	2	2	2	9	9	8	1	0	0	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	0	**6**
65	a	35	1	3	3	7	3	7	1	0	0	1	0	0	0	0		1	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	0	**5**
66	l	59	2	2	2	8	4	7	1	0	0	1	1	1	1	1	1	1	0	1	1	0	1	1	0	1	1	0	0	1	0	0	1	1	1	**9**
67	v	47	2	4	4	7	7	7	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	1	1	0	**5**
68	v	34	2	3	3	7	4	5	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	1	0	1	**7**
2	b	29	2	2	2	5	2	4	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0	0	0	0	1	1	0	1	1	1	0	0	0	**5**
70	b	58	1	4	4	7	3	6	1	1	0	1	1	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	1	1	1	1	1	1	1	**7**
71	a	32	2	3	3	7	4	6	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	1	**5**
72	l	60	1	2	2	7	6	7	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
73	v	54	2	2	2	6	6	5	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
74		58	2	3	3	7	3	6	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
75	v	31	2	3	3	7	4	6	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
76	b	46	2	2	2	7	6	7	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	1	**6**
77	b	50	2	4	4	6	6	5	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	1	**5**
78	a	56	2	3	4	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
79	l	44	1	2	2	9	9	8	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
80	v	42	1	3	3	7	3	7	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
81	v	29	1	3	3	7	6	7	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
82	b	53	2	3	3	6	6	5	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	0	1	**6**
83	b	32	2	2	3	7	3	6	1	0	1	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0	1	0	0	1	1	0	1	0	1	**7**
84	a	43	2	2	2	6	3	5	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
85	l	45	2	3	3	9	9	8	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	1	1	0	**5**
86	v	52	2	2	2	7	3	7	1	0	1	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	**5**
87		53	2	4	4	7	4	6	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	**6**

ID	Initials	Age	Gender	Morning stiff BT	Morning stiff AT	VAS BT	VAS AT	VAS FU	constipation BT	constipation AT	constipation FU	heaviness BT	heaviness AT	heaviness FU	Loss of taste BT	Loss of taste AT	Loss of taste FU	loss of appetite BT	loss of appetite BT	loss of appetite FU	loss of thirst BT	loss of thirst AT	loss of thirst FU	bad belching BT	bad belching AT	bad belching FU	pain BT	pain AT	pain FU	enthusiasm BT	enthusiasm AT	enthusiasm FU	letharg BT	letharg AT	letharg FU	TOTAL BT
88	v	60	2	3	3	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	0	1	0	1	**6**
89	b	60	1	2	2	7	4	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	1	**6**
90	b	57	1	4	4	7	6	7	1	0	1	1	1	1	0	0	0	1	0	1	0	0	0	0	0	0	1	1	1	1	0	0	1	1	1	**6**
91	a	56	2	3	3	6	6	5	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	**7**
92	l	35	2	2	2	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
93	v	53	2	2	2	7	6	7	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
94	v	51	2	3	3	6	6	5	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
95	b	41	2	3	3	7	3	6	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
96	b	47	2	2	2	6	3	5	1	0	1	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0	1	0	0	1	1	0	1	0	1	**7**
97	a	53	2	4	4	9	9	8	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
98	l	52	2	4	4	7	3	7	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	1	1	0	**5**
99	v	53	2	3	2	7	4	6	1	0	1	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	**5**
100	l	43	2	3	3	7	3	6	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	1	**6**
101	v	50	2	3	3	7	4	6	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	**7**
102	v	52	2	2	2	7	6	7	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	1	1	0	0	1	1	0	**8**
103	b	42	2	2	2	6	6	5	1	0	0	1	0	0	1	0	0	1	0	1	0	0	0	0	0	0	1	1	1	0	0	0	1	0	0	**6**
104	b	57	2	3	3	7	3	6	1	0	0	1	0	0	0	0		1	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	0	**5**
105	a	60	2	3	3	9	9	8	1	0	0	1	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	0	1	0	0	1	1	1	**9**
106	l	52	2	2	2	7	3	7	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	1	1	0	**5**
107	l	53	2	4	4	7	4	6	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	1	0	1	1	1	1	1	0	1	**7**
108	v	29	2	2	1	7	3	6	0	0	0	1	1	1	1	0	0	1	0	0	0	0	0	0	0	0	1	1	0	1	1	1	0	0	0	**5**
109	v	40	1	3	3	7	4	6	1	1	0	1	1	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	1	1	1	1	1	1	1	**7**
110	b	47	2	2	2	7	6	7	1	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	1	**5**
111	b	44	2	3	3	6	6	5	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	0	0	1	0	1	**6**
112	a	34	2	2	2	7	3	6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**7**
113	l	51	1	3	3	7	6	7	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	1	0	0	1	1	0	1	0	0	**7**
114	m	53	2	3	3	6	6	5	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	1	1	**6**
115	p	46	2	2	2	6	5	5	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	0	1	**6**

VAIDYARATNAM AYURVEDA COLLEGE

Thaikkattussery PO, Ollur, Thrissur

ETHICAL CLEARANCE CERTIFICATE

Ref No. IEC - 30/4/16 – 5/ECC 02.05.2016

To

Dr. P.V.Giri
PhD Scholar

Supervisor: Dr. Nitin Madhav Kamat

Dear investigator,

The Institutional Ethics Committee, in its meeting held on 30.04.2016 at this institution reviewed and discussed in detail about your research project titled:

'Assessment of ama pachana effect of *Amrutottaram kashayam* in Rheumatoid arthritis'.

The IEC suggested a few modifications related to ethical issues, and subject to your undertaking in writing that these will be incorporated; the project is now approved by the IEC for implementation at Vaidyaratnam Ayurveda College.

It will be your responsibility to keep the IEC informed of the progress of the study. Any modification in the protocol and informed consent format shall be done only after prior approval of the IEC. On completion of the project, a copy of the final report shall be submitted to the IEC. In case the project is discontinued/abandoned, the matter shall be duly reported to the Secretary in writing.

Yours sincerely

Dr. T.Sreekumar,
Secretary
Institutional Ethics Committee
Vaidyaratnam Ayurveda College,
Ollur, Thrissur

Member Secretary
Institutional Ethics Committee
VAC, Ollur, Thrissur.

Dr.K.C.Chacko
Chairperson
Institutional Ethics Committee
Vaidyaratnam Ayurveda College,
Ollur, Thrissur

Dr. K. C. Chacko
Konnath House
St. Paul's Lane, Lourdpuram
Thrissur East - 680 005
Phone : 9447618335

VAIDYARATNAM
OUSHADHASALA PVT. LTD.

To,

Dr. P.V GIRI, MD (Ay), MHA
Professor,Dept. Of Kayachikitsa
Vaidyaratnam Ayurveda College
Thaikkattussery (P.O),Ollur, Thrissur

Sub: Amruthotharam Kashaya Choornam for clinical trials at Vaidyaratnam Ayurveda College Hospital - Clinical Programe of Dr. P.V Giri.,MD (Ay), MHA ,Professor, Dept. Of Kayachikitsa, Vaidyaratnam Ayurveda College, Thaikkattussery (P.O),Ollur, Thrissur

The Amruthotharam Kashaya Choornam (500 Gm * 200 Packets, ie, 100Kg) Batch No: 16A1644 was prepaired as a single lot as per the request from Dr. P.V Giri.

Yours Faithfully,

06/08/16
Dr. Manoj P.S
Manager production