

Clinical Evaluation of Coded Drugs UNIM-304, UNIM-312 along with Munzij (UNIM-308), Mushil (UNIM-309) and Tabreed (UNIM-310) Therapy with Cupping in Waja-ul-Mafasil (Rheumatoid arthritis)

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Abstract

The study was carried out in a total number of 65 patients of Waja-ul-Mafasil of either sex satisfying the criteria of American Rheumatism association. All the patients received treatment with coded Unani drugs UNIM-312 along-with local application of UNIM-304 for a period of 90 days after complete therapy of Munzij (UNIM-308), Mushil (UNIM-309) and Tabreed (UNIM-310) with Hijamah (cupping). Out of 65 cases 56 patients completed the study, 42 patients were sero-positive, 13 patients got complete remission, 35 patients got partially remission, 08 patients got no relief and 09 patients dropped out. No hepatotoxic and nephrotoxic side effects noticed during the course of study. The clinical and laboratory findings after treatment have shown that coded drugs possessed efficacy in the treatment of Waja-ul-Mafasil.

Keywords: Waja-ul-Mafasil, UNIM-304, UNIM-312, UNIM-308, UNIM-309, UNIM-310, Unani medicine.

Introduction

Unani System of Medicine is based on the theory of Akhlat (humours) and it is generally considered by Unani physicians that diseases are caused by impairment in these humours, accumulation of Insabab-e-Maadda (viscous matter) mostly. Waja-ul-Mafasil (Waja- means pain and Mafasil- means joints) also known as Hudar or Gathia is a disease in which joints become painful and swollen with reduction of their normal activity. On the basis of causative factors sue-mizaj saada and humours, it is of two types. (i) Saada (simple): Waja-ul-mafasil occurs due to sue-mizaj Saada (Derangement of temperament) i.e. temperament may be hot, cold, wet and dry. (ii) Maaddi (materialistic): It may be developed due to humoral disturbances i.e. Balgham, Safra, Sauda and Dam. It may be caused by single humour or may occur by conglomeration of two or more humours (Khan, 2003)

It is a condition of pain, swelling, tenderness and morning stiffness in the joints of hands, feet, knee and ankle joints. Maadda (substance) causing disease enters into the joints and it neither absorbed nor expels from them due to lack of Quawwat-e-Jazibah (power of absorption) and Quawwat-e-dafia (power of expulsion) in the joints and retained in the joints (Majoosi, 1889). According to the causative organism of the disease is Ajsam-e-Khabisa (Foul bodies). Depending upon the maadda affecting the joints, Balgham (Phlegm) predominate, Dam (Sanguine), Safra (Yellow bile) and Sauda (Black bile) are involved. In some cases more than one Khilt (Humour) is involved (Arzani, Y.N.M.).

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Four types of the disease have been described on the basis of the Khilt involved:

- (i) Damvi: Redness and swelling of the skin over the affected joints are visibly marked and the pain is severe. Other symptoms of Ghalba-e-dam (Blood dominance) are also present.
- (ii) Safravi: There is a slight yellow discoloration of the skin. Swelling is less than that of damvi type. Pain and burning sensation along with other symptoms of Galba-e-safra (Bile dominance) are also found.
- (iii) Balghami: Besides other symptoms of Ghalba-e-balgham (Phlegm dominance), skin color over the affected joint is whitish and swelling is less. The pain is deep seated and the patients are often obese.
- (iv) Saudavi: There is a hard swelling and dryness over the joint and the colour of overlying skin is blackish blue. Other symptoms of Ghalba-e-sauda (Black bile dominance) are also present.

When Maadda (Substance) is retained in the joints for a long period, its Ghilazat (Viscosity) and Lazoojat (Viscidty) are increased and it becomes hard, Tahajjur-e- Mafasil (Osteoarthritis) and the condition is incurable (Jurjani, 1903).

Rheumatoid arthritis is a systemic disease of unknown etiology characterized by a chronic proliferative and inflammatory reaction in the synovial membrane which eventually results in erosion and destruction of joints cartilage and supporting structure. Usually the pattern of joint involvement is characteristically symmetrical and its cause typically prolonged with the symptoms occasionally, however a typical, asymmetrical and incomplete forms do occur, confusing the diagnosis. It has a worldwide distribution and affects approximately 3% of population, mostly occurs above 30 years of age. Females are affected three times as frequently than males. Arthritis occurs throughout the world in all climates and among all ethnic groups; almost 16% of female and 5% of male population is affected. The disease commences most commonly in the third and fourth decades but no age group is exempted. Prevalence is higher in twins and first degree relatives but not in spouses, suggesting a weak genetic predisposition (Boon *et al.*, 2006).

In majority of patients, the onset of the disease is insidious with pain, Stiffness and symmetrical swelling of a number of small joints as well as major joints. Initially pain is experienced only on moving the affected joints. As the disease advances, pain, muscle spasm and progressive joint destruction results in the limitation of joint movements, joints stability and deformities. At first the deformities are correctable, but later permanent contracture develops and the joints may become completely disorganized (Harvey *et al.*, 1976).

Material and Method

Type of trial: An open-level clinical study

Research Methodology: Each participant well informed about the trial and written consent obtained before initiation of the study. Demographic data and information on the present disease condition, concomitant disease and therapy recorded. Thorough general physical and systemic clinical examination carried out. Signs and Symptoms pertaining to Rheumatoid arthritis recorded in CRF. The vital parameters like blood pressure, heart rate, temperature and respiratory rate also recorded. X-Ray of affected joints conducted and blood sample collected for the evaluation of laboratory parameters, Haemogram, CRP and RA factor to establish and confirm inclusion criteria and other laboratory test like CBP, KFT, LFT and Urine- Routine and microscopic examination done. All clinical and laboratory follow-up were done every 4 weeks.

Selection criteria

Inclusion criteria

- Patients of either sex.
- Patients in the age group of 15-70 years
- Systemically healthy individuals
- With Signs and symptoms of Rheumatoid Arthritis (pain, swelling, Tenderness, Morning stiffness, Loss of function).
- Patients fulfilling the ACR-EULAR criteria.

Exclusion criteria

- Patients below 15 and above 70 years
- Gout/Osteo-arthritis
- Rheumatoid Nodules or Deformity
- Obesity
- Pregnancy/lactating women
- Hypertension and other cardiovascular diseases
- Diabetes and other metabolic disorders
- Tuberculosis and other respiratory diseases
- Gastrointestinal disorders
- Renal/Hepatic impairment
- History of presence of malignancy
- History of alcohol and drug abuse
- Epilepsy and other neurological disorders

Subject selection

The patients of Waja-ul-mafasil attending O. P. D. of CRIUM, Lucknow selected for the study. A detailed clinical history taken and complete physical examination carried out to make the clinical diagnosis of Waja-ul-mafasil and laboratory investigations conducted to fulfill the ACR-EULAR criteria.

Investigation: All the patients were investigated for their routine haematology, LFT, KFT, R.A. Factor, C-Reactive protein (C.R.P.), Urine exam (Routine & microscopic) and Radiological examination of affected joints were also done.

Treatment schedule and drugs

Munzij and Mushil Therapy

Munzij (UNIM-308): Combination of ten single drugs soaked in water all over night and boiled in 200 ml. Water in the morning; decoction given orally on empty stomach up to Nuzj appears in the urine or maximum 20 days.

Mushil (UNIM-309): Combination of single drugs soaked in water all over night and boiled in 250 ml. Water, decoction given orally on empty stomach for 03 to 05 days as purgative on alternate days followed by Tabreed.

Tabreed (UNIM-310): 5 gm UNIM-310 for 03 to 05 days orally with water alternate days.

Cupping (Hijamah): Cupping applied on affected joints after Munzij, Mushil therapy and biweekly for 90 days.

UNIM-312: Two tablets (500 mgs. each) twice in a day, given orally with lukewarm water for 90 days after M. M. Therapy.

UNIM-304: Oil for local application on affected joints twice a day for 90 days.

Follow up of subject: Patients were followed up every 15 days to record change in symptoms and signs. Clinical follow up and investigations were performed at the base line, after M.M. Therapy and every 30 days gap and at the end of study. Follow up of relieved cases were performed after every three months for one year.

Safety assessment: The safety was assessed by monitoring adverse events when reported by the patients or elicited by the investigator by clinical as well as laboratory investigations before and after treatment. The laboratory tests included Haematological tests (Hb, TLC, DLC, ESR), Liver function test (Serum bilirubin, SGOT, SGPT and alkaline phosphatase) and Kidney function tests (Blood urea and serum creatinine).

Statistical data recording: Data recording was done on separate case sheet for each subject at base line, after M. M. Therapy and every follow up at 15 days up

to three months. Active and passive complaints of patients were recorded in grades starting from “+” to “+++” at the time of Base line and at different follow up. Percentage in grading was calculated and results were assessed in terms of complete remission (more than 70%), partially remission (50% to 70%), Poor remission (less than 50%).

Results and Discussion

Temperament and response

The data shows that out of 56 cases studied maximum 48 cases having Balghami temperament followed by 06 cases Saudavi, 01 Safravi and 01 Damvi case. As per temperament and response of the formulae concerned, it is more effective in Balghami temperament as out of 48 cases 08 cases got complete remission, 33 cases got partially remission and 07 got poor response. In Saudavi out of 06 cases, 04 cases got complete remission and 02 cases got partially remission. In Safravi only case got poor remission and Damvi temperament only case got complete remission as presented in table-1 and figure-1.

Table 1: Response according to Mizaj (Temperament)

Mizaj (Temperament)	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Balghami	08	33	07	48 (85.71)
Saudavi	04	02	-	06 (10.71)
Safravi	-	-	01	01 (01.79)
Damvi	01	-	-	01 (01.79)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

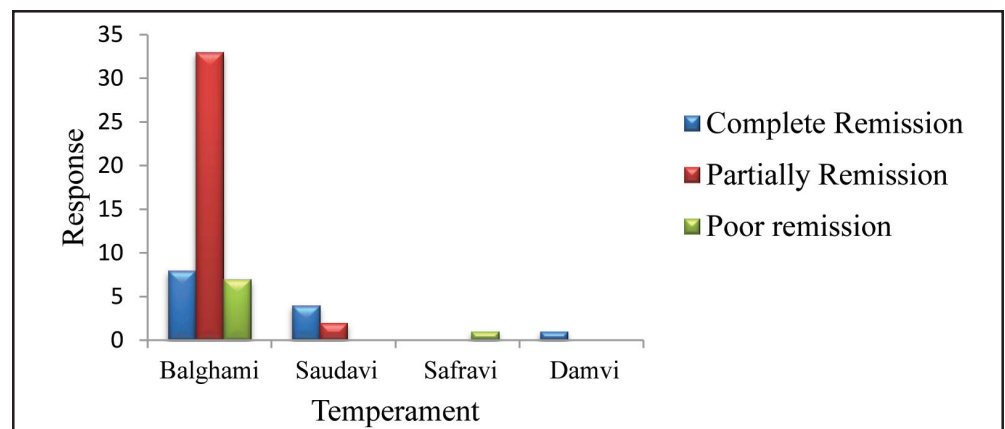


Figure 1: Response according to Mizaj

Chronicity and response

Study data shows that maximum cases were having chronicity up to 02 years, out of 26 cases 07 cases got complete remission, 16 cases got partially remission and 03 cases showed poor remission followed by 09 cases having chronicity 2-4 years, 05 cases 4-6 years, 07 cases 6-8 years, 04 cases 8-10 years and above 10 years 05 cases. As chronicity and response of the formulae concerned, it is effective in the cases having chronicity up to 04 years and 05 cases having above 10 years chronicity 01 case got complete remission, 03 cases got partially remission and 01 case got poor remission (Table 2 & Figure 2).

Table 2: Response according to chronicity of the disease

Chronicity	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Up to 02 year	07	16	03	26 (46.42)
02-04 year	02	06	01	09 (16.07)
04-06 year	-	03	02	05 (08.93)
06-08 year	02	05	-	07 (12.50)
08-10 year	01	02	01	04 (07.14)
Above 10 year	01	03	01	05 (08.93)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

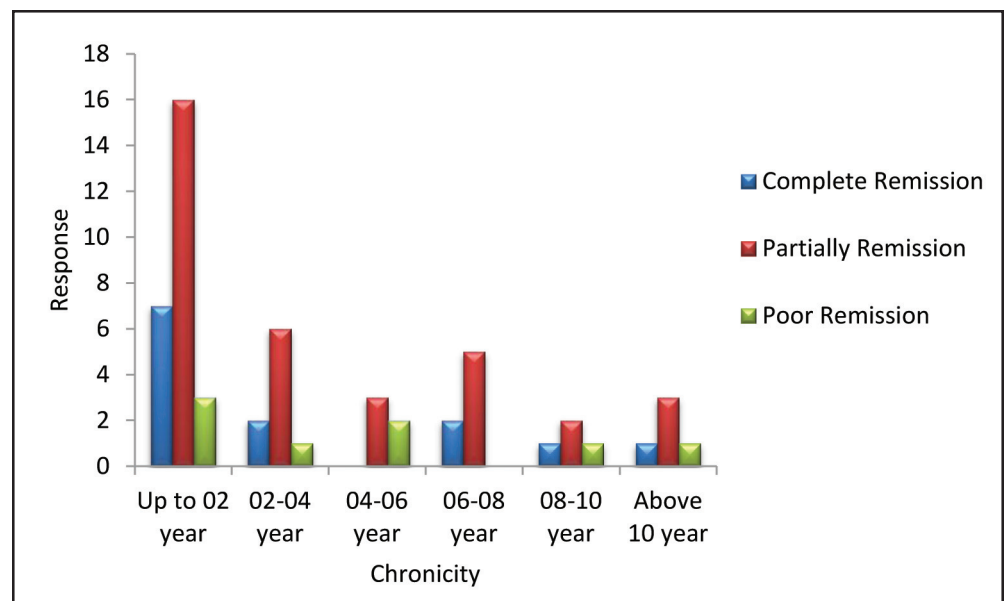


Figure 2: Response according to chronicity of the disease

Sex and response

In the table 3 and figure 3, the study shows that this disease is three times more common in females than males as out of 56 cases studied 47 were female and only 09 cases were males. As per response concerned, drug is somewhat equally effective in both the sexes, out of 47 females cases 08 cases got complete remission, 31 cases got partially remission and 8 cases got poor remission. While in 09 male's cases, 05 cases got complete remission and 04 cases got partial remission.

Table 3: Response according to sex of patients

Sex	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Male	05	04	-	09 (16.07)
Female	08	31	08	47 (83.93)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

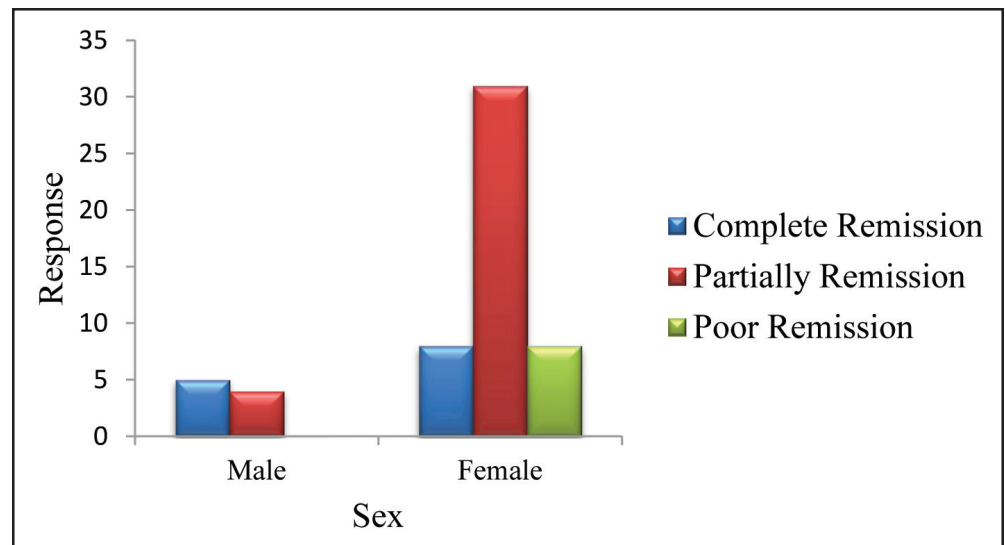


Figure 3: Response according to sex of patients

Dietary habits and response

Data projected from study also shows that it is equally common in non-vegetarian and vegetarian approximately; out of 56 cases studied 31 cases were vegetarian and 25 non-vegetarian. As per response concerned, good response recorded in both the types of habits, out of 31 vegetarian cases 07 got complete remission,

19 cases got partial remission and 05 cases got poor remission. Likewise 25 non-vegetarian cases, 06 cases got complete remission, 16 cases got partial remission and 03 cases got poor remission as presented in table 4 and figure 4.

Table 4: Response according to dietary habits

Dietary Habits	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Vegetarian	07	19	05	31 (55.36)
Non-vegetarian	06	16	03	25 (44.64)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

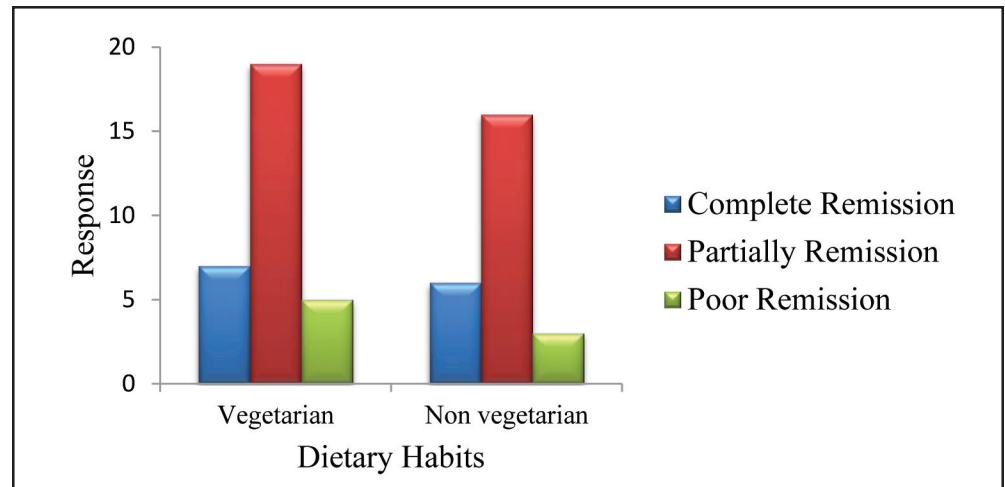


Figure 4: Response according to dietary habits

Social status and response

Study also shows that out of 56 cases, 28 cases from lower income group, followed by 22 cases from middle income group and only 06 cases from high income group. As per income group and response of the drug concerned, good response recorded in HIG as out of 06 cases, 02 cases got complete remission, 03 cases got partial remission and 01 case got poor remission. In MIG out 22 cases studied 05 cases got complete remission, 14 cases got partial remission and 03 cases got poor remission. In LIG group, out of 28 cases studied, 06 cases got complete remission, 18 cases got partial remission and 04 cases got poor remission (Table 5 & Figure 5).

Table 5: Response according to social status of patients

Social Status	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Lower Income Group	06	18	04	28 (50.00)
Middle Income Group	05	14	03	22 (39.28)
Higher Income Group	02	03	01	06 (10.72)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

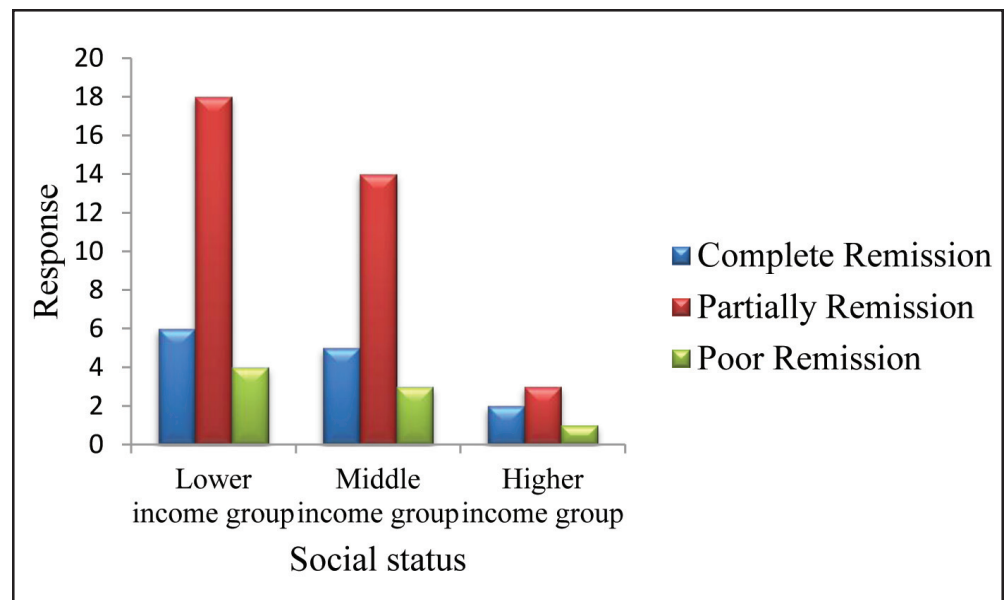


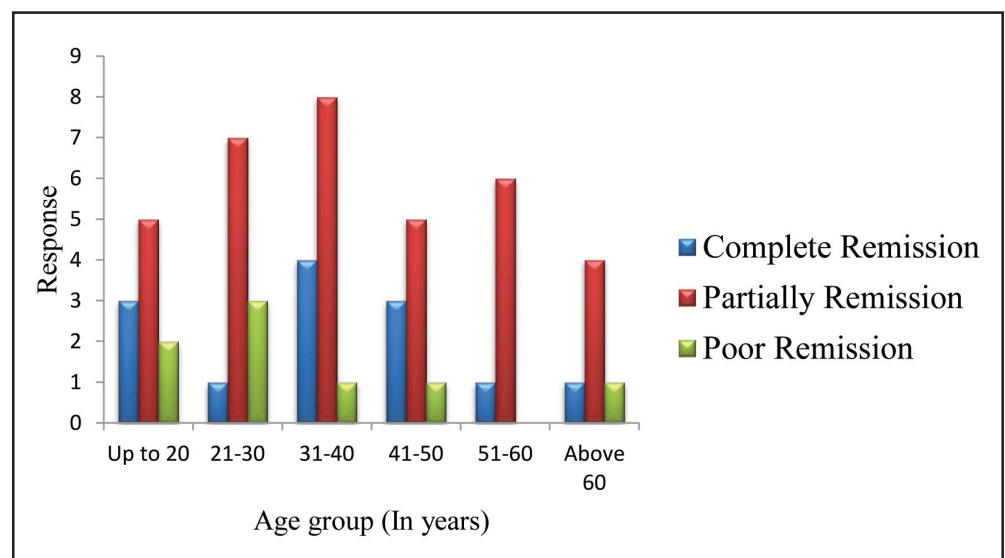
Figure 5: Response according to social status of patients

Age and Response

In the table 6 and figure 6, the study shows that this is very common in the age group of 21 to 40 years as out of 56 cases studied maximum 13 cases were belonging to 31-40 age, followed by 11 cases in the age group of 21-30 years. 07 cases were 51-60 years age group and 06 cases were above 60 years age. As per response is concerned, good response observed in the age group of 31-40 years as out of 13 cases belonging to this group 04 cases got complete remission, 08 cases got partial remission and 01 case got poor remission. In the age group of 31-40 years 04 cases got relived 06 cases were partial relived and 02cases got nil response.

Table 6: Response according to age group of patients

Age Group (In years)	Response			
	Complete Remission	Partially Remission	Poor Remission	Total (%)
Up to 20	03	05	02	10 (17.86)
21-30	01	07	03	11(19.64)
31-40	04	08	01	13 (23.21)
41-50	03	05	01	09 (16.08)
51-60	01	06	-	07 (12.50)
Above 60	01	04	01	06 (10.71)
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100.00)

**Figure 6:** Response according to age group of patients

Clinical signs and symptoms

Clinical signs and symptoms treated with these formulae with cupping, response in the swelling not change in large amount. Tenderness showed before treatment in 55 cases and 01 case had no tenderness and after treatment 07 cases got relieved from tenderness, 48 cases had tenderness and 01 case had no tenderness at before treatment. Pain showed in 56 cases before treatment, after treatment 37 cases got relieved in pain and 19 cases were not relieved pain. Early morning stiffness reduced after treatment, walking time also showed good response (Table 7).

Table 7: Clinical signs and symptoms

Signs and Symptoms	Unit of Measure	Statistics	Day of Examination	
			Before Treatment	After Treatment
Swelling	Inches	Mean \pm SD n=56	92.75 \pm 16.97	92.41 \pm 16.88
Tenderness	Positive	n=56	55	48
	Negative		01	08
Pain	Present	n=56	56	19
	Absent		00	37
Early morning stiffness	Minutes	Mean \pm SD n=56	70.36 \pm 23.25	34.90 \pm 25.00
Walking time	Seconds	Mean \pm SD n=56	30.36 \pm 15.08	25.09 \pm 15.41

Laboratory investigations

On admission 39 patients were R.A. Factor positive and 17 cases sero negative, in 42 cases C.R.P. was positive and 14 cases having C.R.P. negative, with raised/normal ESR, normal renal and liver function test were registered. After treatment level of ESR showed downwards trend and no change in R.A. Factor, slight change observed in C.R.P. positive cases, 03 cases become negative (Table 8).

Table 8: Laboratory investigations before and after treatments

Parameters	Measurement Unit	Statistics	Before Treatment	After Treatment
Hemoglobin	gm%	Mean \pm SD n=56	10.26 \pm 1.35	10.43 \pm 1.26
E.S.R.	mm/1 st hour	Mean \pm SD n=56	75.31 \pm 30.48	64.57 \pm 27.11
T.L.C.	/Cu mm	Mean \pm SD n=56	9157.41 \pm 1355.72	9248.15 \pm 1053.78
Serum Uric Acid	mg/dl	Mean \pm SD n=56	4.84 \pm 1.12	5.17 \pm 1.32
R.A. Factor C.R.P. Test	Positive	n=56	39	39
	Negative		17	17
	Positive		42	39
	Negative		14	17

Overall response

Overall response of patients, 56 subjects completed the study, out of 56 cases, 13 cases got complete remission, 35 cases got partially remission and 08 cases got poor remission. In the table 9 and figure 7.

Table 9: Showing response of the drugs

	Response			
	Complete Remission	Partially Remission	Poor Remission	
Total (%)	13 (23.21)	35 (62.50)	08 (14.29)	56 (100%)

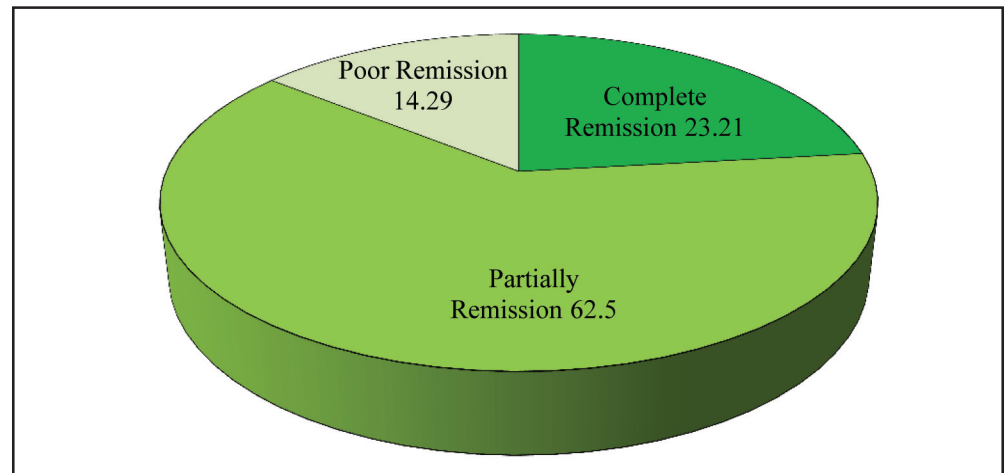


Figure 7: Showing response of the drugs

Conclusion

The study reveals that result of the Unani coded formulae effective, as out of 56 cases studied 13 cases got complete remission, 35 cases got partial remission and 08 cases got poor remission. The formulae reduced signs and symptoms like pain, tenderness, swelling, loss of functions and morning stiffness in uniform way. During the study blood investigations of each patient for haematology, LFT, KFT, R.A. Factor, C- reactive protein were done at base line, after MM therapy, every follow up and after completion of study. We found that there was no significant effect of formulae on RA factor after completion of study, however there was slight increased in Hb% and marked decline ESR in well responded cases. No toxicity and adverse effect of the drugs reported during the study. Blood investigations done to observe any hepatic or renal toxicity at baseline, during follow up and after completion of study. It is observed that drug in safe and has no toxic effect on liver and kidney.

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