



Assessment of Systemic Inflammatory and Metabolic Markers in Patients of Waja' al-Rukba (Knee Pain): A Clinical Laboratory-Based Study

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ABSTRACT: Osteoarthritis (OA) is the most common form of arthritis and a leading cause of disability in older adults. Knee osteoarthritis, a major subtype, closely resembles Waja'-al-Rukba described in Unani medicine, both sharing chronicity, pain, stiffness, and restricted mobility. Unani scholars attribute its origin to Sū'-i-Mizāj (abnormal temperament) and accumulation of Mawād-e-Fuzūni (morbid material) in joints.

Our aim is to evaluate the relationship between Mizāj (temperament) and biochemical markers of inflammation and metabolism (CRP, uric acid, BMI) in patients with Waja'-al-Rukba (knee pain), and to assess their role in disease risk and progression.

A cross-sectional study was conducted on 75 patients (aged 40–80 years) attending the OPD and IPD of of Ilaj bit Tadbeer and Moalejat in Ajmal Khan Tibbiya College and hospital, Ajmal Khan Tibbiya College, AMU, Aligarh. Mizāj was assessed using standard Unani parameters. Laboratory investigations included ESR, CRP, uric acid and BMI.

In our study we have find that most of the patients (76%) were aged between 40–50 years with females predominance (89%). Balghamī Mizāj (phlegmatic) was the most common temperament (41%), followed by Şafrāwī (27%), Damawī (20%), and Sawdāwī (12%). Balghamī individuals had the highest mean BMI (27–29.6 kg/m²) and mean uric acid level (5.98 ± 0.9 mg/dl). CRP positivity was also highest in the Balghamī group (12 cases). These findings indicate a strong association of Balghamī Mizāj with obesity, hyperuricemia, and inflammation.

The study demonstrates a significant correlation between Mizāj (temperament) and metabolic–inflammatory markers, validating Unani concepts through modern biomedical parameters. Balghamī temperament predisposes individuals to inflammatory and metabolic derangements such as osteoarthritis, supporting the integration of Unani temperament-based assessment in preventive and therapeutic frameworks.

KEYWORDS: C-reactive protein, Mizāj, Unani Medicine, Uric acid, Waja'-al-Rukba.

INTRODUCTION

Osteoarthritis is the most common form of arthritis among older adults. It is also one of the most common causes of physical disability among adults. [Zaidi et al.,2022]

Although OA can develop in any joint, most commonly it affects the knee, responsible for 365 million cases globally and 61% of OA-related YLDs. This is followed by the hand, with 142 million cases and 24% of OA YLDs, and the hip, with 33 million cases and 5.5% of the burden.[Global Health Data Exchange, 2019,Zhang, Jordan 2010.(Global Health Data Exchange,2019, Global Burden of Disease Collaborative Network,2020, Zang & Jordan,2010)

Knee osteoarthritis as a subtype of osteoarthritis, is closely aligned with Waja' al-Rukba a subtype of Waja 'al-Mafāşil described in Unani texts. Both conditions are chronic and progressive, sharing hallmark clinical features such as pain, stiffness, swelling, and restricted motility.[Schmitz & Pal et al.,2016]

PATHOGENESIS

The main cause for the development of the Waja 'al-Mafāşil is Sū'-i-Mizāj (abnormal temperament) and accumulation of Mawād-e-Fuzūni (morbid material) in the joint spaces.[Sina, 2015]

Sū'-i-Mizāj (temperament imbalance)



The pathological effects of a disease vary depending on the type of Sū'-i-Mizāj (abnormal temperament) involved. Sū'-i-Mizāj Hār (hot temperament) and Sū'-i-Mizāj Bārid (cold temperament) can directly cause pain, while Sū'-i-Mizāj Yābis (dry temperament) is indirectly associated with pain. In contrast, Sū'-i-Mizāj Raṭb (moist temperament) does not cause pain, either directly or indirectly. [Sina, 2015]

Current theories suggest that osteoarthritis (OA) results from an imbalance between catabolic (breakdown) and anabolic (building) processes, ultimately leading to progressive cartilage damage and destruction. Increased catabolic activity can be triggered by acute injuries, such as meniscal tears, or chronic microtrauma. In the early stages, anabolic responses such as proteoglycan synthesis compensate for cartilage damage. However, with advancing age and persistent stress, anabolic processes diminish, tipping the balance toward degeneration. [Jurjani, 2010, Warrell, 2010]

METHODOLOGY

AIM: To evaluate the relationship between Mizāj (temperament) and biochemical markers of inflammation and metabolism (CRP, uric acid, BMI) in patients with Waja' al-Rukba (knee pain), and to determine their potential role in disease risk and progression.

Type of study:

Observational, Cross-sectional study

Sample size:

A total of 75 patients (Male & female) were included on the basis of inclusion and exclusion criteria.

Place of study:

Department of Ilmul Amraz, Ajmal Khan Tibbiya College, AMU, Aligarh.

Source of data:

Patients attending the Outpatient Department (OPD) and Inpatient department (IPD) of Ilaj Bit Tadbeer and Moalejat with clinical features suggestive of knee osteoarthritis were recruited for the study. After detailed history and clinical examination, relevant blood investigations were carried out in the Central hospital Laboratory under the Department of Ilmul Amraz, AKTC.

Selection Criteria:

Patients who were willing to participate were included in the present study as per study criteria.

Inclusion criteria:

1. Patient with H/O knee joint pain.
2. Patient of either gender.
3. Age group 40-80 years.

Exclusion criteria:

1. Patient with Pregnancy and lactation.
2. Patient with history of any other chronic inflammatory disease.
3. Patient with major systemic and endocrine disease.

Investigation:

1. Erythrocyte Sedimentation Rate (ESR)
2. Uric acid
3. CRP (C- reactive protein)
4. BMI (Basal Metabolic Rate)

Inflammatory and Metabolic Markers

Several biochemical and hematological parameters serve as important indicators in the assessment of osteoarthritis and related conditions.

CRP

C-Reactive Protein (CRP) is an acute-phase protein found in concentrations of upto 5 µg/mL in the serum of healthy persons. However, during an inflammatory response, the levels may increase many folds. [Lopez, 2013]

Uric Acid

Uric acid is the end product of purine metabolism in humans and is excreted mainly through the kidneys. Estimation of serum uric acid is an important biochemical test for the diagnosis and management of gout, renal disorders, leukemia, and in patients undergoing chemotherapy. [Lopez, 2013]



Erythrocyte Sedimentation Rate (ESR)

The erythrocyte sedimentation rate (ESR) is a non-specific hematological test that measures the rate at which red blood cells (RBCs) settle down in a vertical column of anticoagulated blood within a specified period (usually 1 hour). The test indirectly reflects the presence and intensity of inflammation in the body

Considering the conceptual and clinical similarities between knee Osteoarthritis and Waja’ al-Rukba, and the roles of both inflammatory and metabolic disturbances in their pathogenesis, the present study was planned to explore the association between systemic inflammatory and metabolic markers in patients of Waja’ al-Rukba (knee pain).

Procedure:

Patients attending OPD and IPD of Ilaj bit Tadbeer and Moalejat in Ajmal Khan Tibbiya College and hospital who fulfill the inclusion and exclusion criteria of the study were recruited, and written consent was obtained (Annexure-I-Consent form). Demographic data like age and gender were collected in conjunction with relevant history and recorded on predesigned format (Annexure-II- Predesigned proforma). Body Mass Index (BMI) was measured as wt in kg divided by the sq. of height in mt [12,13].

Body Mass Index = Weight (Kg) /Height² (mt).

An intensive clinical examination was additionally conducted and also then numerous findings were recorded on a case record form (CRF). Each patient will be diagnosed for the type of Mizāj based on Ajnas-e- Ashra (Annexure-III), and type of Sū’-i- Mizāj in Waja’ al-Rukba (Annexure-IV) as per description in classical Unani literatures.

Assessment of temperament (Mizāj):

Determination of Mizāj was done on the principles of established parameters in a tool form as per the classical Unani literature, which has been attached with the case report form in the annexure section. [Avicenna,2007]

Assessment of Sū’-i- Mizāj in Waja’ al-Rukba:

Sū’-i- Mizāj in Waja’ al-Rukba is assessed by self-designed questionnaire, compiled by on the basis of Unani classical literature. [Jurjani,2010]

RESULT

In the present study, a total of 75 cases were analyzed according to age and gender distribution [Table-1]. The majority of the patients (57 cases, 76%) belonged to the 40–50 years age group, followed by 14 cases (19%) in the 51–60 years age group. Only 2 cases (3%) each were observed in the 61–70 years and 71–80 years age groups.

With respect to gender distribution, females predominated in all age groups. In the 40–50 years group, 91% were females and 9% were males. Similarly, in the 51–60 years group, 86% were females and 14% were males. In the 61–70 years group, all patients (100%) were females. In the 71–80 years group, males and females were equally distributed (50% each).

Overall, out of 75 cases, 67 (89%) were females and 8 (11%) were males, indicating a strong female predominance across the study population.

Fig 1 represent gender distribution by age group

Table 1: - Study patients age group wise

Sr No	Age group (yrs)	Number/age group (N)	Cases (n=75)	
			Male N (%)	Female N (%)
1	40-50	57	5 (9%)	52 (91%)
2	51-60	14	2(14%)	12(86%)
3	61-70	2	0(0%)	2(100%)
4	71-80	2	1(50%)	1(50%)
	Total all ages	75	8(11%)	67 (89%)

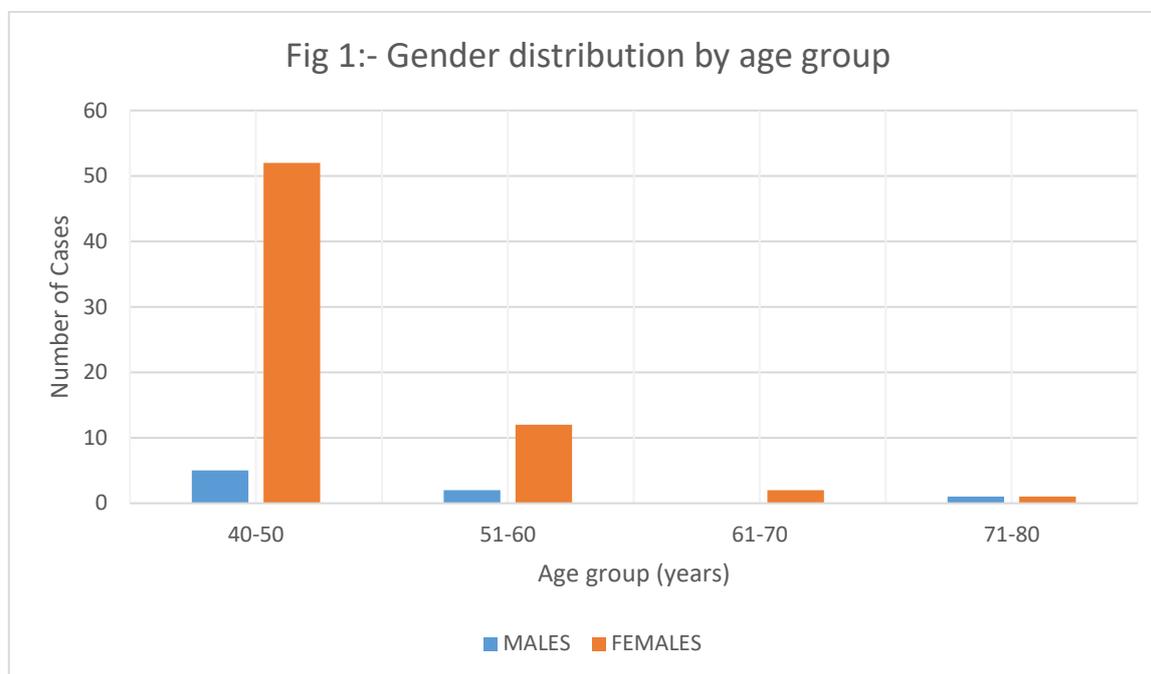


Table 2: - Study patients age group wise

Sr No	Age group (yrs)	Mizāj	Number (%) /age group- N (%)	BMI (mean±SD)
1	40-50	Balghamī	21 (37%)	27.0±2.9
		Damawī	11 (19%)	27.0±2.6
		Sawdāwī	9 (16%)	23.8±2.4
		Şafrāwī	16 (28%)	24.8±2.8
2	51-60	Balghamī	6 (44%)	26.3±3.0
		Damawī	4 (28%)	25.2±3.0
		Sawdāwī	0 (0%)	0
		Şafrāwī	4(28%)	25.6±3.3
3	61-70	Balghamī	2 (100%)	29.6±1.1
		Damawī	0 (0%)	0
		Sawdāwī	0 (0%)	0
		Şafrāwī	0 (0%)	0
4	71-80	Balghamī	2 (100%)	27.1±0.4
		Damawī	0 (0%)	0
		Sawdāwī	0 (0%)	0
		Şafrāwī	0 (0%)	0
Total all ages			75	

In the present study, the Mizāj (temperament) and Body Mass Index (BMI) of 75 patients were analyzed across different age groups [Table 2].



- In the **40–50 years** age group (n=57), the predominant Mizāj was Balghamī (21 cases, 37%), followed by Şafrāwī (16 cases, 28%), Damawī (11 cases, 19%), and Sawdāwī (9 cases, 16%). The mean BMI ranged from 23.8 ± 2.4 in Sawdāwī patients to 27.0 ± 2.9 in Balghamī.
- In the **51–60 years** group (n=14), Balghamī was again the most frequent (6 cases, 44%), followed by Damawī (4 cases, 28%) and Şafrāwī (4 cases, 28%). No Sawdāwī case was observed. The mean BMI was highest in Balghamī patients (26.3 ± 3.0).
- In the **61–70 years** group (n=2), both patients (100%) had Balghamī Mizāj with a mean BMI of 29.6 ± 1.1.
- In the **71–80 years** group (n=2), again both cases (100%) had Balghamī Mizāj with a mean BMI of 27.1 ± 0.4.

Overall, across all age groups, Balghamī Mizāj predominated (31 cases, 41%), followed by Şafrāwī (20 cases, 27%), Damawī (15 cases, 20%), and Sawdāwī (9 cases, 12%). Mean BMI values were generally higher in Balghamī patients compared to other Mizāj.

Table 3: - Association Between Mizāj (temperament) and Inflammatory (CRP) & metabolic marker (Uric acid).

Mizāj (Mizāj)	Uric Acid (mean ± SD)	CRP (+) Number (n)
Balghamī (n=31)	5.98± 0.9	12
Damawī (n=15)	5.58±0.4	5
Sawdāwī (n=9)	5.46±0.5	1
Şafrāwī (n=20)	5.44±0.7	4

The mean serum uric acid levels and positivity of inflammatory marker (CRP) were assessed across different Mizāj (temperament).

- **Balghamī (n=31):** Mean uric acid was **5.98 ± 0.9 mg/dl**, the highest among all groups. CRP positivity was seen in 12 cases.
- **Damawī (n=15):** Mean uric acid was **5.58 ± 0.4 mg/dl**. CRP positivity was reported in 5 cases.
- **Sawdāwī (n=9):** Mean uric acid was **5.46 ± 0.5 mg/dl**. Only 1 case was CRP positive.
- **Şafrāwī (n=20):** Mean uric acid was **5.44 ± 0.7 mg/dl**. CRP positivity was observed in 4 cases.

Overall, **Balghamī Mizāj showed the highest mean uric acid levels** and a greater number of CRP positive cases, suggesting a stronger association with hyperuricemia and inflammatory markers.

DISCUSSION

In the present study, Waja’-al-Rukba was most prevalent in the 40–50 years age group (76%), followed by 51–60 years (19%), while only few cases occurred in older groups (≥61 years) [Table-1]. This indicates that knee disorders begin early in middle age and progress with advancing years. Similar findings have been reported in several epidemiological studies, where knee osteoarthritis prevalence rises after 40 years due to various reasons like cartilage degeneration, metabolic decline, and reduced repair mechanisms.[Zang & Jordan,2010, Felson,2006, Hunter & Bierma-Zeinster, 2019]

Gender-wise distribution revealed a striking predominance of females (89%) compared to males (11%). This observation is consistent with previous reports showing higher prevalence of knee osteoarthritis in women.[Sharma,2021,Blagojevic et al.,2010, Sowers,2001, Hanna et al., 2009]

Srikanth et al. (2005) and Cui et al. (2020) confirmed greater incidence and severity of knee OA in females.[Srikanth et al.,2005, Cui et al., 2020]

From the Unani perspective, women have Bārid-Ratb Mizāj (cold-moist temperament), making them prone to phlegmatic accumulation and joint disorders.[Sina,1993, Jurjani,2010, Razi,2001]

Classical texts also highlight that advancing age leads to Su’-i-Mizāj and deposition of Mawād-e-Fāsida, predisposing to Waja’-al-Rukba.

Thus, both Unani and modern evidence support that “Waja’-al-Rukba” peaks in middle age and disproportionately affects females, justifying gender- and age-specific preventive approaches.

In the present study, the age-wise distribution of Mizāj (temperament) with respect to BMI showed that the majority of patients in the 40–50 years age group had a Balghamī temperament (37%), followed by Şafrāwī (28%), Damawī (19%), and Saudāwī (16%).



This indicates that Balghamī individuals were more prone to being affected in this age group [Table-2]. According to Unani medicine, women and middle-aged individuals often possess a Bārid-Ratab Mizāj (cold-moist temperament), which predisposes them to excessive phlegm (Balgham) production and metabolic disturbances leading to obesity and joint disorders.[Cui et al., 2020, Sina, 1993, Jurjani, 2010, Razi, 2001].

In the 51–60 years age group, Balghamī Mizāj again predominated (44%), whereas Şafrāwī and Damawī accounted for 28% each. Saudāwī temperament was not observed in this group. This reflects the fact that with advancing age, the body tends to lose its natural Ḥarārat Gharīziyya

(innate heat) and becomes more Bārid (cold) and Ratb (moist), thereby favoring a Balghamī dominance.[Jurjani,2010]

In the 61–70 years and 71–80 years groups, all patients (100%) were of Balghamī temperament. This finding strongly supports the Unani principle that ageing itself is a process of cooling and moistening, leading to predominance of phlegmatic disorders such as obesity, arthritis, and sluggish metabolism.[Razi,2001, Central council for Research in Unani Medicine,2012] Modern research also shows that elderly individuals often have reduced basal metabolic rate and increased fat deposition, correlating with Balghamī features.[Itrat et al., 2025]

With respect to BMI, Balghamī individuals consistently showed higher BMI values (mean ~27–29.6) compared to other Mizāj types. This suggests a close association between Balghamī Mizāj and overweight/obesity. Damawī and Şafrāwī individuals showed intermediate BMI values (~25–27), while Sawdāwī Mizāj patients showed the lowest mean BMI (~23.8). This correlates with classical Unani descriptions where Balghamī individuals are predisposed to corpulence, while Sawdāwī persons are lean and underweight due to their dry temperament.[Cui et al., 2020, Sina, 1993, Jurjani,2010, Razi,2001]

Thus, the findings of this study validate the classical Unani concept of Mizāj and its role in determining predisposition to metabolic disorders such as obesity. It also highlights that Balghamī individuals, particularly in advancing age, should be considered at higher risk and may benefit from preventive Unani regimens such as Ilāj-bi'l-Tadbeer (regimental therapy) including exercise, massage, and dietary modifications.[Irfan et al., 2025, World Health Organization, 2000, Kabiruddin, 1954]

In the present study, the mean uric acid level was found to be highest among patients with a Balghamī temperament (5.98 ± 0.9 mg/dl), followed by Damawī (5.58 ± 0.4 mg/dl), Sawdāwī (5.46 ± 0.5 mg/dl), and Şafrāwī (5.44 ± 0.7 mg/dl) [Table-3]. This observation correlates with the Unani concept that Balgham (phlegm) is a cold and moist temperament, predisposing individuals to metabolic sluggishness, impaired digestion, and accumulation of waste products such as uric acid, thereby contributing to conditions like gout and Osteoarthritis.[Sina,1993, Jurjani,2010]

Furthermore, C-reactive protein (CRP) was also positive among Balghamī patients (12 cases), followed by Damawī (5), Şafrāwī (4), and only (1) case in Sawdāwī. CRP is an established modern biomarker of systemic inflammation, and its correlation with Balghamī temperament strengthens the Unani principle that phlegmatic individuals are more prone to inflammatory and degenerative conditions.[Razi,2001, Kasper et al., 2018]

Modern literature also supports these findings, where hyperuricemia is associated with both inflammatory and degenerative joint diseases. Studies indicate that elevated uric acid can act as a pro-inflammatory mediator, stimulating CRP production and perpetuating arthritis.[Firestein,2017]

CONCLUSION

Thus, the present study establishes a significant association between Mizāj (temperament) and inflammatory and metabolic markers (CRP, Uric acid), bridging Unani classical wisdom with modern pathophysiological understanding.

The present study systematically examined the relationship between Mizāj (temperament) and a spectrum of inflammatory, metabolic and anthropometric parameters. The findings reaffirm the classical Unani principle that Mizāj (temperament) influences health and disease predisposition, while also providing objective laboratory-based evidence for this traditional concept.

Taken together, the results highlight a strong and statistically significant association of Mizāj with BMI, uric acid levels & CRP positivity. These observations strengthen the evidence base for the Unani doctrine that Mizāj (temperament) is a key determinant of physiological balance and pathological susceptibility. Importantly, the convergence of traditional Mizāj-based assessment with modern hematological and biochemical indices underscores the relevance of integrating Unani principles into contemporary biomedical frameworks.



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