

Prevalence of types of arthritis and its association with biochemical parameters among pre- and post-menopausal women in different cities of Pakistan.

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Abstract:

Introduction: The prevalence of arthritis among both pre and post menopausal is alarmingly high. Old age, gender, obesity, unhealthy life style, poor nutrition, less physical activity, genetics, lack of knowledge about disease, lack if education are the factors which are strongly associated with onset of arthritis.

Objective: To document prevalence of different types of arthritis and its association with biochemical parameters among pre- and post-menopausal women in different cities of Pakistan.

Methodology: A total of 300 females' patients who were diagnosed as case of arthritis from different aetiology, during April 2022 to September 2022, aged above 40 years were enrolled for this cross-sectional observational questionnaire and laboratory-based study. Their demographic and disease-related biochemical parameters were recorded and analysed.

Results: Over all prevalence of rheumatoid arthritis was high (39%) among both pre- and post-menopausal females. Biochemical laboratory analysis showed mean low (11.90 ± 2.18) level of haemoglobin. 66.6% and 60.6 % of the female patients were seropositive for Rheumatoid factor (RF) and Anti Cyclic Citrullinated Protein (Anti-CCP) which is clinical characteristics of Arthritis patients.

Conclusion: Women with different type of arthritis have border line mean levels of biochemical parameters which indicate co-morbidities like diabetes, cardiovascular and renal diseases, hypertension, obesity and osteoporosis.

Keywords: Post-menopausal, rheumatoid, psoriatic, osteoarthritis, biochemical parameters.

Introduction:

Arthritis is a serious health issues among pre- and post-menopausal females. It is an autoimmune disease affecting older age person age above 45 years. This disease has different types which include, polyarthritis, psoriatic arthritis, rheumatoid arthritis and osteoarthritis. In females this disease ratio is seen high as they are either close or at menopause when their menstrual cycle begins to cease.¹ In recent decade this disease has been more prevalent among menopausal females in Asia, America and Europe. According to a study there has been 13% of prevalence of osteoarthritis is seen in women with age 60 years or above, also 17% prevalence of rheumatoid arthritis has been diagnosed in women age above 50 years.² In Pakistan 13% of women have been diagnosed with arthritis in Karachi.³ In older women obesity, knee joint pain and muscle weakness has also been diagnosed as major symptoms of arthritis. In recent years it has been estimated that arthritis can affect females' joints which include,

hip, neck, shoulder, feet and hand joints. Old age, gender, obesity, unhealthy life style, poor nutrition, less physical activity, genetics, lack of knowledge about disease, lack if education are the factors which are strongly associated with onset of arthritis.⁴

Due to arthritis in females many biochemical profile changes have also been identified, which include serum haemoglobin, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, and sugar levels. As this disease progresses in females, chances of anaemia, cardiovascular disease, stroke and renal comorbidity chances also increases.⁵ Low levels of haemoglobin were measured in menopausal women who were diagnosed with different type of arthritis.⁶ Female with arthritis have also been found diabetic in previous literature, in a study 47% of women who were diabetic have also been diagnosed with arthritis.⁷ Older age females who were diagnosed with arthritis were at higher risk of getting diabetes as well. This finding in addition to autoimmunity, supports the notion that inflammatory pathways play key role in the pathogenesis of diabetes.^{8,9}

In arthritis disease, obesity and poor nutrition can lead to high levels of triglyceride, low HDL and high LDL levels in body that may lead to cardiovascular diseases. Renal comorbidity has been identified in arthritis patient with excessive levels of uric acid, urea and creatinine in blood.^{10,11} In a study, uric acid and

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creatinine identified as strong predictor of renal dysfunction among rheumatoid and psoriatic arthritis patient.¹² In other study excessive levels of uric acid was found in patients with osteoarthritis.¹³ According to different studies high levels of urea, uric acid and creatinine in arthritis patients may viewed as inflammatory markers for severity of joint inflammation and sign of renal dysfunction.^{14,15}

For diagnosis of different types of arthritis, biochemical test which include serum C- reactive protein (CRP), rheumatoid Factor (RF), anti-cyclic citrullinated peptide (anti-CCP) and erythrocyte sedimentation rate (ESR) are used clinically. These biochemical test levels can indicate disease stages or severity of arthritis in pre- and post-menopausal patients. The aim of the present study was to assess prevalence of types of arthritis and its association with biochemical parameters among pre- and post-menopausal women in different cities of Pakistan.

Objective:

To identify the risk factors associated with chronic suppurative otitis media, for early detection of disease and prevention of its complications.

Methodology:

This cross-sectional study was conducted from April 2022 to September 2022 in different cities (Joharabad, Khushab and Sargodha) of Pakistan. Total 300, both pre- and post-menopausal women participated in study. Written informed consent was taken from all participants. The survey included participants who were diagnosed with arthritis of different types from qualified orthopaedic consultants. The demographic information and nutritional assessment of the female patients was recorded on a structured questionnaire. The participants were also evaluated for different biochemical parameters (Triglycerides, LDL, HDL, fasting blood sugar, HBA1c, Creatinine, uric acid, Urea, ESR, haemoglobin, C-reactive protein (CRP), Anticyclic citrullinated protein (Anti-CCP) and cholesterol). Date was collected, recorded and analysed in SPSS version 23. Descriptive statistics was applied with frequency, percentage and mean \pm SD for all variables.

Results:

The demographic profiles and disease related parameters of female patients are shown in table 1.

Table No 1: Demographic and disease related parameters.

Characteristic	Frequency (%)
Age (years)	
40-49	36(12)
50-59	55(18.3)
60-69	119 (39.6)
≥ 70	90 (30)
Education level	
illiterate	124 (41.3)
Primary	102 (34.1)
Secondary	65(21.6)
Higher education	9 (3)
Residence	
Rural	128 (42.6)
Urban	172 (57.4)
Menopause	
Yes	220 (73.3)
No	80 (26.6)
Type of arthritis	
Polyarthritis	34 (11.3)
Osteoarthritis	112 (37.3)
Psoriatic arthritis	12 (4.2)
Rheumatic arthritis	142 (47.3)
Duration of disease	
> 1 year	18 (6.1)
1-2 year	34 (11.3)
2-5 years	89 (29.6)
5-10 years	159 (53)
BMI	
Low (<18.5)	38 (12.6)
Normal (18.5-24)	106 (35.4)
Obesity (≥ 25)	156 (52)

Among 300 patients', majority (39%) of patients were belonging to age group 60-69 years. Among all, 41.3% of the females were illiterate and 34.1% went to primary level. 57.4% of the females were residing in urban areas. In disease related parameters, among type of arthritis, rheumatoid arthritis (47.3%) was more prevalent, followed by osteoarthritis (37.3%), polyarthritis (11.3%) and psoriatic arthritis (4.2%). Majority of the patients (53%) were having the disease duration of 5-10 years. 51.3% of the female patients reported knee pain, followed by wrist pain 45%. Body mass index (BMI) levels were high in more than 52% patients which indicate obesity. Biochemical profile of female patients is shown in table 2. The mean \pm SD levels of haemoglobin was 11.90 \pm 2.18. The mean ESR and CRP levels, in almost all cases were found above the borderline in arthritis patients,

indicating on going inflammation/damage in affected joint (s).

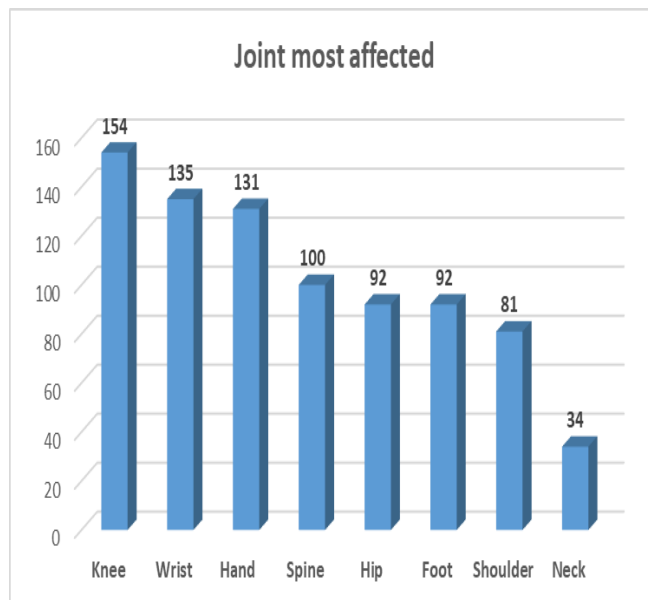
Table No 2: Biochemical clinical profiles of female patients (n=300)

Characteristics	frequency (%) / mean \pm SD
Hemoglobin (g/dL)	11.90 \pm 2.18
ESR (mm/h)	32.05 \pm 2.80
Cholesterol (mg/dL)	246.97 \pm 51.69
Triglyceride (mg/dL)	154.84 \pm 27.25
LDL (mg/dL)	102.22 \pm 21.20
HDL (mg/dL)	40.41 \pm 6.14
FBS (mg/dL)	121.32 \pm 32.11
HBA1c (%)	6.28 \pm 2.53
Creatinine (mg/dL)	1.9 \pm 0.87
Uric Acid (mg/dL)	7.28 \pm 1.87
Urea (mg/dL)	68.94 \pm 32.47
CRP (mg/L)	26.40 \pm 9.14
RF	200 (66.6%)
Anti-CCP	182 (60.6)

ESR: erythrocyte sedimentation rate, **FBS:** Fasting blood sugar, **LDL:** Low density lipoprotein, **HDL:** High density lipoproteins, **CRP:** C-Reactive protein, **RF:** Rheumatoid Factor, **Anti-CCP:** Anti Cyclic Citrullinated Protein.

Total cholesterol (246.97 \pm 51.69) levels were quite high. Fasting blood sugar was above the borderline with mean of 121.32 \pm 32.11. Patients were also evaluated for HBA1c, whose mean levels (6.28 \pm 2.53) were found just above the borderline value that indicate majority of patients are pre-diabetic or potential diabetic. Triglyceride (154.84 \pm 27.25) and low-density lipoproteins (102.22 \pm 21.20) both were at or just above borderline. Mean of High-density lipoprotein found in low range (40.41 \pm 6.14). Unexpectedly rise of creatinine (1.9 \pm 0.87), uric acid (7.28 \pm 1.87) and urea levels (68.94 \pm 32.47) were also observed in arthritis female patients. 66.6% and 60.6 % of the female patients were seropositive for Rheumatoid factor (RF) and Anti Cyclic Citrullinated Protein (Anti-CCP) respectively which is clinical characteristics of arthritic patients.

Graph No 1: Showing the frequency of joint most affected.



Discussion:

Arthritis is a serious threat to health of women especially pre- and post-menopausal women. Prevalence of arthritis disease and its symptoms, in current study found high in females aged above 50 years. In different studies around the world, it is observed that arthritis disease ratio is much higher among menopausal females (aged 55-70 years) as compared to young ones.¹⁶ Biochemical parameters when use for diagnosis, may predict and identify different type of arthritis among pre- and post-menopausal women which otherwise can cause serious health damages.¹⁷ Among type of arthritis, during current study, rheumatoid arthritis and osteoarthritis found to be most prevalent. The results are consistent with published studies.^{18,19} In a study rheumatoid arthritis was identified among post-menopausal women due to obesity and hormonal imbalance at the onset of menopause.²⁰ In another study osteoarthritis ratio was high in aged females as compared to males.²¹ Lack of knowledge about menstrual cycle changes, sedentary life style in older age, excessive body weight, no physical activities, and lack of medication may precipitate arthritis in females. In our result BMI was found to be high ≥ 25 in 52% females. In this study many patients complained about knee pain, several studies indicated that knee osteoarthritis is positively correlated with BMI and age of females.

In addition to obesity, hypertension, biochemically female having low haemoglobin level, suffer most with rheumatoid, poly and osteoarthritis than by chance.²¹ Overall, the mean levels of cholesterol were high, triglyceride and low density lipoproteins (LDL) levels were at borderline and high density lipoprotein levels (HDL) were low. In previous studies it was observed that

serum cholesterol and triglyceride levels were significantly raised in arthritis patients especially in females due to obesity.²²

Based on regular assessment of renal function urine and serum parameters in older female arthritis patients' renal co-morbidity is common.²³ In patients of psoriatic arthritis, rheumatoid and osteoarthritis; elevated serum levels of urea, uric acid and creatinine are significantly correlated with age, duration and disease activity. This probably explains above normal levels of urea, creatinine and uric acid in current study. C- reactive protein (CRP) is a characteristics of arthritis patients, that indicate severe inflammation of joints and high disease activity which is further confirmed by erythrocyte sedimentation rate (ESR).²⁴ Anti-CCP and rheumatoid factor (RF) are considered as important tests for diagnosis of arthritis.²⁵ In our study both anti-CCP and RF were positive for more than 50% females. These tests can help in indicating arthritis at early stage, which can be helpful in managing and treating arthritis in both pre and post-menopausal females.

Conclusion:

Prevalence of different types of arthritis were found to be high among post- menopausal females. Women with different type of arthritis have border line mean levels of biochemical parameters which indicate co-morbidities like diabetes, cardiovascular and renal diseases, hypertension, obesity and osteoporosis in these women. Further investigation is needed at large scale so that preventive measure can be taken in order to prevent this disease and its outcomes.

References:

- Wang B, Deng H, Hu Y, Han L, Huang Q, Fang X, Yang K, Wu S, Zheng Z, Yawalkar N, Zhang Z, Yan K. The difference of lipid profiles between psoriasis with arthritis and psoriasis without arthritis and sex-specific downregulation of methotrexate on the apolipoprotein B/apolipoprotein A-1 ratio. *Arthritis Res Ther*. 2022 Jan 7;24(1):17. doi: 10.1186/s13075-021-02715-4.
- Bugatti S, Bogliolo L, Vitolo B, Manzo A, Montecucco C, Caporali R. Anti-citrullinated protein antibodies and high levels of rheumatoid factor are associated with systemic bone loss in patients with early untreated rheumatoid arthritis. *Arthritis Res Ther*. 2016 Oct 6;18(1):226. doi: 10.1186/s13075-016-1116-9.
- Shakil M, Saleem DM, Zafar A, Ali A, Raziq M, Shams S. Clinical and hematological parameters in patients of Rheumatoid arthritis in a tertiary care hospital. *RMJ*. 2021; 46(1): 45-47.
- Hanna FS, Teichtahl AJ, Wluka AE, Wang Y, Urquhart DM, English DR, Giles GG, Cicuttini FM. Women have increased rates of cartilage loss and progression of cartilage defects at the knee than men: a gender study of adults without clinical knee osteoarthritis. *Menopause*. 2009 Jul-Aug;16(4):666-70. doi: 10.1097/gme.0b013e318198e30e.
- Mushtaq, M., Salim, B., Samreen, S., Nasim, A., & Gul, H. Risk of cardiovascular disease in patients of rheumatoid arthritis (ra) presenting in a tertiary care hospital of Pakistan. *Pakistan Armed Forces Medical Journal*, 2018: 68(6), 1691-95.
- Smyrnova G. Relação entre o nível de hemoglobina e a atividade da doença em pacientes com artrite reumatoide [The relationship between hemoglobin level and disease activity in patients with rheumatoid arthritis]. *Rev Bras Reumatol*. 2014 Nov-Dec;54(6):437-40. Portuguese. doi: 10.1016/j.rbr.2014.06.002. Epub 2014 Sep 28.
- Veronese N, Cooper C, Reginster JY, Hochberg M, Branco J, Bruyère O, Chapurlat R, Al-Daghri N, Dennison E, Herrero-Beaumont G, Kaux JF, Maheu E, Rizzoli R, Roth R, Rovati LC, Uebelhart D, Vlaskovska M, Scheen A. Type 2 diabetes mellitus and osteoarthritis. *Semin Arthritis Rheum*. 2019 Aug;49(1):9-19. doi: 10.1016/j.semarthrit.2019.01.005.
- Tian Z, McLaughlin J, Verma A, Chinoy H, Heald AH. The relationship between rheumatoid arthritis and diabetes mellitus: a systematic review and meta-analysis. *Cardiovasc Endocrinol Metab*. 2021 Feb 19;10(2):125-131. doi: 10.1097/XCE.0000000000000244.
- Dal Bello G, Gisondi P, Idolazzi L, Girolomoni G. Psoriatic Arthritis and Diabetes Mellitus: A Narrative Review. *Rheumatol Ther*. 2020 Jun;7(2):271-285. doi: 10.1007/s40744-020-00206-7.
- Anders HJ, Vielhauer V. Renal co-morbidity in patients with rheumatic diseases. *Arthritis Res Ther*. 2011 Jun 29;13(3):222. doi: 10.1186/ar3256.
- Nada D, Gaber R, Mahmoud AS, Elkhoully R, Alashkar D. Hyperuricemia Among Egyptian Rheumatoid Arthritis Patients. Is It an Association or an Inflammatory Marker? A Cross-Sectional Observational Study. *Open Access Rheumatol*. 2021 Oct 5;13:305-314. doi: 10.2147/OARRR.S331488.
- Atzeni F, Muto P, Rodríguez-Carrio J, Masala IF. Frequency of Renal Function Parameter Abnormalities in Patients with Psoriatic Arthritis and Rheumatoid Arthritis: Real-World Evidence from Clinical Practice. *J Clin Med*. 2022 Feb 16;11(4):1029. doi: 10.3390/jcm11041029.
- Denoble AE, Huffman KM, Stabler TV, Kelly SJ, Hersfield MS, McDaniel GE, Coleman RE, Kraus VB. Uric acid is a danger signal of increasing risk for osteoarthritis through inflammasome activation. *Proc Natl Acad Sci U S A*. 2011 Feb 1;108(5):2088-93. doi: 10.1073/pnas.1012743108.
- Raksasuk S, Ungprasert P. Patients with rheumatoid arthritis have an increased risk of incident chronic kidney disease: a systematic review and

- meta-analysis of cohort studies. *Int Urol Nephrol*. 2020 Jan;52(1):147-154. doi: 10.1007/s11255-019-02346-4.
15. Y.Tang, Y.Varavko,R. Aringazina et al., Changes in renal function and morphological variations of kidney diseases in rheumatoid arthritis patients. *Asian Journal of Urology*: <https://doi.org/10.1016/j.ajur.2022.06.005>
 16. Eun Y, Jeon KH, Han K, Kim D, Kim H, Lee J, Lee DY, Yoo JE, Shin DW. Menopausal factors and risk of seropositive rheumatoid arthritis in postmenopausal women: a nationwide cohort study of 1.36 million women. *Sci Rep*. 2020 Nov 27;10(1):20793. doi: 10.1038/s41598-020-77841-1.
 17. Agrawal U, Agrawal S, Agrawal V. Assessment of Biochemical Parameters in Patients with Rheumatoid Arthritis for Cardiovascular Diseases at Tertiary Care Centre. *Int J Med Res Prof*. 2017; 3(3):462-64.
 18. Chavan VU, Ramavataram D, Patel PA, Rupani MP. Evaluation of serum magnesium, lipid profile and various biochemical parameters as risk factors of cardiovascular diseases in patients with rheumatoid arthritis. *J Clin Diagn Res*. 2015 Apr;9(4):BC01-5. doi: 10.7860/JCDR/2015/12206.5740.
 19. Ryu M, Ha JS, Lee S, Baek WC, Kimm H, Gym H. Association of the Risk of Osteoarthritis and Hypertension in the Korean Adult Population Aged 40 -59 in Pre- and Postmenopausal Women: Using Korea National Health and Nutrition Examination Survey 2012-2016 Data. *Int J Hypertens*. 2021 Feb 23;2021:8065838. doi: 10.1155/2021/8065838.
 20. de Resende Guimarães MFB, Rodrigues CEM, Gomes KWP, Machado CJ, Brenol CV, Krampe SF, de Andrade NPB, Kakehasi AM. High prevalence of obesity in rheumatoid arthritis patients: association with disease activity, hypertension, dyslipidemia and diabetes, a multi-center study. *Adv Rheumatol*. 2019 Oct 16;59(1):44. doi: 10.1186/s42358-019-0089-1.
 21. Alisa Wilson, Hsing-Ting Yu, Lawrence Tim Goodnough, Allen R Nissenson, Prevalence and outcomes of anemia in rheumatoid arthritis: a systematic review of the literature, *The American Journal of Medicine*, Volume 116, Issue 7, Supplement 1, 2004, Pages 50-57, <https://doi.org/10.1016/j.amjmed.2003.12.012>
 22. Lim HS, Kim TH, Lee HH, Park YH, Kim JM, Lee BR. Hypertension and age at onset of natural menopause in Korean postmenopausal women: Results from the Korea National Health and Nutrition Examination Survey (2008-2013). *Maturitas*. 2016 Aug;90:17-23. doi: 10.1016/j.maturitas.2016.04.019. Epub 2016 Apr 30. PMID: 27282789.
 23. Mori S, Yoshitama T, Hirakata N, Ueki Y. Prevalence of and factors associated with renal dysfunction in rheumatoid arthritis patients: a cross-sectional study in community hospitals. *Clin Rheumatol*. 2017 Dec;36(12):2673-2682. doi: 10.1007/s10067-017-3804-5.
 24. Kotulska A, Kopeć-Mędrek M, Grosicka A, Kubicka M, Kucharz EJ. Correlation between erythrocyte sedimentation rate and C-reactive protein level in patients with rheumatic diseases. *Reumatologia*. 2015;53(5):243-6. doi: 10.5114/reum.2015.55825.
 25. Takeuchi T, Miyasaka N, Inui T, Yano T, Yoshinari T, Abe T, Koike T. High titers of both rheumatoid factor and anti-CCP antibodies at baseline in patients with rheumatoid arthritis are associated with increased circulating baseline TNF level, low drug levels, and reduced clinical responses: a post hoc analysis of the RISING study. *Arthritis Res Ther*. 2017 Sep 2;19(1):194. doi: 10.1186/s13075-017-1401-2.