

Gender Differences In Clinical Course Of Rheumatoid Arthritis

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Abstract:

Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by progressive joint destruction and systemic manifestations. Gender plays a significant role in disease prevalence, severity, and clinical presentation; however, sex-specific differences in RA progression remain insufficiently explored.

Objective: To investigate gender-related differences in the clinical course, articular involvement, systemic manifestations, and bone metabolism parameters among patients with rheumatoid arthritis.

Methods: A total of 293 patients diagnosed with RA aged 17–79 years were examined, including 20% men and 80% women. Clinical assessments included disease activity, radiographic staging, joint damage scoring, bone mineral density evaluation, and laboratory analysis of osteoassociated hormones and trace elements. Statistical analyses were performed using ANOVA, MANOVA, and correlation methods.

Results: Women demonstrated a more severe clinical course, with higher disease activity and more advanced radiographic stages compared to men. Female patients more frequently exhibited involvement of proximal interphalangeal, maxillary, and knee joints, while men showed a greater prevalence of sacroiliac joint lesions, tendovaginitis, and intra-articular Hoffa bodies. Extra-articular manifestations also displayed sexual dimorphism: pulmonary and peripheral nervous system complications were more common in men, whereas Sjögren's syndrome and central nervous system involvement were predominantly observed in women. Bone metabolism disturbances were identified in both sexes, with distinct hormonal and mineral profile variations depending on gender.

Conclusion: Rheumatoid arthritis demonstrates substantial gender-specific differences in disease severity, joint distribution, systemic manifestations, and metabolic alterations. Recognition of these distinctions may improve personalized diagnostic strategies, therapeutic planning, and long-term disease monitoring.

Keywords: rheumatoid arthritis, gender differences, osteoporosis, systemic manifestations, bone metabolism, autoimmune disease.

Introduction

Rheumatoid arthritis (RA) is one of the most prevalent chronic systemic autoimmune diseases, leading to progressive synovial inflammation, joint destruction, disability, and multiple extra-articular complications. Epidemiological studies indicate that women are affected

approximately three to four times more often than men, suggesting that biological sex significantly influences susceptibility and disease progression.

Previous investigations have demonstrated that female sex is associated with increased disease severity, while male patients may experience distinct patterns of systemic involvement. Gender-related variations have been reported in metabolic syndrome prevalence, thrombotic risk, pulmonary complications, and skeletal damage. Nevertheless, the influence of sex on radiographic progression, specific joint distribution, osteoporosis development, and biochemical markers of bone metabolism remains incompletely characterized.

A clearer understanding of gender-specific RA manifestations is essential for optimizing diagnostic precision, treatment individualization, and prognostic assessment. Therefore, this study aimed to comprehensively evaluate the impact of gender on clinical presentation, radiological changes, systemic manifestations, and metabolic disturbances in patients with rheumatoid arthritis.

Materials and Methods

Study Population

This cross-sectional study included 293 patients diagnosed with rheumatoid arthritis according to established clinical criteria. Participants ranged from 17 to 79 years of age (mean age: 45.6 ± 0.68 years). Among them, 20% were male (mean age: 43.5 ± 1.36 years) and 80% were female (mean age: 46.2 ± 0.78 years).

The average disease duration was 7.9 ± 0.91 years in men and 9.6 ± 0.46 years in women. Seropositive RA was identified in approximately 75% of patients.

Clinical Assessment

Disease severity was evaluated through:

- Rheumatoid factor positivity
- Disease activity grading (I–III)
- Radiographic staging (I–IV)
- Joint count scoring
- Ritchie Articular Index
- Lansbury Index
- Arthritis Progression Index (API)

Imaging and Bone Density Evaluation

Patients underwent:

- Standard radiography of affected joints
- Ultrasound examination
- Sacroiliac joint and spinal imaging
- Dual-energy X-ray absorptiometry (DEXA)

Bone mineral density and the Barnett–Nordin metacarpal index were used to assess systemic osteoporosis.

Laboratory Analysis

Serum biomarkers included:

- Parathyroid hormone (PTH)
- Calcitonin
- Osteocalcin
- Alkaline phosphatase
- Calcium
- Magnesium
- Phosphorus
- Copper
- Iron

- Zinc
- Manganese
- Strontium
- Lead

Statistical Analysis

Data were processed using:

- Descriptive statistics
- Student's t-test
- Wilcoxon–Rao analysis
- ANOVA/MANOVA
- Correlation analysis

A p-value < 0.05 was considered statistically significant.

Results

Clinical Severity and Disease Activity

Women exhibited significantly higher rates of moderate-to-severe RA activity and more advanced radiographic stages than men, confirming a generally more aggressive disease course.

- Moderate/high activity: 82% in women vs. 72% in men
- Advanced stages (III–IV): 55% in women vs. 43% in men

Articular Landscape Differences

Significant gender-specific differences were identified in joint involvement:

Men:

- Increased sacroiliac joint damage
- More frequent tendovaginitis
- Higher prevalence of intra-articular Hoffa bodies

Women:

- Greater proximal interphalangeal joint involvement
- Increased maxillary joint lesions
- More frequent knee joint damage

Extra-Articular Manifestations

Sexual dimorphism was also evident in systemic RA complications:

Men:

- Higher prevalence of pulmonary pathology
- Increased peripheral neuropathy

Women:

- Exclusive association with Sjögren's syndrome
- More frequent central nervous system disturbances

Bone Metabolism and Osteoporosis

Systemic osteoporosis was identified in both sexes:

- 43% of men
- 49% of women

While both groups demonstrated metabolic disturbances, hormonal patterns differed:

Men with osteoporosis:

- Elevated PTH
- Increased osteocalcin

Women with osteoporosis:

- Elevated PTH and osteocalcin
- Increased alkaline phosphatase
- Reduced calcitonin and magnesium

These findings indicate sex-specific biochemical pathways contributing to osteodeficiency in RA.

Discussion

The present study confirms that rheumatoid arthritis demonstrates marked gender-related heterogeneity. Female patients generally experience more severe inflammatory progression and broader peripheral joint destruction, whereas men are more likely to develop axial skeletal involvement and certain systemic complications.

Hormonal influences, immune response modulation, and genetic factors may underlie these differences. Estrogen-mediated immune activation may partially explain the heightened severity in women, while differences in bone metabolism and inflammatory pathways may contribute to distinct patterns of osteoporosis and systemic manifestations.

Understanding these sex-specific distinctions has practical clinical implications:

- Improved personalized treatment strategies
- Enhanced monitoring for sex-predominant complications
- Better osteoporosis prevention protocols
- More accurate prognostic evaluation

Conclusion

Rheumatoid arthritis exhibits significant gender-associated differences across multiple clinical dimensions.

1. Women experience a more aggressive disease course with greater peripheral joint destruction.
2. Men more frequently develop sacroiliac lesions, tendovaginitis, and pulmonary/systemic complications.
3. Bone metabolism disturbances differ substantially between sexes, necessitating individualized metabolic monitoring.
4. Gender should be considered an important factor in RA diagnosis, treatment planning, and long-term management.

Incorporating gender-specific approaches into rheumatologic practice may substantially improve patient outcomes and therapeutic precision.

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