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CLINICAL SIGNIFICANCE OF ANTI-CITRULLINATED CYCLIC PEPTIDE (ASSP) IN EARLY DIAGNOSIS OF RHEUMATOID ARTHRITIS AND ITS IMPACT ON REPRODUCTIVE HEALTH: A PRELIMINARY OBSERVATIONAL STUDY

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Abstract. Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that predominantly affects women of reproductive age. In addition to joint inflammation, systemic autoimmunity can impair hormonal regulation and reproductive function. Early diagnosis plays a crucial role in preventing irreversible joint damage and reproductive complications.

Objective: To evaluate the diagnostic value of Anti-Citrullinated Cyclic Peptide (ASSP) antibodies in comparison with Rheumatoid Factor (RF) and to assess their clinical significance in women of reproductive age with RA.

Methods: A total of 50 patients from the Fergana Region (40 females, 10 males; aged 18–65 years) diagnosed with RA were enrolled. ASSP was determined by ELISA, and RF by immunoturbidimetric assay. Inflammatory markers (ESR, CRP) were analyzed. Statistical analysis was performed using SPSS 25.0, with $p < 0.05$ considered significant.

Results: ASSP positivity was observed in 80% of patients, while RF positivity was found in 64%. Among them, 27 patients (54%) were positive for both markers, 13 (26%) were ASSP-positive but RF-negative, 5 (10%) were RF-positive but ASSP-negative, and 5 (10%) were negative for both. The difference was statistically significant ($p < 0.05$). ASSP positivity correlated with early disease activity, especially in women aged 18–45 years.

Conclusion: ASSP demonstrates higher sensitivity than RF for early RA diagnosis. Early testing in women of reproductive age can support timely treatment, preserve fertility, and reduce adverse pregnancy outcomes.

Keywords: Rheumatoid arthritis, ASSP, Rheumatoid factor, Reproductive health, Autoimmunity.

Introduction. Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic synovial inflammation and joint destruction. It affects about 0.5–1% of the global population and occurs three times more frequently in women than in men. Reproductive-age women are particularly vulnerable, as hormonal and immunological factors influence disease onset and progression.

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RA can negatively affect fertility, menstrual regularity, and pregnancy outcomes. Hence, early diagnosis is crucial for both joint preservation and reproductive well-being. Anti-Citrullinated Cyclic Peptide (ASSP) antibodies are highly specific and sensitive markers that may appear years before clinical symptoms, enabling early detection.
This preliminary study evaluates the diagnostic performance of ASSP compared to RF in patients with RA and its potential implications for reproductive health among women of childbearing age.

Materials and Methods. Study Design and Population
A total of 50 patients diagnosed with RA from the Fergana Region were included in this observational study, comprising 40 females (80%) and 10 males (20%), aged 18–65 years (mean ± SD: 52 ± 6.4). Women aged 18–45 years were classified as the reproductive-age group.
Diagnostic Evaluation
ASSP antibodies were detected using the Enzyme-Linked Immunosorbent Assay (ELISA) method, while RF was measured via immunoturbidimetric assay. ESR and CRP were determined to evaluate inflammatory activity.
Ethical Approval
The study protocol was approved by the Institutional Ethics Committee of Andijan State Medical Institute (Approval No. ASMI-2025/02). All participants provided written informed consent prior to sample collection.
Statistical Analysis
Data were analyzed using SPSS 25.0 software. Descriptive statistics were expressed as mean ± SD. Comparisons between ASSP and RF positivity were performed using the chi-square test, with significance set at $p < 0.05$.
Results
Serological Findings
Marker Combination Number of Patients (n=50) Percentage (%)

ASSP(+), RF(+)	27	54%
ASSP(+), RF(-)	13	26%
ASSP(-), RF(+)	5	10%
ASSP(-), RF(-)	5	10%

ASSP positivity (80%) was significantly higher than RF positivity (64%) ($p < 0.05$). Among women of reproductive age, ASSP levels showed strong association with early-stage disease activity and lower rates of joint deformity, suggesting improved detection potential before irreversible damage occurs.

Discussion. This preliminary observational study confirms that ASSP antibodies are more sensitive and specific than RF for the early diagnosis of RA. ASSP can be detected years before clinical symptoms, making it a valuable tool for early intervention.
In women of reproductive age, delayed diagnosis or untreated inflammation can cause subfertility, menstrual irregularities, and miscarriage risks. Early identification through ASSP

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testing allows for timely immunomodulatory therapy, improving both rheumatologic and reproductive outcomes.

Our results are consistent with prior studies (Smolen JS, et al. 2020; Mankia K, et al. 2021) and align with recent evidence highlighting the link between autoimmune markers and reproductive health (Kobayashi et al., 2022; Ahmed et al., 2023). The combined use of ASSP and RF enhances diagnostic precision and should be considered as a standard approach for women presenting with unexplained joint pain or infertility.

Conclusion

1. ASSP demonstrated higher diagnostic sensitivity (80%) than RF (64%) in rheumatoid arthritis patients.
2. ASSP-positive but RF-negative cases (26%) highlight ASSP's role in early disease detection.
3. In women of reproductive age, early diagnosis supports fertility preservation and reduces pregnancy complications.
4. Combined testing of ASSP and RF improves diagnostic reliability and facilitates personalized management.

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