

Research Article

Diagnostic Delay in Rheumatoid Arthritis Patients at a Tertiary Care Hospital: a Retrospective Observational Study

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease in which early diagnosis and initiation of disease-modifying antirheumatic therapy are important for limiting persistent inflammation, joint damage, and long-term disability. Despite advances in diagnostic criteria and treatment, delays in diagnosis remain common, particularly in settings where access to specialist rheumatological care and effective referral pathways is limited. This study assessed the magnitude of diagnostic delay and factors associated with prolonged delay among patients with RA attending a tertiary-care hospital in Multan, Pakistan.

Objective: To determine the duration of diagnostic delay among patients with RA and assess its association with selected demographic and diagnostic characteristics, including age, sex, place of residence, and documented diagnostic approach.

Methods: A retrospective observational study was conducted at Mukhtar A. Sheikh Hospital, Multan, Pakistan, over a period of six months. A total of 103 patients with documented RA were included through retrospective consecutive sampling. Data were extracted from medical records regarding age, sex, residence, date of first rheumatology clinic visit, documented diagnostic approach, date of diagnosis, and total diagnostic delay in months. Diagnostic delay was summarized using mean $\pm$ standard deviation (SD) and median with interquartile range (IQR). Because diagnostic delay was positively skewed, non-parametric tests were used for inferential analysis. Spearman's rank correlation was used to assess the relationship between age and diagnostic delay, while the Mann-Whitney U test and Kruskal-Wallis test were used for comparisons between residence and diagnostic-approach groups, respectively. A p-value <0.05 was considered statistically significant.

Results: The mean age of participants was 38.11 ± 11.15 years, with a median age of 36 years (IQR: 28.5-48.0); 102 (99.0%) patients were female. The median diagnostic delay was 5 months (IQR: 3-8), with a mean of 7.75 ± 15.97 months and a range of 1-156 months. Overall, 67 (65.0%) patients experienced a diagnostic delay exceeding 3 months, while 35 (34.0%) experienced a delay exceeding 6 months. Diagnostic delay demonstrated a significant positive correlation with age (Spearman's $\rho = 0.654$, $p < 0.001$). Patients aged ≥ 50 years had a median delay of 11 months compared with 3 months among those aged ≤ 29 years. Patients residing outside Multan had a significantly longer median diagnostic delay than those residing in Multan (10 vs. 4 months; Mann-Whitney U = 351.0, $p < 0.001$). Diagnostic approach was also significantly associated with diagnostic delay (Kruskal-Wallis H = 11.01, $p = 0.004$), although the smaller size of some diagnostic subgroups limits interpretation.

Conclusion: Diagnostic delay was common among patients with RA attending this tertiary-care hospital, with approximately two-thirds experiencing a delay exceeding three months. Older age and residence outside Multan were significantly associated with longer diagnostic delays. Strengthening early recognition of inflammatory arthritis, improving referral pathways, and

facilitating timely access to rheumatological services may help reduce diagnostic delays and promote earlier initiation of appropriate RA management.

Keywords: Rheumatoid Arthritis, Diagnostic Delay, Early Diagnosis, Rheumatology, Referral, Tertiary-Care Hospital, Pakistan.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized predominantly by persistent synovitis, progressive joint destruction, functional impairment, and a range of extra-articular manifestations. It represents one of the most important inflammatory rheumatic diseases because of its potential to cause irreversible structural damage and long-term disability. RA commonly affects individuals during their economically productive years and may consequently impose substantial personal, social, and healthcare-related burdens. The disease is heterogeneous in its clinical presentation, and early manifestations may overlap with other inflammatory or musculoskeletal disorders, making timely recognition and diagnosis challenging, particularly in settings where access to specialist rheumatological care is limited. [1,2] The diagnosis of RA is primarily clinical and is supported by serological and inflammatory markers and imaging findings. The 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria were developed specifically to facilitate identification of patients with RA at an earlier stage of disease. These criteria incorporate the number and distribution of involved joints, serological abnormalities including rheumatoid factor and anti-citrullinated protein antibodies (ACPA), acute-phase reactants, and symptom duration. Their emphasis on early disease characteristics represents a major shift from older criteria that were largely developed for patients with established disease. [1] Nevertheless, classification criteria are not intended to replace clinical diagnosis, and patients with early inflammatory arthritis may not initially fulfill all classification requirements. Consequently, clinical assessment and timely referral remain essential components of early RA management. [3]

The timing of diagnosis is particularly important because RA is associated with a limited therapeutic window during which early disease-modifying antirheumatic drug (DMARD) treatment may produce better clinical and structural outcomes. The concept of a "window of opportunity" suggests that

intervention early in the disease course may alter the subsequent trajectory of inflammation, joint damage, and functional disability. Evidence from early RA cohorts indicates that patients receiving treatment very early have better disease activity outcomes and less radiographic progression than patients whose treatment is initiated after a longer disease duration. [4,5] Accordingly, contemporary recommendations emphasize that DMARD therapy should be initiated as soon as RA is diagnosed and that disease activity should be monitored closely to achieve remission or low disease activity. [6]

Despite advances in diagnostic criteria and therapeutic strategies, delays between symptom onset, initial healthcare consultation, specialist assessment, diagnosis, and initiation of appropriate treatment remain common. Diagnostic delay is multifactorial and may occur at several levels of the healthcare pathway. Patient-related factors may include limited awareness of inflammatory arthritis, normalization of symptoms, use of alternative healthcare providers, financial constraints, and difficulties accessing healthcare. Physician- and system-related factors may include inadequate recognition of inflammatory arthritis in primary care, inappropriate referral pathways, limited availability of rheumatologists, and delays in specialist appointments. [7,8] These factors may be particularly important in low- and middle-income countries, where specialist rheumatology services are concentrated in major urban centers.

Evidence from Pakistan demonstrates that delays in accessing rheumatological care remain substantial. A Pakistani study involving 235 patients reported a median patient-related delay of 6 months and a median physician-related delay of 8 months, while the median interval from symptom onset to rheumatological evaluation was 24 months. The most frequently reported contributing factor was inadequate assessment at the primary-care level. [7] Another Pakistani study of patients with RA found that diagnostic and therapeutic delays were associated with clinical outcomes, emphasizing the potential consequences of prolonged delays within the disease pathway. [8] More recently, a

Pakistani cohort reported a mean diagnostic delay of approximately 17.8 months and highlighted differences according to disease presentation and onset pattern, further demonstrating that delayed recognition remains a relevant issue in local clinical practice. [9]

Although these studies provide important evidence regarding delayed diagnosis and referral in Pakistan, diagnostic delay may vary considerably according to geographic location, healthcare infrastructure, referral patterns, patient characteristics, and the organization of specialist services. There is therefore a need for institution-specific data describing the magnitude and distribution of diagnostic delay and identifying characteristics associated with prolonged delay. Such information may help identify potentially modifiable gaps in the pathway from symptom recognition to definitive diagnosis.

The present study was therefore conducted to assess the diagnostic delay among patients with rheumatoid arthritis attending a tertiary-care hospital and to examine its association with selected demographic and clinical characteristics, including age, sex, place of residence, and documented diagnostic approach. By quantifying the duration of diagnostic delay and identifying groups experiencing longer delays, this study aims to provide locally relevant evidence that may contribute to improved recognition, referral, and timely diagnosis of RA in tertiary-care settings.

Objective: The objective of this study was to determine the magnitude of diagnostic delay among patients with rheumatoid arthritis (RA) presenting to a tertiary-care hospital and to identify demographic and clinical factors associated with prolonged diagnostic delay.

MATERIALS AND METHODS

A retrospective observational study was conducted at Mukhtar A. Sheikh Hospital (MASH), Multan, Pakistan, a tertiary-care hospital providing specialized medical and rheumatological services to patients from Multan and surrounding districts of Southern Punjab. The study was conducted over a period of six months. The study population comprised patients with a documented diagnosis of rheumatoid arthritis (RA) who had attended the hospital and had sufficient clinical information available to assess the diagnostic pathway. A retrospective consecutive sampling

technique was used, and all eligible patient records available during the study period were reviewed. A total of 103 patients fulfilling the predefined eligibility criteria were included in the final analysis.

Patients were included if they had a documented diagnosis of RA, had undergone rheumatological or relevant clinical assessment, and had sufficient information regarding the diagnostic process to determine the duration of diagnostic delay. Patients were excluded if essential demographic or clinical information was missing, if the duration of diagnostic delay could not be determined from the available medical records, or if the diagnosis of RA could not be adequately established from the documented clinical information.

Data were retrospectively extracted from hospital medical records using a structured data-extraction proforma. The variables included age, sex, residential address, date of first rheumatology clinic visit, documented diagnostic approach, date of diagnosis, and total diagnostic delay in months. Residential status was categorized as Multan or outside Multan according to the address documented in the medical record. The documented diagnostic approach was standardized for analysis into RA/clinical diagnosis, RA factor, and RA factor with anti-cyclic citrullinated peptide (anti-CCP) assessment. The primary outcome variable was total diagnostic delay, expressed in months. For descriptive analysis, diagnostic delay was categorized into ≤ 3 months, 4–6 months, 7–12 months, and >12 months. Additional analyses considered delays exceeding 3 and 6 months. Age was analyzed as a continuous variable and categorized into ≤ 29 , 30–39, 40–49, and ≥ 50 years.

Data were entered, coded, cleaned, and analyzed using IBM SPSS Statistics version 25.0. Continuous variables were summarized using mean $\pm$ standard deviation (SD) when appropriate, while skewed variables were summarized using median and interquartile range (IQR). Categorical variables were presented as frequencies and percentages. Since diagnostic delay demonstrated a positively skewed distribution, non-parametric statistical methods were applied. The relationship between age and diagnostic delay was assessed using Spearman's rank correlation coefficient. The Mann–Whitney U test was used to compare diagnostic delay between patients residing in Multan and those residing outside Multan, while the Kruskal–

Wallis test was used to compare diagnostic delay across the different documented diagnostic-approach groups. Graphical methods, including bar charts and scatter plots, were used to illustrate the distribution of diagnostic delay and its relationship with selected variables. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. As the study involved retrospective review of existing medical records and did not involve any intervention or additional procedures, no direct risk was posed to the participants. Patient confidentiality was maintained throughout data extraction, analysis, and reporting. Identifying information was excluded from the analytical dataset, and the collected information was used solely for

research purposes. Institutional permission and ethical approval were obtained from the relevant institutional authority/ethics committee of Mukhtar A. Sheikh Hospital, Multan, in accordance with institutional requirements.

RESULTS

A total of 103 patients with rheumatoid arthritis (RA) were included in the retrospective observational study. The mean age of the study population was 38.11 ± 11.15 years, with a median age of 36 years (IQR: 28.5–48.0 years) and an age range of 19–64 years. The study population was predominantly female, comprising 102 (99.0%) females and 1 (1.0%) male. Seventy-five patients (72.8%) were residents of Multan, whereas 28 (27.2%) were from outside Multan.

Table 1. Demographic Characteristics of the Study Population

Characteristic	Value
Total patients	103 (100.0%)
Age, mean $\pm$ SD (years)	38.11 ± 11.15
Age, median (IQR), years	36 (28.5–48.0)
Age range, years	19–64
Female	102 (99.0%)
Male	1 (1.0%)
Residence in Multan	75 (72.8%)
Residence outside Multan	28 (27.2%)

The distribution of total diagnostic delay was positively skewed. The median diagnostic delay was 5 months (IQR: 3–8 months), whereas the mean diagnostic delay was 7.75 ± 15.97 months, with a range of 1–156 months. Among the participants, 36 (35.0%) had a diagnostic delay of ≤ 3 months, 32

(31.1%) had a delay of 4–6 months, 27 (26.2%) had a delay of 7–12 months, and 8 (7.8%) had a delay exceeding 12 months. Overall, 67 (65.0%) patients experienced a delay of more than 3 months, while 35 (34.0%) experienced a delay exceeding 6 months.

Table 2. Distribution of Diagnostic Delay

Diagnostic delay	N (%)
≤ 3 months	36 (35.0%)
4–6 months	32 (31.1%)
7–12 months	27 (26.2%)
>12 months	8 (7.8%)
>3 months, overall	67 (65.0%)
>6 months, overall	35 (34.0%)
Median (IQR), months	5 (3–8)
Mean $\pm$ SD, months	7.75 ± 15.97
Range, months	1–156

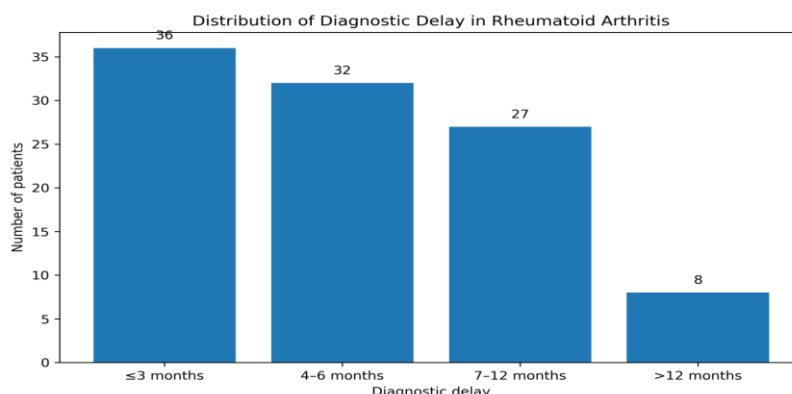


Figure 1. Distribution of Diagnostic Delay among Patients with Rheumatoid Arthritis.

A statistically significant positive correlation was observed between age and diagnostic delay. Spearman's rank correlation demonstrated a moderate-to-strong positive association ($\rho = 0.654$, $p < 0.001$), indicating that increasing age was associated with longer

diagnostic delay. When patients were stratified by age, the median diagnostic delay was 3 months among those aged ≤29 years, 4 months among those aged 30–39 years, 7 months among those aged 40–49 years, and 11 months among those aged ≥50 years.

Table 3. Diagnostic Delay According To Age Group

Age group	n	Median delay (months)	Mean ± SD (months)
≤29 years	30	3	3.53 ± 4.12
30–39 years	32	4	4.61 ± 2.45
40–49 years	20	7	7.45 ± 4.68
≥50 years	21	11	18.86 ± 32.76

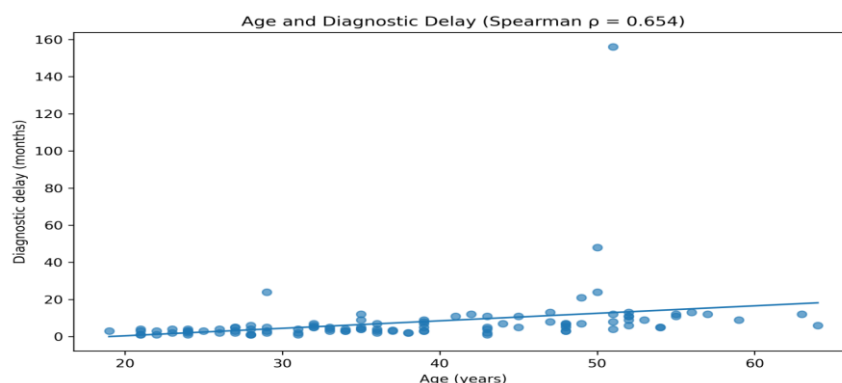


Figure 2. Relationship between Age and Diagnostic Delay. Each Point Represents An Individual Patient; The Fitted Line Illustrates The Overall Positive Association.

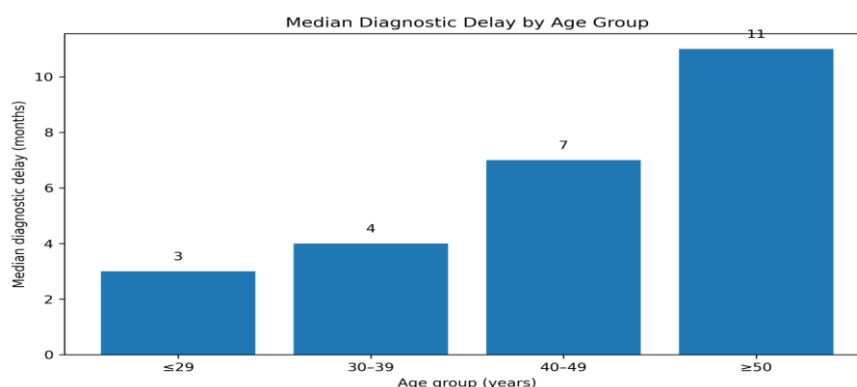


Figure 3. Median Diagnostic Delay According To Age Group.

Diagnostic delay also differed significantly according to place of residence. Patients residing outside Multan had a substantially longer diagnostic delay than those residing in Multan. The median diagnostic delay was 10 months among patients from outside Multan

compared with 4 months among Multan residents. The mean diagnostic delays were 16.43 ± 28.84 months and 4.51 ± 2.99 months, respectively. The difference was statistically significant according to the Mann-Whitney U test ($U = 351.0$, $p < 0.001$).

Table 4. Diagnostic Delay According To Place of Residence

Residence	n	Median delay (months)	Mean $\pm$ SD (months)	p-value
Multan	75	4	4.51 ± 2.99	
Outside Multan	28	10	16.43 ± 28.84	$<0.001^*$

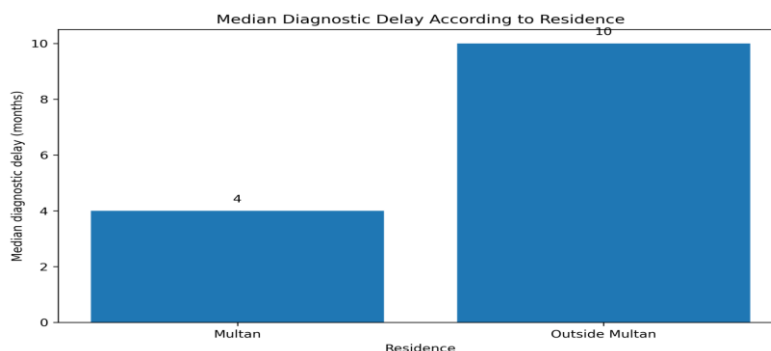


Figure 4. Median Diagnostic Delay According To Place of Residence.

The documented diagnostic approach was also evaluated in relation to diagnostic delay. After standardizing the terminology used in the dataset, patients were categorized as RA/clinical diagnosis ($n = 87$, 84.5%), RA factor ($n = 12$, 11.7%), and RA factor combined with anti-CCP ($n = 4$, 3.9%). The median diagnostic delay was 4 months in the RA/clinical diagnosis group, 12 months in the RA factor group, and 5 months in the RA

factor plus anti-CCP group. The corresponding mean diagnostic delays were 5.26 ± 3.64 , 26.33 ± 42.76 , and 6.25 ± 4.27 months, respectively. The overall difference was statistically significant (Kruskal-Wallis $H = 11.01$, $p = 0.004$). Because the latter two categories contained relatively few patients, this association should be interpreted cautiously.

Table 5. Diagnostic Delay According To Documented Diagnostic Approach

Diagnostic approach	n (%)	Median delay (months)	Mean $\pm$ SD (months)
RA/clinical diagnosis	87 (84.5%)	4	5.26 ± 3.64
RA factor	12 (11.7%)	12	26.33 ± 42.76
RA factor + anti-CCP	4 (3.9%)	5	6.25 ± 4.27
Overall	103 (100.0%)	5	7.75 ± 15.97
Kruskal-Wallis H		11.01	$p = 0.004$

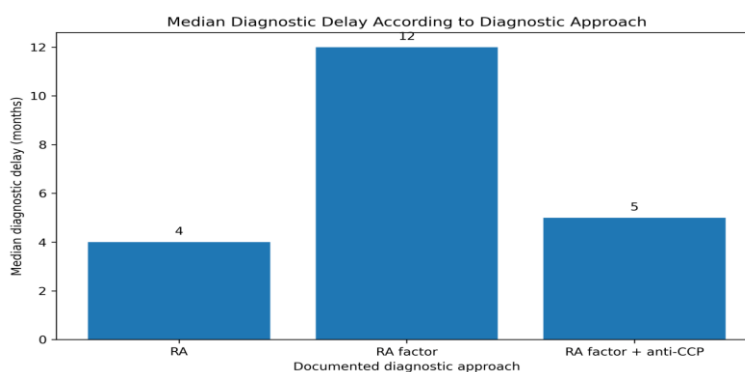


Figure 5. Median Diagnostic Delay According To Documented Diagnostic Approach.

Because only one male patient was included, a meaningful statistical comparison of diagnostic delay according to sex was not possible. Overall, the findings demonstrate that diagnostic delay was common in this tertiary-care cohort of patients with rheumatoid arthritis. Approximately two-thirds of patients experienced a delay exceeding 3 months, and one-third experienced a delay exceeding 6 months. Older age and residence outside Multan were significantly associated with longer diagnostic delay, while the documented diagnostic approach also showed a statistically significant association. Given the marked positive skewness of diagnostic delay and the presence of an extreme 156-month observation, median and IQR are considered the more appropriate primary descriptive measures for this outcome.

DISCUSSION

The present retrospective observational study evaluated diagnostic delay among 103 patients with rheumatoid arthritis (RA) attending a tertiary-care hospital in Multan. The principal finding was that diagnostic delay remained substantial, with a median delay of 5 months (IQR: 3–8) and 65.0% of patients experiencing a delay of more than 3 months. Furthermore, increasing age and residence outside Multan were significantly associated with longer diagnostic delay. The findings are clinically relevant because early recognition and treatment of RA are important for preventing persistent inflammation, structural joint damage, functional impairment, and long-term disability.

The median diagnostic delay observed in the present study was shorter than that reported in several Pakistani studies. Naeem et al. reported a median diagnostic delay of 12 months (IQR: 3–48 months) among 102 patients with RA presenting to a rheumatology service in Lahore, while another Pakistani study involving 235 patients reported a median interval of 24 months from symptom onset to rheumatological evaluation. [10,11] A more recent Pakistani cohort of 1,200 patients reported a mean diagnostic delay of 17.8 ± 27.9 months. [12] Differences between these estimates may reflect variations in study populations, definitions of diagnostic delay, referral pathways, healthcare settings, and methods used to determine the onset of disease [16]. The comparatively shorter delay in the present cohort may partly reflect its

setting in a tertiary-care hospital with direct access to rheumatological assessment.

Despite this relatively shorter median delay, the finding that approximately two-thirds of patients experienced delays exceeding 3 months remains important. Early treatment is particularly relevant in RA because evidence supports a therapeutic window during the early phase of disease. Very early initiation of disease-modifying antirheumatic drugs (DMARDs) has been associated with improved disease activity and reduced radiographic progression compared with later treatment. [13] Contemporary EULAR recommendations therefore emphasize that DMARD therapy should be initiated as soon as RA is diagnosed, with treatment aimed at achieving sustained remission or low disease activity. [14] Consequently, even several months of diagnostic delay may represent a clinically meaningful missed opportunity.

A significant positive association was identified between age and diagnostic delay in the present study (Spearman's $\rho = 0.654$, $p < 0.001$). Median delay increased from 3 months among patients aged ≤ 29 years to 11 months among those aged ≥ 50 years. This observation is consistent with findings from Pakistan, where older age has been identified among factors contributing to delayed referral and diagnosis. [10,15] Older patients may have more complex presentations, multiple musculoskeletal complaints, or a greater likelihood of attributing symptoms to age-related conditions, potentially complicating early recognition. However, the present observational design does not establish causality, and age may also act as a marker for other unmeasured patient- or healthcare-related factors.

Residence was another significant determinant of diagnostic delay. Patients residing outside Multan had a median delay of 10 months, compared with 4 months among Multan residents ($p < 0.001$). This geographical difference may reflect barriers related to accessibility of specialist services, referral pathways, transportation, healthcare costs, or delays in reaching rheumatological care. A Pakistani study similarly identified delayed referral at the primary-care level as the most frequently reported contributor to prolonged access to rheumatologists. [11] These findings highlight the potential importance of strengthening referral pathways and improving recognition of inflammatory arthritis outside major urban centers.

The documented diagnostic approach was also significantly associated with diagnostic delay. Patients categorized as RA/clinical diagnosis had a median delay of 4 months, compared with 12 months among those with an RA-factor-based approach. However, this finding should be interpreted cautiously because the diagnostic subgroups were small and the observational dataset does not establish whether the diagnostic test itself caused delay. Previous Pakistani evidence has also suggested that rheumatoid factor positivity was not independently responsible for diagnostic or therapeutic delay. [10] Thus, the present finding is more appropriately interpreted as an association between the documented diagnostic pathway and delay rather than evidence that a particular diagnostic test increases diagnostic delay.

The study has several limitations. Its retrospective single-center design limits generalizability, and the predominance of female participants restricts sex-based comparisons. Important potential determinants such as socioeconomic status, education, first healthcare provider consulted, number of consultations before diagnosis, disease presentation, and treatment initiation were not consistently available. In addition, the extreme 156-month delay may influence the mean; therefore, median and IQR provide a more robust representation of the distribution. Nevertheless, the study provides useful local evidence regarding diagnostic delay in RA and identifies age and geographical residence as important characteristics associated with prolonged diagnostic pathways.

CONCLUSION

The present study demonstrated that diagnostic delay remains a considerable problem among patients with rheumatoid arthritis attending a tertiary-care hospital in Multan. The median diagnostic delay was 5 months, and nearly two-thirds of patients experienced a delay exceeding 3 months. Increasing age was significantly associated with longer diagnostic delay, with older patients demonstrating progressively greater delays. Patients residing outside Multan also experienced significantly longer diagnostic delays than those residing within the city, suggesting that geographical accessibility and referral pathways may contribute to delayed diagnosis. The documented diagnostic approach was additionally associated with diagnostic delay, although this finding should

be interpreted cautiously because of the small number of patients in some diagnostic categories. These findings emphasize the importance of early recognition of inflammatory arthritis, timely referral to rheumatology services, improved diagnostic pathways, and equitable access to specialist care, particularly for patients from areas outside major urban centers. Strengthening primary-care awareness and referral mechanisms may help reduce diagnostic delays and facilitate earlier initiation of appropriate disease-modifying therapy. Further multicenter prospective studies are recommended to identify patient-, physician-, and health-system-level determinants of diagnostic delay and to evaluate interventions aimed at reducing these delays.

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