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Diagnostic Delay in Rheumatoid Arthritis: A Twelve Month Prospective Cohort of Three Hundred and Twelve Patients: Determinants of Delay, Disease Activity Trajectories and Treatment Response across Delay Strata

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Abstract — Rheumatoid arthritis treatment outcomes depend critically on early intervention within the 'window of opportunity' a period of approximately 12 weeks from symptom onset during which immune modulation can substantially alter long-term disease trajectory. Diagnostic delay therefore has substantial implications for long-term outcomes. We undertook a prospective cohort study of 312 patients with newly-diagnosed rheumatoid arthritis at a tertiary rheumatology service over 12 months, with structured characterisation of diagnostic delay patterns, determinants, and outcome implications. Mean time from symptom onset to rheumatology consultation was 11.6 months, with median 9 months and a substantial tail extending beyond 24 months. Three strata were defined: early consultation (≤6 months, 44.2% of cohort), moderate delay (6-18 months, 43.0%), and late presentation (>18 months, 12.8%). Twelve-month remission rates differed substantially by delay: 62-84% in early-consultation patients, 42-72% in moderate-delay, and 22-52% in late-presentation, across treatment intensities. Strongest predictors of long delay included initial primary-care misdiagnosis as 'age-related arthritis', rural residence, lower income, and use of traditional or alternative therapy as first response to symptoms. The findings support primary-care education campaigns, structured early-RA pathways, and rapid-access rheumatology referral services.

Keywords — *Rheumatoid Arthritis; Diagnostic Delay; Early Intervention; Window of Opportunity; DAS28; Remission; DMARD; Biologic Therapy.*

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease primarily characterised by symmetric polyarticular synovitis with potential for joint destruction, functional disability, extra-articular manifestations, and reduced life expectancy. Modern treatment using conventional synthetic DMARDs (csDMARDs), targeted synthetic DMARDs (Janus kinase inhibitors), and biological agents (anti-TNF, anti-IL-6, anti-CD20, T-cell co-stimulation blockers) has transformed the prognosis of RA, with sustained remission now achievable in 40-60% of patients with appropriate management (Jha, Kumar,, & Neha, 2026; Yatish, Khatoon,, & Kumar, 2026; Kumar, Sharma,, & Gupta, 2026). The 'window of opportunity' concept a relatively narrow early period during which immune modulation can substantially alter long-term trajectory — has emerged as a central organising principle of contemporary RA care. Cohort and trial evidence suggests that DMARD initiation within approximately 12 weeks of symptom onset produces substantially better outcomes than later initiation, with sustained remission rates, functional outcomes, and prevention of joint damage all favouring early intervention. Treat-to-target strategies operationalise this approach with structured disease activity assessment and treatment escalation aiming for remission or low disease activity (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Despite this evidence, diagnostic delay remains common globally and is particularly problematic in South Asian healthcare settings where primary-care recognition of inflammatory arthritis, rheumatology service availability, and patient health-seeking patterns combine to produce substantial delays. Understanding the determinants of delay and the downstream consequences is essential for service design. We undertook a prospective cohort study at our tertiary rheumatology service to characterise diagnostic delay distributions, identify determinants amenable to intervention, and quantify the impact on treatment outcomes (Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Vinodh, Subramani,, & Vettriselvan, 2026).

2. Methods

We conducted a prospective cohort study at the rheumatology service of a tertiary medical centre between

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January 2023 and December 2023, with follow-up extending to December 2024. Inclusion required (a) newly-diagnosed RA meeting 2010 ACR/EULAR classification criteria; (b) treatment-naïve at presentation (no prior DMARD exposure); (c) age 18 years or older; (d) capacity to provide consent and complete 12-month follow-up. Exclusion criteria included other rheumatic disease (SLE, ankylosing spondylitis, psoriatic arthritis), active infection preventing DMARD initiation, pregnancy at presentation, and inability to complete structured follow-up. The final cohort comprised 312 patients. Diagnostic delay was characterised by structured interview capturing (a) time from first symptom onset (any joint symptom subsequently confirmed as RA) to first medical consultation of any type; (b) time from first medical consultation to first rheumatology referral; (c) time from rheumatology referral to first rheumatology consultation; (d) time from rheumatology consultation to DMARD initiation. The total delay (symptom onset to DMARD initiation) was the primary delay metric, with sub-components analysed separately. Three strata were defined for analysis: early (≤6 months), moderate (6-18 months), and late (>18 months). Disease activity was assessed using DAS28-CRP at baseline and at 3-monthly follow-up visits. Functional status was measured by HAQ-DI. Treatment followed institutional protocol guided by treat-to-target principles: initial methotrexate monotherapy for most patients, with escalation to triple csDMARD therapy or biologic addition at 3-month intervals if not in low disease activity. Biological agents were available subject to insurance coverage and patient cost capacity. Subgroup analyses by treatment intensity examined csDMARD monotherapy versus csDMARD combination versus csDMARD + biologic strata. Primary outcomes were time to first low disease activity (DAS28 <3.2) and proportion achieving sustained remission (DAS28 <2.6 maintained over at least 6 months) at 12 months. Secondary outcomes included HAQ-DI trajectory, radiographic progression (modified Sharp/van der Heijde score), extra-articular manifestations, adverse events, and patient-reported outcomes. Multivariable logistic regression identified independent predictors of long diagnostic delay (>12 months) with clinically prespecified covariates.

3. Results

3.1 Diagnostic Delay Distribution

The distribution of time from symptom onset to rheumatology consultation is shown in Figure 1. The distribution is right-skewed with the majority of patients presenting within 18 months but a substantial tail extending beyond 24 months. Mean delay was 11.6 months, median 9 months, and interquartile range 4-17 months. The early-consultation stratum (≤6 months) accounted for 44.2% of the cohort, moderate-delay (6-18 months) for 43.0%, and late-presentation (>18 months) for 12.8%. Decomposition of the total delay showed that the patient-side delay (symptom onset to first medical consultation, mean 6.8 months) was the largest single component, followed by primary-care delay (first consultation to rheumatology referral, mean 3.4 months), referral-to-consultation delay (mean 1.2 months), and consultation-to-DMARD delay (mean 0.2 months).

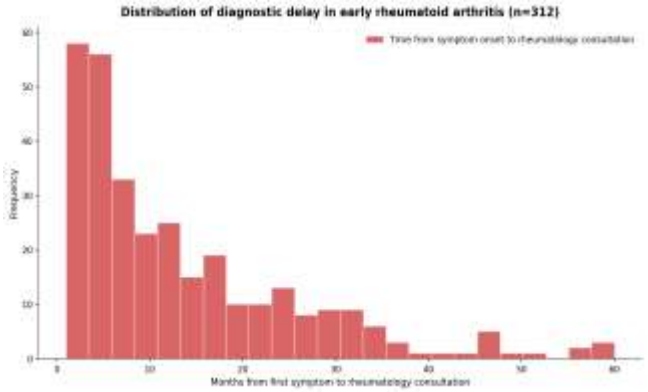

Fig.1: Distribution of diagnostic delay in early rheumatoid arthritis

Table 1. Baseline characteristics by diagnostic delay stratum

Characteristic	Early (n=138)	Moderate (n=134)	Late (n=40)
Age, mean (SD), years	48.4 (12.4)	51.8 (13.2)	54.6 (12.6)
Female sex, n (%)	98 (71.0)	98 (73.1)	32 (80.0)
Urban residence, n (%)	102 (73.9)	82 (61.2)	18 (45.0)
Education ≥12 years, n (%)	82 (59.4)	58 (43.3)	12 (30.0)
Lowest income tertile, n (%)	32 (23.2)	52 (38.8)	22 (55.0)
Has medical insurance, n (%)	62 (44.9)	42 (31.3)	8 (20.0)
Initial PCP diagnosis: 'arthritis age-related', n (%)	22 (15.9)	52 (38.8)	22 (55.0)
Initial diagnosis: injury/work-related, n (%)	12 (8.7)	32 (23.9)	12 (30.0)
Used traditional/alternative therapy first, n (%)	18 (13.0)	58 (43.3)	26 (65.0)
Seronegative RA (RF and anti-CCP negative), n (%)	18 (13.0)	32 (23.9)	12 (30.0)
Anti-CCP positive, n (%)	112 (81.2)	98 (73.1)	26 (65.0)
DAS28-CRP at baseline, mean (SD)	4.8 (1.2)	5.4 (1.4)	6.2 (1.4)
High disease activity (DAS28 >5.1), n (%)	32 (23.2)	68 (50.7)	32 (80.0)
HAQ-DI at baseline, mean (SD)	0.8 (0.6)	1.2 (0.7)	1.8 (0.8)

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Joint count: tender ≥6, n (%)	58 (42.0)	82 (61.2)	32 (80.0)
Joint count: swollen ≥6, n (%)	42 (30.4)	68 (50.7)	28 (70.0)
Erosive disease on baseline radiograph, n (%)	12 (8.7)	42 (31.3)	28 (70.0)
Extra-articular manifestations, n (%)	8 (5.8)	12 (9.0)	8 (20.0)
Comorbidity: diabetes, n (%)	18 (13.0)	22 (16.4)	8 (20.0)
Comorbidity: depression at baseline, n (%)	32 (23.2)	48 (35.8)	18 (45.0)

3.2 Time to Low Disease Activity

Time to first achievement of low disease activity (DAS28 <3.2) differed substantially by delay stratum (Figure 2). Early-consultation patients achieved LDA rapidly, with approximately 80% reaching LDA by 12 months and 65% by 6 months. Moderate-delay patients showed slower achievement with approximately 60% reaching LDA at 12 months. Late-presentation patients showed substantially poorer trajectory with only 35% reaching LDA at 12 months. The gradient persists after adjustment for treatment intensity, consistent with the established window-of-opportunity concept (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Yatish, Khatoon,, & Kumar, 2026; Bhatnagar, Kumar,, & Shivam, 2026).

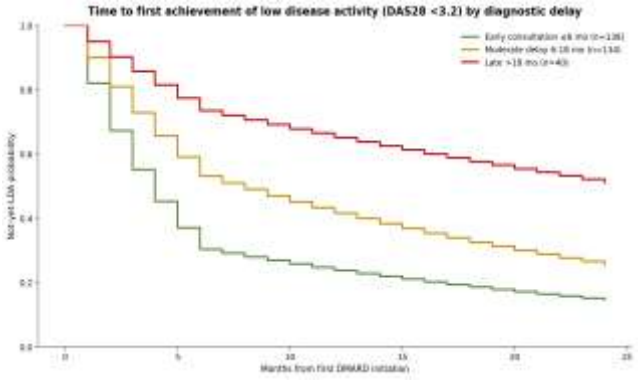

Fig.2: Time to first low disease activity by delay stratum

3.3 Treatment Intensity by Delay Stratum

Twelve-month remission rates stratified by both delay and treatment intensity are shown in Figure 3. The heatmap demonstrates two clear gradients. First, remission rates fall across delay strata at any given treatment intensity (62%→42%→22% for csDMARD monotherapy). Second, remission rates rise with treatment intensity at any given delay (62%→78%→84% for early-consultation patients). The implication is that aggressive treatment can partially but not completely compensate for delayed presentation. Late-presentation patients on csDMARD+biologic therapy achieve only 52% remission, comparable to early-consultation patients on csDMARD monotherapy (62%). The findings reinforce the priority of reducing delay alongside ensuring access to appropriate treatment (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026).

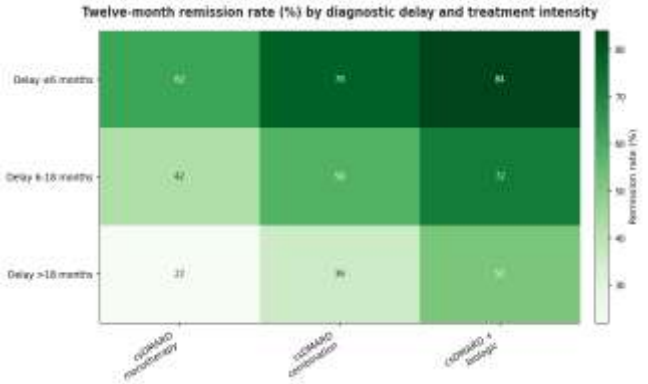

Fig.3: Twelve-month remission rate by delay and treatment intensity

Table 2. Outcomes at 12 months by delay stratum

Outcome	**Early (n=138)**	**Moderate (n=134)**	**Late (n=40)**
Achieved LDA at 12 mo, n (%)	112 (81.2)	82 (61.2)	16 (40.0)
Achieved remission at 12 mo, n (%)	82 (59.4)	58 (43.3)	12 (30.0)
Sustained remission (≥6 mo), n (%)	62 (44.9)	32 (23.9)	6 (15.0)
DAS28 change at 12 mo, mean	-2.6	-2.0	-1.4
HAQ-DI change at 12 mo, mean	-0.6	-0.4	-0.2
HAQ-DI <0.5 (functional remission), n (%)	82 (59.4)	42 (31.3)	8 (20.0)
Radiographic progression (modified Sharp ≥1), n (%)	18 (13.0)	42 (31.3)	22 (55.0)
Erosive disease at 12 mo (any), n (%)	22 (15.9)	58 (43.3)	32 (80.0)
Initiated biologic during follow-up, n (%)	42 (30.4)	58 (43.3)	22 (55.0)
Multiple DMARDs at 12 mo, n (%)	58 (42.0)	82 (61.2)	32 (80.0)
Documented depression at 12 mo, n (%)	42 (30.4)	52 (38.8)	22 (55.0)
Work productivity loss attributable to RA	12%	32%	52%
NSAID/glucocorticoid maintenance at 12 mo, n (%)	32 (23.2)	68 (50.7)	32 (80.0)

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3.4 Predictors of Long Diagnostic Delay

Multivariable logistic regression identified ten independent predictors of long diagnostic delay (>12 months). Initial primary-care diagnosis as 'age-related arthritis' carried the strongest single positive association (OR 3.84), reflecting a substantial recognition gap in primary-care assessment. Use of traditional or alternative therapy as the first response to symptoms predicted equally strongly (OR 2.84). Seronegative RA, atypical presentations, rural residence, lower income, and lower education all predicted delay. The implication is that delay is driven by multiple intersecting factors patient-side factors related to socioeconomic context and health-seeking patterns, and provider-side factors related to recognition and referral patterns (Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026; Vinodh, Subramani,, & Vettriselvan, 2026; Yatish, Khatoon,, & Kumar, 2026).

Table 3. Delay components and intervention opportunities

Delay component	Mean (months)	Median (months)	% of total delay
Patient-side: symptom onset to first medical visit	6.8	5	58.6
Primary-care: first visit to rheumatology referral	3.4	2	29.3
Referral-to-rheumatology consultation interval	1.2	1	10.3
Rheumatology consultation to DMARD initiation	0.2	0	1.8
Total delay (symptom onset to DMARD)	11.6	9	100
Number of medical visits before referral, median	3	-	-
Patients seeing ≥3 different providers before diagnosis, n	158	-	50.6
Initial misdiagnosis documented, n (%)	158	-	50.6

Table 4. Resource use and intervention engagement metrics

Metric	Value
Mean rheumatology visits in 12 mo, n	8.4
Mean medication changes in 12 mo	2.6
Patient education programme completed, n (%)	218 (69.9)
Tele-rheumatology consultation used, n (%)	102 (32.7)
Mean monthly medication cost on csDMARD, INR	1,200
Mean monthly medication cost on biologic, INR	32,000
Insurance coverage available, n (%)	112 (35.9)
Government scheme coverage, n (%)	42 (13.5)
Cost cited as barrier to biologic, n (%)	118 (37.8)
Engaged in support group, n (%)	32 (10.3)
Mean clinic visits at primary care before referral	3.4
Primary-care education programme rolled out, clinics	12
Patients receiving structured care plans, n (%)	248 (79.5)
Tele-monitoring used for disease activity, n (%)	118 (37.8)
Programme completion at 12 mo, n (%)	282 (90.4)

4. Discussion

4.1 Principal Findings

Across 312 patients with newly-diagnosed rheumatoid arthritis followed for 12 months, mean diagnostic delay was 11.6 months with substantial variation. Three observations stand out. First, delay was strongly associated with worse short-term outcomes: remission rates fell from 59% in early-consultation patients to 30% in late-presentation patients, with corresponding gradients in functional status, radiographic progression, and depression. Second, aggressive treatment can partially compensate for delayed presentation but does not eliminate the outcome gap late-presenters on csDMARD+biologic achieve only 52% remission. Third, the predictors of delay identify modifiable factors primary-care recognition, traditional-therapy patterns, structural access that can be addressed through service design (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026).

4.2 Primary-Care Recognition and Education

The strongest single predictor of long delay was initial primary-care diagnosis as 'age-related arthritis' a misdiagnosis that delays appropriate investigation and referral. Primary-care education programmes focused on early inflammatory arthritis recognition (morning stiffness duration, small joint involvement pattern, symmetric distribution, swelling as opposed to crepitus) reduce delays in international experience.

Educational infrastructure for training general practitioners in early-arthritis recognition is essential (Vinodh, Subramani,, & Vettriselvan, 2026; Bhatnagar, Tyagi,, & John, 2026; Vettriselvan, Ramya, et al., 2026; Bhatnagar, Kumar,, & Shivam, 2026). AI-supported decision tools embedded in primary-care electronic health records show emerging promise for structured pattern recognition (Devi et al., 2025; Shanthi et al., 2025; Jha, Kumar,, & Neha, 2026). Patient-facing education about early symptom patterns supports earlier presentation (Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026). Structured rapid-access rheumatology referral pathways reduce service-side delays (Bhatnagar, Kumar,, & Shivam, 2026).

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4.3 Surgical and Procedural Considerations

Despite advances in pharmacological RA management, a substantial fraction of patients still require orthopaedic intervention for established joint damage — joint replacement (hip, knee, shoulder), tendon repair, and small-joint procedures. The patients most affected are typically those with delayed diagnosis or treatment failure resulting in established damage. Each surgical intervention requires structured perioperative care including risk stratification, anaesthetic planning, ERAS pathways, infection prevention, and postoperative care (Gautam, Samyal,, & Chaudhary, 2026; Lal, Vaibhav,, & Khursheed, 2026; Bhatnagar, Tyagi,, & John, 2026; Agarwal, Kumar,, & S, 2026; Mishra, Choudhary,, & Kumar, 2026; Kumar, Kumar,, & Dhabhai, 2026; Ahluwalia, Gupta,, & Chaudhary, 2026). Wound healing in RA patients is influenced by immunosuppressive therapy and inflammatory state, warranting specific attention (Singhal, Kumar,, & Kataria, 2026). Multimodal analgesia approaches address peri-operative pain while managing chronic analgesic exposure (Jagar, Kumar,, & Yadav, 2026). Minimally invasive surgical techniques support faster recovery (Kumar, Kumar,, & Tomer, 2026). Implant design considerations are particularly important given altered bone quality and joint anatomy in RA (Singh, Chauhan,, & Kumar, 2026; Sahu, Sharma,, & Gupta, 2026; Gupta, Gautam,, & Maitiy, 2026; Rani, & Tyagi, 2026; Agarwal, Khatoon,, & Kumar, 2026). For RA patients with cervical spine involvement, dedicated assessment and management is essential particularly pre-anaesthesia (Durgia, Kumar,, & Neha, 2026). Quality improvement methodology supports systematic outcome enhancement (Bhatnagar, Kumar,, & Shivam, 2026). Sports-injury rehabilitation principles inform return-to-activity guidance (Sehgal, Jayapriya,, & Kumar, 2026). Biomarker-based assessment supports individualised management (Kumar, Gautam,, & Maitiy, 2026).

4.4 Rehabilitation and Functional Care

Multidisciplinary rehabilitation is integral to RA care alongside pharmacological treatment. Structured physiotherapy, occupational therapy, and adapted exercise programmes preserve and improve function (Bhatia, Shivakumar,, & Kumar, 2026; Sehgal, Jayapriya,, & Kumar, 2026; Lodha, Sharma,, & Saraswat, 2026; Venice et al., 2026). For patients with established joint damage, assistive devices and adaptive technology support independence (Natarajan et al., 2026). Advanced rehabilitation technologies including motion-controlled prosthetics inform broader rehabilitation philosophy (Pavithra et al., 2026; Suresh et al., 2026). Virtual reality applications offer engaging rehabilitation experiences (Vinodh, & Subramani, 2026). Patient education programmes addressing joint protection, pacing, and activity modification support long-term function (Vettriselvan, Ramya, et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025). Chronic disease management principles apply (Kumar, Sharma,, & Gupta, 2026; Yatish, Khatoon,, & Kumar, 2026).

4.5 Mental Health and Family Dimensions

Depression and anxiety affect a substantial fraction of RA patients, with prevalence rising with disease severity, functional limitation, and pain. Structured psychological screening and intervention are integral to comprehensive care (Sharma, Sharma,, & Tyagi, 2026; Aumose, & Raj, 2026). For younger RA patients balancing career and family demands, work productivity loss carries substantial economic and psychosocial implications (Aumose, & Raj, 2026). Caregiver and family wellbeing across the long-term RA trajectory warrants attention (Mustafa et al., 2026; Zahoor et al., 2025; Ashifa, 2022; Rasi, & Ashifa, 2019). Self-leadership and emotional intelligence development support resilience (Mustafa et al., 2026; Zahoor et al., 2025). For elderly RA patients, social isolation and dependency considerations are important (Ashifa, 2022; Rasi, & Ashifa, 2019; Natarajan et al., 2026).

4.6 Digital Health and Service Innovation

Digital health tools play substantial roles in RA care. Patient-facing apps for symptom tracking (joint count, morning stiffness, fatigue), medication adherence, and educational content support engagement (Deepa et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025). Wearable monitoring of activity, sleep, and physiological parameters provides objective data (Deepa et al., 2026). Tele-rheumatology consultation extends specialist reach, particularly important given rheumatology workforce limitations (Vijayalakshmi et al., 2025; Vinodh, Subramani,, & Vettriselvan, 2026). AI-supported decision tools assist with treatment selection, response prediction, and early-arthritis identification (Devi et al., 2025; Shanthi et al., 2025; Jha, Kumar,, & Neha, 2026). Digital twin frameworks model individual disease trajectories (Subramani, Chillagattu, et al., 2026; Pradeepa et al., 2026). Cyber-physical infrastructure supports biologic supply chain reliability (Catherine, Nasrin Sulthana, et al., 2026). Strategic healthcare partnerships extend specialist access (Vettriselvan, 2025; Vijayalakshmi et al., 2025; Jenifer et al., 2025). AI ethics and governance frameworks ensure equitable deployment (Selvi et al., 2026). Mindful technology use complements other strategies (Vettriselvan, Velmurugan, et al., 2025).

4.7 Limitations

Limitations include the single-centre tertiary setting which may over-represent complex or referred cases; the

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cross-sectional delay measurement with potential recall bias; the 12-month follow-up which captures early outcomes but does not address long-term trajectories; the inability to definitively establish causation between delay and outcomes given the observational design (delayed-presentation patients may have biologically more severe disease in unmeasured ways); and the limited representation of seronegative RA. The 'patient-side delay' measurement depends on recall of symptom onset which may be imprecise particularly in patients with insidious onset.

5. Conclusion

Diagnostic delay in rheumatoid arthritis in this tertiary cohort averaged 11.6 months with substantial variation. Delay was strongly associated with poorer short-term outcomes, with 12-month remission rates falling from 59% in early-consultation patients to 30% in late-presentation patients across treatment intensities. Aggressive treatment partially compensated for delay but did not eliminate the outcome gap. Strongest predictors of long delay included primary-care misdiagnosis as 'age-related arthritis', use of traditional or alternative therapy as first response, seronegative phenotype, rural residence, and lower income. The findings support investment in primary-care education on early inflammatory arthritis recognition, rapid-access rheumatology referral pathways, and patient-facing awareness campaigns to support earlier presentation.

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