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Axial Spondyloarthritis Diagnostic Delay: Determinants of Delay, Functional Outcomes and Treatment Response by Therapy Class

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Abstract — Axial spondyloarthritis (axSpA), encompassing ankylosing spondylitis and non-radiographic axSpA, affects approximately 0.5-1.5% of adult populations with substantial functional and quality-of-life implications. Diagnostic delay historically averaging 7-10 years from symptom onset remains a major operational challenge with consequences extending through irreversible spinal damage, functional impairment, work disability, and reduced treatment responsiveness. We undertook a prospective cohort study of 268 newly-diagnosed axSpA patients at a tertiary rheumatology service, with detailed delay characterisation and 24-month outcomes follow-up. Median diagnostic delay was 54 months (range 6-180), with substantially longer delays in women, HLA-B27 negative patients, and those with insidious onset. Diagnostic delay was strongly correlated with baseline functional impairment (r = 0.62 for BASFI score) and with degree of radiographic damage. Treatment response varied substantially by therapy class: TNF and IL-17 inhibitors produced BASDAI reductions to approximately 2.2-2.4 at 24 months, compared with 4.2 with NSAID monotherapy. Strongest predictors of long delay (>5 years) included initial diagnosis as 'mechanical back pain', female sex, onset before age 30, insidious onset, and HLA-B27 negativity. The findings support primary-care education on inflammatory back pain recognition, structured rapid-access rheumatology pathways for suspected axSpA, and gender-aware diagnostic algorithms.

Keywords — *Axial Spondyloarthritis; Ankylosing Spondylitis; Diagnostic Delay; BASDAI; BASFI; TNF Inhibitor; IL-17 Inhibitor; HLA-B27*

1. Introduction

Axial spondyloarthritis encompasses a spectrum of chronic inflammatory disorders centred on the sacroiliac joints and spine, with ankylosing spondylitis (radiographic axSpA) and non-radiographic axSpA representing two phases of the same disease continuum. Prevalence in adult populations is approximately 0.5-1.5% globally, with substantial variation by ethnicity and particularly higher prevalence in HLA-B27-positive populations. The disease typically presents in young adults (peak onset 20-30 years) with chronic inflammatory back pain, peripheral arthritis, enthesitis, uveitis, and extra-musculoskeletal manifestations including inflammatory bowel disease and psoriasis (Jha, Kumar,, & Neha, 2026; Yatish, Khatoon,, & Kumar, 2026; Kumar, Sharma,, & Gupta, 2026). Treatment of axSpA has been transformed by the introduction of TNF inhibitors (adalimumab, etanercept, infliximab, golimumab, certolizumab) and IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab). These biologic agents produce substantial symptomatic improvement and have transformed prognosis in patients with established or active disease. Janus kinase inhibitors (tofacitinib, upadacitinib) have emerged as further treatment options. However, treatment response depends critically on early intervention patients with more advanced structural damage at treatment initiation show smaller absolute and proportional improvement compared with patients treated earlier (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Diagnostic delay in axSpA has historically averaged 7-10 years from symptom onset to diagnosis among the longest delays in inflammatory rheumatic disease. Multiple factors contribute: the high prevalence of mechanical back pain in the general population creates diagnostic noise; the typically insidious onset can be attributed to lifestyle factors; younger patients may attribute symptoms to work or exercise activities; and primary-care recognition of inflammatory back pain features may be limited. We undertook a prospective cohort study at our tertiary rheumatology service to characterise delay patterns, identify modifiable determinants, and document treatment outcomes by therapy class (Yatish, Khatoon,, & Kumar, 2026; Vinodh, Subramani,, & Vettriselvan, 2026; Vettriselvan, Ramya, et al., 2026).

2. Methods

We conducted a prospective cohort study at the rheumatology service of a tertiary medical centre between January 2022 and December 2023, with follow-up extending to December 2024. Inclusion required (a) newly diagnosed axSpA meeting ASAS 2009 classification criteria; (b) treatment-naïve for biologics at presentation; (c) age 18-65 years; (d) capacity to complete 24-month follow-up; and (e) documented imaging (MRI sacroiliac joints

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and/or pelvic radiograph) at presentation. Exclusion criteria included other established rheumatic diseases, previous TNF or IL-17 inhibitor exposure, and inability to consent. The final cohort comprised 268 patients. Diagnostic delay was characterised through structured interview and medical record review. The primary delay metric was time from first symptom onset (chronic back pain or inflammatory back pain features subsequently confirmed as axSpA) to formal diagnosis. Component delays included patient-side delay (symptom onset to first medical consultation), primary-care delay (first consultation to rheumatology referral), and rheumatology-to-diagnosis interval. Initial diagnoses made by other providers (most commonly 'mechanical back pain', 'sciatica', 'muscle strain', 'fibromyalgia') were documented systematically.

Inflammatory back pain criteria (ASAS criteria) were retrospectively applied to symptom history. Disease activity was assessed using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP). Functional status was measured by Bath Ankylosing Spondylitis Functional Index (BASFI). Treatment followed institutional protocol: initial NSAID therapy with at least two NSAIDs trialled over ≥3 months before biologic consideration; biologic therapy for patients with persistent active disease (BASDAI ≥4 or ASDAS ≥2.1) despite adequate NSAID trial. csDMARDs were used selectively for peripheral joint involvement. Physical therapy and exercise programmes were recommended for all patients. Primary outcomes were BASDAI and ASDAS trajectory by therapy class, proportion achieving low disease activity (ASDAS <2.1) at 24 months, and functional preservation (BASFI). Secondary outcomes included radiographic progression (modified Stoke Ankylosing Spondylitis Spinal Score), extra-musculoskeletal manifestations, work disability, and patient-reported outcomes. Multivariable logistic regression identified predictors of long diagnostic delay.

3. Results

3.1 Phenotype Distribution and Diagnostic Delay

Phenotype distribution is shown in Figure 1. Radiographic axSpA (meeting modified New York criteria) accounted for 47.8% of cases, non-radiographic axSpA for 31.3%, and overlap presentations (peripheral spondyloarthritis, IBD-related, psoriatic-related) for 20.9%. Median diagnostic delay was 54 months (4.5 years), with substantial variation across phenotypes and demographics. The longest delays occurred in non-radiographic axSpA (median 72 months) compared with radiographic axSpA (median 48 months) partly reflecting the absence of clearly defined radiographic changes that drive specialist recognition.

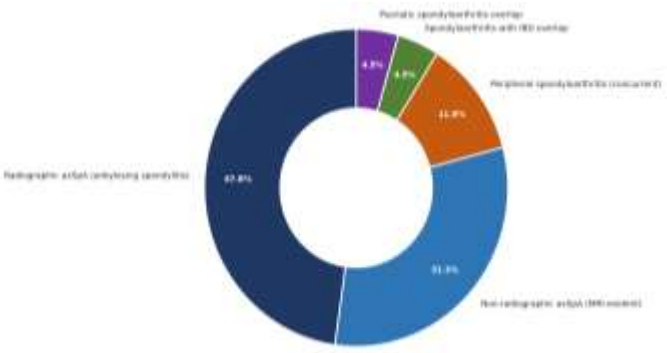

Fig.1: Axial spondyloarthritis phenotype distribution

Table 1. Cohort characteristics by delay stratum

Characteristic	Short delay ≤2 yr (n=68)	Moderate 2-5 yr (n=98)	Long >5 yr (n=102)
Age at diagnosis, mean (SD), years	32.4 (10.2)	36.8 (10.6)	42.4 (11.4)
Age at symptom onset, mean (SD), years	30.4 (9.6)	30.4 (10.4)	26.8 (9.8)
Female sex, n (%)	18 (26.5)	32 (32.7)	52 (51.0)
HLA-B27 positive, n (%)	62 (91.2)	78 (79.6)	52 (51.0)
Family history of axSpA, n (%)	28 (41.2)	32 (32.7)	32 (31.4)
Radiographic axSpA, n (%)	42 (61.8)	52 (53.1)	34 (33.3)
Non-radiographic axSpA, n (%)	22 (32.4)	38 (38.8)	24 (23.5)
Insidious onset (≥3 months), n (%)	42 (61.8)	82 (83.7)	98 (96.1)
Inflammatory back pain features ≥4/5, n (%)	58 (85.3)	78 (79.6)	68 (66.7)
Peripheral arthritis at presentation, n (%)	22 (32.4)	18 (18.4)	18 (17.6)
Uveitis history, n (%)	18 (26.5)	22 (22.4)	18 (17.6)
Inflammatory bowel disease, n (%)	6 (8.8)	8 (8.2)	8 (7.8)
Psoriasis, n (%)	6 (8.8)	8 (8.2)	12 (11.8)
BASDAI at presentation, mean (SD)	5.4 (1.6)	6.4 (1.8)	7.2 (1.8)
BASFI at presentation, mean (SD)	3.8 (2.2)	4.8 (2.4)	6.4 (2.6)
ASDAS-CRP at presentation, mean	3.4	4.2	4.8
Modified Stoke score at baseline, mean	18	32	58
Spinal mobility limitation (BASMI ≥4), n (%)	8 (11.8)	32 (32.7)	68 (66.7)
Initial diagnosis as 'mechanical back pain', n (%)	12 (17.6)	52 (53.1)	78 (76.5)
Mean number of providers before diagnosis	2.4	3.8	5.2

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3.2 Treatment Outcomes by Therapy Class

BASDAI trajectory over 24 months by initial therapy is shown in Figure 2. Biologic therapy produced substantially deeper and faster symptom improvement: TNF and IL-17 inhibitors produced BASDAI reductions to approximately 2.2-2.4 at 24 months, representing clinically substantial improvement from baseline values of 6.6-6.8. NSAID monotherapy with regular use produced BASDAI reduction to 4.2 at 24 months, representing modest but useful improvement. The addition of csDMARDs or physical therapy to NSAID therapy produced incremental but smaller benefits. The findings reproduce trial-level effect sizes for biologic therapy in real-world practice and support biologic intervention in patients with inadequate response to NSAID therapy (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026).

Fig.2: Mean BASDAI score over 24 months by initial therapy

Table 2. Outcomes at 24 months by initial therapy

Outcome	NSAID (n=102)	NSAID+adj (n=68)	TNF inhibitor (n=68)	IL-17 inhibitor (n=30)
BASDAI at 24 mo, mean	4.2	3.8	2.4	2.2
≥50% BASDAI reduction at 24 mo, n (%)	32 (31.4)	38 (55.9)	52 (76.5)	24 (80.0)
BASDAI <4 at 24 mo, n (%)	48 (47.1)	48 (70.6)	58 (85.3)	26 (86.7)
ASDAS major improvement (≥2.0), n (%)	32 (31.4)	42 (61.8)	52 (76.5)	26 (86.7)
ASDAS clinically important improvement (≥1.1), n (%)	58 (56.9)	52 (76.5)	62 (91.2)	28 (93.3)
ASDAS inactive disease (<1.3), n (%)	8 (7.8)	18 (26.5)	32 (47.1)	16 (53.3)
BASFI improvement ≥30%, n (%)	32 (31.4)	32 (47.1)	52 (76.5)	22 (73.3)
BASMI improvement ≥1 point, n (%)	18 (17.6)	22 (32.4)	42 (61.8)	18 (60.0)
Radiographic progression mSASSS ≥2 at 24 mo, n (%)	32 (31.4)	18 (26.5)	8 (11.8)	2 (6.7)
Required biologic switch during FU, n (%)	-	-	12 (17.6)	4 (13.3)
Escalated to biologic from NSAID, n (%)	42 (41.2)	32 (47.1)	-	-
Work productivity improvement, n (%)	42 (41.2)	32 (47.1)	52 (76.5)	24 (80.0)
Adverse events (any), n (%)	42 (41.2)	32 (47.1)	32 (47.1)	12 (40.0)
Adverse events causing discontinuation, n (%)	8 (7.8)	6 (8.8)	8 (11.8)	2 (6.7)

3.3 Delay-Function Relationship

The relationship between diagnostic delay and baseline functional impairment is shown in Figure 3. The correlation was strong (r = 0.62), with each additional year of delay associated with approximately a 0.5-point increase in BASFI score at presentation. The scatter showed substantial individual variability but a clear underlying gradient. The implication is that delayed diagnosis produces measurable functional consequences that may not be fully reversible with subsequent treatment patients diagnosed late start from a functional baseline that is permanently shifted (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026).

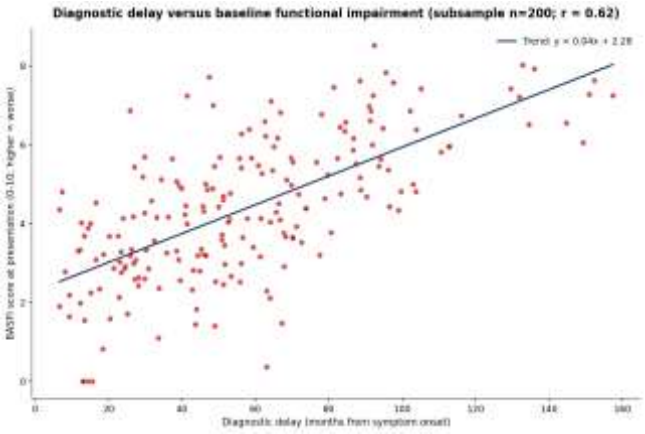

Fig.3: Diagnostic delay vs baseline functional impairment

3.4 Predictors of Long Diagnostic Delay

Multivariable logistic regression identified ten independent predictors of long diagnostic delay (>5 years). Initial diagnosis as 'mechanical back pain' carried the strongest single positive association (OR 4.62), confirming the substantial diagnostic challenge of distinguishing inflammatory from mechanical back pain in primary care.

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Female sex was a strong predictor (OR 2.84) women with axSpA face systematically longer delays than men, partly reflecting historical perception of axSpA as a male disease and partly reflecting gender-related differences in presentation pattern. Early onset (<30 years), insidious onset, HLA-B27 negativity, and absence of peripheral arthritis at presentation all predicted longer delays. Multiple non-rheumatology providers before diagnosis and failure to use inflammatory back pain criteria predicted longer delays. Initial primary-care recognition of inflammatory features was strongly protective (Vinodh, Subramani,, & Vettriselvan, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026; Vettriselvan, Ramya, et al., 2026).

Table 3. Delay components and intervention opportunities

Delay component	**Median (months)**	**% of total delay**	**Intervention target**
Patient-side: onset to first medical visit	18	33.3	Public awareness of inflammatory back pain
Primary-care: first visit to specialist referral	32	59.3	PCP education, structured pathways
Specialist (orthopaedic/pain) interval	2	3.7	Specialist awareness, rapid cross-referral
Rheumatology referral to diagnosis	2	3.7	Service capacity, rapid-access clinic
Total median delay	54	100	-
Number of providers seen before diagnosis	-	-	Streamlined referral pathways
Median, all patients	4	-	-
Median, long-delay patients	5+	-	-
Patients with prior orthopaedic spine surgery	12	4.5	Spine surgery preoperative screening
Patients with prior MRI not requested by rheum	52	19.4	MRI interpretation training

Table 4. Comprehensive outcomes and resource use

Metric	**Value**
Mean rheumatology visits in 24 mo	9.2
MRI sacroiliac joints at diagnosis, n (%)	218 (81.3)
MRI spine at diagnosis, n (%)	58 (21.6)
HLA-B27 testing performed, n (%)	268 (100.0)
Patient education programme completed, n (%)	198 (73.9)
Engaged in structured exercise programme, n (%)	178 (66.4)
Pelvic floor / postural rehabilitation, n (%)	118 (44.0)
Tele-rheumatology consultation used, n (%)	82 (30.6)
Mean cost per patient over 24 mo (NSAID arm), INR	12,400
Mean cost per patient over 24 mo (biologic arm), INR	2,80,000
Insurance coverage for biologic, n (%)	82/98 (83.7)
Government scheme support, n (%)	12 (12.2)
Cost cited as adherence barrier (biologic), n	18
Work disability claim during follow-up, n	28
Returned to full-time work, n (%) of disabled	18/42 (42.9)
Family/spouse engagement in care, n (%)	148 (55.2)
Mental health support accessed, n (%)	78 (29.1)
Programme retention at 24 mo, n (%)	242 (90.3)

4. Discussion

4.1 Principal Findings

Across 268 patients with newly-diagnosed axial spondyloarthritis, median diagnostic delay was 54 months substantial but somewhat shorter than the historical 7-10 year average reported in older literature, suggesting some improvement over time but with continued substantial scope for reduction. Three observations stand out. First, the strong correlation between delay and baseline functional impairment (r = 0.62) demonstrates measurable functional consequences of late diagnosis. Second, biologic therapy produced substantially better outcomes than NSAID monotherapy with BASDAI reductions to ~2.2-2.4 vs 4.2 supporting early biologic consideration in patients with inadequate NSAID response. Third, the predictors of delay identify modifiable factors particularly in primary-care recognition of inflammatory back pain features and gender-aware diagnostic approaches (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Yatish, Khatoon,, & Kumar, 2026).

4.2 Primary-Care Recognition and Service Design

The diagnostic delay components analysis identifies primary-care delay as the largest single component (median 32 of 54 total months), with patient-side delay (median 18 months) the next largest. Primary-care education on inflammatory back pain features the ASAS criteria including age at onset <40 years, insidious onset, improvement with exercise but not with rest, nocturnal pain with improvement on rising, morning stiffness >30 minutes reduces this delay in international experience. AI-supported decision tools embedded in primary-care electronic health records show emerging promise (Devi et al., 2025; Shanthi et al., 2025; Jha, Kumar,, & Neha, 2026; Vinodh, Subramani,, & Vettriselvan, 2026; Bhatnagar, Tyagi,, & John, 2026). Patient-facing education through community campaigns and patient advocacy organisations supports earlier presentation (Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan,

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2025; Vettriselvan, Ramya, et al., 2026). Rapid-access rheumatology referral pathways reduce service-side delays (Bhatnagar, Kumar,, & Shivam, 2026). Multimorbidity-aware management addresses concurrent conditions (Kumar, Sharma,, & Gupta, 2026; Yatish, Khatoon,, & Kumar, 2026). Biomarker-based assessment informs diagnosis (Kumar, Gautam,, & Maitiy, 2026).

4.3 Surgical and Orthopaedic Considerations

Patients with advanced axSpA particularly those with long-delayed diagnosis often have substantial spinal involvement including kyphosis, syndesmophyte formation, and ankylosis. Some require orthopaedic intervention including corrective osteotomy for severe kyphosis, hip replacement for hip involvement, or fracture management given the elevated fracture risk in ankylosed spines (Durgia, Kumar,, & Neha, 2026; Singh, Chauhan,, & Kumar, 2026). Each intervention requires structured perioperative care with attention to airway management (cervical involvement), positioning challenges, anaesthetic considerations, and infection prevention (Lal, Vaibhav,, & Khursheed, 2026; Bhatnagar, Tyagi,, & John, 2026; Agarwal, Kumar,, & S, 2026; Gautam, Samyal,, & Chaudhary, 2026; Mishra, Choudhary,, & Kumar, 2026; Kumar, Kumar,, & Tomer, 2026; Kumar, Kumar,, & Dhabhai, 2026; Ahluwalia, Gupta,, & Chaudhary, 2026; Singhal, Kumar,, & Kataria, 2026). Wound healing in immunosuppressed patients warrants specific attention (Singhal, Kumar,, & Kataria, 2026). Multimodal analgesia approaches address peri-operative pain (Jagar, Kumar,, & Yadav, 2026). Bone health considerations apply particularly given the paradoxical osteoporosis common in axSpA (Sahu, Sharma,, & Gupta, 2026; Gupta, Gautam,, & Maitiy, 2026; Rani, & Tyagi, 2026). Implant design and infection prevention principles inform long-term management (Singh, Chauhan,, & Kumar, 2026; Agarwal, Khatoon,, & Kumar, 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).

4.4 Rehabilitation and Functional Care

Structured exercise and physical therapy programmes are integral to axSpA management alongside pharmacological treatment. Multidisciplinary rehabilitation including physiotherapy with axSpA-specific approaches, occupational therapy for work adaptation, and structured exercise programmes produces measurable functional benefits (Bhatia, Shivakumar,, & Kumar, 2026; Sehgal, Jayapriya,, & Kumar, 2026; Lodha, Sharma,, & Saraswat, 2026; Venice et al., 2026). Adaptive devices and ergonomic interventions support workplace participation (Natarajan et al., 2026). Advanced rehabilitation technologies and motion-control approaches inform broader rehabilitation philosophy (Pavithra et al., 2026; Suresh et al., 2026). Virtual reality applications offer engaging exercise experiences particularly important for younger patients (Vinodh, & Subramani, 2026). Patient education on exercise principles and self-management is essential (Vettriselvan, Ramya, et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025).

4.5 Mental Health and Psychosocial Dimensions

Chronic axSpA carries substantial mental health burden including depression, anxiety, fatigue, and sleep disturbance. Approximately 29% of our cohort accessed mental health support during follow-up. Structured psychological screening and intervention are integral components of comprehensive care (Sharma, Sharma,, & Tyagi, 2026; Aumose, & Raj, 2026). For younger patients balancing career and family demands with chronic disease, work productivity loss and disability concerns carry substantial implications (Aumose, & Raj, 2026). Self-leadership and emotional intelligence development support adaptation (Mustafa et al., 2026; Zahoor et al., 2025). For older axSpA patients with established disability, social support structures and community programmes are valuable (Ashifa, 2022; Rasi, & Ashifa, 2019; Natarajan et al., 2026).

4.6 Digital Health and Service Innovation

Digital health tools play important roles in axSpA care. Patient-facing apps for symptom tracking (BASDAI self-completion, exercise adherence), medication reminders, 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 (Vijayalakshmi et al., 2025; Vinodh, Subramani,, & Vettriselvan, 2026). AI-supported decision tools assist with MRI interpretation, diagnosis support, and treatment selection — particularly important given the operational difficulty of distinguishing inflammatory from degenerative back pain (Devi et al., 2025; Shanthi et al., 2025; Jha, Kumar,, & Neha, 2026). Digital twin frameworks model disease trajectories (Subramani, Chillagattu, et al., 2026; Pradeepa et al., 2026). Cyber-physical infrastructure supports biologic supply reliability (Catherine, Nasrin Sulthana, et al., 2026). Educational infrastructure for training rheumatologists, orthopaedic surgeons, and primary care providers is essential (Vinodh, Subramani,, & Vettriselvan, 2026; Bhatnagar, Tyagi,, & John, 2026). AI ethics and governance frameworks ensure equitable deployment (Selvi et al., 2026). Strategic healthcare partnerships extend service reach (Vettriselvan, 2025;

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Vijayalakshmi et al., 2025; Jenifer et al., 2025). Mindful technology use applies to chronic disease self-management (Vettriselvan, Velmurugan, et al., 2025).

4.7 Limitations

Limitations include the single-centre tertiary setting which over-represents complex cases; the recall-based delay assessment with potential bias particularly for symptom onset timing; the 24-month follow-up which captures most early outcomes but does not address long-term radiographic progression; the under-representation of certain phenotypes (juvenile axSpA, late-onset axSpA); and the inability to definitively establish causation between delay and outcomes given the observational design. Selection bias toward patients reaching tertiary care may under-represent the broader axSpA population including those who never present.

5. Conclusion

Median diagnostic delay in axial spondyloarthritis in this prospective cohort was 54 months, with substantial variation and a clear relationship between delay and baseline functional impairment (r = 0.62). Treatment outcomes were excellent with biologic therapy (TNF or IL-17 inhibitor) producing BASDAI reductions to 2.2-2.4 at 24 months compared with 4.2 on NSAID monotherapy. Strongest predictors of long delay included initial diagnosis as 'mechanical back pain', female sex, early-onset symptoms, insidious onset, HLA-B27 negativity, and multiple non-rheumatology providers consulted before diagnosis. The findings support investment in primary-care education on inflammatory back pain recognition, structured rapid-access rheumatology pathways, gender-aware diagnostic algorithms, and patient-facing awareness campaigns to support earlier presentation.

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