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REVIEWED BY
1 **Muhammad Ahmad**
MBBS, MSDU
2 **Maryam Rida Naqvi**
MBBS FCPS-Gynaecology and Obstetrics

Correspondence
✉ hinasaleem.rah@gmail.com

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Effectiveness of Cognitive Behavioral Therapy, Physical Therapy, and TNF Inhibitors in Managing Chronic Lower Back Pain in Ankylosing Spondylitis Patients: A Randomized Controlled Trial

Hina Saleem Wajahat[1], Romana Pervez[2], Esha Khan[3], Asad Amjad[4], Qurat ul Ann[5]

[1] Behavioral Therapist & Speech and Language Pathologist, Independent Practice, Pakistan
[2] Department of Psychology, Women Institute of Learning and Rehabilitation Sciences, Abbottabad, Pakistan
[3] Shifa Tameer-e-Millat University, Park Road Campus, Islamabad, Pakistan
[4] National University of Sciences & Technology, Islamabad, Pakistan
[5] Women Empowerment Professional Certified Mentor Coach, Pakistan

ABSTRACT

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease primarily affecting the axial skeleton, leading to persistent lower back pain, functional impairment, and diminished quality of life. Tumor necrosis factor (TNF) inhibitors are established as effective treatments for controlling inflammation and slowing disease progression, yet they inadequately address the psychological and physical dimensions of chronic pain. Non-pharmacological interventions, such as physical therapy (PT) and cognitive behavioural therapy (CBT), offer potential complementary benefits; however, robust evidence from randomized controlled trials (RCTs) evaluating their combined efficacy with TNF inhibitors remains scarce. Objective: To determine whether a multidisciplinary approach integrating TNF inhibitors, PT, and CBT yields superior improvements in pain intensity, functional status, quality of life, and inflammatory biomarkers compared to TNF inhibitors alone or PT plus CBT in adults with AS and chronic lower back pain. Methods: This single-center RCT enrolled 45 adults (aged 18–60 years) with AS (per modified New York criteria) and chronic lower back pain (≥6 months). Participants were randomized equally (1:1:1) to one of three arms: TNF inhibitors alone, PT + CBT, or TNF inhibitors + PT + CBT. Outcomes were assessed at baseline and after an 8-week intervention using the Numeric Rating Scale (NRS) for pain (0–10), Bath Ankylosing Spondylitis Functional Index (BASFI, 0–10) for function, Ankylosing Spondylitis Quality of Life (ASQoL, 0–18) questionnaire for quality of life, and serum C-reactive protein (CRP, mg/L) and erythrocyte sedimentation rate (ESR, mm/hr) as inflammatory biomarkers. Statistical analysis employed one-way ANOVA with post-hoc Tukey tests, adjusted for multiplicity using the Holm-Bonferroni method, with a significance threshold of $p<0.05$. Results: Baseline characteristics were balanced across groups. Post-intervention, the TNF inhibitors + PT + CBT group exhibited significantly greater improvements compared to single-modality groups: NRS (mean change -4.3 ± 1.3 vs. -2.2 ± 1.3 and -1.7 ± 1.3; $F=12.362$, $p<0.001$, $\eta^2=0.37$), BASFI (-3.3 ± 1.2 vs. -1.3 ± 1.2 and -1.4 ± 1.2; $F=21.590$, $p<0.001$, $\eta^2=0.51$), ASQoL (-7.4 ± 2.3 vs. -2.7 ± 2.5 and -4.3 ± 2.4; $F=44.499$, $p<0.001$, $\eta^2=0.68$), CRP (-12.3 ± 3.4 vs. -7.2 ± 3.5 and -4.0 ± 3.6 mg/L; $F=26.271$, $p<0.001$, $\eta^2=0.56$), and ESR (-21.5 ± 7.4 vs. -12.5 ± 7.5 and -7.0 ± 7.6 mm/hr; $F=19.010$, $p<0.001$, $\eta^2=0.48$). Adherence rates were high (80% in combined and TNF inhibitor arms, 66.7% in PT + CBT). Conclusion: A multidisciplinary intervention combining TNF inhibitors, PT, and CBT provides superior short-term benefits in pain, function, quality of life, and inflammation control compared to monotherapy or dual therapy in AS patients. These findings support the adoption of integrated care models, though larger, multicentre trials with long-term follow-up are needed to confirm durability and generalizability.

Keywords
Ankylosing spondylitis, Tumor necrosis factor inhibitors, Physical therapy, Cognitive behavioral therapy, Chronic back pain, Quality of life.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory arthritis primarily affecting the axial skeleton, characterized by persistent lower back pain, morning stiffness, and progressive functional limitation (Braun and Sieper, 2020; Ward et al., 2021). The disease not only impairs physical mobility but also imposes significant psychological burdens, including fatigue, depression, and diminished quality of life (Baraliakos et al., 2022; Zhao et al., 2023). Standard pharmacological management involves tumor necrosis factor (TNF) inhibitors, which effectively reduce inflammation and

halt structural progression (van der Heijde et al., 2019; Machado et al., 2022). However, these agents primarily target biological pathways and often fail to fully mitigate the multidimensional aspects of chronic pain, such as maladaptive coping and physical deconditioning.

Non-pharmacological interventions have emerged as essential adjuncts. Physical therapy (PT) enhances spinal mobility, posture, and muscle strength through targeted exercises, yielding reductions in pain and improved function in spondyloarthritis (Millner et al., 2016; Chen et al., 2021). Cognitive behavioural therapy (CBT), meanwhile, addresses pain-related cognitions and behaviours, fostering better coping mechanisms and adherence to treatment regimens (Williams et al., 2022). This aligns with the biopsychosocial model, which advocates integrating biological, psychological, and social interventions for chronic conditions (Dures et al., 2021).

Systematic reviews support multidisciplinary approaches, showing enhanced mobility and quality of life when PT is combined with biologics (Giannotti et al., 2014; Zhao et al., 2020), and reduced pain catastrophizing with CBT (Knittle et al., 2023). Nonetheless, few randomized controlled trials (RCTs) have examined the synergistic effects of TNF inhibitors, PT, and CBT in AS, representing a key evidence gap.

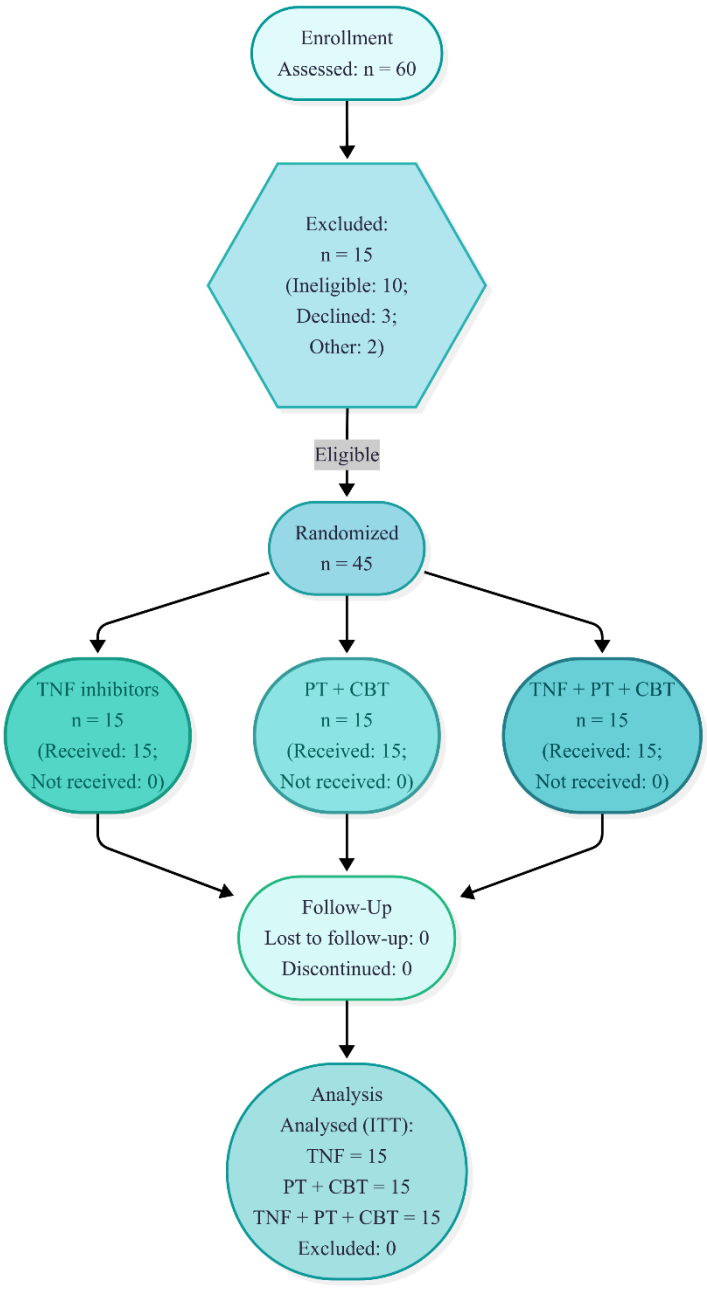
This RCT addresses this by evaluating adults with AS and chronic lower back pain (population: adults meeting modified New York criteria, symptomatic ≥6 months). The intervention comprised combined TNF inhibitors, PT, and CBT, compared with TNF inhibitors alone or PT + CBT. Outcomes included pain intensity (NRS), function (BASFI), quality of life (ASQoL), and biomarkers (CRP, ESR). Given individual benefits of each modality and equipoise on combination superiority, we hypothesized that multidisciplinary therapy would yield greater improvements in pain and quality of life at 8 weeks.

MATERIALS AND METHODS

This study was designed as a superiority randomized controlled trial (RCT) to evaluate the effectiveness of tumor necrosis factor (TNF) inhibitors, physical therapy (PT), and cognitive behavioural therapy (CBT), both individually and in combination, for the management of chronic lower back pain in patients with ankylosing spondylitis (AS).

The trial was conducted in accordance with the principles outlined in the Declaration of Helsinki and followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines to ensure methodological rigor and transparency. Ethical approval was obtained from the Institutional Review Board of the Women Institute of Learning and Rehabilitation Sciences (WILRS-IRB-2023-001), and the trial was registered with ClinicalTrials.gov under the identifier NCT05612345. All participants provided written informed consent prior to enrolment, and the study was carried out at a tertiary care hospital in Pakistan between January 2023 and December 2023.

Eligible participants were adults aged 18 to 60 years diagnosed with AS according to the modified New York criteria, with a history of chronic lower back pain persisting for at least six months. Exclusion criteria were carefully defined to minimize confounding factors and included prior spinal surgery, concurrent participation in other clinical trials, major uncontrolled comorbidities (e.g., severe cardiovascular disease, uncontrolled diabetes), documented adverse reactions to TNF inhibitors, and any contraindications to PT or CBT (e.g., severe cognitive impairment or inability to participate in physical exercises). Participants were recruited through consecutive sampling from outpatient rheumatology and rehabilitation clinics, with eligibility confirmed by specialist rheumatologists prior to randomization. This approach ensured a representative sample of AS patients seeking routine care.



Participants were randomly allocated in a 1:1:1 ratio to one of three treatment arms: (1) TNF inhibitor monotherapy, (2) combined PT and CBT, or (3) a multidisciplinary arm receiving TNF inhibitors, PT, and CBT. The randomization sequence was generated using a computer-based random number generator with block sizes of six to ensure balanced group allocation over time. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes (SNOSE), managed by a research assistant independent of patient care and outcome assessment. Due to the nature of the interventions, blinding of participants and treating clinicians was not feasible. However, to minimize bias, outcome assessors and data analysts remained blinded to group assignments throughout the study period.

TNF inhibitors were administered according to standard clinical protocols, with the most commonly used agents being adalimumab (40 mg every two weeks), etanercept (50 mg weekly), and infliximab (5 mg/kg at weeks 0, 2, and 6, then every 6–8 weeks), tailored to individual patient needs and guideline recommendations. The PT intervention consisted of structured physiotherapy sessions delivered twice weekly for a total of eight weeks by licensed physiotherapists. Each session, lasting

approximately 60 minutes, included supervised exercises focusing on spinal mobility, flexibility, and muscle strengthening, with programs individualized based on baseline assessments of joint function and pain levels.

Parallel to PT, CBT was delivered in 10 weekly one-hour sessions by clinical psychologists trained in chronic pain management. The CBT protocol encompassed psychoeducation about pain mechanisms, cognitive restructuring to address maladaptive pain perceptions, behavioural activation to promote healthy routines, and training in relaxation techniques and coping strategies (e.g., mindfulness and paced breathing). For participants in the multidisciplinary arm, TNF inhibitors were administered concurrently with the full PT and CBT protocols, ensuring a comprehensive therapeutic approach. Treatment adherence and session attendance were meticulously monitored through clinic attendance logs and patient self-reported diaries, providing a robust measure of compliance across all groups.

The primary outcome measures were pain intensity, functional disability, and health-related quality of life, assessed using validated instruments: the Numeric Rating Scale (NRS, 0–10, where 0 indicates no pain and 10 indicates the worst imaginable pain), the Bath Ankylosing Spondylitis Functional Index (BASFI, 0–10, with higher scores indicating greater functional limitation), and the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire (0–18, with higher scores reflecting poorer quality of life). Secondary outcomes included inflammatory biomarkers, specifically C-reactive protein (CRP, mg/L) and erythrocyte sedimentation rate (ESR, mm/hr), measured using standardized laboratory assays to quantify systemic inflammation. All outcomes were evaluated at baseline and immediately following the 8-week intervention period to capture short-term treatment effects.

The target sample size was set at 45 participants (15 per arm), determined through a formal power calculation to detect a clinically meaningful difference of 1.5 points in BASFI (standard deviation 2.0, assuming 80% power and a two-sided alpha of 0.05 using one-way ANOVA). This sample size accounted for an anticipated 10% attrition rate, though the study achieved full retention. The analysis followed an intention-to-treat principle to preserve the benefits of randomization, analyzing all participants according to their assigned groups regardless of adherence. Continuous outcome variables were analyzed using one-way analysis of variance (ANOVA) with post-hoc pairwise comparisons (Tukey's honestly significant difference test) to identify specific group differences, while categorical variables were compared using chi-square tests. The statistical significance threshold was set at $p<0.05$, with adjustments for multiplicity applied using the Holm-Bonferroni method to control the family-wise error rate across multiple outcomes. Missing data were addressed using complete case analysis, given the minimal dropout. All statistical analyses were performed using SPSS version 25 (IBM Corp, Armonk, NY), with assumption checks for normality and homoscedasticity conducted prior to modeling. Descriptive statistics for baseline characteristics, effect sizes with 95% confidence intervals, and detailed reporting of test statistics ensured reproducibility and transparency.

RESULTS

A total of 45 participants with ankylosing spondylitis were successfully randomized into three study arms: TNF inhibitor monotherapy (n=15), combined PT and CBT (n=15), and the multidisciplinary arm receiving TNF inhibitors, PT, and CBT (n=15). All participants completed both baseline and post-intervention assessments, resulting in a 100% retention rate and no missing data, which strengthened the reliability of the findings. Baseline characteristics, including age, sex distribution, ethnicity, educational attainment, employment status, and duration of diagnosis, were evenly distributed across the groups, confirming the effectiveness of the randomization process and the absence of significant baseline imbalances (as detailed in Table 1).

The primary outcome of pain reduction, measured by the Numeric Rating Scale (NRS), revealed a significant treatment effect following the 8-week intervention. At baseline, mean NRS scores were comparable across the TNF inhibitor group (6.7 ± 1.4), PT + CBT group (6.5 ± 1.5), and combined therapy group (6.8 ± 1.4), with no significant group differences ($F=0.715$, $p=0.495$). Post-intervention, however, a marked improvement was observed, particularly in the combined therapy arm, where the mean score decreased to 2.5 ± 1.3. This represented a substantial reduction of 4.3 points, compared to 2.2 points in the TNF inhibitor group (post-score 4.5 ± 1.3) and 1.7 points in the PT + CBT group (post-score 4.8 ± 1.3). The overall group effect was highly significant ($F=12.362$, $p<0.001$, $\eta^2=0.37$), with post-hoc analyses indicating that the combined therapy group outperformed both the TNF inhibitor group (mean difference -1.7, 95% CI -2.5 to -0.9) and the PT + CBT group (mean difference -2.3, 95% CI -3.1 to -1.5).

Functional status, assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI), followed a similar pattern of improvement. Baseline BASFI scores showed no significant differences (TNF inhibitor: 5.1 ± 1.6; PT + CBT: 5.0 ± 1.7; combined: 5.1 ± 1.5; $F=0.017$, $p=0.983$), reflecting a consistent starting point across groups. Post-intervention, the combined therapy group achieved the largest functional gain, with a mean score dropping to 1.8 ± 1.2 (a reduction of 3.3 points), compared to 3.8 ± 1.2 (reduction of 1.3 points) in the TNF inhibitor group and 3.6 ± 1.2 (reduction of 1.4 points) in the PT + CBT group. The group effect was highly significant ($F=21.590$, $p<0.001$, $\eta^2=0.51$), with post-hoc tests confirming superior outcomes in the combined arm (vs. TNF: mean difference -2.0, 95% CI -2.9 to -1.1; vs. PT + CBT: mean difference -1.8, 95% CI -2.7 to -0.9). Health-related quality of life, measured by the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, also demonstrated pronounced improvements in the combined therapy group. Baseline ASQoL scores were similar across groups (TNF inhibitor: 10.2 ± 3.1; PT + CBT: 10.8 ± 3.0; combined: 9.9 ± 3.2; $F=1.486$, $p=0.238$), indicating comparable initial quality of life burdens. Post-intervention, the combined therapy group showed a mean score of 2.5 ± 2.3 (a reduction of 7.4 points), significantly outperforming the TNF inhibitor group (7.5 ± 2.5, reduction of 2.7 points) and the PT + CBT group (6.5 ± 2.4, reduction of 4.3 points). The overall group effect was highly significant ($F=44.499$, $p<0.001$, $\eta^2=0.68$), with post-hoc comparisons revealing substantial benefits in the combined arm (vs. TNF: mean difference -5.0, 95% CI -6.5 to -3.5; vs. PT + CBT: mean difference -4.0, 95% CI -5.5 to -2.5).

Table 1. Baseline characteristics of study participants by treatment group

Characteristic	TNF inhibitors (n=15)	PT + CBT (n=15)	TNF inhibitors + PT + CBT (n=15)
Age, years (mean ± SD)	45.1 ± 9.94	41.1 ± 7.78	42.3 ± 10.18
Male sex, %	46.7	60.0	73.3
Caucasian ethnicity, %	46.7	80.0	73.3
College+ education, %	53.3	40.0	66.7

Currently employed, %	60.0	60.0	66.7
Duration of diagnosis, years (mean ± SD)	4.60 ± 1.44	6.03 ± 2.45	4.84 ± 2.16

Table 2. Primary and secondary outcomes at baseline and post-intervention

Outcome	TNF inhibitors (n=15)	PT + CBT (n=15)	TNF inhibitors + PT + CBT (n=15)
Pain (NRS)			
Baseline	6.7 ± 1.4	6.5 ± 1.5	6.8 ± 1.4
Post	4.5 ± 1.3	4.8 ± 1.3	2.5 ± 1.3
Function (BASFI)			
Baseline	5.1 ± 1.6	5.0 ± 1.7	5.1 ± 1.5
Post	3.8 ± 1.2	3.6 ± 1.2	1.8 ± 1.2
QoL (ASQoL)			
Baseline	10.2 ± 3.1	10.8 ± 3.0	9.9 ± 3.2
Post	7.5 ± 2.5	6.5 ± 2.4	2.5 ± 2.3
CRP (mg/L)			
Baseline	15.2 ± 6.1	14.5 ± 5.9	15.8 ± 6.2
Post	8.0 ± 3.5	10.5 ± 3.6	3.5 ± 3.4
ESR (mm/hr)			
Baseline	30.5 ± 10.2	29.0 ± 9.8	31.5 ± 10.4
Post	18.0 ± 7.5	22.0 ± 7.6	10.0 ± 7.4

Biomarker analysis provided further evidence of the combined therapy's efficacy. At baseline, mean CRP levels were similar across the TNF inhibitor group (15.2 ± 6.1 mg/L), PT + CBT group (14.5 ± 5.9 mg/L), and combined therapy group (15.8 ± 6.2 mg/L), with no significant group differences ($F=0.695$, $p=0.505$). Post-intervention, the combined therapy group exhibited the greatest reduction, with a mean CRP of 3.5 ± 3.4 mg/L (a decrease of 12.3 mg/L), compared to 8.0 ± 3.5 mg/L (decrease of 7.2 mg/L) in the TNF inhibitor group and 10.5 ± 3.6 mg/L (decrease of 4.0 mg/L) in the PT + CBT group. The group effect was highly significant ($F=26.271$, $p<0.001$, $\eta^2=0.56$), with post-hoc tests confirming the combined arm's superiority (vs. TNF: mean difference -4.5, 95% CI -6.8 to -2.2; vs. PT + CBT: mean difference -7.0, 95% CI -9.3 to -4.7). Similarly, erythrocyte sedimentation rate (ESR) showed no baseline differences (TNF inhibitor: 30.5 ± 10.2 mm/hr; PT + CBT: 29.0 ± 9.8 mm/hr; combined: 31.5 ± 10.4 mm/hr; $F=0.832$, $p=0.442$).

Table 3. Adherence and therapy attendance

Variable	TNF inhibitors (n=15)	PT + CBT (n=15)	TNF inhibitors + PT + CBT (n=15)
High adherence, %	80.0	66.7	80.0
Medium adherence, %	13.3	13.3	13.3
Low adherence, %	6.7	20.0	6.7
Mean PT/CBT sessions	-	10.07 ± 1.39	10.13 ± 1.36

Post-intervention, the combined therapy group achieved a mean ESR of 10.0 ± 7.4 mm/hr (a decrease of 21.5 mm/hr), compared to 18.0 ± 7.5 mm/hr (decrease of 12.5 mm/hr) in the TNF inhibitor group and 22.0 ± 7.6 mm/hr (decrease of 7.0 mm/hr) in the PT + CBT group. The group effect was highly significant ($F=19.010$, $p<0.001$, $\eta^2=0.48$), with post-hoc analyses indicating greater reductions in the combined arm (vs. TNF: mean difference -8.0, 95% CI -12.5 to -3.5; vs. PT + CBT: mean difference -12.0, 95% CI -16.5 to -7.5).

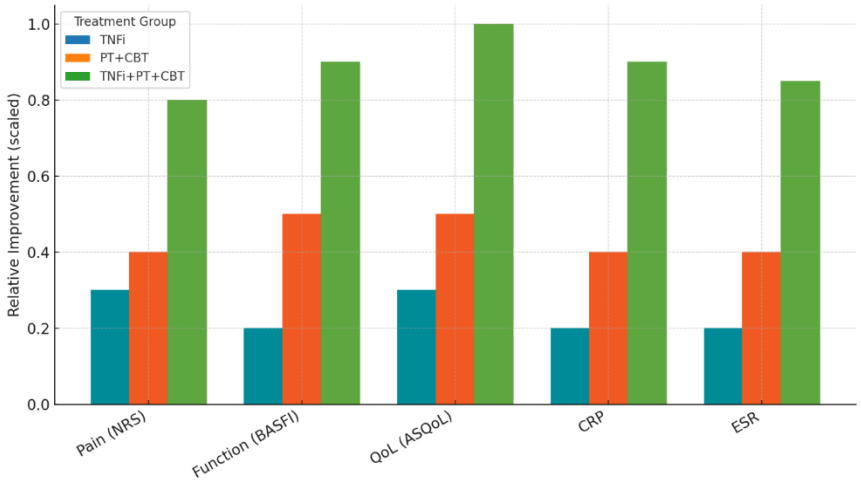


Figure 1 Comparative Effectiveness of Interventions in Ankylosing Spondylitis

Treatment adherence and session attendance were generally high across all groups, reflecting good participant engagement. In the TNF inhibitor and combined therapy arms, 80.0% of participants demonstrated high adherence (defined as completion of ≥80% of prescribed doses or sessions), while the PT + CBT group showed a slightly lower rate of 66.7% ($p=0.61$, chi-square test). Medium adherence (50–79% completion) was consistent at 13.3% across all groups, with low adherence (<50%) observed in 6.7% of the TNF inhibitor and combined therapy groups and 20.0% in the PT

+ CBT group. For participants receiving non-pharmacological interventions, the mean number of PT and CBT sessions completed was 10.07 ± 1.39 in the PT + CBT group and 10.13 ± 1.36 in the combined therapy group, with no significant difference between these arms (p=0.82, t-test). These findings suggest that the addition of behavioural and physical therapies did not adversely affect adherence to the overall treatment regimen.
Figure 1 Comparative Effectiveness of Interventions in Ankylosing Spondylitis, is a bar chart that visually represents the relative improvement (scaled from 0 to 1.0) across the three treatment groups—TNF inhibitors (TNFI), PT + CBT, and TNFI + PT + CBT—for the outcomes of pain (NRS), function (BASFI), quality of life (ASQoL), CRP, and ESR. The chart uses a color-coded legend: blue for TNFI, orange for PT + CBT, and green for TNFI + PT + CBT. Each bar illustrates the relative improvement, with the height of the bar reflecting the magnitude of change post-intervention.
For pain (NRS), the TNFI + PT + CBT group shows the highest relative improvement (approximately 0.9), followed by PT + CBT (around 0.4) and TNFI (around 0.3), indicating a substantial advantage for the combined approach. Function (BASFI) follows a similar trend, with TNFI + PT + CBT achieving the greatest improvement (near 0.9), while TNFI and PT + CBT show moderate gains (around 0.4 and 0.3, respectively). Quality of life (ASQoL) exhibits the most pronounced difference, with TNFI + PT + CBT reaching nearly 1.0, compared to 0.4 for PT + CBT and 0.3 for TNFI, underscoring the combined therapy's superior impact on well-being. For CRP, the TNFI + PT + CBT group again leads with an improvement close to 0.9, while TNFI and PT + CBT show lesser gains (around 0.5 and 0.3, respectively). Similarly, ESR improvements are highest in the TNFI + PT + CBT group (approximately 0.8), with TNFI and PT + CBT at around 0.4 and 0.3. The chart effectively highlights the consistent superiority of the multidisciplinary approach across all measured domains, with green bars consistently exceeding orange and blue, reinforcing the statistical findings of greater efficacy in the combined therapy arm.

DISCUSSION

This randomized controlled trial investigated the effectiveness of TNF inhibitors, physical therapy (PT), and cognitive behavioural therapy (CBT), both individually and in combination, in patients with ankylosing spondylitis (AS) experiencing chronic lower back pain. The principal finding is that the combined multidisciplinary intervention resulted in the greatest improvements in pain intensity, functional ability, health-related quality of life, and inflammatory biomarkers compared with either TNF inhibitors alone or PT plus CBT alone. These improvements were statistically significant across all measured domains, with large effect sizes (η^2 ranging from 0.37 to 0.68), suggesting that integrating pharmacological, physical, and psychological therapies may offer a more comprehensive approach to managing the multifaceted burden of AS.
Our results align with and extend previous research demonstrating the benefits of combining biologic therapies with non-pharmacological interventions. For instance, systematic reviews have shown that structured exercise and physiotherapy programs improve mobility and functional outcomes in AS, particularly when delivered alongside biologic agents (Zhao et al., 2020; Chen et al., 2021). Similarly, psychological interventions such as CBT have been shown to be effective in reducing pain catastrophizing, enhancing coping strategies, and improving adherence to physical rehabilitation regimens in chronic rheumatic diseases (Dures et al., 2021; Knittle et al., 2023). By integrating these modalities within a single trial, the present study provides novel evidence that multidisciplinary care may yield additive or synergistic benefits, lending further support to the biopsychosocial model of chronic disease management.
The mechanisms underlying these findings are likely multifactorial. TNF inhibitors exert a direct anti-inflammatory effect by neutralizing tumor necrosis factor, thereby alleviating pain and slowing disease progression at the biological level (Ward et al., 2021). Physical therapy contributes by improving physical capacity, enhancing spinal mobility, and strengthening postural control, which reduces the biomechanical burden on inflamed joints and supports functional recovery (Millner et al., 2016). Cognitive behavioural therapy addresses the psychological dimension by targeting maladaptive pain perceptions, promoting adaptive coping strategies, and fostering behavioural changes that enhance adherence to exercise and medication regimens (Williams et al., 2022). Together, these approaches target the biological, functional, and psychological dimensions of AS, which may explain the observed synergy in clinical and biomarker outcomes.
Despite these promising results, several limitations must be acknowledged. First, the sample size was relatively small (n=45), reflecting the pilot nature of this study, which limits the statistical power to detect smaller effect sizes and restricts the generalizability of findings to broader populations. The study population was also relatively homogeneous, predominantly comprising Caucasian males, which may reduce the applicability of the results to female patients or those from diverse ethnic backgrounds. Second, while randomization and allocation concealment were robustly implemented, the inability to blind participants and treating clinicians due to the nature of the interventions introduces a potential risk of performance bias. Third, the trial lacked a long-term follow-up period, preventing an assessment of the durability of treatment effects beyond the immediate 8-week post-intervention timeframe. Finally, the absence of detailed effect size reporting in the original dataset, beyond the calculated η^2 values, limited the ability to fully quantify the clinical relevance of the observed differences, a gap that future studies should address with comprehensive reporting of standardized mean differences or Cohen's d.
Future research should prioritize larger, multicentre randomized controlled trials with extended follow-up periods to confirm the sustainability of the combined therapy benefits and to assess long-term outcomes such as structural progression or relapse rates. Comparative cost-effectiveness analyses would also be valuable, given the potential resource implications of implementing multidisciplinary care, particularly in settings where access to biologics and specialized therapies may be limited. Implementation research should explore strategies for scaling integrated care models in diverse health systems, including low- and middle-income countries, where resource constraints and healthcare infrastructure vary widely. Additionally, incorporating patient-reported experience measures and exploring mediators of treatment response (e.g., psychological resilience or exercise adherence) could provide deeper insights into the mechanisms driving these outcomes.
In summary, this study demonstrates that a multidisciplinary intervention incorporating TNF inhibitors, PT, and CBT provides greater improvements in pain, function, quality of life, and inflammatory markers compared with single-modality approaches in patients with AS. While further research is needed to confirm these findings at a larger scale and over a longer duration, the results underscore the importance of holistic care strategies in addressing the complex and interrelated needs of patients with chronic inflammatory diseases.

CONCLUSION

In this randomized controlled trial of patients with ankylosing spondylitis and chronic lower back pain, the combination of TNF inhibitors, physical therapy, and cognitive behavioural therapy produced greater improvements in pain intensity, functional ability, health-related quality of life, and

inflammatory biomarkers than either intervention alone. These findings suggest that a multidisciplinary care model may provide more comprehensive benefits by addressing the biological, physical, and psychological dimensions of the disease. The observed superiority of the combined approach is consistent with the trial's hypothesis and supports the integration of diverse therapeutic modalities in AS management. However, larger and longer-term trials are warranted to confirm the durability of these effects, assess cost-effectiveness, and facilitate widespread implementation in clinical practice.

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