Research Paper

Effect of Manual Therapy Combined With Aerobic Exercise on Psychological Well-being in Patients With Chronic Low Back Pain

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ABSTRACT

Purpose: Chronic low back pain (CLBP) is often related to both physical disability and mental health impairments, such as anxiety, depression, and fatigue. While manual therapy and aerobic exercise independently demonstrate benefits for physical symptoms, few studies have investigated their combined effects on psychological well-being, leaving a critical gap in the evidence for multimodal rehabilitation strategies. Existing research prioritizes pain and disability outcomes, with psychological factors often assessed secondarily.

Methods: A preliminary trial was conducted with 40 participants (aged 32–49 years) diagnosed with CLBP. Participants were randomly allocated to either an intervention group (group 1) receiving manual therapy and aerobic training, or a control group (group 2) performing self-directed exercises after screening for eligibility based on inclusion and exclusion criteria. Pain (numerical pain rating scale [NPRS]), perceived fatigue modified borg rating of perceived exertion [MRPE] scale), and mental health status (hospital anxiety and depression scale [HADS]) were assessed pre- and post-intervention over four weeks.

Results: Compared with the control group, the intervention group achieved greater reductions in pain intensity, perceived exertion, and psychological distress. ANCOVA adjusting for baseline values confirmed statistically significant between-group differences across all outcomes ($P<0.01$). Within-group analyses indicated improvements from baseline to post-intervention in both groups, with larger changes observed in the intervention arm.

Conclusion: Combining manual therapy and aerobic training may be an effective strategy for improving physical and psychological outcomes in middle-aged individuals with CLBP. This supports the need for integrated, multimodal rehabilitation protocols.

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Highlights

● Combined manual therapy and aerobic training significantly reduced pain intensity in middle-aged individuals with CLBP compared to self-directed exercise alone.

● Within the intervention group, significant pre-to-post improvements in pain, fatigue, and psychological well-being were observed over four weeks.

● The findings support integrated rehabilitation protocols combining physical and psychological treatment approaches for enhanced outcomes in CLBP management.

Plain Language Summary

Chronic low back pain (CLBP) is a common condition that causes ongoing pain and can affect both physical ability and mental health, often leading to anxiety, depression, and tiredness. While treatments, such as manual therapy (hands-on techniques to relieve pain) and aerobic exercise (physical activities that increase heart rate), are known to help with physical symptoms, little is known about how they interact when combined, especially regarding mental well-being. A study involving 40 adults aged 32-49 found that combining manual therapy and aerobic exercise can improve both physical and mental health. Combined therapy led to a greater decrease in pain and tiredness and a significant improvement in anxiety and depression symptoms compared to self-directed exercises. This suggests that an integrated approach to managing CLBP may be more effective. These findings can help healthcare providers design better treatment plans, improving the quality of life for people with this condition.

Introduction

Chronic low back pain (CLBP) is a pervasive musculoskeletal condition that significantly impairs quality of life and is a leading cause of disability worldwide [1]. CLBP not only impairs mobility and physical functioning but is intricately linked with psychological distress, including anxiety, depression, and fatigue [2]. CLBP is among the most prevalent syndrome, with approximately 85-95% of patients lacking a specific pathoanatomical diagnosis [3].

Low back pain (LBP) impacted 619 million individuals worldwide in 2020, with the number expected to rise to 843 million by 2050, primarily due to population growth and aging [4]. The pooled point, yearly, and lifetime prevalence of LBP in India were 48%, 51%, and 66%, respectively, and the pooled prevalence rates were higher among females, rural populations, and elementary school personnel [5].

Between 1990 and 2019, disability related to LBP rose across all age groups, with the 50-54 age group experiencing the biggest increase. People in their working years (20–65 years) accounted for almost 70% of lifespan lost due to disability [4, 6]. It is believed that less than one-third of patients with CLBP have had significant limitations in employment, social activities, and self-care tasks for six months or more (high-impact LBP) [7, 8]. There are also reciprocal impacts on mental health CLBP is connected with greater depression, and depression is linked to higher disability and poor recovery in those with LBP [4].

While pharmacological and surgical interventions are sometimes employed, conservative management, including exercise and manual therapy, remains the cornerstone of treatment for most patients [9–11]. Exercise therapy, particularly aerobic exercise, has demonstrated benefits in reducing pain intensity and improving both physical and psychological function among individuals with CLBP [12, 13]. Aerobic activities such as walking, cycling, and swimming not only enhance cardiorespiratory endurance but may also contribute to better psychological outcomes by reducing anxiety and depression associated with chronic pain [12].

Manual therapy, including mobilization and manipulation techniques, is frequently used in conjunction with exercise to address musculoskeletal dysfunctions in CLBP [9, 14]. Manual therapy can modulate central sensitization and interrupt maladaptive neural pathways that reinforce chronic pain states [15–17]. This neuromodulation is believed to decrease hyperalgesia and reduce the perception of pain, which is a significant driver of psychological distress in CLBP [16, 18]. Similarly, aerobic exercise programs have shown beneficial effects not only on cardiovascular health but also on mood and fatigue levels through neurochemical modulation [19, 20]. Although physical therapy remains the cornerstone of CLBP management, addressing psychological factors has emerged as crucial for optimal recovery.

Given the multidimensional nature of CLBP, which encompasses both physical and psychological domains, there is a growing interest in multimodal interventions that target both aspects concurrently [21]. Despite the independent benefits of these interventions, limited studies have evaluated their combined impact on physical and psychological domains in CLBP, especially among middle-aged individuals. The combined approach may offer several benefits by addressing both biomechanical and cardiovascular aspects of pain, while also improving psychological well-being through reductions in fear-avoidance behavior and pain catastrophizing. This intervention will not only enhance physical function and relieve pain but may also decrease the risk of symptom recurrence by promoting sustained physical activity and confidence in movement. Ultimately, targeting both physical and psychological domains together provides a more holistic and potentially more effective management strategy for CLBP, particularly among middle-aged individuals. This study aims to assess the effect of manual therapy combined with aerobic exercise on psychological well-being among individuals with CLBP, addressing an important gap in current clinical knowledge and potentially informing more holistic approaches to CLBP management.

Materials and Methods

Study design

A randomized pre-test–post-test study was conducted at a tertiary rehabilitation facility in New Delhi, India, between May and July 2024.

Sample size

The sample size for the trial was determined based on calculations for the selected outcome the hospital anxiety and depression scale (HADS). G*Power was used to determine the number of participants to be included in the intervention and control groups. The initial calculations indicated a required sample of 40 participants. To account for a potential 15% dropout rate, the final target sample size was set at 46 participants (23 per group). This corresponds to an effect size of 0.6, with a significance level (α) of 0.05 and a statistical power of 0.8.

Participants

A total of 46 individuals with non-specific CLBP were recruited according to predefined eligibility criteria. The inclusion criteria included age 32-49 years, diagnosis of non-specific CLBP lasting >3 months, ability to follow instructions, and willingness to participate. The exclusion criteria included history of spinal surgery, severe cardiopulmonary, neurological, or psychiatric disorders, current participation in other rehabilitation programs, history of metabolic disorder, uncontrolled hypertension, pregnancy, history of major trauma in the last six months, history of major surgery in the last year, and cancer.

Randomization and blinding

A sealed opaque envelope approach was used to ensure allocation concealment, and participants were randomly assigned in a 1:1 ratio to either the intervention group (IG) or control group (CG). An independent researcher who was not involved in recruitment or assessment produced the group allocations in sequentially numbered, identical, and sealed envelopes. At enrolment, each participant was assigned the next available envelope to determine group allocation. To minimize bias, participants remained blinded to their group designation throughout the trial, and outcome assessors were blinded to group allocation.

Ethical approval

Prior to commencement, the study was reviewed and approved by the Jamia Hamdard Institutional Ethics Committee (JHIEC). The present study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, ensuring the protection of the rights of all research participants.

Interventions

For IG patients, aerobic exercise and manual therapy were administered, while the CG patients were prescribed conventional LBP protocol (home program) consisting of self-exercises for four weeks [22]. Physiotherapists with more than ten years of expertise managed for every patient in the IG and CG. A flyer handout was provided, and an exercise was demonstrated to all the CG patients. The physiotherapist phoned them at the end of every week throughout the intervention period to assess and record any changes in their pain. The treatment was implemented three times a week for four weeks, for a total of 12 sessions (Figure 1).

Figure 1. Intervention procedure

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Aerobic exercise: The aerobic training procedure for the IG involved participants beginning each session with a 5-10 minute warm-up of low-intensity cycling to gradually elevate heart rate and prepare the muscles, followed by moderate-intensity stationary cycling (targeting 50-70% heart rate reserve) for 15 minutes initially, with the duration increased by 5 minutes per week up to 30 minutes as tolerated; each session concluded with 5-10 minute cool-down of low-intensity cycling to safely return heart rate to baseline and promote recovery, and post-exercise stretching was recommended to enhance flexibility and reduce muscle soreness [23].

Manual therapy: Soft tissue mobilization (STM)

Three STM techniques were used: quadratus lumborum myofascial release, thoracolumbar myofascial release, and transverse sliding of the lumbar muscles. The therapist used their elbow to slide across the paraspinal muscles three times on each side while the patient lay prone to perform the transverse sliding technique. The therapist placed their hands in the participant's T12-L1 region and sacrum to facilitate thoracolumbar myofascial release, which was also performed in the prone position. After making contact, the therapist massaged along the fascia for at least five minutes without slipping over the skin or applying intense pressure. The participant remained prone during the quadratus lumborum myofascial release procedure, and the therapist used the opposite hand to hold and stabilize the participant's leg while placing their elbow on the quadratus lumborum muscle above the iliac crest. The therapist gently moved the hand on the thigh lower and applied pressure with the elbow towards the spine. Each half of this approach was used for seven minutes [24].

Maitland's mobilization procedure and technique Maitland's mobilization procedure and technique [25]

Patient position: The patient is lying in the prone position, with their arms resting either beside their body or outstretched overhead, and their head cocked slightly to one side. The therapist should stand on the patient's right side and place the ulnar edge of their hand just above the spinous process, between the pisiform and hamate bones. The therapist placed their shoulder directly over the spinous process and maintained full wrist extension while keeping the forearm neutral, neither supinated nor pronated [26].

Direction: Mobilization was directed in a posteroanterior direction. Joint oscillations in grades I and II lasted 30 seconds each. The three spinous processes around the pathologic region were subjected to grade I joint mobilizations in a sequential manner, followed by grade II joint mobilizations. Mobilization had six glides on each spinous process. After mobilization, patients were given a hydrocollator pack for 10 minutes to alleviate pain

Table 1. Overview of combined intervention for CLBP

Intervention	Description	Parameters	Frequency/Duration
Aerobic exercise	Stationary cycling: Warm-up, moderate-intensity cycling, cool-down, post-exercise stretching	Warm-up: 5–10 min low-intensity cycling Main: 15 min moderate-intensity (50–70% HRR), increasing by 5 min/week to 30 min as tolerated Cool-down: 5–10 min low-intensity cycling Stretching: Post-exercise	Sessions: 3/week Duration: 4 weeks
Manual therapy	1. STM: Thoracolumbar, quadratus lumborum myofascial release, transverse sliding of lumbar muscles. 2. Maitland's mobilization: Posteroanterior joint oscillations	STM: Lumbar muscle sliding (3x/side), Thoracolumbar fascia (≥5 min) Quadratus lumborum (7 min/side) Maitland's: - Grade I/II oscillations on spinous processes (6 reps each, 30 sec/grade), hydrocollator pack (10 min)	Sessions: 3/week Duration: 4 weeks

HRR: Heart rate reserve; STM: Soft tissue mobilization.

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caused by increased paraspinal muscle activity from mechanical stress during mobilization. Follow-up: The treatment was administered for four weeks, with three visits per week, each lasting one hour (Tables 1 and 2).

Outcome measures

Pain: Numerical pain rating scale (NPRS)

The NPRS is an 11-point rating system with 0 representing no pain and 10 representing severe pain. The triple NPRS, which generates the global average by utilizing the patient's maximum and minimum pain readings from the current and previous 24 hours, was utilized in this study to assess NPRS (Figure 2). The triple NPRS's test re-test reliability had an intraclass correlation coefficient (ICC) ranging from 0.61 to 0.77 and a nominal clinically significant difference (minimal clinically important difference [MCID]) of two points [27].

Psychological factor examination

HADS: This self-assessment tool is used to gauge the degree and severity of change as well as to determine a patient's risk for anxiety and depression. There are 14 questions on the scale, seven of which measure anxiety and the other seven of which measure sadness. From both subscales, patients can receive a maximum score of 21 and a minimum score of 0 [28].

Method of measurement of perceived fatigue

Modified Borg rating of perceived exertion (MRPE): Participants provided subjective feedback on training using the MRPE at baseline and after four weeks as a secondary outcome. Participants were asked to tick the

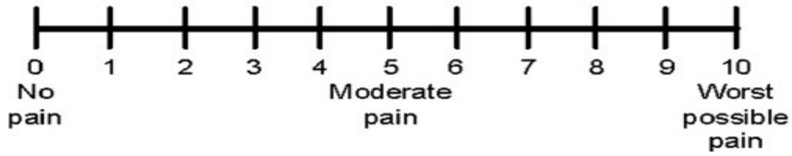

Figure 2. 0-10 NPRS

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Table 2. Overview of home-based exercise program

Exercise Type	Description	Repetitions/ Duration	Frequency/Duration
Stretching	Hamstring, gluteal, and lower back stretches; gentle movements to improve flexibility	2–3 repetitions, 20-30 sec hold	Daily/ 4 weeks
Aerobic exercise	Walking or Pedo-cycling: at patient specific self-selected speed and seat height, moderate intensity	20–30 minutes per session	3 times per week / 4 weeks
Strengthening	Core stabilization (e.g. bridges, abdominal bracing, bird-dog), bodyweight exercises	2–3 sets, 10–15 reps	3 times per week / 4 weeks
Post-exercise cool-down	Gentle stretching and relaxation	5–10 minutes	3 times per week / 4 weeks

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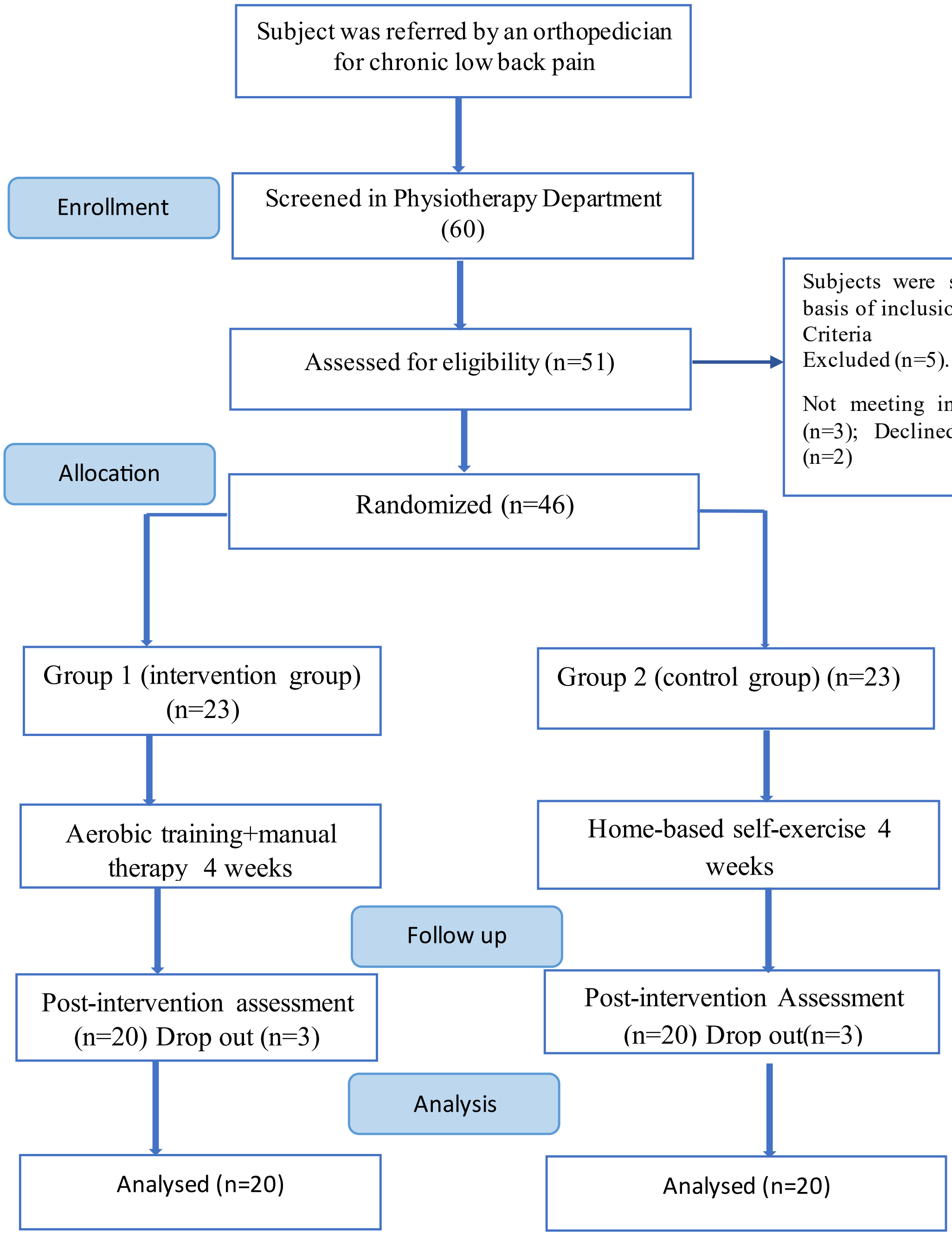

Figure 3. Consort flow diagram

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appropriate answer to the given questions, how you exerted during cycling it ranges from 0-10 on the conscious intensity scale [29]. Participants were asked to rate their exercise using an MRPE scale.

Statistical analysis

SPSS software, version 25 was used to analyze the data. The skewness and kurtosis values were analyzed to assess whether the data were normally distributed. Prior to statistical analysis, the Shapiro-Wilk and Kolmogorov-Smirnov tests were used to assess normality. Continuous post-intervention outcomes were compared between groups using independent t-tests and analysis of covariance (ANCOVA) models adjusting for each outcome's baseline value (pre-specified primary approach for handling baseline variability and any imbalance). Effect sizes, adjusted mean differences, 95% confidence intervals (CI), and P-values are reported to emphasize magnitude and precision. Given the limited number of

Table 3. Baseline characteristics for both groups

Demographic	Mean±SD	
	Group 1 (n=20)	Group 2 (n=20)
Age (y)	38.8±4.5	39.5±4.2
Gender (M/F)	8.12	10/10
BMI (kg/m²)	27.3±4.2	25.8±2.9
NPRS (0–10)	7.0±1.2	6.8±1.1
HADS total (0–42)	18.5±3.2	19.0±3.4
MRPE (0–10)	6.5±1.5	7.2±1.4

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Abbreviations: NPRS: Numerical pain rating scale; HADS: Hospital anxiety and depression scale; MRPE: Modified Borg rating of perceived exertion; BMI: Body mass index; M: Male; F: Female.

prespecified outcomes, P values are presented unadjusted; conclusions were consistent in direction and significance after baseline adjustment. Assumptions were checked using model diagnostics; ANCOVA is appropriate in randomized designs and increases statistical power while reducing bias due to baseline differences.

Procedure

Patients with CLBP were referred to the physiotherapy department for screening. Eligible participants provided written informed consent following screening, according to predetermined inclusion and exclusion criteria. Baseline measurements of pain, anxiety, depression, and fatigue were collected and reassessed at the termination of the four-week intervention period. All information was systematically recorded and compiled into a master chart.

Of the 60 individuals screened, 51 were assessed for eligibility. Three did not meet the inclusion criteria, and two declined to participate. A total of 46 participants were randomized: 23 to the IG (manual therapy aerobic exercise) and 23 to the CG (home-based self-exercise). During follow-up, 3 participants in each group withdrew (for reasons, including relocation, competing work commitments, or family reasons). Thus, 40 participants (20 in each group) completed the study and were analyzed. Six participants did not complete the follow-up assessments owing to relocation, competing work commitments, or personal/family reasons. No adverse events were reported in either group during the intervention or follow-up period (Figure 3).

Results

Participant characteristics

The baseline characteristics of all anthropometric measures were consistent across the groups. No statistically significant baseline differences were observed between groups (all P>0.05). The average age of participants was similar in both groups, with group 1 at approximately 39 years and group 2 at approximately 39 years. The gender distribution was balanced, with group 1 comprising 8 males and 12 females and group 2 comprising 10 males and 10 females. Body mass index (BMI) was also comparable between groups, with group 1 averaging just over 27 kg/m² and group 2 averaging just under 26 kg/m². Table 3 presents the characteristics of the participants in the initial assessment (Table 3).

Outcome measures

At baseline, no significant differences were observed between groups for NPRS, HADS, or MRPE (all P>0.05). After the 4-week intervention, the IG showed significantly greater improvements across all outcomes (Table 4). Table 4 presents a between-group analysis between the intervention and the CG. Figure 4 shows a graphical representation of pre- and post-intervention comparative findings (Table 4 and Figure 4).

Values are presented as Mean±SD. Between-group differences are adjusted for baseline values using ANCOVA. Effect sizes are reported as Cohen's d with 95% CIs. P values represent unadjusted significance levels from ANCOVA models adjusting for baseline values. MCID thresholds: NPRS ≥2 points; HADS ≥1.5–2 points. No validated MCID is available for MRPE; changes are interpreted based on magnitude and effect size.

Table 4. Primary and secondary outcomes at baseline and post-intervention with ANCOVA adjusted between-group differences

Timepoint	Mean±SD		ANCOVA Adjusted Group Difference (95% CI)	P	Cohen's d (95% CI)
	Group 1	Group			
NPRS Pre	7±1.2	6.8±1.1	−1.08 (−1.43, −0.74)	<0.001	−2.01 (−2.78, −1.25)
NPRS Post	4±1.3	5.1±1.4			
HADS Pre	18.5±3.2	19±3.4	−5.6 (−6.9, −4.2)	<0.001	−2.65 (−3.51, −1.79)
HADS Post	11.2±2.9	16.8±3.1			
MRPE Pre	6.5±1.5	7.2±1.4	−1.4 (−2.1, −0.8)	0.002	−1.58 (−2.29, −0.86)
MRPE Post	4.1±1.2	5.8±1.5			

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Pain intensity (NPRS): Scores decreased to 4±1.3 from 7±1.2 in the IG and to 5.1±1.4 from 6.8±1.1 in the CG. ANCOVA indicated a significant between-group difference of −1.08 (95% CI, −1.43%, −0.74%; P<0.001; d=−2.01). Both groups exceeded the MCID of two points, with greater improvement in the IG.

Psychological distress (HADS): Scores declined to 11.2±2.9 from 18.5±3.2 in the IG versus 16.8±3.1 from 19.0±3.4 in the control. The between-group difference was −5.6 (95% CI, −6.9%, −4.2%; P<0.001; d=−2.65), exceeding the MCID of 1.5–2 points.

Perceived exertion (MRPE): Scores reduced to 4.1±1.2 from 6.5±1.5 in the IG and to 5.8±1.5 from 7.2±1.4 in the control. The between-group mean difference was −1.4 (95% CI, −2.1%, −0.8%; P=0.002), corresponding to a large effect size (Cohen's d=−1.58).

Discussion

This study demonstrated that manual therapy combined with aerobic exercise significantly improved physical pain, fatigue, and psychological symptoms among middle-aged individuals with CLBP. The large effect sizes validated these findings. The moderate resolution of pain and substantial mental health improvements sug-

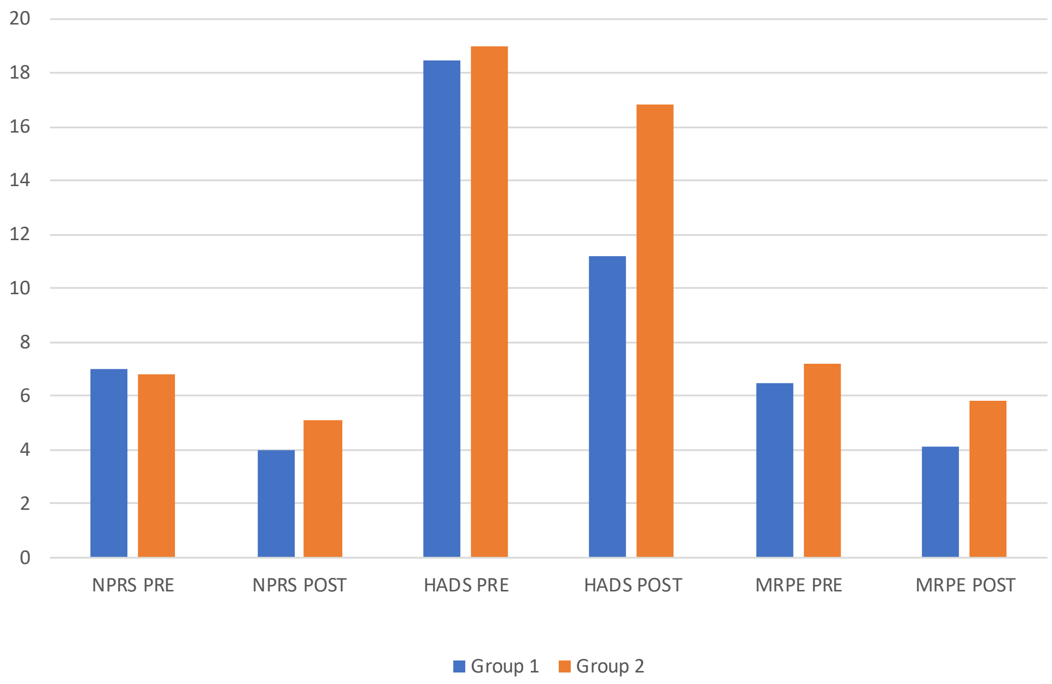

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Figure 4. Graphical representation of pre- and post-intervention comparative findings a) NPRS, b) HADS, and c) MRPE

gest a multimodal therapeutic mechanism, potentially addressing both nociceptive pathways and psychosocial contributors to CLBP. These outcomes suggest the intervention should be integrated into clinical protocols for middle-aged individuals with CLBP and comorbid mental health concerns.

Previous studies have typically examined these interventions in isolation, whereas this study's design intends to harness their potential synergistic benefits. Second, by concentrating on middle-aged individuals who often experience both the mechanical and psychological burdens of CLBP, the study addresses the clinical need for holistic treatments that target both pain and psychological parameters simultaneously. This study's results indicated that IG experienced significantly greater improvement in pain, as evidenced by a reduced NPRS.

Manual treatment generates mechanical stimulation by applying pressure to the joints. This procedure triggers the gate control mechanism, which prevents thin A-delta and C fibers from transmitting pain signals. Rather, it activates the thick, myelinated A-β fibers that transmit these sensations and are connected to joint mechanoreceptors [30]. By stretching the joint capsule, manual therapy activates proprioceptors in the joint capsule and surrounding muscles, which provide sensory signals to the spinal cord. These signals subsequently stimulate the midbrain's periaqueductal grey matter. Pain is reduced when the descending noradrenergic and serotonergic pathways are activated [31, 32]. Consistent with previous findings, several studies in the literature have shown that individuals with LBP experience a significant decrease in pain when manual therapy and exercise are used [1]. This pain alleviation facilitates improved exercise participation, thereby allowing aerobic training to further supplement the process of neuromuscular rehabilitation. These findings are well aligned with prior observations supporting the beneficial role of combined physical intervention in CLBP management [1]. Consistent with our findings, several studies in the literature have also documented that both manual therapy and exercise lead to a significant decrease in pain among individuals with LBP.

This study is the first to explore the use of manual therapy in conjunction with aerobic exercise for treating psychological symptoms. The findings of our study indicate reduced HAD scores among participants receiving the combined treatment. A randomized trial found that individuals who had ten sessions of manual therapy had significantly lower levels of depression and kinesiophobia, which is in line with the findings of our study [33]. Another study showed that manual therapy can lead to significant enhancements in mental health outcomes, including reduced anxiety and depression levels [1, 34]. Jayakody et al. emphasized that moderate-intensity aerobic exercise is effective in reducing anxiety and depressive symptoms, findings that mirror the trends seen in our IG [35]. Regular aerobic exercise has been linked to significant reductions in anxiety and depression. It serves as a non-pharmaceutical intervention that can improve mood and overall mental health [36].

Perceived fatigue, assessed using the modified Borg scale, showed significant improvement in the IG relative to the CG. Aerobic exercise has been shown to diminish fatigue by enhancing oxygen delivery and utilization at the muscular level, and, when combined with manual therapy, it further reduces fatigue. Another study states that multimodal intervention is beneficial for energy levels and endurance in patients with chronic conditions [37]. Furthermore, aerobic exercise is known to modulate inflammatory cytokines and increase endorphin release, thereby improving fatigue and mood symptoms [38].

The study found that self-directed exercise did not yield the same improvement as integrated interventions, highlighting the need for supervised, multi-model interventions to ensure adherence, motivation, and technique. The absence of consistent manual therapy and structured aerobic training in self-directed exercise protocols may lead to suboptimal exercise intensity and lower engagement, potentially resulting in inadequate physical outcomes and mental health improvement [1].

CLBP patients often experience psychological distress, anxiety, and depression, which can exacerbate pain perception and hinder recovery. This study suggests investigating manual therapy as an adjuvant therapy option to reduce depressive symptoms in patients with CLBP. Manual therapy and aerobic exercise are safe and effective interventions that can be incorporated into regular physical therapy practice. Traditional physiotherapy often fails to address mental health outcomes; therefore, examining these conditions in a combined intervention environment could guide future integrated multimodal rehabilitation procedures.

Limitations

This study has some limitations that should be considered when interpreting the findings. First, the small sample size and short intervention duration may limit the generalizability and sustainability of the observed effects. Second, the absence of long-term follow-up eliminates assumptions about the strength of improvements in psychological well-being and the recurrence of symptoms after the intervention period. Third, although the study focused on middle-aged individuals, the homogeneity of the sample may restrict its applicability to other age groups or populations with different clinical characteristics, moreover the lack of blinding for researchers could introduce performance and detection bias.

Future research directions

Future studies should address the limitations of current research by using larger, more diverse samples, extending follow-up periods, investigating underlying mechanisms, and incorporating rigorous methodological controls. They should also use comprehensive psychological health measures, involve diverse populations, and evaluate real-world implementation and cost-effectiveness.

Conclusion

The study found that combining manual therapy and aerobic training effectively reduced pain, fatigue, and mental health symptoms in middle-aged individuals with CLBP, promoting the inclusion of multimodal rehabilitation approaches in clinical practice.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Jamia Hamdard Institutional (JHIEC), New Delhi, India (CODE: 03/24 (12/04/2024). The subjects provided informed consent to participate in this study.

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Authors' contributions

Conceptualization, methodology, review and editing:: All authors; Investigation: Firdaus Jawed, Rabia Aziz, and Aatika Khan; Writing the original draft: Firdaus Jawed and Rabia Aziz; Supervision: Sohrab Ahmad khan and Sahar Zaidi.

Conflict of interest

The authors declared no conflict of interest.

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