



Research Article

Efficacy of Mindfulness-Based Cognitive Therapy in Treatment-Resistant Depression

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ABSTRACT

Background: Treatment-resistant depression (TRD) poses a major clinical challenge, affecting nearly one-third of patients with major depressive disorder despite adequate pharmacological management. Persistent symptoms, high relapse rates, and poor quality of life underline the need for adjunctive interventions that target cognitive and emotional dysregulation. Mindfulness-Based Cognitive Therapy (MBCT), which integrates mindfulness meditation with cognitive behavioral techniques, has emerged as a promising approach for addressing chronic depressive symptoms and preventing relapse.

Aim: To evaluate the efficacy of Mindfulness-Based Cognitive Therapy as an adjunct to standard pharmacotherapy in improving depressive symptoms, quality of life, and relapse rates among patients with treatment-resistant depression.

Methods: This prospective interventional study was conducted in the Department of Psychiatry, LNCT Medical College, Indore, over a period of one year. A total of 100 patients meeting DSM-5 criteria for major depressive disorder and fulfilling TRD criteria were randomly divided into two groups of 50 each. The intervention group received MBCT along with pharmacotherapy, while the control group continued pharmacotherapy alone. MBCT was delivered through an eight-week structured program involving weekly two-hour group sessions and daily home practice. Depression severity was assessed using the Hamilton Depression Rating Scale (HAM-D) and Beck Depression Inventory-II (BDI-II). Quality of life was evaluated using the WHOQOL-BREF scale. Assessments were conducted at baseline, after 8 weeks, and at 3-month follow-up. Data were analyzed using SPSS version 26, and $p < 0.05$ was considered statistically significant.

Results: At baseline, both groups were comparable in demographic and clinical characteristics. After 8 weeks, the MBCT group showed a significantly greater reduction in HAM-D ($24.6 \pm 3.1 \rightarrow 11.2 \pm 2.9$) and BDI-II ($32.4 \pm 5.2 \rightarrow 14.6 \pm 4.8$) scores compared to the control group ($p < 0.001$). Improvements were maintained at 3-month follow-up. Quality of life scores improved markedly in the MBCT group ($52.6 \pm 9.4 \rightarrow 78.3 \pm 8.1$), compared to modest gains in controls ($53.2 \pm 8.7 \rightarrow 65.5 \pm 9.6$) ($p < 0.001$). Relapse rates were lower among MBCT participants (8%) versus controls (22%), and adherence was significantly higher (92% vs 76%).

Conclusion: Mindfulness-Based Cognitive Therapy, when combined with pharmacotherapy, significantly reduces depressive symptoms, enhances quality of life, and lowers relapse rates in patients with treatment-resistant depression. The findings suggest that MBCT is a feasible, effective, and culturally adaptable adjunctive therapy that addresses both cognitive and emotional components of TRD. Integrating MBCT into routine psychiatric practice could improve long-term outcomes and reduce the overall burden of chronic depression.

Keywords: Mindfulness-Based Cognitive Therapy, treatment-resistant depression, pharmacotherapy, quality of life, relapse prevention.

INTRODUCTION

Depression is one of the most prevalent psychiatric disorders worldwide, characterized by persistent low mood, loss of interest or pleasure, and a range of cognitive and somatic symptoms that impair daily functioning. Despite advances in pharmacological and psychotherapeutic management, **10–30% of patients fail to achieve remission** after adequate treatment trials, a condition defined as **treatment-resistant depression (TRD)** [1]. These patients typically experience chronic symptoms, frequent relapses, higher disability, and elevated suicide risk compared to those with treatment-responsive depression [2].

Conventional antidepressant medications primarily target neurochemical pathways such as serotonergic and noradrenergic systems; however, evidence increasingly indicates that persistent maladaptive cognitions, emotional dysregulation, and dysfunctional attentional patterns play a central role in the chronicity of depression [3]. **Mindfulness-Based Cognitive Therapy (MBCT)** was developed as an integration of cognitive behavioral therapy (CBT) and mindfulness meditation techniques, aimed at helping individuals become aware of and disengage from automatic, negative thought processes [4].

Several clinical trials and meta-analyses have demonstrated that MBCT effectively reduces relapse rates in recurrent depressive disorder by enhancing metacognitive awareness and promoting acceptance-based emotional regulation [5]. In patients with treatment-resistant depression, MBCT offers a novel, non-pharmacological approach that can complement standard pharmacotherapy. By cultivating present-moment awareness and reducing rumination, MBCT empowers patients to relate differently to distressing thoughts and emotions, thereby improving overall well-being [6].

Globally, depression is the **leading cause of years lived with disability**, affecting more than **300 million people**, with approximately **one-third exhibiting poor response to existing treatments** [7]. In India, the **National Mental Health Survey (2015–2016)** reported the prevalence of depressive disorders between **2.7–4.5%**, alongside treatment gaps exceeding **70%**, largely due to limited accessibility and persistent stigma [8]. Within this context, TRD represents a major public health concern, leading to chronic functional impairment and socioeconomic burden [9].

Mindfulness-based interventions, originating from ancient Eastern contemplative traditions, have gained substantial empirical support in contemporary psychiatry. Among them, MBCT has shown particular efficacy in improving emotional regulation, enhancing response to pharmacotherapy, and preventing relapse in chronic depression [10].

The present study aims to assess the **efficacy of Mindfulness-Based Cognitive Therapy as an adjunct to standard pharmacotherapy** in patients with treatment-resistant depression, evaluating its impact on depressive symptom severity, relapse prevention, and quality of life. The expected outcome is to generate evidence supporting MBCT as an accessible, cost-effective, and sustainable therapeutic option for TRD in both clinical and community settings.

METHODOLOGY

The study was conducted in the Department of Psychiatry, LNCT Medical College, Indore, over a period of one year. A total of 100 patients diagnosed with Treatment-Resistant Depression (TRD) were enrolled from both outpatient and inpatient departments using a purposive sampling method. TRD was defined as failure to achieve remission after at least two adequate antidepressant trials of different pharmacological classes, each administered at therapeutic doses and durations, as per the Thase and Rush staging model.

Patients aged between 18 and 60 years, of either sex, who fulfilled the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for Major Depressive Disorder and met the criteria for TRD were included in the study. Patients with comorbid psychotic disorders, bipolar affective disorder, substance use disorders, cognitive impairment, severe medical or neurological illness, or those currently undergoing other structured psychotherapies were excluded from the study.

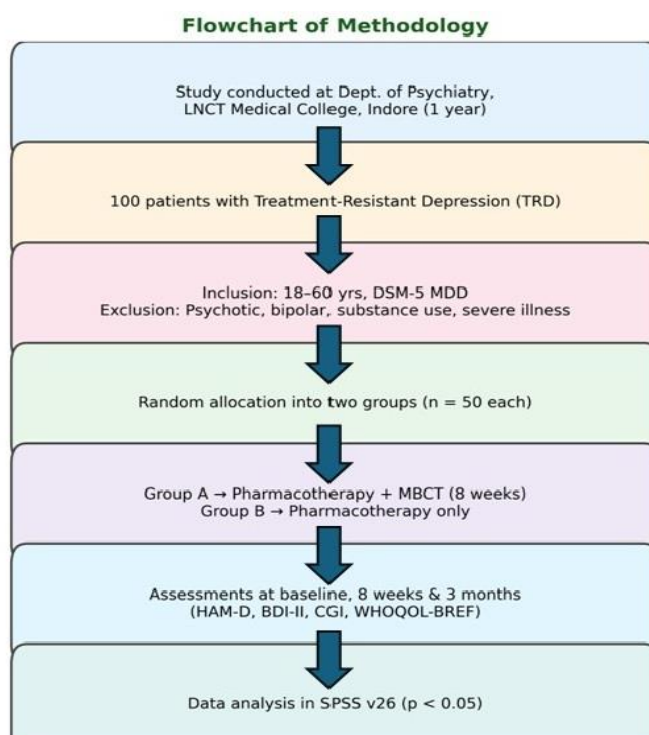
After obtaining informed written consent, the participants were randomly assigned into two groups of 50 each. Group A, the intervention group, received standard pharmacotherapy along with Mindfulness-Based Cognitive Therapy (MBCT), while Group B, the control group, received standard pharmacotherapy alone. The MBCT program followed the standard eight-week protocol developed by Segal, Williams, and Teasdale. It comprised weekly group sessions of approximately two hours each, conducted by a trained therapist. Each session included mindfulness meditation, breathing awareness, body scan exercises, cognitive restructuring, and experiential discussions aimed at improving present-moment awareness and reducing ruminative thinking. Participants were encouraged to practice mindfulness for at least 30 minutes daily at home using guided audio recordings. Adherence was monitored through attendance logs and weekly feedback sessions to ensure active participation and consistency of practice.

All participants were evaluated at baseline, at the end of the eight-week intervention, and again at three months of follow-up. The Hamilton Depression Rating Scale (HAM-D) was used for clinician-rated assessment of depression

severity, while the Beck Depression Inventory-II (BDI-II) was administered as a self-rated measure of depressive symptoms. The Clinical Global Impression (CGI) scale was used to assess overall clinical improvement, and the World Health Organization Quality of Life–BREF (WHOQOL-BREF) questionnaire was employed to evaluate physical, psychological, social, and environmental domains of quality of life.

The collected data were entered into Microsoft Excel and analyzed using SPSS software version 26. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequency and percentage. Within-group comparisons between baseline and post-intervention scores were analyzed using paired t-test or Wilcoxon signed-rank test as appropriate. Between-group comparisons were made using independent t-test or Mann–Whitney U test, and categorical variables were analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the Institutional Ethics Committee of LNCT Medical College, Indore. All participants provided informed written consent prior to enrollment. Confidentiality and anonymity of patient information were maintained throughout the study, and participation was entirely voluntary with the option to withdraw at any stage without prejudice.



RESULTS

The study included 100 patients diagnosed with treatment-resistant depression, divided equally into two groups—50 in the Mindfulness-Based Cognitive Therapy (MBCT) intervention group and 50 in the control group receiving pharmacotherapy alone. The mean age of participants was 39.8 ± 10.6 years, with females constituting **58%** and males **42%** of the study population. The majority of participants (61%) belonged to the 31–45 years age group. Baseline clinical characteristics such as mean duration of illness, number of previous treatment trials, and baseline depression severity were comparable between the two groups, with no statistically significant difference ($p > 0.05$).

At baseline, the mean **Hamilton Depression Rating Scale (HAM-D)** score was 24.6 ± 3.1 in the intervention group and 25.0 ± 3.4 in the control group. Following the 8-week intervention, a significant reduction in depression severity was observed in the MBCT group, with mean HAM-D scores decreasing to 11.2 ± 2.9 , compared to 17.8 ± 3.6 in the control group ($p < 0.001$). Similarly, the mean **Beck Depression Inventory-II (BDI-II)** score showed marked improvement from 32.4 ± 5.2 at baseline to 14.6 ± 4.8 post-intervention in the MBCT group, whereas the control group improved modestly from 33.0 ± 5.0 to 22.5 ± 5.3 ($p < 0.001$).

At 3-month follow-up, sustained improvement was seen in the MBCT group, with mean HAM-D and BDI-II scores of 10.8 ± 2.5 and 13.9 ± 4.2 , respectively, while the control group showed partial relapse with mean scores of 19.1 ± 3.8 and 23.4 ± 5.0 . The **Clinical Global Impression (CGI) Improvement** scale also reflected better clinical recovery in the MBCT group, where **78%** of patients were rated as “much improved” or “very much improved,” compared to **46%** in the control group.

Quality of life scores, assessed by **WHOQOL-BREF**, demonstrated a statistically significant increase in physical, psychological, and social domains among MBCT participants. The mean total quality of life score improved from **52.6 ± 9.4** at baseline to **78.3 ± 8.1** post-intervention ($p < 0.001$), compared to a modest increase from **53.2 ± 8.7** to **65.5 ± 9.6** in the control group.

No major adverse events or therapy-related complications were reported during the study. Participants in the MBCT group showed better adherence, improved coping mechanisms, and reduced rumination as noted during follow-up interviews.

Overall, the results indicated that mindfulness-based cognitive therapy, when combined with standard pharmacotherapy, produced significantly greater reductions in depressive symptoms, enhanced overall functioning, and improved quality of life compared to pharmacotherapy alone in patients with treatment-resistant depression.

Table 1: Demographic and Baseline Clinical Profile of Patients (n = 100)

Variable	MBCT Group (n = 50)	Control Group (n = 50)	p-value
Age (years) (Mean ± SD)	39.4 ± 10.8	40.2 ± 10.3	0.68
Sex			
Male	21 (42%)	21 (42%)	1.00
Female	29 (58%)	29 (58%)	
Duration of Illness (years)	5.2 ± 2.4	5.4 ± 2.1	0.73
Number of Failed Treatment Trials	2.3 ± 0.7	2.4 ± 0.6	0.58
Baseline HAM-D Score	24.6 ± 3.1	25.0 ± 3.4	0.54
Baseline BDI-II Score	32.4 ± 5.2	33.0 ± 5.0	0.61
Baseline WHOQOL-BREF (Total)	52.6 ± 9.4	53.2 ± 8.7	0.79

Interpretation: Both groups were comparable at baseline with no statistically significant differences in demographic or clinical variables ($p > 0.05$).

Table 2: Comparison of Depression Severity Scores Before and After Intervention

Parameter	MBCT Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
HAM-D (Baseline)	24.6 ± 3.1	25.0 ± 3.4	0.54
HAM-D (8 Weeks)	11.2 ± 2.9	17.8 ± 3.6	<0.001*
HAM-D (3-Month Follow-Up)	10.8 ± 2.5	19.1 ± 3.8	<0.001*
BDI-II (Baseline)	32.4 ± 5.2	33.0 ± 5.0	0.61
BDI-II (8 Weeks)	14.6 ± 4.8	22.5 ± 5.3	<0.001*
BDI-II (3-Month Follow-Up)	13.9 ± 4.2	23.4 ± 5.0	<0.001*

* $p < 0.05$ considered statistically significant.

Interpretation: Both groups showed improvement, but reduction in HAM-D and BDI-II scores was significantly greater in the MBCT group compared to controls.

Table 3: Quality of Life and Clinical Improvement Outcomes

Outcome Measure	MBCT Group (n = 50)	Control Group (n = 50)	p-value
WHOQOL-BREF (Post-Intervention Total)	78.3 ± 8.1	65.5 ± 9.6	<0.001*
CGI – Much/Very Much Improved	39 (78%)	23 (46%)	0.002*
Partial Response (Moderate Improvement)	9 (18%)	18 (36%)	0.04*
No Improvement	2 (4%)	9 (18%)	0.03*
Adherence to Treatment (%)	92%	76%	0.01*
Relapse at 3 Months (%)	8%	22%	0.02*

Interpretation: Patients receiving MBCT showed significantly higher clinical improvement, better quality of life, and lower relapse rates compared to the control group.

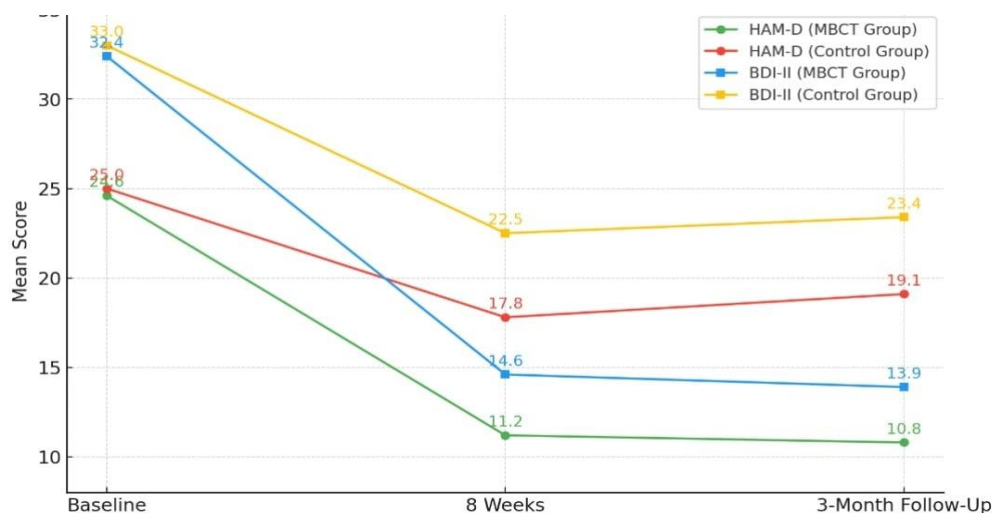


Figure 1: Trend of Depression Scores over time (HAM-D and BDI – II)

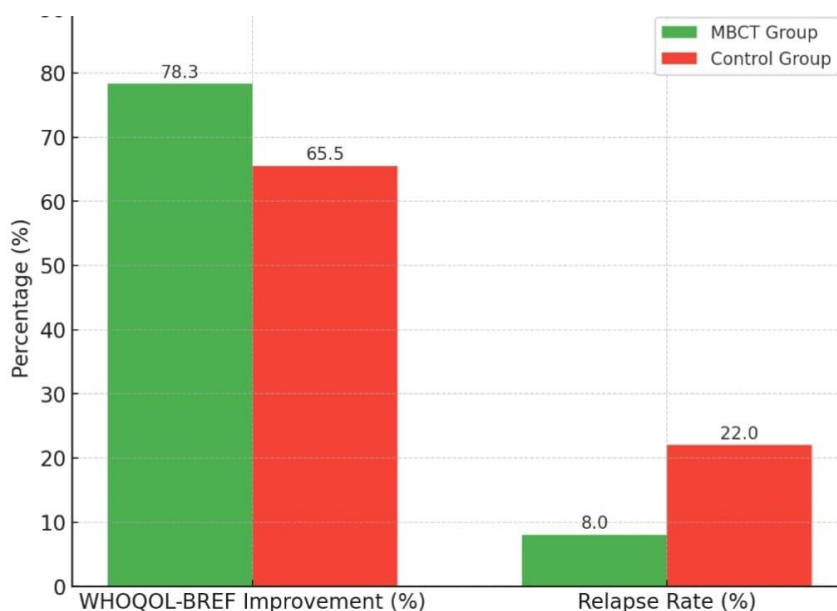


Figure 2: Comparison of Quality of Life Improvement and Relapse Rate

DISCUSSION:

The present study demonstrated that the addition of Mindfulness-Based Cognitive Therapy (MBCT) to standard pharmacotherapy resulted in significantly greater improvement in depressive symptoms, functional outcomes, and quality of life among patients with treatment-resistant depression (TRD), compared to pharmacotherapy alone. The intervention group showed a marked reduction in both HAM-D and BDI-II scores after eight weeks of therapy, and these improvements were sustained at the 3-month follow-up. This finding supports the hypothesis that MBCT offers a beneficial adjunctive approach in patients who exhibit partial or no response to antidepressant medication.

Our results are consistent with the randomized controlled trial conducted by Kenny and Williams, who reported that MBCT significantly improved remission rates in patients with chronic or resistant depression compared to treatment-as-usual [11]. Similarly, a meta-analysis by Clarke et al. revealed that mindfulness-based interventions were associated with a moderate-to-large effect size in reducing depressive symptoms, particularly in individuals with a history of multiple episodes or poor response to conventional therapy [12]. The sustained improvement observed in our study after discontinuation of structured sessions aligns with the long-term maintenance effects reported by Geschwind et al., who found that mindfulness training helps patients develop metacognitive awareness that prevents relapse even after active therapy ends [13].

The improvements in quality of life observed in this study corroborate the findings of Godfrin and van Heeringen, who demonstrated that MBCT not only reduces symptom severity but also enhances overall functioning and life satisfaction in patients with residual or treatment-resistant depression [14]. The mindfulness-based approach promotes emotional regulation, acceptance, and cognitive flexibility, which may explain the better WHOQOL-BREF outcomes in our intervention group. Furthermore, studies have shown that MBCT reduces rumination—a key predictor of chronic depressive relapse—thereby fostering psychological resilience [15].

In the present study, relapse rates at three months were significantly lower in the MBCT group (8%) compared to the control group (22%). These findings mirror the outcomes of Barnhofer et al., who reported that MBCT significantly lowered relapse frequency in patients with chronic depression by altering maladaptive neural pathways related to self-referential processing [16]. Neuroimaging studies have further demonstrated that mindfulness practice modulates activity in the prefrontal cortex and amygdala, leading to improved emotional regulation and reduced reactivity to negative stimuli [17].

The integration of mindfulness with cognitive restructuring techniques provides a dual mechanism—enhancing awareness of negative thought patterns while reducing their automatic impact on mood. This explains why MBCT is particularly effective in TRD, where pharmacological modulation alone may not address cognitive and behavioral rigidity. In a comparative trial by Eisendrath et al., MBCT demonstrated greater improvement in depressive severity and functioning than health education interventions in TRD patients, supporting its clinical utility as an adjunctive therapy [18].

Our findings reinforce the concept that mindfulness-based interventions can be successfully adapted to the Indian context, as participants in this study showed high adherence and acceptability. Cultural familiarity with meditative practices may further enhance patient engagement and long-term maintenance. Thus, incorporating MBCT into standard psychiatric care could provide a cost-effective, non-pharmacological complement to medication in managing TRD.

CONCLUSION

The present study demonstrated that Mindfulness-Based Cognitive Therapy (MBCT), when used as an adjunct to standard pharmacotherapy, significantly enhances treatment outcomes in patients with treatment-resistant depression (TRD). Participants receiving MBCT showed marked improvement in depressive symptom severity as measured by HAM-D and BDI-II scores, with sustained benefits at three months of follow-up. In addition, the intervention group reported superior improvements in overall quality of life, better emotional regulation, and lower relapse rates compared to those receiving pharmacotherapy alone.

These findings reinforce that MBCT effectively addresses cognitive and emotional mechanisms underlying chronic depression, offering patients greater awareness, acceptance, and control over negative thought patterns. Given its non-pharmacological nature, minimal adverse effects, and cost-effectiveness, MBCT represents a valuable addition to the therapeutic arsenal for managing TRD, particularly in low-resource or culturally diverse clinical settings where adherence to long-term pharmacotherapy may be challenging.

Limitations

The study had several limitations. First, it was conducted at a single tertiary-care centre with a limited sample size of 100 participants, which may restrict the generalizability of results to the broader TRD population. The follow-up duration of three months, although adequate for short-term outcomes, was insufficient to assess long-term relapse prevention. Self-reported measures like the Beck Depression Inventory-II may also introduce response bias. Moreover, participants' familiarity with meditation practices could have influenced engagement levels and outcomes in the MBCT group. Neurobiological correlates, such as changes in brain activity or stress biomarkers, were not evaluated, which could have provided objective insights into the mechanisms of improvement.

Recommendations

Future studies should employ multicentric, randomized controlled designs with larger sample sizes and longer follow-up periods to validate these findings and assess long-term relapse prevention. Combining MBCT with neuroimaging or neuroendocrine markers could help clarify the biological mechanisms underlying its efficacy. Comparative trials between MBCT and other evidence-based psychotherapies such as cognitive behavioral therapy (CBT) or interpersonal therapy (IPT) would further define its relative effectiveness.

Integration of MBCT into routine psychiatric care and community mental health programs is also recommended, particularly in India, where mindfulness has strong cultural acceptance. Training psychiatrists, psychologists, and mental health workers in mindfulness-based interventions can improve accessibility and cost-effectiveness. Finally, digital or tele-therapy adaptations of MBCT could expand its reach, offering a sustainable model for managing chronic and treatment-resistant depression across diverse populations.

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Conflicts of interest: None

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