

Transcranial Magnetic Stimulation (rTMS) Outcomes in Cases of Treatment-Resistant Depression

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ABSTRACT

Major depressive disorder (MDD) is a prevalent and debilitating mental health condition characterized by persistent low mood, anhedonia, and impaired functioning. Although many patients respond to first-line treatments such as antidepressant medications and psychotherapy, a significant subset—referred to as treatment-resistant depression (TRD)—fails to achieve adequate symptom relief despite multiple therapeutic trials. In recent years, non-invasive neuromodulation techniques have been introduced as alternative options for patients with TRD. Among these, repetitive transcranial magnetic stimulation (rTMS) has gained prominence due to its efficacy, safety profile, and favorable tolerability. rTMS involves delivering focused magnetic pulses to targeted regions of the brain, particularly the left dorsolateral prefrontal cortex (DLPFC), which is associated with mood regulation. Compared to electroconvulsive therapy (ECT), which is generally more efficacious, rTMS is often preferred by patients as it does not require general anesthesia, does not induce seizures, and has fewer cognitive side effects. Several studies have demonstrated significant improvement in depressive symptoms following rTMS, yet more data are needed from real-world clinical settings to assess its effectiveness across different populations. This study contributes to this growing body of evidence by evaluating the clinical impact of rTMS on symptomatology in patients with treatment-resistant depression using structured outcome measures at different phases of therapy.

INTRODUCTION

Major depressive disorder (MDD) is a prevalent and debilitating mental health condition characterized by persistent low mood, anhedonia, and impaired functioning. Although many patients respond to first-line treatments such as antidepressant medications and psychotherapy, a significant subset—referred to as treatment-resistant depression (TRD)—fails to achieve adequate symptom relief despite multiple therapeutic trials¹.

In recent years, non-invasive neuromodulation techniques have been introduced as alternative options for patients with TRD. Among these, repetitive transcranial magnetic stimulation (rTMS) has gained prominence due to its efficacy, safety profile, and favorable tolerability^{2,3}. rTMS involves delivering focused magnetic pulses to targeted regions of the brain, particularly the left dorsolateral prefrontal cortex (DLPFC), which is associated with mood regulation⁴.

Compared to electroconvulsive therapy (ECT), which is generally more efficacious, rTMS is often preferred by patients as it does not require general anesthesia, does not induce seizures, and has fewer cognitive side effects^{5,6}. Several studies have demonstrated significant improvement in depressive symptoms following rTMS, yet more data are needed from real-world clinical settings to assess its effectiveness across different populations^{3,7}.

This study contributes to this growing body of evidence by evaluating the clinical impact of rTMS on symptomatology in patients with treatment-resistant depression using structured outcome measures at different phases of therapy.

Objectives: To assess the clinical effectiveness of repetitive transcranial magnetic stimulation (rTMS) in reducing depressive symptoms among patients diagnosed with treatment-resistant depression, by comparing symptom scores across pre-treatment, on-treatment, and post-treatment phases using validated clinical scales.

METHOD

Ethical considerations: the study was conducted following approval from the Bahrain defence force royal medical services, military hospital institutional review board (RMS-MH/IRB/2024-761).

To ensure patient privacy, all collected data were anonymized using unique codes assigned to each patient before analysis.

As this research utilized a retrospective cohort study design, formal patient consent was taken.

The study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki.

This retrospective study investigates the effectiveness of transcranial magnetic stimulation on treatment-resistant depression cases among 20 patients, age ranged from 26-85. Using Hamilton Depression Scale in three phases: pretreatment, on treatment and post treatment.

Statistical Analysis: Continuous variables were represented as Median (Interquartile Range) or Mean \pm Standard deviation, whereas categorical variables were represented as frequencies and percentages N (%). The Wilcoxon signed-rank test was used to compare patients'

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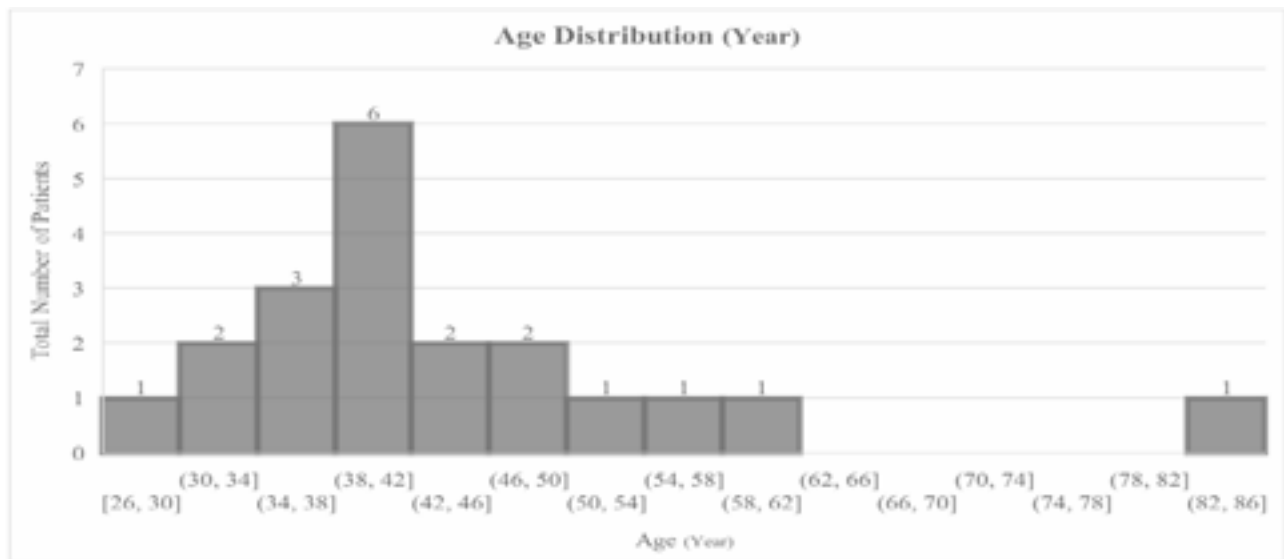


Figure 1. Patients' age distribution, represented as frequencies.

Table 1. Machine Settings

Machine Settings	Frequency	Duration	Number of pulses	Waiting time	Number of trains	Total number of pulses
	10	4	40	26	75	3000

Machine settings were not recorded for one patient.

Table 2. Descriptive statistics for patients' activities on pre, on, and post-treatments, represented as median (Interquartile range)

Activity	Pre – Treatment n = 20	On – Treatment n = 17	Post – Treatment n = 9
Depressed mood			
Feelings of guilt	2 (1 – 3.75)	1 (1 – 2.5)	1 (0.5 – 2)
Suicide			
Early insomnia	2 (1 – 2)	1 (1 – 2)	1 (0 – 1)
Middle insomnia	2 (0 – 2)	0 (0 – 2)	0 (0 – 1.5)
Late insomnia	1 (0.25 – 2)	0 (0 – 1)	0 (0 – 0.5)
Work and activities Retardation	1 (0.25 – 2)	1 (0 – 1)	1 (0 – 1)
Agitation	1 (0.25 – 2)	0.5 (0 – 1)	1 (0 – 1.5)
Anxiety, psychic	2.5 (1 – 4)	2 (1 – 3.5)	0 (0 – 1.5)
Anxiety, somatic	1.5 (1 – 2)	1 (0 – 1)	1 (0 – 1.5)
Somatic symptoms: gastrointestinal	1 (0 – 1)	1 (0 – 1)	0 (0 – 1)
Somatic symptoms: general	1 (1 – 2.75)	1 (0.5 – 3)	0 (0 – 1)
General symptoms			
Hypochondriasis	2 (0.25 – 3)	1 (1 – 2)	0.5 (0 – 1.75)
Loss of weight			
	1 (0.25 – 1.75)	1 (0 – 1)	0 (0 – 0.5)
	1 (0 – 1)	1 (0 – 1)	1 (0 – 1.5)
Insight	0.5 (0 – 2)	1 (0 – 1.5)	0 (0 – 1)
	1 (0 – 1.75)	0 (0 – 0.5)	0 (0 – 1)
	0 (0 – 1)	0 (0 – 0)	0 (0 – 0)
	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)
Total score	20 (15 – 24)	16 (7.5 – 18.5)	9 (4 – 14.5)

scores across the three phases: pre-treatment, on-treatment, and post-treatment. SPSS version 26.0 (IBM Corp., Armonk, NY) software was used to conduct all analyses. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 20 patients were included in the analysis, 13 (65%) were males, and 7 (35%) were females. Patients age ranged from 26 – 85, with mean and standard deviation of 44 ± 13 . Age distribution is illustrated in figure 1.

All patients had the same machine settings, except for one, he had a total number of 80 strains instead of 75 Table 1.

Comparisons of Patients' Total Scores for Depression Across Different Phases

A total of 20 patients were assessed in the pre-treatment phase. Among these, 17 patients continued to the on-treatment phase, and only 9 patients completed the assessments in the post-treatment phase.

The ranks in Wilcoxon signed-rank test are interpreted as follows:

Negative rank → The number of patients whose scores decreased from phase to phase (improvement). **Positive rank** → The number of patients whose scores increased from phase to phase (worsening).

Ties → The number of patients whose scores remained the same in both phases.

On-treatment phase had one un-applicable patient in late insomnia activity, and post-treatment phase had one un-applicable patient in somatic anxiety.

There was a statistically significant difference in patients' depression, suicide, early, middle, and late insomnia, work and activities, retardation, somatic symptoms (gastrointestinal), and total score between the pre-treatment and on-treatment phases, with a reduction in depression scores, as shown in Table 2 and Table 3.

Table 3. Comparison of patients' total scores between pre-treatment and on-treatment phases, represented as median (Interquartile range), (n = 17)

Activity	Pre – Treatment	On – Treatment	Ranks			P-value
			Neg.	Pos.	Ties	
Depressed mood	2 (1 – 3.5)	1 (1 – 2.5)	8	2	7	0.032*
Feelings of guilt	2 (1 – 2)	1 (1 – 2)	5	1	11	0.238
Suicide	2 (0 – 2.5)	0 (0 – 2)	8	1	8	0.018*
Early insomnia	1 (0 – 2)	0 (0 – 1)	8	0	9	0.008**
Middle insomnia	1 (1 – 2)	1 (0 – 1)	8	0	9	0.008**
Late insomnia	1 (0.5 – 2)	0.5 (0 – 1)	7	1	8	0.035*
Work and activities	3 (1.5 – 4)	2 (1 – 3.5)	6	0	11	0.026*
Retardation	2 (1 – 2)	1 (0 – 1)	10	1	7	0.003**
Agitation	1 (0 – 1)	1 (0 – 1)	3	2	12	0.48
Anxiety, psychic	2 (1 – 3)	1 (0.5 – 3)	5	3	9	0.393
Anxiety, somatic	2 (0 – 3)	1 (1 – 2)	7	4	6	0.821
Somatic symptoms: gastrointestinal	1 (0 – 1.5)	1 (0 – 1)	7	1	9	0.034*
Somatic symptoms: general	1 (0 – 1)	1 (0 – 1)	4	2	11	0.739
General symptoms	0 (0 – 2)	1 (0 – 1.5)	1	3	13	0.317
Hypochondriasis	0 (0 – 1)	0 (0 – 0.5)	5	1	11	0.332
Loss of weight	0 (0 – 0.5)	0 (0 – 0)	2	1	14	0.564
Insight	0 (0 – 0)	0 (0 – 0)	1	1	15	>0.05
Total Score	20(15-24)	16(7.5-18.5)	14	3	0	0.002**

* Significant p-value <0.05

** Significant p-value <0.01

P-value was calculated using Wilcoxon signed-rank test.

Table 4. Comparison of patients' total scores between pre-treatment and post-treatment phases, represented as median (Interquartile range), (n = 9)

Activity	Pre – Treatment	Post – Treatment	Ranks			P-value
			Neg.	Pos.	Ties	
Depressed mood Feelings of guilt Suicide	2 (1 – 2.5)	1 (0.5 – 2)	5	1	3	0.071
Early insomnia	2 (1 – 2.5)	1 (0 – 1)	7	0	2	0.014*
Middle insomnia	0 (0 – 2)	0 (0 – 1.5)	2	1	6	0.414
Late insomnia	1 (0 – 1.5)	0 (1 – 0.5)	5	1	3	0.096
Work and activities Retardation	1 (1 – 2)	1 (0 – 1)	5	0	4	0.034*
Agitation	1 (1 – 2)	1 (0 – 1.5)	5	1	3	0.096
Anxiety, psychic	2 (1 – 4)	0 (0 – 1.5)	6	1	2	0.041*
Anxiety, somatic	2 (0.5 – 2)	1 (0 – 1.5)	6	3	0	0.327
Somatic symptoms: gastrointestinal	1 (0 – 1.5)	0 (0 – 1)	3	0	6	0.083
Somatic symptoms: general	2 (0.5 – 3)	0 (0 – 1)	5	1	3	0.057
General symptoms Hypochondriasis Loss of weight	2 (1.5 – 3)	0.5 (0 – 1.75)	5	0	3	0.042*
	1 (0 – 1.5)	0 (0 – 0.5)	4	0	5	0.063
	1 (1 – 1)	1 (0 – 1.5)	3	1	5	0.705
Insight	1 (0 – 2)	0 (0 – 1)	3	0	6	0.102
	1 (0 – 1.5)	0 (0 – 1)	3	1	5	0.257
	0 (0 – 0)	0 (0 – 0)	1	1	7	> 0.05
	0 (0 – 0.5)	0 (0 – 0)	2	0	7	0.157
Total score	20 (16.5 – 24)	9 (4 – 14.5)	9	0	0	0.008**

* Significant p-value <0.05

** Significant p-value <0.01

P-value was calculated using Wilcoxon signed-rank test.

Table 5. Comparison of patients' total scores between on-treatment and post-treatment phases, represented as median (Interquartile range), (n = 9)

Activity	Pre – Treatment	On – Treatment	Ranks			P-value
			Neg.	Pos.	Ties	
Depressed mood	1 (1 – 2)	1 (0.5 – 2)	2	1	6	0.785
Feelings of guilt	1 (1 – 2)	1 (0 – 1)	4	0	5	0.059
Suicide	0 (0 – 1.5)	0 (0 – 1.5)	1	2	6	0.564
Early insomnia	0 (0 – 1)	0 (0 – 0.5)	2	1	6	> 0.05
Middle insomnia	1 (0 – 1)	1 (0 – 1)	2	2	5	0.705
Late insomnia	0.5 (0 – 1)	1 (0 – 1.5)	1	1	6	0.655
Work and activities	1 (0 – 2)	0 (0 – 1.5)	4	1	4	0.157
Retardation	1 (0 – 1)	1 (0 – 1.5)	2	3	4	0.48
Agitation	0 (0 – 1)	0 (0 – 1)	2	1	6	0.564
Anxiety, psychic	1 (0 – 2.5)	0 (0 – 1)	2	0	7	0.157
Anxiety, somatic	1 (1 – 2)	0.5 (0 – 1.75)	5	0	3	0.034*
Somatic symptoms: gastrointestinal	1 (0 – 1)	0 (0 – 0.5)	4	0	5	0.046*
Somatic symptoms: general	1 (0.5 – 1)	1 (0 – 1.5)	2	2	5	0.705
General symptoms	1 (0.5 – 2)	0 (0 – 1)	4	0	5	0.063
Hypochondriasis	0 (0 – 1.5)	0 (0 – 1)	2	3	4	> 0.05
Loss of weight	0 (0 – 0)	0 (0 – 0)	0	1	8	0.317
Insight	0 (0 - 0.5)	0 (0 - 0)	2	0	7	0.157
Total score	12(8-17.5)	9(4-14.5)	7	2	0	0.108

*Significant p-value < 0.05

P-value was calculated using Wilcoxon signed-rank test.

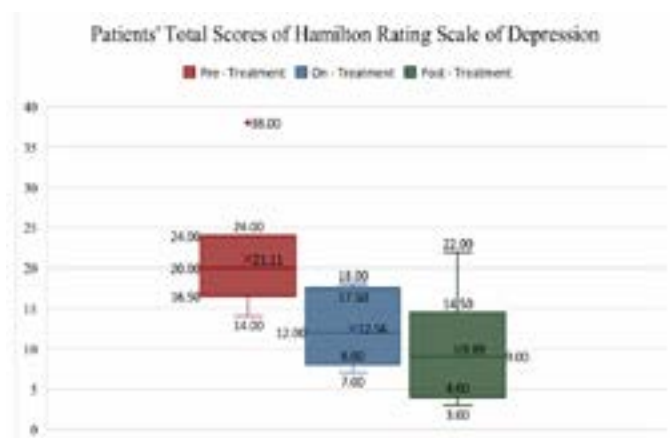


Figure 2. Comparison of Patients' total scores of Hamilton rating scale in pre, on, and post-treatment (n = 9).

There was a statistically significant difference in patients' feelings of guilt, middle insomnia, work and activities, somatic anxiety, and total score between the pre-treatment and post-treatment phases, with a reduction in depression scores, as shown in Table 4.

There was a statistically significant difference in patients' somatic anxiety, and somatic symptoms (gastrointestinal) between the on-treatment and post-treatment phases, with a reduction in depression scores, as shown in Table 5. A comparison of patients' total scores is illustrated in figure 2.

DISCUSSION

Research has examined the clinical effectiveness of repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT) in treating depression. In the current study, we assessed a total of 20 patients undergoing (rTMS) during the pre-treatment phase, with 17 progressing to the on-treatment phase and only 9 completing

the assessments in the post-treatment phase. Despite the small sample size, our findings revealed statistically significant differences in various measures, including depression, suicide ideation, insomnia (early, middle, and late), work and activities, retardation, somatic symptoms (particularly gastrointestinal), and total scores between the pre-treatment and on-treatment phases, indicating a reduction in depression scores (refer to Table 2).

Additionally, we observed statistically significant differences in feelings of guilt, middle insomnia, work and activities, somatic anxiety, and total scores between the pre-treatment and post-treatment phases, again highlighting a reduction in depression scores (refer to Table 3).

Numerous patients with unipolar major depression are candidates for noninvasive neuromodulation techniques like repeated transcranial magnetic stimulation (TMS) and electroconvulsive therapy (ECT) because they do not respond to conventional treatment with medication and psychotherapy. Because repeating TMS is better tolerated and doesn't require general anesthesia or seizure induction, as ECT does, patients may prefer it, even if ECT is more effective. The US Food and Drug Administration authorized contemporary TMS for treatment-resistant depression in 2008 after it was developed in 1985⁸.

According to a study, electroconvulsive therapy improved mood more than repeated transcranial magnetic stimulation, which was tested for two weeks. In terms of cognitive outcome measures, electroconvulsive therapy had a negative but temporary impact on several memory components that were no longer noticeable two weeks after treatment ended; nevertheless, there was proof of persistent retrograde amnesia following electroconvulsive therapy treatment. Following therapy with recurrent transcranial magnetic stimulation, there was no indication of either anterograde or retrograde memory loss, but overall, patients only saw a slight decrease in the intensity of their depression⁹.

In another study, Hamilton Rating Scale for Depression scores decreased by 50% or more in 46% of the ECT group and 44% of the rTMS group, indicating a similar treatment response. Memory complaints decreased

and cognitive performance stayed the same or improved in patients treated with rTMS, but memory recall deficits and memory complaints persisted in the ECT group¹⁰.

In a retrospective case-control study, 35 patients at Örebro University Hospital in Sweden who received treatment for depression using rTMS (left dorsolateral prefrontal cortex, 90% observed motor threshold, 10 Hz, 2000 pulses/session, 15 sessions) were compared to a control group of 35 patients who received treatment for depression using ECT. The remission rate was 43% for controls and 26% for cases ($p = .3$). For cases, the response rate was 40%, whereas for controls, it was 51% ($p = .63$)¹¹.

A meta-analysis was published evaluating the impact of rTMS stimulus parameters on rTMS's effectiveness in treating serious depression in comparison to ECT. Nine studies with 395 individuals were meta-analyzed by evaluating the chances of response, dropout, and remission. Two subgroups of rTMS showed non-significant superiority over ECT: ≥ 1200 daily stimuli (OR = 1.06; $P > 0.05$) and 20 Hz (odds ratio (OR) = 1.20; $P > 0.05$). A subset of rTMS showed non-significant inferiority to ECT after four weeks of treatment (OR = 0.65; $P > 0.05$). Compared to ECT, the other rTMS subgroups performed noticeably worse. A 30% relative decrease in dropout probabilities was linked to repetitive transcranial magnetic stimulation; however this relationship was not statistically significant (95% CI: 0.36-1.39)¹².

In another meta-analysis of numerous treatments and a systematic review, data were gathered from 25 trials that included 1288 MDD patients. The most effective but least well-tolerated treatment for MDD was ECT, whereas the best-tolerated treatment was R-rTMS. It seems that B-rTMS offers the best compromise between tolerability and efficacy¹³.

In a different investigation, behavioral performance on a series of cognitive tasks was assessed in TMS patients. They discovered that TMS treatment improved working memory performance in a visuospatial 2-back task and a verbal digit span¹⁴.

Moreover, chronic pain and related depression symptoms can be alleviated by high-frequency (HF) repetitive transcranial magnetic stimulation (rTMS) on the dorsolateral prefrontal cortex (DLPFC). A study extracted the evaluation indicators for pain and depression. While HF rTMS has a strong mid- and long-term analgesic effect on chronic pain, its short-term analgesic effect over the left DLPFC is not statistically significant. Patients with chronic pain can effectively reduce their depressed symptoms by using HF rTMS over the DLPFC. Therefore, chronic pain and related depressed symptoms can be alleviated by HF rTMS on the left DLPFC¹⁵.

How to best optimize rTMS procedures and methods to make them applicable in standard clinical practice is still up for debate. Professionals doing rTMS procedures should also receive extensive training to guarantee the correct treatment of patients, ensure the quality of the technical realization, and increase the likelihood of success. In the upcoming years, the therapeutic application of rTMS ought to be able to grow under these circumstances¹⁶.

In A Systematic Review and Meta-Analysis of Randomized Controlled Trials, six RCTs compared rTMS with electroconvulsive treatment (ECT), whereas 23 RCTs compared rTMS with sham. In comparison to ECT, rTMS trials revealed a statistically and clinically significant difference favoring ECT. The risk ratios favoring ECT were 1.44 (95% CI 0.64-3.23, $P = .38$) for remission and 1.72 (95% CI 0.95-3.11, $P = .07$) for response. A statistically significant improvement in depression scores was observed in rTMS versus sham trials¹⁷.

Rapidly emerging clinical research is examining the possibility of rTMS in a number of different neurological disorders. Both clinical researchers and practitioners may find this difficult. The results are promising and pave the way for TMS in neurology, even though the majority of these neurological applications have not yet been subjected to the same degree of scientific or empirical examination as neuropathic pain and motor stroke. However the most recent clinical data supporting rTMS in cutting-edge neurological applications, such as multiple sclerosis, epilepsy, movement disorders, and Alzheimer's disease/mild cognitive impairment¹⁸.

While the current study's limited sample size may restrict the generalizability of the positive findings, it also underscores the strength of our results in demonstrating the potential efficacy of rTMS. In contrast to larger studies that often report on broader populations, our focused investigation allows for a more detailed examination of individual patient responses. There is a need for larger-scale studies to further validate the effectiveness of rTMS in treating depression and related symptoms.

CONCLUSION

In Conclusion, our results align with existing literature that supports the efficacy of rTMS, suggesting that even within a small study, significant positive outcomes can be achieved, warranting further exploration in larger populations; repetitive transcranial magnetic stimulation (rTMS) represents a promising and innovative approach in the treatment of various neurological and psychiatric disorders, offering a new hope for patients where traditional therapies have failed.

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Competing Interest: None

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