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Efficiency of Transcranial Magnetic Stimulation in Depressive States in Patients with Anemia

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Abstract: ***Depression in patients with anaemia is often under-recognised and undertreated, partly due to symptom overlap and pharmacological limitations. This study aimed to evaluate the clinical efficiency of repetitive transcranial magnetic stimulation (rTMS) in treating depressive states in anaemic patients. Forty adult patients with mild to moderate anaemia and clinically diagnosed depression received 15 sessions of high-frequency rTMS over the left dorsolateral prefrontal cortex. Significant reductions in depressive symptoms were observed, with a 42.5% mean decrease in HAM-D scores and a parallel reduction in fatigue severity and improvement in quality of life (SF-12). The treatment was well-tolerated with minimal side effects. These findings suggest that rTMS is a safe and effective non-pharmacological intervention for managing depression in anaemic individuals, offering rapid relief and improved daily functioning.***
Keywords: Anaemia, depression, transcranial magnetic stimulation, rTMS, fatigue, neurostimulation, quality of life.

I. INTRODUCTION

Depressive disorders are among the most prevalent neuropsychiatric conditions globally, significantly impacting quality of life, social functioning, and productivity. The interplay between somatic and psychological health is increasingly recognised, with a growing body of evidence suggesting that anaemia—a condition characterised by reduced haemoglobin and oxygen-carrying capacity—can contribute to the onset and persistence of depressive states. Fatigue, cognitive slowing, irritability, and mood disturbance are common in anaemic patients, and these symptoms often overlap or exacerbate clinical depression, particularly in individuals with chronic or untreated anaemia [3, 6].

Conventional antidepressant therapy in anaemic patients is frequently complicated by drug intolerance, delayed therapeutic response, and interactions with haematological treatments. As a result, there is increasing interest in non-pharmacological, neuromodulatory approaches that can safely and effectively address depressive symptoms in this unique patient population. One such method is transcranial magnetic stimulation (TMS)—a non-invasive brain stimulation technique that modulates cortical excitability through electromagnetic pulses, particularly targeting the left dorsolateral prefrontal cortex (DLPFC), a region implicated in affective regulation [4, 7].

TMS has shown clinical efficacy in treatment-resistant depression and has been approved by international regulatory bodies as a safe and evidence-based option. However, its potential in anaemic patients with depressive symptoms remains under-investigated. Considering the physiological vulnerability of anaemic individuals, a non-invasive and systemic side-effect–free intervention such as TMS could be highly beneficial.

This study aims to evaluate the clinical efficiency of repetitive transcranial magnetic stimulation (rTMS) in alleviating depressive symptoms in patients with anaemia. By assessing changes in depression severity scores, fatigue, and functional status before and after a structured TMS protocol, this research seeks to contribute to a more integrated and tailored approach to the management of depression in patients with concurrent haematological conditions.

II. METHOD

This was a prospective, open-label clinical study conducted between January and October 2024 at the Departments of Neurology and Psychiatry in collaboration with the Haematology Unit of the Samarkand Regional Multi-Profile Medical Centre. The aim was to assess the effect of repetitive transcranial magnetic stimulation (rTMS) on depressive symptoms in patients with mild to moderate anaemia. A total of 40 adult patients (aged 20–60) were included based on the following inclusion criteria: (1) confirmed diagnosis of anaemia (haemoglobin level <12 g/dL for women, <13 g/dL for men), (2) clinically significant depressive symptoms as measured by a Hamilton Depression Rating Scale (HAM-D) score ≥17, and (3) no prior exposure to TMS.

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Patients with severe anaemia (Hb <7 g/dL), psychotic features, epilepsy, metallic implants in the skull, or concurrent psychiatric or neurological disorders unrelated to anaemia were excluded.

All patients underwent a baseline clinical and laboratory assessment, including haemoglobin, serum ferritin, and complete blood count, along with psychiatric evaluation using HAM-D and the Beck Depression Inventory (BDI-II). After medical clearance from haematology specialists, participants received 15 sessions of high-frequency rTMS (10 Hz) targeting the left dorsolateral prefrontal cortex (DLPFC), administered over a 3-week period (5 sessions per week). Stimulation was performed using a Magstim Rapid^2 system, with parameters set at 110% of the motor threshold, 3000 pulses per session, and a train duration of 4 seconds with inter-train intervals of 26 seconds.

Throughout the study, patients continued to receive standard supportive therapy for anaemia (iron supplementation or vitamin B12 as indicated), but no new antidepressants were initiated. Participants maintained stable doses of prior medications, if any.

Depressive symptoms were re-evaluated at Day 1 (baseline), Week 2, and Week 4 using the HAM-D and BDI-II scales. Additionally, fatigue severity was measured using the Fatigue Severity Scale (FSS), and patient-reported quality of life was assessed using the SF-12 Health Survey.

All participants provided written informed consent, and the study protocol was approved by the Ethics Committee of Samarkand State Medical University. The procedure followed all ethical principles outlined in the Declaration of Helsinki.

Statistical analysis was conducted using SPSS version 26.0. Data were expressed as mean ± standard deviation, and comparisons between pre- and post-treatment scores were performed using the paired t-test. A p-value of <0.05 was considered statistically significant.

III. RESULTS

All 40 patients completed the 3-week rTMS treatment protocol without serious adverse events or dropouts. The mean age of participants was 42.6 ± 9.3 years, with 67.5% female and 32.5% male. The average baseline haemoglobin level was 10.4 ± 1.1 g/dL, confirming the presence of mild to moderate anaemia. Prior to treatment, patients demonstrated moderate to severe depressive symptoms, with a mean HAM-D score of 22.8 ± 3.5 and BDI-II score of 27.4 ± 5.1.

Following the 15-session rTMS protocol, there was a significant reduction in depressive symptom severity. The mean HAM-D score decreased to 13.1 ± 3.2 by Week 4 ($p < 0.001$), reflecting a 42.5% mean reduction from baseline. Similarly, the BDI-II score dropped to 16.0 ± 4.3 ($p < 0.001$), indicating meaningful clinical improvement. Notably, 65% of patients achieved a reduction of ≥50% in HAM-D scores, while 30% reached remission status (HAM-D ≤ 7) by the end of treatment.

In addition to mood improvement, fatigue levels decreased significantly. The average Fatigue Severity Scale (FSS) score was reduced from 5.6 ± 0.8 at baseline to 3.9 ± 0.7 at Week 4 ($p < 0.01$), correlating with patients' reports of improved daytime functioning. The SF-12 Health Survey showed corresponding increases in both the Mental Component Summary (MCS) and Physical Component Summary (PCS) scores, with the greatest gains noted in emotional role functioning and energy domains.

Minor side effects such as transient scalp discomfort (15%), mild headache post-session (12.5%), and light dizziness (7.5%) were reported, but none required intervention or led to treatment discontinuation.

Overall, the application of high-frequency rTMS significantly improved depressive symptoms, fatigue, and overall quality of life in anaemic patients with coexisting depressive states, highlighting the method's safety and efficacy in this population.

IV. DISCUSSION

The results of this study demonstrate that repetitive transcranial magnetic stimulation (rTMS) is a safe and effective treatment modality for reducing depressive symptoms in patients with anaemia. The significant reduction in both HAM-D and BDI-II scores over the 3-week stimulation period indicates that neuromodulation using high-frequency stimulation of the left dorsolateral prefrontal cortex (DLPFC) can meaningfully alleviate mood disorders even in individuals with underlying somatic vulnerabilities such as reduced haemoglobin levels.

One of the most notable aspects of this study is the rapid and clinically significant improvement observed in patients who may not be ideal candidates for traditional antidepressant pharmacotherapy due to metabolic limitations, fatigue, or drug intolerance associated with anaemia. By circumventing systemic pharmacological effects, rTMS provided a well-tolerated, non-invasive alternative that led to mood improvement and, importantly, reductions in fatigue—one of the hallmark symptoms of both anaemia and depression. The substantial decline in Fatigue Severity Scale scores parallels the overall psychological improvement and reflects enhanced neurocognitive and physical functioning, which is critical in restoring quality of life for this patient population.

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These findings are consistent with broader rTMS research, particularly in treatment-resistant depression, and expand its relevance to populations previously underrepresented in clinical trials. While most studies of rTMS exclude patients with significant comorbid medical conditions, the present study supports its application in haematologically compromised individuals. The results also underscore the value of neuromodulation as part of a multimodal treatment strategy that addresses both neuropsychiatric and systemic aspects of depression in anaemic individuals.

The improvement in patient-reported quality of life as assessed by the SF-12 confirms that symptom relief translated into better day-to-day functionality. Increased energy, social engagement, and emotional well-being were frequently mentioned by patients during follow-up interviews, and these subjective reports reinforce the objective improvements documented by clinical scales. The absence of serious adverse events further enhances the appeal of rTMS in this context. Minor discomfort and mild headache were transient and did not interfere with treatment adherence.

However, several limitations must be acknowledged. The sample size was moderate and the study design lacked a sham or placebo control group, making it difficult to rule out non-specific treatment effects. Additionally, the follow-up period was limited to the short term, and long-term durability of symptom remission remains untested. Future studies should incorporate control conditions, larger sample sizes, and extended follow-up durations to validate these findings and explore maintenance protocols. Biomarker studies could also help elucidate the mechanisms by which rTMS improves both mood and fatigue in anaemic individuals—potentially involving neural plasticity, cerebral oxygenation, or neuroinflammation modulation.

In conclusion, this study provides encouraging evidence for the use of transcranial magnetic stimulation as a complementary intervention in the treatment of depressive states among patients with anaemia. Given its non-invasive nature, rapid onset of effect, and favourable tolerability profile, rTMS represents a promising option for integrated neuropsychiatric care, especially when standard pharmacological interventions are insufficient or contraindicated.

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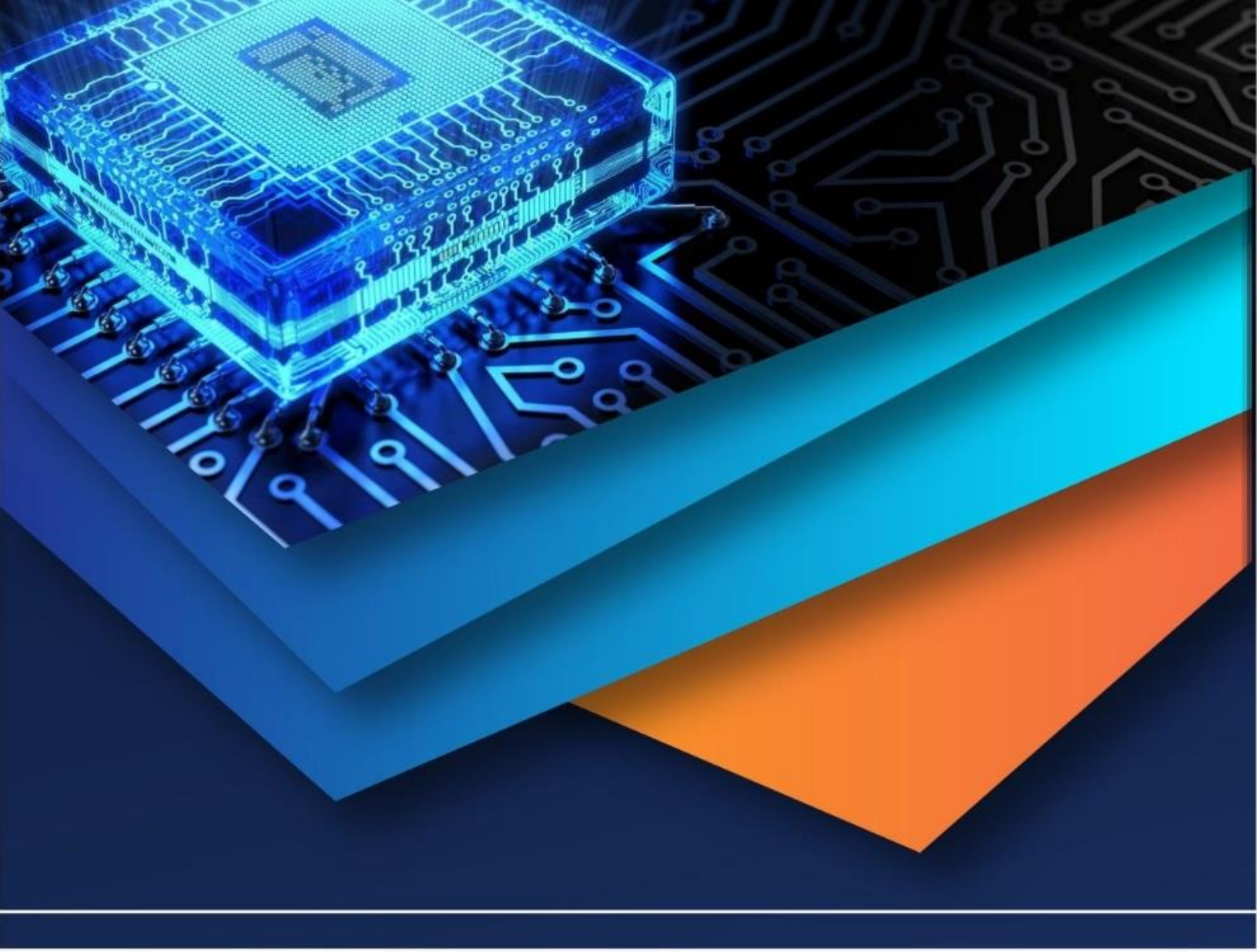
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