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Case Series

Integrating Unani medicine in managing major depressive disorder: a series of case reports

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ABSTRACT

Major depressive disorder (MDD) is a chronic condition affecting mood, cognition, and physical well-being. In Unani medicine, MDD is similar to *Mālankhūliyā*. This case series aimed to integrate Unani medicine into an outpatient model for holistic MDD treatment. Seven participants (four females, three males) with moderate to severe MDD were diagnosed using the DSM-V and Unani criteria for *Mālankhūliyā Sawdāwī*. They underwent a 19-week treatment protocol, consisting of 17 weeks of active treatment and 2 weeks of observation. The Unani-based approach combined *Ilāj bi'l Tadbīr* (regimenal therapy) like *Naṭūl* (forehead irrigation with medicated oil), *Sa'ūṭ* (nasal drops), and *Tadhīn* (oiling). Pharmacotherapy included *Majoon Njah*, *Jawarish Shahi* (5 g twice daily), and *Dawa-ul-Misk Sada* with *Arq Gawzaban* (5 g and 60 ml twice daily). Conventional antidepressants were tapered and discontinued. Outcomes were assessed using primary self-reported questionnaires and secondary measures including quality of life (QoL) and routine blood tests. The intervention showed significant reductions in the Hamilton depression rating scale (HDRS-21) ($p<0.001$), Beck depression inventory (BDI) ($p<0.002$), and insomnia, measured by the insomnia severity index (ISI) ($p<0.004$). QoL improved significantly ($p<0.007$). Thus, the integrative Unani medicine approach demonstrated efficacy in managing MDD. The combination of pharmacotherapy and regimenal therapy significantly alleviated depressive symptoms and improved QoL. However, further rigorous studies are needed to confirm its broader applicability in MDD treatment.

Keywords: Depression, Ilāj bi'l Tadbīr, Major depressive disorder, Mālankhūliyā, Unani system of medicine

INTRODUCTION

Major depressive disorder (MDD) is a common and debilitating mental health condition that significantly impacts both emotional and physical well-being. It affects mood, engagement in activities, and overall quality of life. MDD is a major health issue worldwide and is the second leading cause of illness.[1] As one of the leading causes of disability worldwide, MDD's severity was highlighted by the World Health Organization's choice of "Depression: Let's Talk" as the theme for World Health Day in 2017. In India, the prevalence of depression is high, affecting about 48.5 million people.[2] Studies show that MDD is more prevalent in women, who are 2.1 times more likely to experience it than men.[3] Additionally, many people with MDD also struggle with substance abuse.[4] The risk of suicide is particularly high, with 30-40% of MDD patients attempting suicide.[5] The causes of depression are complex, involving a mix of genetic, environmental, and personal factors, as well as issues related to the body's biological systems like the brain, immune system, and hormones.[6] About 20-25% of patients have a chronic, unremitting form of MDD. MDD is also linked to an increased risk of developing other health problems, such as diabetes, heart disease, and stroke.[7]

The standard treatments for MDD typically involve a combination of medication and psychotherapy, especially for moderate to severe cases. These treatments are generally delivered in two phases: an initial phase aimed at symptom reduction and a maintenance phase designed to prevent relapse.[8] Medications commonly used in treatment include selective serotonin receptor inhibitors (SSRIs), tricyclic and tetracyclic antidepressants, serotonin and norepinephrine receptor inhibitors (SNRIs), and monoamine oxidase (MAO) inhibitors. Transcranial magnetic stimulation (TMS) and vagus nerve stimulation (VNS) are also effective treatments for depression. Several types of psychotherapy have been shown to help, including cognitive behavioral therapy (CBT), interpersonal therapy, behavioral activation therapy, psychodynamic therapy, problem-solving therapy, and mindfulness-based therapy.[9] However, only about 40% of patients respond to this current treatment, and many experience significant side effects, such as drowsiness, weight gain, and sexual dysfunction.[10] These challenges result in low patient adherence and highlight the need for alternative or complementary treatment approaches. In Unani medicine, MDD is conceptually similar to the condition known as *Mālankhūliyā*, and in severe cases, *Mālankhūliyā Sawdāwī*. These are categorized under *Amraaz-i-Nafsānī* (mental disorders) in classical Unani texts, where symptoms such as persistent sadness, overthinking, fear, anxiety, insomnia palpitation, hallucinations and suicidal tendencies are described—symptoms that closely mirror those of MDD.[11]

This case series, conducted following CARE guidelines, involves seven participants who received an Unani treatment regimen aimed at alleviating symptoms of MDD and improving overall quality of life. The results from this study may contribute to the expanding body of research supporting Unani medicine as a promising, complementary therapeutic option for the management of MDD.

METHODS

This study presents a case series involving seven individuals—four females and three males, aged 26 to 40 years—who sought treatment at the outpatient department (OPD) of the Hakim Syed Ziaul Hasan Government (Autonomous) Unani Medical College and Hospital, Bhopal, Madhya Pradesh. Each participant presented with a constellation of chronic emotional symptoms, including disturbed sleep, persistent sadness, feelings of worthlessness, helplessness, death wishes, and frequent crying spells. The duration of these symptoms spanned between 5 to 7 years. All participants had previously consulted multiple psychiatric facilities and received various antidepressants; previously received medications are shown in (Table 1).

Patients were given clear information about the study procedures and told that their data, without revealing their identity, might be published. This was explained in a language they could understand, and a written consent was obtained from them.

Upon general examination, all participants' vitals were within normal limits, and no abnormalities were detected through systemic examination. Each participant underwent a thorough psychiatric work-up based on information provided by the patients and their relatives. All participants appeared dull, spoke in low voices, avoided eye contact, and exhibited passive behaviour. They frequently experienced crying episodes, irritability, impulsivity, neglect of personal hygiene, excessive worry, and feelings of worthlessness and helplessness. Additionally, all participants reported thoughts of death and had withdrawn from their families and friends. Other symptoms included sleep disturbances, headaches, fatigue, and bilateral tinnitus.

All participants underwent routine blood tests, including HbA1c, and the results were within normal limits. They were all diagnosed with major depressive disorder based on the diagnostic and statistical manual of mental disorders, fifth edition (DSM-V). The main outcomes measured were reductions in depression severity, assessed through self-reported questionnaires, including the Hamilton depression rating scale (HDRS-21) and the Beck depression inventory (BDI).

Sleep disruption was evaluated using the insomnia severity index (ISI), and quality of life was assessed using the quality-of-life scale (QoLS). The response to treatment was assessed by comparing data collected at baseline, on the 17-weeks post-treatment initiation, and two weeks after the treatment concluded (week 19).

Table 1: Clinical-demographic profile of the seven participants studied.

Case no.	Age (years)	Sex	BMI (kg/m^2)	*Mizāj* (temperament)	Family history	Disease duration (years)	Past interventions	Outcome of past interventions	Other clinical findings	Timeline of trial therapy (dd/mm/yy)
1	26	F	23.5	*Sawdāwī* (melancholic)	Not present	6	Allopathic SSRIs (drug combination of paroxetine 12.5 mg and clonazepam 0.5 mg) twice a day	Experienced temporary relief from the symptoms with intolerable side effect	Not significant	08/02/2024 to 20/05/2024
2	38	F	25.6	*Sawdāwī* (melancholic)	Not present	7	Allopathic tricyclic anti-depressant (drug combination of amitryptiline 25 mg and chlordiazepoxide 10 mg) twice a day	Got temporary relief in the symptoms, also got intolerable side effect	Not significant	10/02/2024 to 22/05/2024
3	35	M	28.7	*Ṣafrāwī* (bilious)	Not present	5	Allopathic tricyclic anti-depressant (drug combination of amitryptiline 12.5 mg and chlordiazepoxide 5 mg) twice a day	Experienced temporary relief from the symptoms with intolerable side effect	Not significant	10/02/2024 to 22/05/2024
4	40	F	23.5	*Ṣafrāwī* (bilious)	Not present	7	Allopathic SSRIs (drug combination of paroxetine 12.5 mg and clonazepam 0.5 mg) twice a day	Got temporary relief in the symptoms, also got intolerable side effect	Not significant	12/02/2024 to 24/05/2024
5	36	F	27.5	*Sawdāwī* (melancholic)	Not present	5	Allopathic SSRIs (drug combination of paroxetine 12.5m g and clonazepam 0.5 mg) twice a day	Do not experience satisfactory relief	Not significant	12/02/2024 to 24/05/2024
6	34	M	26.3	*Sawdāwī* (melancholic)	Not present	5	Allopathic tricyclic anti-depressant (drug combination of amitryptiline 12.5 mg and chlordiazepoxide 5 mg) twice a day	Got temporary relief in the symptoms, also got intolerable side effect	Not significant	15/02/2024 to 27/05/2024
7	29	M	28.4	*Sawdāwī* (melancholic)	Not present	6	Allopathic tricyclic anti-depressant (drug combination of amitryptiline 12.5 mg and chlordiazepoxide 5 mg) twice a day	Got temporary relief in the symptoms, also got intolerable side effect	Not significant	16/02/2024 to 28/05/2024

The outpatient model was based on traditional Unani medicine. All participants underwent a 17-week outpatient department management, which included treatments from traditional Unani medicine. The treatment consisted of *Ilāj bi'l Tadbīr* (regimenal therapy), which involved interventions such as *Naṭūl* (irrigation therapy), *Sa'ūṭ* (nasal drop) and *Tadhīn* (oiling) (Table 2). Participants also received *Ilāj bi'l Dawā* (pharmacotherapy), which included oral medications such as *Majoon Najah*, *Jawarish Shahi* and *Dawa-ul-Misk Sada* with *Arq Gawzaban*.

Patients underwent *Naṭūl* therapy, which involved the gentle and continuous dripping of *Ravghan Nilofar* onto the forehead. The aim of this therapy is to promote *Taskīn-i-Alam* (analgesic), *Ta'dīl-i-Mizāj* (alteration of temperament), and alleviate *Tanwīm* (hypnosis). During the session, patients were instructed to lie down comfortably while taking necessary precautions. To ensure safety and prevent oil from entering sensitive areas, gauze pieces were carefully placed over the eyes and ears. The oil was dropped steadily from a distance of 12 cm for 45 minutes, using 1 liter of *Ravghan Nilofar*. This precise and controlled application helps evenly distribute the oil, maximize its therapeutic effects, and provide a deeply calming experience. Patients received *Sa'ūṭ* therapy, which involved the administration of 3 drops of *Ravghan Banafsha* in each nostril overnight, using a nasal dropper.

Participants received *Tadhīn* therapy, a traditional Unani approach involving the application of therapeutic oils. Each participant was advised to apply 5 ml of *Ravghan Kahu* on the forehead overnight. After application, participants were instructed to cover the forehead with a cotton cloth to keep the oil undisturbed, enhancing absorption and optimizing therapeutic effects overnight. The covering also helps retain warmth, potentially aiding in the oil's penetration and aligning with traditional Unani practices.

Participants in this case series received a 17-week course of oral Unani medications. The treatment regimen included potent pharmacological interventions: 5 grams each of *Majoon Najah* and *Jawarish Shahi*, taken twice daily after meals. Additionally, participants were given 5 grams of *Dawa-ul-Misk Sada* along with 60 ml of *Arq Gawzaban*, also administered twice daily after meals. For this case study, the formulations were manufactured by Hamdard Laborities, Delhi and supplied by the Government of Madhya Pradesh, ensuring adherence to traditional Unani standards and practices.

Data analysis

Statistical analysis was conducted using statistical package for the social sciences (SPSS) software, version 27.0. $P<0.05$ was considered as statistically significant. Descriptive statistics were calculated, including minimum, maximum, and mean values. For within-group comparisons, the paired t-test was applied to data with a normal distribution, while the Wilcoxon rank-sum test was used for data with a non-normal distribution.

Results

The study included a 19-week follow-up of participants, with a mean age of 34±4.93 years. The average duration since MDD diagnosis was 5.85±0.89 years. No side effects were reported throughout the treatment period. All participants were on allopathic medication (Table 1). Based on symptom improvement, medication was reduced to once daily by day 42 (6 weeks) and discontinued by day 84 (12 weeks) per the psychiatric physician's recommendation. Evaluation tools, including HDRS-21, BDI, ISI, and QoLS, showed consistent declines in scores from baseline to two-weeks post-treatment, indicating significant symptom improvement (Table 3). Hematological analyses revealed no significant changes from baseline to post-treatment (Table 4).

Table 2: Seventeen-week-long healthcare model schedule describing the frequency of interventions (times per week).

Regimenal therapy	Baseline to 8 weeks	9 to 14 weeks	15 to 17 weeks
***Naṭūl* (irrigation therapy)/week**	3 times	2 times	1 time
***Sa'ūṭ* (nasal drop)/week**	7 times	5 times	3 times
***Tadhīn* (oiling)/week**	7 times	5 times	4 times

Table 3: Change in symptom severity of MDD patients that before and after 8 weeks of treatment (n=7).

Variables	Baseline mean (SD)	17 weeks mean (SD)	19 weeks mean (SD)	Difference mean (SD)	T value	P value
HDRS-21	17.3333 (1.15470)	4.6667 (0.57735)	3.6667 (0.57735)	13.66667 (0.57735)	41.000	<0.001
BDI	27.3333 (1.15470)	4.3333 (0.57735)	3.3333 (0.57735)	24.00000 (1.73205)	24.000	0.002
ISI	19.3333 (1.15470)	4.3333 (1.52753)	4.6667 (0.57735)	14.66667 (1.52753)	16.630	0.004
QoLS	42.6667 (0.57735)	49.0000 (1.00000)	49.6667 (0.57735)	-7.00000 (1.00000)	-12.124	0.007

HAMD-21: Hamilton depression scale; BDI: Beck depression inventory scale; ISI: insomnia severity scale; QoLS: quality of life scale

Table 4: Blood sample results comparison means before and after treatment in MDD patients (n=7).

Variables	Baseline mean (SD)	17 weeks mean (SD)	Difference mean (SD)	T value	P value
HbA1c (%)	4.7000 (0.26458)	4.6667 (0.28868)	0.03333 (0.05774)	1.000	0.423
Hb (g/dl)	12.6667 (1.15470)	12.6000 (1.03923)	0.06667 (0.11547)	1.000	0.423
RBC count (10^{12}/l)	4.4300 (0.14731)	4.3967 (0.10017)	0.03333 (0.04933)	1.170	0.362
Platelet count (PLT) (10^{12}/l)	298.3333 (3.05505)	297.9967 (2.64387)	0.33667 (0.57449)	1.015	0.417
WBC (10^{12}/l)	8.7667 (0.92916)	8.7267 (0.93388)	0.04000 (0.05292)	1.309	0.321
ESR (mm/hour)	7.3333 (1.52753)	7.4933 (1.31154)	-0.16000 (0.29462)	-0.941	0.446
Bilirubin (total) (mg/dl)	0.6333 (0.32146)	0.6600 (0.29462)	-0.02667 (0.06429)	-0.718	0.547
AST (U/l)	27.3333 (6.42910)	26.8333 (6.82520)	0.50000 (0.50000)	1.732	0.225
ALT (U/l)	30.0000 (10.00000)	29.3333 (10.50397)	0.66667 (0.57735)	2.000	0.184
Creatinine-serum (mg/dl)	0.5333 (0.35119)	0.4633 (0.30989)	0.07000 (0.05196)	2.333	0.145
BUN (mg/dl)	14.1733 (3.75235)	14.0000 (4.00000)	0.17333 (0.28308)	1.061	0.400
Sodium (mmol/l)	140.0000 (2.00000)	139.5000 (1.50000)	0.50000 (0.50000)	1.732	0.225
Potassium (mmol/l)	3.9667 (0.15275)	3.9433 (0.14364)	0.02333 (0.07506)	0.538	0.644
Chloride (mmol/l)	101.0000 (1.00000)	100.6167 (1.06810)	0.38333 (0.53929)	1.231	0.343

HbA1c: glycated hemoglobin, Hb: hemoglobin, RBC: red blood cell, WBC: white blood cells, ESR: erythrocyte sedimentation rate, AST: aspartate aminotransferase, ALT: aspartate aminotransferase, BUN: blood urea nitrogen

DISCUSSION

MDD is a common mental health condition that profoundly impacts mood, interest in activities, thought patterns, and overall quality of life. In the context of Unani medicine, MDD closely resembles *Mālankhūliyā*, and in severe cases, *Mālankhūliyā Sawdāwī*. Classical Unani texts attribute its etiology to the derangement of *Sawdā* (Black bile), which affects both mental and physical health.[12] Symptoms such as *Ikhtilāṭ al-'Aql* (mental derangement), *Idmān al-Tafakkur* (persistent overthinking), *Gham* (sadness without cause), *Al-Faz* (fear), palpitation, liking of loneliness, hallucinations, insomnia, and suicidal ideation align closely with modern diagnostic criteria for depression.[13]

In this case series patients were diagnosed with MDD based on DSM V criteria and Unani diagnostic criteria for *Mālankhūliyā*. Each patient's treatment was personalized according to their *Mizāj* (temperament), ensuring a holistic balance of mental and physical health. The Unani approach, which categorizes *Mālankhūliyā* under *Amraaz-i-Nafsānī* (mental diseases), emphasized therapies to *Tanqiya* (cleanse morbid matter), *Taskīn-i-Alam* (analgesic), *Tarṭīb-i-Dimāgh* wa *Badan* (producing moistness in the brain and the body), *Tafrih-i-Taba* (exhilaration), *Tarwīḥ* (moderation of vital pneuma), *Tanwīm* (hypnosis) and *Taqwiyat-i-Dimāgh* wa *Qalb* (toning up of brain and heart).[14,15]

We used Naṭūl therapy as part of traditional Unani medicine, which has been extensively studied and shown to be safe and effective for generalized anxiety disorder (GAD) and insomnia.[16,17] According to Unani theory, *Naṭūl* facilitates *Taḥlīl-i-Mawād*—the dispersion of *akhlāṭ-i-fāsida* (morbid humors) from the affected part, *Ta'dīl-i-Mizāj*—the normalization of *Su-i-Mizāj* (altered temperament), *Taskīn-i-Alam*—the relief of pain by diverting morbid humors (*Imālah-i-akhlāṭ-i-fāsida*), and *Muqawwi-i-A'ṣāb*—the strengthening of nerves by enhancing circulation and nutrition.[18] Physiologically, its effects include bradycardia and reduced sympathetic tone, leading to increased blood circulation and skin temperature.[19] Biochemical changes involve the suppression of noradrenalin and alpha receptors, resulting in sympathetic suppression. Stimulation of the trigeminal nerve and somato-autonomic reflexes also alters neurotransmitter levels, including serotonin and catecholamines, creating psycho-neuro-immunologic effects.[20] *Sa'ūṭ* with *Ravghan Banafsha* was employed, as classical Unani scholars documented its benefits for *Mālankhūliyā* (MDD) and insomnia.[11,21] Traditional literature suggests that *Sa'ūṭ* aids in evacuating morbid materials and stimulating the nerves and brain. *Tadhīn* was also used, specifically with *Ravghan Kahu*, which is noted for its calming and sedative effects. Studies suggest that *Tadhīn* with *Ravghan Kahu* is particularly beneficial in managing insomnia, a common symptom in MDD.[22] Both *Naṭūl* and *Tadhīn* serve as transcranial routes for drug delivery. Studies suggest that applying oil-based formulations to the scalp can effectively deliver medicines to the brain and the central nervous system.[23]

The Unani scholar *Jalinus* recommended *Majoon Najah* as a primary treatment for *Mālankhūliyā*.[11] Animal studies and reports on its ingredients, such as *Emblica officinalis*, *Terminalia bellirica*, *Terminalia chebula*, *Cuscuta reflexa* and *Lavandula officinalis*, support its antidepressant properties.[24-27] *Ibn Sina* recommended *Dawa ul Misk* with *Arq Gawzaban* for *Mālankhūliyā*, emphasizing its role in *Taqwiyat Qalb* (heart toning).[11] In this case series, *Dawa ul Misk Sada* was used for its pharmacological actions as a general and cardiac tonic, aiding conditions like *Zof-e-Aza-e-Raeesa* (vital organ insufficiency), *Khafaqān* (palpitation), *Mālankhūliyā* (melancholia), and *Waswas* (psychosis).[28] *Jawarish Shahi* was prescribed for

gastrointestinal symptoms often observed in MDD. Studies demonstrate its benefits in managing GIT problems and depression.[29] Its ingredients, include *Phyllanthus emblica L., Terminalia chebula Retz., Elettaria cardamomum (L.) Maton, Coriandrum sativum L. and Salix caprea L.*, exhibit anxiolytic, antidepressant, sedative, and antioxidant properties, making it effective in addressing both digestive and mental health challenges.[30-34] Each of the regimenal therepies and oral Unani medicines was selected for their specific actions and was well-tolerated, with no adverse effects observed throughout the study. While this case series focuses on traditional Unani interventions, the findings suggest that Unani treatments may complement conventional psychiatric care for MDD. These interventions could reduce the need for high-dose pharmaceuticals, offering a holistic, sustainable approach to mental health. The Unani system, with its focus on balance and integration of the physical, mental, and emotional aspects, has the potential to serve as an adjunct in the management of MDD.

CONCLUSION

The therapeutic interventions utilized in this case series, including *Naṭūl, Sa'ūṭ, Tadhīn*, and oral medications such as *Majoon Najah, Jawarish Shahi*, and *Dawa-ul-Misk*, demonstrated efficacy in managing MDD. These traditional Unani therapies, grounded in the Unani conceptualization of *Mālankhūliyā*, provide a holistic treatment model that addresses both the mental and physical dimensions of depression. The improvements observed in depressive symptoms, sleep quality, and overall quality of life indicate that these therapies effectively target the multifaceted nature of MDD. All interventions were safe and well-tolerated by the participants, with no significant adverse effects reported. Nevertheless, to strengthen the scientific basis for these findings, a larger, rigorously designed study with a well-defined protocol and a more substantial sample size is necessary. This case series underscores the potential of Unani medicine as a valuable complementary approach in contemporary mental health care, highlighting the need for further research into its role in the management of MDD.

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