Effects of Mindfulness Meditation on Quality of Sleep, Perceived Stress, Serum Cortisol, and C-reactive Protein in Hemodialysis Patients

Study Protocol

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1. Introduction

End-stage renal disease (ESRD), or kidney failure, happens when the kidneys almost completely stop working, usually below 10-15% of normal function (1). It has been documented as a significant factor in rising rates of disability and mortality worldwide, particularly due to the rising rates of diabetes and hypertension(1). Globally, the population of individuals with ESRD falls from 4.902 to 9.701 million, with most found in low and middle-income nations (1). In North Africa and the Middle East, ESRD rates exceed 500 per 100,000 population when age-standardized (2). In Gulf Cooperation Council (GCC) countries, the average rate of end-stage renal disease was 551 per million people, with Oman having the highest prevalence at 1000 per million and Qatar the lowest at 347 per million (3). In Kuwait, there were 465 cases of dialysis per million people, while the incidence of dialysis was 100 per million populations (4).

The Global Burden of Disease reports that impaired fasting plasma glucose, hypertension, sodium-rich diet, heart disease, urinary tract blockages, inflammation, and certain genetic disorders are common risk factors for end-stage kidney disease (1, 5). The last phase of chronic kidney disease necessitates renal replacement therapy, like dialysis or a kidney transplant, to ensure survival (1). Both forms of dialysis, hemodialysis or peritoneal dialysis, effectively eliminate toxins and excess fluids from the body, but they do not cure kidney disease (1). Nevertheless, hemodialysis is an extremely important treatment for individuals with ESRD that enhances health by removing toxins from the body, typically done multiple times a week and lasting several hours (1).

However, the lives of ESRD patients are impacted by hemodialysis treatment, which brings about various physical and psychosocial stressors during their lengthy

treatment (1). In relation to physical indications, hemodialysis patients are constantly in danger of experiencing intradialytic hypotension, muscle cramps, headache, fatigue, nausea, vomiting, itching, acute hemolysis, air embolism, bloodstream infections, and vascular access stenosis (6). While stress, insomnia, depression, and anxiety are among the psychological indicators in this group (7, 8). Additionally, most of these individuals have observed elevated amounts of pro-inflammatory markers in the blood, like C-reactive protein (9). In this situation, continual stress can harm the immune system by activating the hypothalamic-pituitary-adrenal (HPA) system, including hormones like cortisol, which rises 15 minutes after the stress situation and stays high for multiple hours (10, 11). During chronic stress and frequent exposure to stressors, a long-term elevation in cortisol levels can harm the hippocampus, reduce sensitivity to cortisol, and enhance cortisol binding to the mineralocorticoid receptor (12). When cortisol binds to the mineralocorticoid receptor, it triggers the release of pro-inflammatory factors like C-reactive protein (CRP) as a pro-inflammatory response (10) and psychological stress (13). It often leads to changes in body fluid balance, uremia, and frequent nocturnal muscle cramps, all of which disturb sleep (14). As the hemodialysis treatment often involves three or more sessions per week, each lasting several hours, it is taxing on the patient’s body and disrupts natural circadian rhythms, compounding the effects of sleep disorders (14). Sleep disorders such as insomnia, restless leg syndrome, and obstructive sleep apnea are common among hemodialysis patients, leading to fatigue, cognitive decline, and increased risk for depression and anxiety (15). Additionally, poor sleep can exacerbate cardiovascular risks, worsen pain perception, and weaken the immune system, all of which are critical concerns for ESRD patients (16). These issues are particularly problematic because they affect patients' rest, physiological recovery, and mental

health (17). That's why sleep quality is often severely impaired in patients with ESRD, with rates of sleep disturbances much higher than in the general population or among those with other chronic illnesses (1).

As a result, reports have shown that ESRD patients sometimes employ ineffective or harmful coping strategies when facing multiple stressors, resulting in negative impacts on their overall physical and psychological well-being, increased vulnerability to infections, and higher rates of mortality and morbidity among this population (18, 19). On the other hand, mind-body techniques are believed to be beneficial for health by promoting a connection between the mind and body, enhancing present-moment awareness and acceptance without judgment (20). Mindfulness meditation, a widely practiced mind-body technique, involves focusing on the present moment with an attitude of acceptance and nonjudgment (21). Mindfulness meditation is hypothesized to target multiple cognitive and emotional processes that contribute to stress and poor sleep quality. It has been shown to enable psychological distance and positive reappraisals, helping to stop automatic, uncontrollable appraisals and decreasing stress and cortisol levels (22, 23). It has also been shown to decrease ruminative thoughts, diminish emotional reactivity, and promote impartial reappraisal of salient experiences, which together may facilitate sleep (24-27). In addition, it has been found to improve physiological indices of stress by cultivating stress and amygdala reactivity, resulting in decreased cortisol responses and pro-inflammatory markers such as CRP (28, 29). Decreased amygdala reactivity associated with activation of the parasympathetic nervous system decreases cortisol levels, which is its high prolonged levels can cause an increase in glucocorticoid receptor resistance to cortisol and increased circulating markers of inflammation, such as CRP (30).

Smith (2005)(31) suggested in his Attentional Cognitive Behavioral (ABC_2) Relaxation theory that two 30-minute sessions of mindfulness meditation per week are necessary to induce relaxation, reduce stress, and enhance overall health on the broader community (31). His mindfulness format has been suggested as a standardized format with five consecutive parts, each lasting 5 minutes, for a total session time of 30 minutes (31). Research has shown that this mindfulness meditation is as successful as the more extended method in decreasing stress levels (9, 32) . Also, mindfulness meditation has been shown to be a suitable therapy that improves various aspects of well-being in Arabic societies (33). In general, studies have shown that mindfulness meditation is a proven method to decrease stress and biomedical markers and improve sleep quality in both ESRD and other chronic patients, impacting them physically, emotionally, and mentally (9, 32, 34-44).

Since mindfulness meditation offers the potential to address psychological and physiological symptoms in different patient groups, it has not been widely utilized in hemodialysis patients compared to other chronic illnesses (45). Further, sleep issues are often under-recognized in clinical care, especially with ESRD patients receiving hemodialysis despite their high prevalence and impact on health outcomes (46, 47). Additionally, no studies have been conducted to investigate mindfulness meditation's impact on sleep quality and stress levels and inflammatory markers such as serum cortisol and C-reactive protein among hemodialysis patients. Thus, it is essential to have efficient nursing strategies for managing hemodialysis to ensure the best possible care for this group (45, 48-50). Therefore, the main goal of this research is to assess how effective mindfulness meditation is in improving sleep quality, reducing stress levels, and impacting serum cortisol and C-reactive protein levels in end-stage renal disease patients undergoing hemodialysis. Practically, the findings of this

research could advise the Kuwaiti Ministry of Health on incorporating mindfulness meditation in Kuwait hospitals. Theoretically, the current study could also broaden the nursing field's understanding and address the existing literature gap on how mindfulness meditation impacts sleep quality, stress perception, cortisol levels, and C-reactive protein in hemodialysis patients in Kuwait and culturally similar countries to enhance disease satisfaction.

2. Method

2.1. Design

This study used a repeated-measures, randomized, parallel control design and was conducted between September 2024 and February 2025 in the dialysis center at Jahra Hospital, Kuwait. The recruitment took approximately ten weeks, and the data collection and intervention took approximately nine weeks. Fifty-six ESRD patients undergoing hemodialysis were recruited using simple random sampling. Jahra Hospital is a governmental hospital with one of the biggest dialysis centers in Kuwait, with a female ward, male ward, and isolation ward. The center holds 70 dialysis machines/beds, with an average of 30 patients managed daily. The location was chosen because of its capacity to supply an adequate number of participants for the planned research. So, the researcher discovered that conducting an interventional study by enrolling patients from multiple Kuwait hospitals was costly and required a significant amount of time. Additionally, the researcher focusing on evaluating the efficacy of this treatment for ESRD patients receiving hemodialysis in Kuwait should prioritize addressing factors impacting internal validity over those impacting external validity or generalizability. Choosing a homogenous sample from a single setting is a method that can be used to enhance internal validity (51).

The inclusion criteria for participation in this study were being a patient with ESRD undergoing hemodialysis three times a week for a minimum of one year, being aged 18 years old or over, having a urea reduction rate greater than 65% or Kt/V greater than 1.2 in the past month, and possessing Arabic literacy skills. The exclusion criteria included being a patient with cognitive dysfunction or mental retardation, suffering from rheumatoid arthritis, using a hearing aid, regularly consuming psychopharmacological drugs to reduce stress and improve sleep, participating in other psychological therapies at the time, or had prior formal training in mindfulness methods or a current meditation practice. Criteria for exclusion were built based on the chronic condition of the participants' status, which would make participation in the mindfulness sessions and home practice of mindfulness meditation problematic or distressing. Having serious psychiatric conditions, receiving psychopharmacological drugs, participating in other psychological or mindfulness therapies, or having severe hearing impairment would potentially risk failure in the intervention or limit participation in the mindfulness sessions. Further, patients with rheumatoid arthritis may have an increased burden of both age-related and disease-related cognitive decline, and elevated C-reactive protein levels may indicate an inflammatory process in the body (52, 53). The trial is reported in accordance with the CONSORT guidelines.

The required sample size was calculated using G-power version 3.1. Given a mixed-design (within groups and between groups) repeated measures ANOVA, power of 0.95, moderate effect size of 0.25, and α of 0.05, the required sample size was 44 subjects. A similar study reported an attrition rate of 60% (54). Considering an expected attrition rate of 60%, 24 subjects should be added. Thus, the final required sample size was 68 participants.

2.2. Data collection instruments

The study data were collected using an Arabic self-report questionnaire with five parts.

2.2.1. Demographic characteristics

This section included a question for each variable: Age, gender, nationality, marital status, dialysis vintage, Kt/V, educational attainment, employment status, family status, and any comorbidities.

2.2.2. Quality of sleep

The Pittsburgh Sleep Quality Index (PSQI) aims to evaluate sleep quality in clinical populations. The PSQI includes seven dimensions of sleep characteristics: subjective sleep quality (1 item), sleep latency (2 items), sleep duration (1 item), habitual sleep efficiency (3 items), sleep disturbances (9 items), use of sleeping medication (1 item), and daytime dysfunction (2 items). When the PSQI is scored, seven different scores are calculated for each component, ranging from 0 (no problems) to 3 (severe problems) (55). The PSQI shows internal consistency and a reliability coefficient (Cronbach's alpha) of 0.83 for its seven components (55). The Arabic PSQI had a Cronbach's alpha coefficient of 0.77, indicating satisfactory reliability (56). The Arabic version provided accurate and dependable outcomes within Arabic cancer communities (56). In our study, Chronbach's α coefficient for the PSQI was 0.77.

2.2.3. Perceived stress

The Perceived Stress Scale (PSS) assesses how stressful situations in one's life are perceived based on their unpredictability, lack of control, and feeling overwhelmed. It consists of 10 elements assessed using a 5-point Likert scale (0=never, 4=very often) that are mostly not specific to any particular subgroup.

Scores range from 0 to 40, with higher scores indicating greater perceived stress levels (57). The PSS showed internal consistency coefficients varying from 0.84 to 0.36 and a test-retest reliability of 0.85 (57). The Arabic PSS had a Cronbach's alpha coefficient of 0.80 and an intra-correlation coefficient of 0.90 for test-retest reliability, indicating satisfactory reliability levels (58). Almadi, Cathers, Mansour, and Chow (2012) (58) confirmed the suitability of PSS for Arabic individuals. The Chronbach's α coefficient for the PSS was 0.76.

2.2.4. Biomedical markers

The Access Cortisol Assay-33600 and CRP Reagent-447280 protocols, which involved blood sampling, were strictly followed. The Access Cortisol Assay is a paramagnetic particle, competitive binding immuno-enzymatic assay for the quantitative determination of cortisol levels in human serum, plasma (heparin, EDTA), and urine using the Access Immunoassay Systems, aiding in the diagnosis of adrenal-related disorders (59). The CRP reagent, in conjunction with IMMAGE Immunochemistry Systems, is intended for the quantitative determination of C-reactive protein (CRP) in human serum or plasma (heparin, EDTA), aiding in the evaluation of stress, trauma, infection, inflammation, and surgery (60).

Both protocols were precise, specific, and sensitive in accurately measuring serum cortisol and C-reactive protein concentration (59, 60). It is necessary to do the serum cortisol test multiple times a day or several days (61). However, it is important to carefully consider the timing of cortisol testing because it follows a strong circadian rhythm, peaking during the first hour after waking up and decreasing throughout the day until midnight. Hence, routinely checking serum cortisol levels during the first hour after waking up is viewed as a consistent and trustworthy biological indicator (61-63).

2.3. Intervention

2.3.1. Experimental group

The experimental group received the Smith's version of mindfulness meditation (31), a standardized theory-based intervention found to be effective in improving stress and its related health problems. Smith's version of mindfulness meditation (31) comprises the following components.

(1) Being mindful of breathing, which includes easily taking in a full, deep breath, filling the lungs, simply exhaling, and then breathing naturally. It also includes noticing and simply attending to the air as it flows in and out of the nose and moves deeper into the throat and lungs (5 min).

(2) Being mindful of the body includes attending to how the body feels from head to toe and noticing any sensations that come and go. Upon noticing a sensation, the individual must gently note it, let it go, and continue attending to how the body feels (5 min).

(3) Being mindful of thought includes attending to the mind as thoughts come and go. Whenever a thought or feeling comes to mind, the individual should notice it, let it go, and continue attending to the mind repeatedly (5 min).

(4) Being mindful of sounds includes attending to the sounds one hears without thinking about them. The individual must gently notice the sound, let it go, and continue waiting (5 min).

(5) Being mindful of taste, which includes imagining a wonderful bowl of pieces of one's favorite fruit and simply attending to a taste sensation without thought, analysis, or effort (5 min)

(6) Full meditation includes gently opening one's eyes and being mindful of the world of the moment, quietly attending, and waiting. When noticing something, be it a sight,

sound, thought, or sensation, the individual must let it go and then resume attending, doing nothing else, and waiting for what comes next (5 min).

The participants in the intervention group underwent a 30-minute mindfulness meditation program three times a week for eight weeks, scheduled during their dialysis sessions, specifically between the first and second hour of hemodialysis (64). The program is based on ABC_2 theory and incorporates mindfulness meditation techniques, a standardized intervention that has been proven effective in reducing stress and associated health issues (31). The researcher in the study documented the intervention guidelines in Arabic following the protocol Smith (2005) outlined. Following that, two psychologists and meditation experts approved the intervention contents, which were recorded in audio format. Following this, the recorded audio instructions were forwarded to the IT developer for assessment of the intervention program based on functionality, design, user-friendliness, and voice quality. The IT technician was on standby to address any technical issues promptly.

The participants were required to finish a 2-hour introductory course conducted in a private setting by the certified researcher before starting the training sessions in a room in the dialysis center. The introduction course educated the participants on the fundamentals, advantages, procedures, and ways to reach the intervention. Next, the recorded audio instructions were dispatched to the participants through WhatsApp and email to guarantee the uniform administration of the intervention. Participants followed the recommended instructions accessed via their cell phones and headsets during hemodialysis sessions, as documented (9, 54). The individualized intervention was provided and supervised directly at the patients' chairside while they were receiving hemodialysis treatment. The intervention delivery

using audio-recorded instructions allowed the researcher to introduce individual intervention sessions for up to five participants simultaneously.

This method has been shown to be both possible and successful for individuals receiving hemodialysis (9, 32, 54, 65). In his ABC_2 relaxation theory, Smith (2005) (31) stated that general populations should receive at least two 30-minute sessions of mind-body therapy training per week to induce relaxation, alleviate stress, and enhance overall health. Nevertheless, it has been proposed that a concise program structure with a minimum of 400 minutes could increase hemodialysis patients' health advantages (54). Based on physical assessments, there is a theory that morning serum cortisol and serum C-reactive protein levels may decrease after an 8-week period of mindfulness-based practices (1-3 times weekly, totaling 60-180 minutes) (66, 67). As a result, the experimental group participated in a 30-minute mindfulness meditation session three times per week for 8 weeks (720 minutes). Curtains were used to maintain the privacy of each participant during the intervention. Participants were instructed not to disclose any details about the intervention to those in the control group to avoid contamination. The healthcare professionals promptly addressed any possible interruptions, such as the alarm of the dialysis machine (peeps). Over eight weeks, participants were instructed to consistently practice the program at home before going to bed each night.

The researcher responsible for supervising the intervention delivery was an advanced nursing specialist with six years of nephrology nursing experience and a 4-day training course on mindfulness meditation. This researcher attended the sessions to manage any potential interruptions (e.g., machines' peeps and interruptions) and evaluate the intervention delivery and compliance using checklists produced according to Smith's protocol (54). After each session, the researcher completed the

checklist by asking the participants whether they had completed all the intervention protocol. If the participants felt discomfort, nausea, headache, muscle tension or any other uncomfortable symptoms during or immediately after the intervention sessions, the researcher informed the participants to stop the intervention to seek and provide the appropriate healthcare.

2.3.2. Control group

The participants in the control group were instructed to sit with their eyes closed and relaxed for 30 min three times a week for eight weeks during hemodialysis sessions to control for the nonspecific effects of social interaction and environment (Rausch et al., 2006). The timings of the control group sessions were similar to those of the experimental group, whereby if a given experimental group intervention lasted for 30 min, the control group participants would also be asked to sit with their eyes closed and relax for 30 min.

To avoid contamination bias, the experimental group participants were instructed to refrain from discussing any details about the intervention with anyone else throughout the duration of the study. The nurses and doctors at the hemodialysis center were not informed about the experimental group's intervention to avoid sharing details with the control group participants. During the study, the control group participants were given a placebo intervention, which involved closing their eyes and relaxing for 30 minutes. The experimental group participants' hemodialysis sessions were rescheduled to different units from the control group for eight weeks to prevent contamination bias during the intervention period. The participants from the experimental and control groups were allocated to separate hemodialysis units within the hemodialysis treatment center. Approval was obtained from the participants before managing the rescheduling with the nurses and physicians at the hemodialysis

center. The privacy and confidentiality of the participants were upheld by ensuring that no one could observe the data collection and intervention sessions through the use of curtains around each participant. At the end of the intervention, the researcher overseeing the intervention delivery confirmed with the control group participants that they had not engaged in or been provided with any information on mindfulness meditation throughout the study.

2.4. Procedure

First, the permission from the instruments used in the study was obtained. Recruitment of participants was conducted by one of the study researchers who supervised the intervention delivery after obtaining approval from the hospital administrators to conduct the study. The list of all hemodialysis patients' names for both male and female floors, including their personal information (age, contact number, dialysis unit/room, hemodialysis shifts/days, hemodialysis access, hemodialysis starting date, and other chronic diseases) were gathered from the selected dialysis center. After that, all participants' files were checked for the last month Kt/V scores to conduct the inclusion criteria and select the study sample. The study purposes and protocol were explained to the patients in detail. Patients who agreed to participate in the study and met the eligibility criteria were asked to sign a consent form. Participants then completed the study variables' baseline measurements (T0) using the self-report questionnaires and measurements with a research assistant with a bachelor's nursing degree and 10 years of nephrology nursing experience. Another study researcher with a PhD degree, who was not involved in the recruitment process and data collection, randomized the participants to the experimental group (n = 34) or the control group (n = 34), using a simple 1:1 computer-generated sequence. The study variables were measured four weeks post the

start of the intervention (immediately after the twelve session, T1) and at the end of the final session (T2) for both groups. The measurements of the study variables at T0, T1 and T2 were conducted by the same research assistant who was not involved in any other parts of the study and blinded to randomization allocation. All measurements were privately taken at the dialysis center.

2.5. Data analysis

SPSS version 25 (SPSS Inc., Chicago, Illinois, USA) was used to analyze the collected data. Prior to the main analysis, outliers and missing data were examined and managed as appropriate. Then, the assumptions of the statistical tests used, normality using a histogram graph, homogeneity of variance, and sphericity were checked and managed as appropriate. Mauchly's test of sphericity is used to assess whether the assumption of sphericity has been violated. When Mauchly's test of sphericity was significant ($P < 0.05$), the degrees of freedom were corrected using Greenhouse-Geisser or Huynh-Feldt estimates of sphericity. The comparability of the two groups was evaluated in terms of demographic characteristics and the baseline measurements of the dependent variables using a *t*-test and Chi-square based on the measurements of the dependent variables. The main analysis was conducted with repeated-measures ANOVA (mixed design: within and between groups). A *P*-value of 0.05 was set as the significance level for the main analysis tests.

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