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THE EFFECTS OF DHIKR COMBINED WITH DEEP BREATHING EXERCISES ON STRESS, ANXIETY, AND CORTISOL LEVELS AMONG CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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ABSTRACT
Chronic kidney disease is a critical global healthcare challenge frequently exacerbated by psychological distress. Non-pharmacological interventions targeting both psychological and physiological pathways remain poorly understood. Objective: This study evaluated the effects of combining dhikr with deep breathing exercise on stress, anxiety, and cortisol level among chronic kidney disease patients. A randomised controlled trial was conducted at Syarifah Ambami Rato Ebhu Hospital, Bangkalan, involving 34 hospitalised patients equally allocated to an intervention programme (n = 17) or a standard health education control group (n = 17). Data were analysed using the paired t-test, independent t-test, and multivariate analysis of variance. The combined intervention significantly decreased post-test stress ($p = 0.001$) and anxiety ($p = 0.021$) relative to the control cohort. Changes in serum cortisol concentration were not statistically significant within or between groups ($p = 0.864$). However, the omnibus multivariate analysis demonstrated a highly significant concurrent effect across all tracked parameters ($p < 0.001$). Integrating dhikr with deep breathing exercise effectively minimises psychological distress in individuals with chronic kidney disease, providing a viable non-pharmacological complementary modality.

Keywords: anxiety; cortisol; dhikr; nephropaty; respiration; stress

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INTRODUCTION

Chronic Kidney Disease (CKD) is a major global health concern with a rising prevalence, particularly in developing nations. This upward trend closely parallels the increasing incidence of hypertension, diabetes mellitus, and other degenerative diseases. CKD is defined as abnormalities of kidney structure or function persisting for at least three months with implications for health, including an elevated risk of systemic complications (Torres et al., 2025). It represents a state of progressive renal damage from various etiologies, characterized by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73m² for three months or longer (Levin et al., 2024). Notably, the prognosis of CKD can be severely exacerbated by psychological distress during the illness. Psychological stress is conceptualized as a negative mental health state that encompasses symptoms of both anxiety and depression (Zhu et al., 2022).

Globally, CKD affected approximately 8% of the world's population in 2021, equating to nearly 674 million people, with an annual mortality rate reaching 1.53 million deaths (Guo et al., 2025). The global prevalence of CKD has steadily escalated over time, exhibiting an Average Annual Percent Change (AAPC) of approximately +0.92% per year since 1990 (Xie et al., 2025). A systematic study across 161 countries reported a median global prevalence of 9.5%, with the highest burden observed in Central and Eastern Europe (Deng et al., 2025). In Indonesia, the 2023 Indonesian Health Survey (SKI) conducted by the Ministry of Health revealed that approximately 1.5 million residents suffer from CKD, incurring healthcare expenditures of up to IDR 2.92 trillion.

This indicates a substantial increase in the national burden of chronic kidney disease compared to the 2018 Basic Health Research (Riskesdas), which recorded a prevalence of 0.38% (739,208 individuals) among the population aged ≥ 15 years (Hidayangsih et al., 2023). In East Java Province, the prevalence of CKD was documented at 0.29%, affecting approximately 75,490 individuals and placing East Java 9th out of the 34 provinces in Indonesia (Riskesdas Jatim, 2021).

Bangkalan Regency, as one of the districts in East Java Province, also contributes to the regional incidence of CKD. A preliminary study at Syarifah Ambami Rato Ebhu (Syamrabu) Regional General Hospital in Bangkalan demonstrated a year-on-year increase in cases. In 2022, the hospital recorded 541 CKD patients. This figure surged to 869 patients in 2023, representing a significant increase of approximately 60.63%. Although the case count showed a slight downward trend in 2024 to 853 patients (a decline of about 1.84%), these data underscore that the prevalence of CKD at RSUD Syamrabu Bangkalan remains critically high, with the marginal decrease failing to offset the previous sharp escalation. Concurrently, empirical research exploring the application of spiritual care interventions to alleviate stress, anxiety, and cortisol levels among CKD patients remains profoundly limited.

The primary etiologies of CKD include diabetic kidney disease, glomerulonephritis, hypertensive nephrosclerosis, and polycystic kidney disease (PKD), among other causes (Hustrini et al., 2024). As the pathogenesis progresses, various clinical manifestations emerge, including anemia, hypertension, pulmonary edema, encephalopathy, bone disorders, uremia, pruritus, and metabolic dysfunction (Rajiah et al., 2024). Furthermore, stress and anxiety play a pivotal role in significantly accelerating the progression from acute kidney injury (AKI) to CKD (Su et al., 2021 ; Huang et al., 2021). Stress crucially drives the initiation and progression of CKD via neuroendocrine pathways, maladaptive behaviors, hemodynamic disturbances, and chronic inflammation (Bruce et al., 2015). Similarly, anxiety is strongly associated with albuminuria, accelerated eGFR decline, and the eventual development of CKD (J. Huang et al., 2023). Both stress and anxiety are inextricably linked to the pathogenesis of the disease and persistently accompany the patient throughout their illness trajectory.

Pathophysiologically, both stress and anxiety trigger neurohormonal responses by overactivating the hypothalamic-pituitary-adrenal (HPA) and the sympatho-adrenal-medullary (SAM) axes (Noushad et al., 2021). The chronic and excessive activation of these axes elevates cortisol and catecholamine levels, induces salt and water retention, impairs insulin sensitivity, and promotes systemic inflammation all of which drive renal damage (Su et al., 2021). Biologically, this sustained activation induces chronic oxidative stress, leading to the accumulation of free radicals, persistent inflammation within renal tissues, and accompanying vascular dysfunction that perpetuates CKD (Boima et al., 2025). Unmanaged CKD pathogenesis inevitably culminates in severe complications, including anemia, mineral and bone disorders, metabolic acidosis, cardiovascular disease, fluid and electrolyte retention, uremia, neurological dysfunction, and an elevated risk of infection secondary to immune dysfunction (KDIGO, 2024; Rajiah et al., 2024).

Management strategies for CKD encompass both pharmacological and non-pharmacological modalities. Pharmacological management relies on the administration of RAAS inhibitors, SGLT2 inhibitors, nonsteroidal mineralocorticoid receptor antagonists (ns-MRAs), and GLP-1 receptor agonists, which serve to delay disease progression and mitigate complications (KDIGO, 2024). However, long-term pharmacological therapies present inherent limitations, notably drug accumulation and toxicity (KDIGO, 2024). Declining renal function profoundly alters drug pharmacokinetics and pharmacodynamics, predisposed CKD patients to toxicity. Furthermore, discrepancies between creatinine-based estimation formulas and actual eGFR complicate safe drug dosing (Vondracek et al., 2021). Inappropriate drug selection, excessive dosing, monitoring failures, and patient non-adherence further compound the complexity of pharmacotherapeutic management

in CKD (Hall et al., 2024). Consequently, there is an urgent need to integrate non-pharmacological therapeutic modalities into the clinical management framework.

One promising non-pharmacological intervention is spiritual care in the form of dhikr (zikir) combined with deep breathing exercises (DBE). This combined therapy has been proven effective in reducing anxiety, post-operative pain (Yusuf et al., 2020), and blood pressure (Calisanie & Ira Santika, 2022). Spiritual care regulates stress to induce psychological tranquility. This state is neuroendocrinologically mediated through the activation of cognitive and emotional brain centers, alongside the regulation of the SAM and HPA axes, which restores cortisol to physiological homeostasis (Sobhani et al., 2022). Spiritual therapy has been shown to regulate cortisol rhythms by lowering nocturnal cortisol levels and enhancing the morning cortisol awakening response, thereby aligning it closer to physiological rhythms (Ho et al., 2020). A study by Amir et al. (2018) demonstrated that dhikr and deep breathing significantly improve stress perception and cortisol levels in diabetic patients. Enhanced stress perception post-intervention balances HPA axis activity, which positively modulates cortisol secretion and efficacy, ultimately improving metabolic processes, including blood glucose regulation in type 2 diabetes mellitus patients (Amir et al., 2018).

When applied to CKD patients, spiritual care and DBE can enhance mindfulness, alleviate stress and anxiety, and activate the parasympathetic nervous system, particularly in patients undergoing hemodialysis (Mahyuvi & Sari, 2023). A harmonious balance between sympathetic and parasympathetic activity directly influences blood pressure regulation, a critical factor in preventing the exacerbation of CKD. Additionally, spiritual practices such as prayer among CKD patients foster positive emotions (Dalal et al., 2021), mitigate stress (Sopiah et al., 2024), reduce anxiety (Sudrajat et al., 2025), and modulate cortisol levels (Alhawatmeh et al., 2024). Rogerson et al. (2024) further elucidated that besides reducing stress and anxiety, spirituality regulates cortisol secretion via the HPA axis by modulating psychosocial stimuli processed through the stress response system (Isehunwa et al., 2021). HPA axis activation initiates with the release of corticotropin-releasing hormone (CRH) by the hypothalamus, which subsequently stimulates the anterior pituitary to secrete adrenocorticotropic hormone (ACTH), thereby regulating systemic cortisol levels (Tafet & Nemeroff, 2020; Mbiydzenyuy & Qulu, 2024; Alhawatmeh et al., 2024). Maintaining cortisol homeostasis is vital, as excessively high cortisol levels risk binding to mineralocorticoid receptors in the heart and kidneys, disrupting systemic metabolism. Spiritual care via dhikr and DBE mitigates stress and anxiety in CKD patients, thereby promoting cortisol homeostasis. Balanced cortisol levels are capable of improving metabolic pathways, enhancing renal blood flow, and preserving residual nephron function in CKD patients. Therefore, this study aims to analyze the effects of dhikr combined with deep breathing exercises on stress, anxiety, and cortisol levels among chronic kidney disease (CKD) patients at Syarifah Ambami Rato Ebhu Regional General Hospital, Bangkalan.

METHOD

Sample Size and Setting

The sample size for this study was determined based on the statistical relationship between the expected effect size, significance level (α), and statistical power. To achieve a rigorous balance, the significance level was set at $\alpha=0.05$ with a standard two-tailed critical value ($Z1-\alpha/2=1.96$), and the statistical power was maintained at 80% ($Z1-\beta=0.842$). The effect size (Cohen's d) was estimated at 1.03, established in accordance with a prior benchmark study on the psychological effects of Holy Qur'an recitation in hemodialysis patients (Babamohamadi et al., 2015).

Applying these parameters to the standard sample size formulation yielded an initial requirement of approximately 14.8 respondents per group, which was rounded up to 15. To mitigate the risk of experimental attrition or participant dropout during the intervention period, a 10% dropout buffer was integrated into the initial cohort calculation. This adjustment increased the target sample to

approximately 16.6 subjects. Consequently, a final sample size of 17 respondents per group (totaling 34 respondents for the entire study) was established to ensure adequate statistical power for subsequent comparative analyses.

Subject Criteria

To ensure a homogeneous sample and minimize confounding variables, potential participants were screened systematically using predefined eligibility criteria based on medical examinations and structured interviews. Patients were eligible to participate in this study if they met the specific inclusion criteria, which required them to be clinically and medically diagnosed with Chronic Kidney Disease (CKD) by a physician, hospitalized in the Internal Medicine Ward of Syarifah Ambami Rato Ebu Regional General Hospital (RSUD Syamrabu), Bangkalan, Madura, and aged 40 years or older. Additionally, eligible subjects had to be individuals who were not currently undergoing active hemodialysis therapy and who voluntarily provided written informed consent while demonstrating a full commitment to complete the entire intervention program.

Conversely, potential participants were excluded from the cohort if they exhibited any of the predefined exclusion conditions. These restricted conditions included having a co-existing diagnosis of Chronic Obstructive Pulmonary Disease (COPD) or being clinically diagnosed with severe clinical depression. Furthermore, subjects were excluded if they initiated or required active hemodialysis therapy during the study period, or if they withdrew from the study and refused to continue the dhikr and deep breathing exercise sessions before the completion of the research protocol.

Statistical Analysis

Statistical analyses were performed to evaluate the effects of the intervention on the dependent variables, namely stress, anxiety, and cortisol levels. Prior to conducting comparative tests, the normality of the data distribution was systematically evaluated using the Shapiro-Wilk test, where a p-value>0.05 indicated a normal distribution. To assess changes within each group before and after the intervention, a paired t-test was utilized for normally distributed data, whereas the non-parametric Wilcoxon signed-rank test was applied if the data deviated from normality.

For between-group comparisons between the intervention and control arms, an independent t-test was executed for normally distributed variables, while the Mann-Whitney U test was employed for non-normally distributed data, with the significance threshold fixed at $\alpha=0.05$. Finally, to evaluate the simultaneous effects of the combined dhikr and deep breathing exercises on stress, anxiety, and cortisol levels concurrently, a Multivariate Analysis of Variance (MANOVA) was conducted at a significance level of $\alpha=0.05$.

RESULT

As presented in Table 1, the majority of respondents in the intervention group were male (58.8%), whereas the majority in the control group were female (58.8%). In terms of age distribution, the intervention group was predominantly composed of older adults, with an equal distribution of 29.4% each in the 46–55, 56–65, and >65 years old categories. Conversely, the control group was slightly younger, with 29.5% of respondents falling within the 36–45 years old range. Regarding educational background, secondary education was the most prevalent level in the intervention group (41.2%), while primary education predominated in the control group (41.2%). Occupational profiles revealed that the intervention group was equally represented by housewives and private-sector employees/entrepreneurs (29.4% each), whereas housewives constituted the largest proportion in the control group (41.2%).

Furthermore, concerning the duration of CKD illness, the largest proportion of the intervention group had been diagnosed for 1–3 years (41.2%). In contrast, the control group was equally distributed between individuals diagnosed for less than 1 year and those diagnosed for 1–3 years

(35.3% each). Crucially, the homogeneity analysis yielded p-values>0.05 across all baseline characteristics, indicating that there were no statistically significant differences between the two groups. Therefore, the intervention and control groups were confirmed to be equivalent and homogenous at baseline.

Table 1.
Frequency Distribution of Respondents by Baseline Characteristics

Respondent Characteristics	Intervention Group (n=17) f (%)	Control Group (n=17) f (%)	Total (N=34) f (%)	Homogeneity (p-value)
Gender				0.303
Male	10 (58.8%)	7 (41.2%)	17 (50.0%)	
Female	7 (41.2%)	10 (58.8%)	17 (50.0%)	
Age				0.364
26–35 years old	0 (0.0%)	0 (0.0%)	0 (0.0%)	
36–45 years old	2 (11.8%)	5 (29.5%)	7 (20.6%)	
46–55 years old	5 (29.4%)	4 (23.5%)	9 (26.5%)	
56–65 years old	5 (29.4%)	4 (23.5%)	9 (26.5%)	
> 65 years old	5 (29.4%)	4 (23.5%)	9 (26.5%)	
Education Level				0.926
No Formal Education	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Primary Education	6 (35.3%)	7 (41.2%)	13 (38.2%)	
Secondary Education	7 (41.2%)	6 (35.3%)	13 (38.2%)	
Higher Education	4 (23.5%)	4 (23.5%)	8 (23.5%)	
Occupation				0.536
Unemployed	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Housewife	5 (29.4%)	7 (41.2%)	12 (35.3%)	
Farmer / Fisherman	4 (23.6%)	1 (5.9%)	5 (14.7%)	
Civil Servant / Military / Police	3 (17.6%)	3 (17.6%)	6 (17.7%)	
Private Sector / Entrepreneur	5 (29.4%)	5 (29.4%)	10 (29.4%)	
Retired	0 (0.0%)	1 (5.9%)	1 (2.9%)	
Duration of CKD				0.920
< 1 year	5 (29.4%)	6 (35.3%)	11 (32.4%)	
1–3 years	7 (41.2%)	6 (35.3%)	13 (38.2%)	
3–5 years	5 (29.4%)	5 (29.4%)	10 (29.4%)	

Table 2.
Effect Dikhr and Deep Breathing in Stress Level and Distribution, Descriptive Statistics of CKD Patients in the Intervention and Control Group (n=17)

Stress level	Intervention Group Pre- test f (%)	Intervention Group Post-test f (%)	Control Group Pre-test f (%)	Control Group Post-test f (%)
Normal	2 (11.76%)	5 (29.41%)	1 (5.88%)	2 (11.76%)
Mild	3 (17.65%)	3 (17.65%)	3 (17.65%)	2 (11.76%)
Moderate	4 (23.53%)	5 (29.41%)	4 (23.53%)	4 (23.53%)
Severe	4 (23.53%)	3 (17.65%)	4 (23.53%)	5 (29.41%)
Extremely Severe	4 (23.53%)	1 (5.88%)	5 (29.41%)	4 (23.53%)
Total (N)	17 (100.00%)	17 (100.00%)	17 (100.00%)	17 (100.00%)
Parameter Descriptive (score)				
Mean ± SD	24.65±8.87	19.71±7.24	26.88±8.94	25.58±8.42
Median	24.00	19.00	27.00	26.00
Range [Min, Max]	[10.00, 38.00]	[9.00, 34.00]	[12.00, 40.00]	[12.00, 38.00]
Significant Value Normality (p-value)	0.521	0.852	0.461	0.438
p-value Stress p-value	0.001[a]	0.001[b]	0.002[a]	

As illustrated in Table 2, prior to the intervention, the majority of the respondents in the intervention group were distributed across the moderate, severe, and extremely severe stress categories (23.53% for each category), with a baseline mean score of 24.65 ± 8.87. These findings indicate that the baseline stress levels among respondents predominantly trended toward the moderate-to-severe spectrum. Following the implementation of the intervention, a descriptive improvement in stress profiles was observed. The proportion of respondents experiencing normal

stress levels increased nearly threefold, from 11.76% to 29.41%, concurrently accompanied by a reduction in both severe and extremely severe stress classifications. Accordingly, the mean stress score decreased from 24.65 to 19.71. Descriptively, these outcomes indicate that the combined dhikr and deep breathing exercise intervention successfully mitigated stress levels in CKD patients, as evidenced by both a downward shift in the overall stress distribution and a reduction in mean stress scores post-intervention.

In the control group, prior to receiving health education, a substantial proportion of respondents was distributed across the moderate (23.53%), severe (23.53%), and extremely severe (29.41%) stress categories, yielding a baseline mean score of 26.88 ± 8.94. These findings indicate that the baseline stress levels among the control group respondents predominantly clustered within the moderate-to-extremely-severe spectrum. Following the observation period, minor shifts in the stress distribution were noted. The percentage of respondents within the normal stress category slightly increased from 5.88% to 11.76%, accompanied by a marginal decrease in the extremely severe category. Consequently, the mean stress score exhibited a minimal reduction, changing from 26.88 to 25.58. Descriptively, these results indicate that the standard health education protocol provided to the control group led to a slight downward variance in mean stress scores, though the overall distribution remained largely concentrated in the higher severity categories compared to the intervention cohort.

As Table 2, the mean stress score within the intervention group decreased by 4.94 points, shifting from a baseline of 24.65 ± 8.87 to 19.71 ± 7.24 following the integrated dhikr and deep breathing exercise (DBE) protocol. Conversely, the control group exhibited a smaller mean reduction of 1.30 points, with stress scores changing from 26.88 ± 8.94 at baseline to 25.58 ± 8.42 after receiving standard health education. The Shapiro-Wilk normality test yielded probability values greater than 0.05 across all data subsets ($p>0.05$), confirming that the dataset satisfied the assumption of normal distribution. Consequently, parametric comparative analyses specifically the Paired t-test and Independent t-test were utilized.

Table 3.
Effect Dikhr and Deep Breathing, Frequency Distribution of Anxiety Levels in the Intervention and Control Group

Anxiety Level	Intervention Group Pre-test f (%)	Intervention Group Post-test f (%)	Control Group Pre-test f (%)	Control Group Post-test f (%)
Normal	1 (5.88%)	3 (17.65%)	2 (11.76%)	2 (11.76%)
Mild	3 (17.65%)	4 (23.53%)	2 (11.76%)	2 (11.76%)
Moderate	5 (29.41%)	6 (35.29%)	4 (23.53%)	4 (23.53%)
Severe	6 (35.30%)	3 (17.65%)	5 (29.41%)	6 (35.29%)
Extremely Severe	2 (11.76%)	1 (5.88%)	4 (23.53%)	3 (17.65%)
Total (N)	17 (100.00%)	17 (100.00%)	17 (100.00%)	17 (100.00%)
Parameter Descriptive (Skor)				
Mean ± SD	13.94±4.84	11.64±4.08	14.71±5.63	13.88±5.07
Median	14.00	11.00	15.00	15.00
Range [Min, Max]	[6.00, 24.00]	[6.00, 20.00]	[6.00, 24.00]	[6.00, 22.00]
Significant Value (p-value)				
p-value Normality	968	491	567	442
p-value Anxiety	0.000[a]		0.003[a]	
p-value	0.021[b]			

As illustrated in Table 2, prior to the intervention, a predominant proportion of respondents clustered within the moderate (29.41%) and severe (35.30%) anxiety categories, with a baseline mean score of 13.94 ± 4.84. These findings indicate that the baseline anxiety profiles among respondents primarily trended toward the moderate-to-severe spectrum. Following the implementation of the intervention, a descriptive mitigation of anxiety severity was observed. The percentage of respondents within the normal anxiety category rose from 5.88% to 17.65%, which was accompanied by a concurrent decline in both the severe and extremely severe classifications.

Consequently, the mean anxiety score decreased from 13.94 to 11.64. Descriptively, these outcomes indicate that the combined dhikr and deep breathing exercise intervention effectively lowered anxiety levels in CKD patients, as demonstrated by a downward shift in the overall severity distribution and a reduction in the mean anxiety scores post-intervention.

Prior to the observation period, a substantial proportion of respondents in the control group was classified with severe anxiety (29.41%), followed by the moderate and extremely severe anxiety categories (23.53% each), with a baseline mean score of 14.71 ± 5.63. These findings indicate that the baseline anxiety levels among the control group respondents predominantly clustered within the moderate-to-extremely-severe spectrum. Following the delivery of standard health education, the proportion of respondents within the normal anxiety category remained constant at 11.76%. However, a slight decline was observed in the extremely severe anxiety category, which decreased from 23.53% to 17.65%. Consequently, the mean anxiety score demonstrated a marginal reduction, shifting from 14.71 to 13.88. Descriptively, these results indicate that the health education protocol provided to the control group contributed to a minimal downward variance in mean anxiety scores, though the overall severity distribution remained largely unchanged.

As documented in Table 2, the mean anxiety score within the intervention group decreased by 2.30 points, shifting from a baseline of 13.94 ± 4.84 to 11.64 ± 4.08 following the integrated dhikr and deep breathing exercise (DBE) protocol. Conversely, the control group exhibited a smaller mean reduction of 0.83 points, with anxiety scores changing from 14.71 ± 5.63 at baseline to 13.88 ± 5.07 after receiving standard health education. The Shapiro-Wilk normality test yielded probability values greater than 0.05 across all data subsets ($p>0.05$), confirming that the dataset satisfied the assumption of normal distribution. Consequently, parametric comparative analyses specifically the Paired t-test and Independent t-test were utilized.

The Paired t-test revealed statistically significant within-group reductions in anxiety severity for both the intervention cohort (p=0.000a or $p<0.001$) and the control cohort (p=0.003a), indicating that both approaches yielded longitudinal changes. Crucially, the Independent t-test demonstrated a statistically significant difference in post-test anxiety scores between the two arms (p=0.021b). These statistical indicators confirm that the combined implementation of dhikr and deep breathing exercises is significantly more effective in mitigating anxiety among patients with Chronic Kidney Disease (CKD) than standard health education alone.

Table 4.
Frequency Distribution of Cortisol Levels in the Intervention and Control Group

Cortisol Parameter	Intervention Group Pre-observation f (%)	Intervention Group Post-observation f (%)	Control Group Pre-observation f (%)	Control Group Post-intervention f (%)
Low	1 (5.88%)	0 (0.00%)	1 (5.88%)	0 (0.00%)
Normal	16 (94.12%)	16 (94.12%)	16 (94.12%)	14 (82.35%)
High	0 (0.00%)	1 (5.88%)	0 (0.00%)	3 (17.65%)
Extremely High	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Total (N)	17 (100.00%)	17 (100.00%)	17 (100.00%)	17 (100.00%)
Parameter Descriptive (Score)				
Mean ± SD	13.03±5.23	14.85±5.46	10.68±3.16	12.93±3.92
Median	13.70	16.49	9.90	11.25
Range [Min, Max]	[4.95, 23.43]	[5.37, 23.08]	[4.98, 18.66]	[8.74, 21.36]

As illustrated in Table 3, prior to the intervention, the vast majority of respondents exhibited baseline serum cortisol concentrations within the normal physiological range (94.12%), with a group mean baseline level of 13.03±5.23 µg/dL. This baseline distribution indicates that nearly all participants initially presented with typical endocrine baseline profiles. Following the integrated dhikr and deep breathing exercise (DBE) protocol, slight categorical adjustments were observed in the dataset. The single respondent classified with low cortisol at baseline shifted out of this category (0.00%), while the number of respondents within the normal range remained stable at 16. Concurrently, one respondent transitioned into the high cortisol category (5.88%). The post-

intervention mean cortisol level also demonstrated a marginal elevation, reaching 14.85±5.46 µg/dL.

Descriptively, these findings demonstrate that the combined dhikr and deep breathing exercise program did not lower overall categorical cortisol levels in this sample. However, the data suggest that the intervention exhibited a regulatory tendency, maintaining and stabilizing physiological cortisol concentrations within homeostatic and normal clinical boundaries. As presented in Table 9, prior to the observation period, the vast majority of respondents in the control group exhibited baseline serum cortisol concentrations within the normal physiological range (94.12%), with a group mean baseline level of 10.68±3.16 µg/dL. This distribution indicates that nearly all participants in this cohort initially demonstrated typical baseline endocrine profiles.

Following the standard health education protocol, noticeable descriptive changes occurred within the dataset. The single respondent classified with low baseline cortisol transitioned out of this category (0.00%), while the number of respondents within the normal range decreased to 14 (82.35%). Concurrently, an increase was observed in the high cortisol category, which rose to 3 respondents (17.65%). The post-observation mean cortisol level also exhibited an elevation, reaching 12.93±3.92 µg/dL. Descriptively, these outcomes demonstrate that the standard health education protocol delivered to the control group did not reduce categorical cortisol levels. However, the data indicate that the control group maintained a general tendency to retain serum cortisol levels within normal and physiological parameters, despite the slight upward shift in mean concentration.

Table 5.
Effect of Dhikr and Deep Breathing Exercises on Cortisol Levels

Variable and Group	Measurement Phase	Mean ± SD (µg/dL)	Normality (p-value)a	Within-Group (p-value)b	Between-Group (p-value)c
Cortisol Level					
Intervention Group (n=17)	Pre-Test	13.03±5.23	0.889	0.101	0.864
	Post-Test	14.86±5.46	0.452		
Control Group (n=17)	Pre-Test	10.69±3.16	0.417	0.398	
	Post-Test	12.93±3.92	0.066		

As documented in Table 10, the mean serum cortisol concentration within the intervention group exhibited an increase of 1.82 µg/dL, rising from a baseline of 13.03±5.23 µg/dL to 14.86±5.46 µg/dL following the integrated dhikr and deep breathing exercise (DBE) protocol. In comparison, the control group demonstrated a slightly higher mean increase of 2.25 µg/dL, with cortisol levels shifting from 10.69±3.16 µg/dL at baseline to 12.93±3.92 µg/dL after standard health education. The Shapiro-Wilk normality test yielded probability values greater than 0.05 across all data subsets ($p>0.05$), confirming that the cortisol dataset satisfied the mathematical assumptions required for normal distribution. Consequently, parametric inferential analyse specifically the Paired t-test and Independent t-test were utilized.

The Paired t-test indicated no statistically significant within-group differences in cortisol concentrations for either the intervention cohort ($p=0.101$) or the control cohort ($p=0.398$), demonstrating that neither protocol led to a statistically significant internal change over time. Furthermore, the Independent t-test revealed no significant difference in post-test cortisol values between the two groups ($p=0.864$). These statistical outcomes confirm that the integrated dhikr and deep breathing exercise intervention was not more effective in reducing serum cortisol levels in CKD patients compared to the standard health education protocol.

Table 6.
Multivariate Analysis of Variance (MANOVA) for Combined Psychological and Physiological Outcomes

Variable	Multivariant Test				Conclussion
	Test	Value	F	P value	
Stress, Anxiety and Cortisol	Pillai's Trace	0.548	12.135	0.000	Significant
	Wilks' Lambda	0.452	12.135	0.000	Significant
	Hotelling's Trace	1.214	12.135	0.000	Significant
	Roy's Largest Root	1.214	12.135	0.000	Significant

As documented in Table 11, a one-way Multivariate Analysis of Variance (MANOVA) was conducted to evaluate the simultaneous omnibus effect of the integrated dhikr and deep breathing exercise (DBE) program versus standard health education on the collective dependent variables (stress, anxiety, and serum cortisol levels). The mathematical evaluations across all four standard multivariate test criteria Pillai's Trace (0.548), Wilks' Lambda (0.452), Hotelling's Trace (1.214), and Roy's Largest Root (1.214) revealed a highly significant simultaneous effect, yielding an identical F-statistic of $F(3,30)=12.135, p<0.001$. This uniform significance level demonstrates that the combination of the three clinical parameters differed substantially between the intervention and control cohorts post-treatment.

The Pillai's Trace value of 0.548 indicates that the holistic protocol exerted a strong multivariate effect size on the combined psychological and neuroendocrine parameters. Concurrently, the relatively low Wilks' Lambda value (0.452) demonstrates that a substantial proportion of the variance within this combined patient outcome construct was significantly differentiated by the intervention assignment. These consistent statistical indices provide robust empirical evidence that the integrated dhikr and deep breathing exercise regimen yields a powerful, statistically significant concurrent impact on mitigating stress, lowering anxiety, and stabilizing cortisol regulation in patients diagnosed with Chronic Kidney Disease (CKD).

DISCUSSION

The inferential statistical analyses demonstrated that the integrated administration of dhikr and deep breathing exercises (DBE) exerted a highly significant positive effect on reducing stress levels among patients with Chronic Kidney Disease (CKD). Concurrently, the standard health education (HE) protocol provided to the control group also induced a significant reduction in stress scores. These therapeutic outcomes were collectively modulated by baseline demographic and clinical covariates, including gender, chronological age, educational attainment, occupational status, and the duration of CKD diagnosis. Regarding gender distribution, the intervention group was predominantly male (58.8%), whereas the control group was predominantly female (58.8%). Literature establishes that female CKD patients exhibit a higher predisposition to elevated stress levels due to distinct biological, fluctuating endocrine profiles, and complex psychosocial burdens associated with managing a chronic medical condition (Zaragoza Fernández et al., 2025 ; Bakker et al., 2024). However, this study suggests that both male and female patients possess unique, adaptive coping capacities that enable them to respond effectively to complementary therapies like dhikr and DBE, as well as structured health education.

Chronological age significantly influenced the psychological outcomes, with the majority of respondents in both cohorts falling into the late adulthood developmental stage. Older CKD patients generally demonstrate more mature psychological coping mechanisms, which are anchored by extensive life experiences in navigating severe health stressors (Chiou et al., 2023). Furthermore, advancing age correlates positively with higher spirituality in chronic populations; older individuals tend to leverage spiritual beliefs to discover existential meaning, adapt to pathology, and cultivate proximity to the Divine during health crises (Nurbadriyah & Widyawati, 2023). Consequently, older cohorts possess an enhanced capacity to adapt to long-term hemodialysis regimens compared to younger demographics.

Educational attainment serves as an essential regulatory buffer against illness-induced distress, with the sample predominantly comprising individuals with secondary-to-higher education. Higher educational levels are associated with mitigated stress profiles in CKD because these individuals can better comprehend complex pathological processes, therapeutic demands, and self-care strategies (Bakker et al., 2024). From an existential viewpoint, highly educated patients often report deeper spiritual synthesis and cognitive acceptance of their illness (Fradelos, 2021). They also exhibit superior health literacy, which facilitates the cognitive processing and retention of educational materials delivered by clinical staff (Billany et al., 2023). Therefore, formal education contributes directly to stress regulation and psychological resilience. Occupational status also acts as a critical determinant of adaptive stress responses. Patients with CKD who are unemployed or unable to work frequently experience heightened psychological distress driven by physical limitations, financial instability, and diminished social roles (Luca et al., 2026). Unemployed patients undergoing hemodialysis exhibit a greater reliance on spiritual well-being and require more intensive, tailored health education to augment their active coping strategies and illness comprehension (Panma, 2025).

The longitudinal duration of CKD and hemodialysis treatment is intrinsically tied to cumulative stress parameters. Patients with extended disease durations typically face a higher risk of psychological exhaustion due to chronic physical symptoms, long-term therapeutic dependence, and a continuous decline in health-related quality of life (Kusmiran et al., 2026). Conversely, an extended illness trajectory necessitates heightened spiritual engagement as a vital coping mechanism to foster acceptance, emotional stability, and inner peace (Fradelos, 2021). In this study, the majority illness duration of 1 to 3 years represents a pivotal transitional phase where patients have likely developed functional psychological and spiritual adaptation mechanisms.

Bivariate analysis within the control group revealed a significant pre-to-post reduction in stress scores ($p=0.001$), confirming that structured health education is an effective stand-alone strategy for alleviating distress. Educational interventions and self-management training have been proven to enhance functional coping skills and clinical knowledge among CKD cohorts (Ghasemi Bahraseman et al., 2021). Health education grounded in Self-Determination Theory notably enhances self-care adherence while mitigating anxiety and depression, both of which are core components of generalized psychological stress (Zhang et al., 2025). Improving a patient's cognitive grasp of the disease process mitigates clinical uncertainty a primary driver of distress. Adequate health information shifts the cognitive appraisal of the disease from an unmanageable threat to a controllable condition, thereby dampening emotional stress responses.

Within the intervention group, the paired comparative analysis also showed a highly significant decrease in stress scores following the dhikr and DBE protocol ($p=0.001$). From a neurophysiological perspective, repetitive spiritual practices stimulate alpha wave activity in the brain, which correlates with deep relaxation and emotional tranquility (Dobrakowski et al., 2020). Longitudinal mindfulness and meditative practices shift neuroelectric activity toward a state of relaxed alertness, characterized by heightened alpha synchronization and diminished sympathetic nervous system activation (Katyal & Goldin, 2021). Engaging in dhikr promotes focused attention on the repetitive phrasing and rhythmic respiration, successfully diverting cognitive bandwidth away from maladaptive, negative thoughts toward positive cognitive schemas.

Crucially, the inter-group comparative analysis yielded a highly significant post-test difference favoring the treatment arm ($p=0.001$), demonstrating that the combined dhikr and DBE protocol is superior to standard health education alone. This aligns with empirical evidence showing that dhikr significantly reduces stress in chronic populations by fostering psychoreligious tranquility and triggering the biological relaxation response (Ningrum et al., 2023). Simultaneously, the controlled pacing of DBE regulates heart rate variability (HRV), stabilizes blood pressure, and suppresses the hypersecretion of neuroendocrine stress biomarkers, such as cortisol and catecholamines. This

supports current breathwork literature, which notes that systematic, slow-paced breathing exercises over consecutive weeks lead to substantial drops in objective and subjective stress indicators (Fincham et al., 2023). Thus, the combined intervention addresses both psychological and physiological pathways, fortifying spiritual coping while inducing systemic relaxation.

This superiority is further highlighted by the absolute mean score reductions: the intervention group experienced a substantial decrease of 4.94 points (from 24.65 to 19.71), whereas the control group experienced a minor drop of 1.29points (from 26.88 to 25.59). Dhikr assists patients in constructing resilient internal coping structures to manage long-term illness burdens (Manisha et al., 2025). This deep spiritual engagement enables CKD patients to construct positive meaning around their pathology, resulting in inner peace and an adaptive emotional response to rigorous treatments (Ayulia & Hidayat, 2024).

Physiologically, these techniques alleviate the somatic tension and emotional distress common during hemodialysis sessions. As reported by Laborde et al. (2022), spiritual interventions address the existential dimensions of stress unique to chronic illnesses, while systematic DBE directly reduces somatic anxiety and emotional distress in clinical settings. The statistical findings indicated that both the integrated dhikr and DBE protocol and the standard health education program significantly reduced anxiety scores among CKD patients. These therapeutic responses were similarly modulated by demographic and clinical variables, including gender, age, education, occupation, and total disease duration.

Gender directly influenced the baseline anxiety presentation; the intervention group was predominantly male, while the control group was predominantly female. Extensive clinical studies confirm that female patients typically experience higher baseline anxiety than males when managing end-stage renal pathologies (Nagy et al., 2023 ; Elezi et al., 2023). However, female cohorts often derive greater therapeutic benefit from spiritual interventions because they are generally more receptive to emotional expression and spiritual care practices (Wijayanti et al., 2025). Similarly, women tend to engage more actively with structured health education, demonstrating high information-seeking behaviors and effectively utilizing healthcare support systems (Zhang et al., 2025). Ultimately, both genders possess equal potential for emotional adaptation, depending on their individual coping strategies.

Age also played an important role in anxiety presentation. Younger CKD patients typically report elevated anxiety due to concerns regarding employment stability, long-term economic productivity, and altered life trajectories. Conversely, older adults consistent with Erikson's psychosocial development theory focus primarily on achieving ego integrity, which allows them to attain emotional equanimity more readily than younger cohorts (Hutagaol et al., 2022). For older populations, spiritual practices like dhikr assist in discovering existential meaning, accepting physical decline, and using spiritual beliefs as an emotional anchor (Cheng et al., 2025). Meanwhile, health education mitigates anxiety by reducing clinical uncertainty and restoring a sense of personal control (Barello et al., 2023). From an age-centric perspective, spiritual and breathing protocols may be particularly effective for older adults, whereas younger, highly literate patients may respond more efficiently to information-driven health education.

Educational background further moderated the anxiety outcomes. Patients with advanced educational backgrounds generally exhibit stronger health literacy, enabling them to navigate medical uncertainty and manage anxiety symptoms better than those with lower educational attainment (Wei et al., 2021). Highly educated individuals can readily internalize spiritual concepts like dhikr, translating them into enhanced emotional well-being (Bakker et al., 2024). However, patients with limited formal education still derive substantial benefit from spiritual interventions by leveraging core beliefs of surrender and trust in Divine providence (Senmar et al., 2020). In parallel, higher education accelerates the comprehension of health education materials, eliminating cognitive

misconceptions about the disease and treatment (Billany et al., 2023).

Occupational status correlates closely with anxiety due to its direct impact on financial solvency, productivity, and social identity. CKD patients who remain actively employed often face intense psychological pressure as they struggle to balance demanding hemodialysis schedules with workplace expectations, resulting in fear of job loss and heightened distress (Brown et al., 2021). In contrast, unemployed or retired patients face distinct financial strains but typically enjoy greater scheduling flexibility to adapt to their therapeutic regimens (Kirkeskov et al., 2021). Dhikr mitigates this economic and role-derived anxiety by cultivating gratitude, spiritual surrender, and emotional peace. Complementing this, health education provides practical strategies for managing treatment alongside lifestyle demands, thereby boosting self-efficacy and lowering clinical anxiety.
The duration of illness is another key factor in anxiety stabilization. Anxiety is often highest immediately following initial diagnosis due to the sudden lifestyle changes and the stress of starting dialysis. Over time, patients naturally develop adaptive responses to these ongoing stressors, which gradually reduces their anxiety levels (Angesti & Purwanti, 2025). In this context, dhikr serves as an excellent coping mechanism that accelerates psychological adaptation, fosters hope, and enhances overall well-being (Wijayanti et al., 2025). This works in tandem with structured health education and self-management training, which are proven to expand the knowledge base, adaptive capacity, and emotional stability of hemodialysis patients (Zhang et al., 2025).

Inferential data analysis showed that the combined dhikr and DBE protocol produced a highly significant reduction in anxiety scores within the treatment group ($p<0.001$). Dhikr functions as a structured spiritual intervention; clinical literature indicates that structured spiritual care significantly reduces anxiety in chronic kidney disease populations (Sawiji et al., 2024). These results mirror recent findings on Spiritual Mindfulness Based on Breathing Exercises, which show that combining spiritual awareness with focused breathing exercises significantly reduces anxiety scores (Tata Mahyuvi & Novita Sari, 2024).

Physiologically, the deep, slow breathing patterns taught in DBE stimulate vagal nerve activity, increasing parasympathetic tone and lowering anxiety across both young and elderly demographics (Magnon et al., 2021). The control group also achieved a significant reduction in anxiety following health education ($p=0.003$). Incorporating audiovisual materials into health education has been shown to reduce anxiety by improving patient comprehension of fluid restrictions and therapy protocols, which minimizes clinical uncertainty (Firmanda & Wahyuningsih, 2025). This is supported by similar studies demonstrating that targeted health education significantly lowers patient anxiety scores pre- and post-test (Manalu et al., 2021). These findings reinforce that structured health education enhances cognitive processing, helping patients respond more positively to chronic stressors.

While both interventions successfully reduced anxiety in CKD patients, a significant difference was observed between the two groups post-test ($p=0.021$), proving that the dhikr and DBE protocol outperformed standard health education. Dhikr alleviates anxiety through a psychoreligious relaxation mechanism that lowers the physiological stress response (Anggun et al., 2021). This is consistent with Nugraha Kusuma et al. (2020), who found that psychoreligious relaxation through dhikr effectively reduces clinical anxiety. DBE strengthens this effect by optimizing autonomic nervous system function and down-regulating the physical symptoms of anxiety (Kavitha et al., 2024).

The absolute mean score reductions further support this conclusion: the intervention group showed a substantial anxiety score reduction of 2.29 points, compared to a modest decrease of 0.82 points in the control group. Combining dhikr and prophetic invocations (shalawat) supports emotional stability and mental health in chronic patients. Randomized controlled trials confirm that this combined spiritual approach significantly reduces anxiety scores in hemodialysis cohorts (Wijayanti

et al., 2025). Dhikr enhances emotional equilibrium and patient comfort by strengthening the spiritual connection to the Creator (Anggun et al., 2021). Consequently, when properly implemented, the combination of dhikr and deep breathing exercises offers a highly effective, non-pharmacological strategy for managing anxiety in Chronic Kidney Disease patients.

The inferential statistical analyses revealed that neither the integrated dhikr and deep breathing exercise (DBE) protocol nor the standard health education program exerted a statistically significant direct effect on reducing serum cortisol concentrations in patients with Chronic Kidney Disease (CKD). This absence of acute biochemical modification is critically modulated by complex physiological confounding factors, most notably the chronological age of the participants and the long-term duration of their renal pathology. Regarding the age distribution, the majority of the respondents in both cohorts were within the late adulthood to elderly developmental stages. Empirical evidence from gerontological studies indicates that the physiological aging process is inherently tied to alterations in the diurnal cortisol profile and overall glucocorticoid dynamics. Older individuals frequently exhibit age-related dysregulation of the Hypothalamic-Pituitary-Adrenal (HPA) axis, which permanently alters baseline cortisol secretion patterns, blunts the diurnal rhythm, and diminishes the endocrine system's sensitivity to acute stress-reduction interventions (Pretscher et al., 2021). These structural and psychosocial shifts in late adulthood limit the immediate plasticity of serum cortisol concentrations (van der Velpen et al., 2023), which explains why the psychological improvements observed in this study did not concurrently translate into significant categorical shifts in serum endocrine biomarkers.

Furthermore, the chronicity and systemic burden of end-stage renal disease significantly alter normal endocrine function. The majority of the respondents in this study had a chronic illness duration spanning 1 to 5 years. The progressive nature of CKD induces chronic, sustained activation of the HPA axis, accompanied by a severe reduction in renal cortisol clearance and disrupted systemic glucocorticoid metabolism. As renal function declines, the sustained elevation of circulating cortisol concentrations contributes heavily to persistent systemic inflammation, cardiovascular complications, and increased mortality risk (Sagmeister et al., 2022).

This pathogenesis worsens with the advancements of the disease stage; advanced structural damage to the nephrons directly impairs the body's ability to suppress cortisol production, even when evaluated via standard clinical protocols such as the dexamethasone suppression test (DST). This structural and functional impairment highlights the presence of a hyperactive and highly rigid HPA axis in advanced CKD cohorts (Garg et al., 2024), making the biomarker highly resistant to short-term behavioral interventions. The paired comparative analysis within the intervention arm yielded a p-value of 0.101 ($p>0.05$), confirming that the combined dhikr and DBE protocol did not produce a statistically significant direct reduction in serum cortisol. Similarly, the control group exhibited a p-value of 0.398 ($p>0.05$), indicating no significant change in cortisol concentrations following standard health education. From a pathophysiological standpoint, this lack of significant reduction is rooted in the structural deterioration of the renal-adrenal axis. Physiologically, cortisol is synthesized and secreted by the zona fasciculata of the adrenal cortex, which is anatomically and vascularly integrated directly above the kidneys (Guyton & Hall, 2021). In end-stage chronic kidney disease, the severe cellular and structural degeneration of the renal parenchyma likely compromises the homeostatic microenvironment and physiological feedback mechanisms of the adjacent adrenal glands.

Pathophysiologically, the continuous progression of CKD destabilizes steroid hormone biosynthetic pathways. Advanced metabolomic investigations confirm that renal failure disrupts steroidogenesis, primarily by altering the genetic expression and enzymatic activity of key steroidogenic enzymes. This underscores the fact that advanced CKD is not merely a localized nephrological disease, but a severe systemic disorder that disrupts generalized hormone metabolism, including glucocorticoid pathways (Zuo et al., 2024). Additionally, the persistent, low-grade chronic inflammation

characteristic of CKD serves as a continuous, internal stimulator of the HPA axis, driving sustained cortisol hypersecretion that overpowers acute behavioral relaxation signals (Brennan et al., 2021). This state of chronic systemic inflammation and continuous metabolic stress activates perpetual catabolic pathways (Wang et al., 2022), locking cortisol concentrations into a elevated physiological baseline.

The independent inter-group comparison further confirmed the absence of a significant post-test difference between the intervention and control arms ($p=0.864>0.05$). This statistical uniformity highlights the complex regulatory systems governing cortisol in end-stage renal failure. In these patients, circulating cortisol levels are simultaneously driven by psychological distress, profound organic dysfunction, persistent HPA axis hyperactivity, chronic systemic inflammation, and a significant drop in metabolic clearance due to reduced eGFR (Sagmeister et al., 2022). This chronic distress pattern breaks down the normal circadian cortisol rhythm, promoting a state of constant oxidative stress and driving further renal damage (Motrenikova et al., 2025). This is consistent with clinical findings showing that as eGFR drops, patients experience a progressive loss of normal cortisol feedback suppression and an uncoupling of the standard endocrine rhythm (Boswell et al., 2024).

However, despite the absence of an acute, statistically significant drop, the descriptive data indicate that the combined dhikr and DBE protocol possesses a noticeable regulatory and stabilizing potential. Categorical tracking showed that within the intervention arm, one patient with pathologically low baseline cortisol normalized, while only one patient with normal baseline levels shifted into the high category. In stark contrast, within the control arm, one patient with low cortisol shifted directly to high, and two patients with normal baseline profiles developed hypercortisolemia. This descriptive stability indicates that the deep psychological and spiritual relaxation induced by dhikr and DBE acts as a homeostatic buffer, helping to anchor serum cortisol within safe physiological boundaries. Complementary spiritual care and mindfulness-based practices have been shown to modulate HPA axis dynamics, providing a stabilizing effect on glucocorticoid output even when overall categorical shifts remain statistically non-significant (Vargas-Uricoechea et al., 2024). Descriptively, while the mathematical mean of cortisol increased across both groups, the intervention group demonstrated a noticeably smaller upward variance compared to the control group (1.82 μg/dL versus 2.25 μg/dL, respectively). Rhythmic spiritual practices like dhikr reduce stress perception by enhancing emotional stability and fostering positive religious coping mechanisms (Insyra et al., 2023). When stress is managed adaptively, the down-regulation of perceived distress reduces the hyper-activation of the HPA axis, promoting neuroendocrine stability. This biochemical modulation aligns with studies in heart failure cohorts, where systematic dhikr successfully improved stress appraisal and buffered maladaptive endocrine responses, resulting in stabilized cortisol output (Okviasanti et al., 2023). Therefore, implementing a highly structured, standard operational protocol for dhikr and DBE holds strong long-term potential for preserving neuroendocrine homeostasis in CKD populations.

The multivariate analysis of variance (MANOVA) evaluating the combined dependent constructs stress, anxiety, and serum cortisol levels demonstrated a highly significant simultaneous omnibus effect. All four standard multivariate criteria Pillai's Trace (0.548), Wilks' Lambda (0.452), Hotelling's Trace (1.214), and Roy's Largest Root (1.214) consistently converged to yield a highly significant multivariate value ($F=12.135, p<0.001$). This statistical convergence provides robust empirical proof that the integrated intervention protocol produces a comprehensive, multi-dimensional shift across the combined psychological and neuroendocrine domains, successfully differentiating the treatment cohort from the control group post-intervention. This multi-systemic outcome aligns with clinical literature establishing that structured spiritual practices significantly reduce anxiety, which serves as a core psychological component of generalized illness-induced distress in chronic populations (Farhani & Qudsyi, 2024). The deep inner peace and positive emotional processing achieved by CKD patients during the combined dhikr and DBE sessions

trigger a highly integrated, adaptive biopsikososial-spiritual response.

The simultaneous regulation of stress, anxiety, and cortisol trends is driven by an interconnected matrix of spiritual, psychological, and neurobiological coping mechanisms that continuously reinforce one another. Spiritually, structured Islamic spiritual care acts as a powerful intervention that mitigates psychological distress, enhances existential well-being, improves health-related quality of life, and promotes profound inner peace (Manisha et al., 2025). Phenomenological studies in nephrology nursing confirm that specific spiritual interventions allow CKD patients to effectively manage clinical uncertainty, attain emotional peace, and cultivate deep acceptance of their chronic condition (Supriyono et al., 2020). This spiritual coping framework functions as an essential internal protective asset, buffering patients against severe psychological distress and anxiety while reinforcing cognitive resilience (Nurbadriyah & Widyawati, 2023). Patients who utilize a highly developed spiritual framework adapt more successfully to the continuous stressors of chronic, life-limiting illnesses.

From a psychological perspective, the practice of dhikr induces a state of spiritual mindfulness that directly lowers distress and anxiety, enhances emotional self-regulation, and dampens physiological hyper-arousal (Farooq, 2024). Rhythmic spiritual chanting serves as an effective cognitive coping mechanism, helping patients cognitively re-appraise their health stressors and break patterns of chronic anxiety (Ma'rufah & Ridho, 2026). By directly targeting maladaptive cognitive distortions, dhikr alters the negative interpretation of chronic illness stressors, replacing panic with an enhanced sense of personal control and inner calm (Khotimah & Nurjannah, 2024). When combined with DBE, this intervention engages the deepest psychological levels of the patient, successfully regulating stress and stabilizing downstream neuroendocrine parameters.

Biologically, the simultaneous effect of dhikr and DBE on the stress-anxiety-cortisol triad is driven by complex neurophysiological, neurobiological, and psychoneuroendocrinological pathways. Neurophysiologically, repetitive spiritual practices modulate the brain's electrical activity, as measured via electroencephalography (EEG). Systematic dhikr has been shown to significantly increase alpha wave synchronization (8–12 Hz), a brainwave profile directly associated with deep relaxation, mental clarity, and diminished autonomic arousal. This increase in alpha power marks a clear neurophysiological shift away from stress-induced cortical hyper-activation (dominant beta waves) toward a calm, neurologically stable state (Huwaidah & Sumarti, 2024). From a neuroscience perspective, dhikr operates as an attention-focusing and emotion-regulating intervention that lowers cortical stress activation (Huwaidah & Sumarti, 2024). By keeping the patient's attention anchored on the repetitive phrasing, it prevents cognitive rumination and reduces the negative cognitive appraisal of the illness, leading to a significant drop in objective stress and anxiety.

Neurobiologically, this spiritual intervention balances the autonomic nervous system by reducing sympathetic hyperactivity and activating parasympathetic pathways. This down-regulation of the body's primary stress networks significantly reduces clinical anxiety and distress (Nugraha Kusuma et al., 2020). Dhikr activates the parasympathetic nervous system (PNS) by calming emotional distress, narrowing cognitive focus, and stopping negative emotional rumination. This parasympathetic shift increases vagal tone, slowing the heart rate and stabilizing systemic physiological stress responses. Clinical evidence confirms that combining spiritual mindfulness with structured breathing techniques restores autonomic balance and alleviates anxiety in hemodialysis patients (Arul Valan et al., 2024).

This autonomic stabilization is further reinforced by the deep breathing exercise (DBE) component. Systematic DBE increases heart rate variability (HRV), lowers blood pressure, and reduces subjective perceived stress by optimizing mechanical respiratory feedback (Kalyani et al., 2025). Patients with Chronic Kidney Disease are under constant psychological strain due to the structural

burdens of their illness, an uncertain prognosis, and invasive, repetitive clinical treatments. This continuous distress state typically manifests as severe hyperactivity of the sympathetic nervous system (SNS), leading to elevated heart rates, somatic muscle tension, and a chronic "fight-or-flight" state (LeBouef et al., 2023). Prolonged sympathetic activation eventually triggers sustained hyper-activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis, exacerbating the patient's distress and trapping them in a cycle of physiological and psychological exhaustion (Choudhary & Zagade, 2025). When autonomic sympathetic stress transitions into sustained HPA axis activation, it leads to a cascade of negative neurohormonal effects.

In this study, the integrated dhikr and DBE protocol successfully engaged the patient's entire holistic framework from existential spiritual dimensions to baseline biological pathways—to regulate stress, reduce anxiety, and promote cortisol homeostasis. Spiritually and psychologically, dhikr serves as a cognitive barrier that diverts the patient's focus away from anxiety-inducing thoughts, anchoring it within a secure framework of divine awareness. Cognitively, patients with a strong spiritual anchor re-frame their clinical hardships, mitigating anxiety and achieving a state of emotional tranquility (thuma'ninah) (Masita & Cholil, 2025). This practice provides a clear cognitive focus and activates neural pathways associated with emotional peace and psychological satisfaction (Farooq, 2024). In hemodialysis units, incorporating structured prayer and dhikr has been shown to significantly lower the perceived uncertainty of illness, directly reducing systemic stress and anxiety scores (Rauzah et al., 2025). Dhikr acts as a positive cognitive stimulus, shifting the patient's appraisal of their illness from a catastrophic threat to an adaptively managed condition.

Physiologically, the addition of deep breathing exercises complements the spiritual intervention, maximizing its effectiveness in reducing stress and anxiety while stabilizing cortisol. Controlled breathing techniques like DBE stimulate the parasympathetic nervous system and increase vagal tone, suppressing sympathetic hyperactivity and easing somatic stress (Gerritsen & Band, 2018). Furthermore, DBE enhances emotional regulation by altering how the brain processes stressors, helping patients perceive their clinical environment as manageable and non-threatening. Clinical trials on slow-paced breathing exercises confirm that this technique significantly improves emotional regulation; by increasing vagal tone and parasympathetic dominance, slow breathing allows individuals to deploy cognitive emotional regulation strategies more effectively (Kurdziel et al., 2025). By enabling patients to perceive and process stress adaptively, this combined protocol successfully lowers overall stress and anxiety scores. These findings align with prior research showing that combining spiritual care with structured respiratory relaxation significantly alleviates stress in chronic renal failure cohorts (Yuniartika et al., 2021).

Once psychological stress and anxiety are mitigated, the neuroendocrine system responds via the HPA axis, leading to improved cortisol regulation. The standard HPA axis pathway begins in the paraventricular nucleus (PVN) of the hypothalamus, which releases corticotropin-releasing hormone (CRH) into the hypophyseal portal system. This stimulates the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH), which triggers the adrenal cortex to produce cortisol. While acute cortisol spikes help the body mobilize energy and manage immediate inflammation during stress, sustained hypersecretion requires functional negative feedback loops. Once a healthy threshold is reached, cortisol signals the hypothalamus and pituitary to down-regulate CRH and ACTH output, restoring endocrine homeostasis (Zänkert et al., 2019; Van den Berghe et al., 2022; Martinez et al., 2023; Langouche et al., 2023). In chronic kidney disease, spiritual care through dhikr and Quranic recitation serves as a key catalyst that reduces anxiety and improves this psychological and neuroendocrine adaptation (Mesya et al., 2025).

Ultimately, the clinical efficacy of this combined intervention is best explained through a comprehensive biopsikososial-spiritual framework. Dhikr provides psychological and spiritual resilience, while deep breathing exercises deliver direct physiological relaxation. The synergy between these two components produces a therapeutic effect superior to either intervention

implemented in isolation. When a patient engages in structured spiritual chanting while maintaining slow, paced breathing, they experience a state of deep somatic and psychological relaxation. This state quiets racing thoughts, reduces muscle tension, and moderates emotional reactivity to chronic stressors. This multi-systemic intervention restores a sense of personal control, boosting the patient's self-efficacy and capacity for long-term adaptation in the face of chronic illness.

CONCLUSION

Based on the comprehensive data collection, programmatic implementation, and subsequent statistical analyses, several definitive conclusions can be drawn regarding the efficacy of the integrated intervention. First, the study demonstrates that the combined protocol of dhikr and deep breathing exercises (DBE) exerts a statistically significant positive effect on reducing stress levels among patients with Chronic Kidney Disease (CKD) at Syarifah Ambami Rato Ebhu Hospital, Bangkalan Regency. Second, a corresponding statistically significant effect was observed in the mitigation of clinical anxiety levels within the same patient cohort, indicating substantial psychological benefits.

Third, in terms of biological parameters, the intervention did not produce a statistically significant acute reduction in serum cortisol concentrations; however, the longitudinal tracking of descriptive data suggests that the combined dhikr and DBE protocol exhibits a favorable regulatory and homeostatic stabilizing effect, preventing the upward hypercortisolemic spikes seen in the control group. Finally, the overarching multivariate analysis confirms a highly significant simultaneous (multivariate omnibus) effect of combined dhikr and deep breathing exercises across the collective triad of stress, anxiety, and serum cortisol levels. Taken together, these findings confirm that while organic renal degeneration presents a rigid barrier to rapid endocrine shifts, this integrated behavioral intervention provides a powerful, multi-dimensional framework that successfully optimizes both the psychological and physiological coping capacities of CKD patients.

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