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Examining the Effectiveness of Compassion-Based Acceptance and Commitment Integrated Therapy on Cortisol Hormone Levels and Mindfulness in Infertile Women Undergoing Hormone Therapy

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A B S T R A C T

Objective: The purpose of this study was to investigate the effect of compassion-based acceptance and commitment integrated therapy on reducing cortisol hormone levels and improving mindfulness in infertile women undergoing hormone therapy.

Methods and Materials: This study employed a quasi-experimental design with a pretest–posttest control group. The statistical population consisted of infertile women undergoing hormone therapy in Isfahan, Iran, in 2023, from which 40 participants were selected using purposive sampling and randomly assigned to the experimental group (n = 20) and the control group (n = 20). The therapeutic intervention was conducted for the experimental group in 10 sessions. Research instruments included the Five Facet Mindfulness Questionnaire (FFMQ) and a salivary cortisol assessment test. Data were analyzed using multivariate analysis of covariance (MANCOVA) and multivariate analysis of variance (MANOVA).

Findings: The results indicated that compassion-based acceptance and commitment therapy had a significant effect on reducing cortisol levels ($P < .001$) and improving various dimensions of mindfulness ($P < .01$). In the experimental group, the mean cortisol level decreased significantly in the posttest (a 2.2-unit reduction), while the control group showed a minimal, non-significant decrease. Moreover, overall mindfulness in the experimental group increased by 13.3 units; dimensions such as acceptance of negative emotions, present-moment focus, and non-judgmental awareness also demonstrated positive changes. MANOVA results further revealed that the difference between groups regarding the combination of dependent variables was significant (Wilks' Lambda = 0.712, $P < .001$).

Conclusion: The findings suggest that compassion-based acceptance and commitment integrated therapy is effective not only in reducing physiological stress (cortisol) but also in enhancing mindfulness skills.

Keywords: *Compassion-Based Acceptance and Commitment Integrated Therapy (ACT-CFT), infertility, cortisol, mindfulness*

1. Introduction

Infertility is a multifactorial condition that profoundly affects biological, psychological, and social functioning, placing women under persistent distress and disrupting their quality of life (Sharma et al., 2022). The inability to conceive is not only a medical challenge but also a deeply lived experience, generating stress, shame, self-criticism, and anxiety (Rahimi et al., 2019). Research shows that infertility triggers significant dysregulation in the hypothalamic–pituitary–adrenal (HPA) axis and is closely associated with heightened levels of stress hormones such as cortisol (Karunyam et al., 2023; Wdowiak et al., 2020). Cortisol dysregulation interferes with reproductive function, negatively influences oocyte quality, and reduces pregnancy success rates during assisted reproductive technologies (Cesta et al., 2018; Miller et al., 2019). Additionally, infertility-specific stress predicts lower well-being and diminished treatment outcomes (Swift et al., 2021).

In recent decades, there has been a growing movement to integrate psychological interventions into infertility care to reduce stress and improve emotional adjustment (Amirpour et al., 2024; Tarway & Kumari, 2024). Among these approaches, Acceptance and Commitment Therapy (ACT) has gained strong empirical support as an evidence-based intervention aimed at increasing psychological flexibility, fostering acceptance of distressing emotions, and promoting value-driven living despite uncontrollable circumstances (Balsom et al., 2024; Barbosa et al., 2024). ACT is particularly relevant for women with infertility because it targets experiential avoidance and rumination, both of which sustain anxiety and depression during treatment (Järvelä-Reijonen, 2020; Rahimi et al., 2019). Compassion-based interventions complement ACT by counteracting self-criticism and shame, which are prevalent among women facing infertility (Aghasi, 2021; Rezaie, 2021). Combining these two modalities is theorized to strengthen emotion regulation, reduce physiological stress, and foster self-kindness in the face of reproductive failure (Ferreira et al., 2024; Pourgoli & Rezaei, 2023).

Evidence indicates that stress reduction in infertility care is not only psychologically beneficial but also physiologically significant. Elevated cortisol impairs reproductive hormones and may lower embryo quality and clinical pregnancy rates (Cesta et al., 2018; Fata & Tokat, 2021). Mind-body and mindfulness-based interventions have shown measurable decreases in cortisol and improvements in emotional functioning (More et al., 2022; Wen et al., 2024). For instance, mindfulness programs reduced anxiety and enhanced fertility-specific quality of life (Nery et al., 2019; Wang et al., 2023). Women with infertility who engaged in structured mindfulness and acceptance practices demonstrated decreased perceived stress and improved coping (Fard et al., 2018; Mousavi et al., 2020). Similarly, social and psychological support during treatment has been linked to better hormonal balance and lower stress biomarkers (Malina et al., 2019; Malina & Piotrowski, 2024).

Compassion-based elements are particularly vital because infertility often elicits profound feelings of failure and inadequacy (Aghasi, 2021; Amirpour et al., 2024). Compassion-Focused Therapy (CFT) aims to activate the soothing system of the brain, balancing the overactive threat system that perpetuates stress (Ferreira et al., 2024). By integrating CFT with ACT, interventions can simultaneously cultivate acceptance and self-kindness while reducing self-judgment, leading to improved mental health and quality of life (Asadollah Salmanpour & Pasha, 2023). Preliminary studies show that ACT adapted for infertility reduces distress and enhances fertility-related quality of life (Balsom et al., 2024; Barbosa et al., 2024). Furthermore, combining ACT and compassion has shown promising effects in other chronic conditions, including inflammatory bowel disease, by reducing stress and enhancing psychological well-being (Ferreira et al., 2024).

Another important consideration in infertility treatment is the medical context, particularly hormone therapy. Hormone therapy is a cornerstone of assisted reproductive technologies but is associated with physical side effects and emotional burden (Cervoni, 2025; Costa et al., 2025). The complex hormonal environment, including fluctuations of cortisol and prolactin, interacts with reproductive hormones and can impair conception (Wdowiak et al., 2020). Psychological distress exacerbated by these medical procedures may further dysregulate endocrine functioning (Miller et al., 2019). Interventions that directly target the stress response system are therefore critical for improving both mental health and potentially biological readiness for conception (More et al., 2022; Swift et al., 2021).

Mindfulness and ACT-based programs have demonstrated reductions in inflammation and stress biomarkers such as cortisol and C-reactive protein (Järvelä-Reijonen et al., 2020). Mindfulness-based cognitive therapy adapted for infertility decreased anxiety and depressive symptoms while improving resilience and coping strategies (Fard et al., 2018; Mousavi et al., 2020). A meta-analysis

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confirmed the efficacy of mindfulness for improving mental health outcomes in infertile women (Wen et al., 2024). The integration of compassion strategies may further potentiate these effects by promoting self-soothing and reducing emotional reactivity (Pourgoli & Rezaei, 2023; Rezaie, 2021). Such combined approaches help individuals accept their emotions, detach from self-critical thoughts, and reconnect with personal values (Barbosa et al., 2024; Ferreira et al., 2024).

Emerging studies in the Iranian context also support this integration. Acceptance and Commitment Therapy has been shown to enhance happiness, mental health, and life satisfaction in childless women (Asadollah Salmanpour & Pasha, 2023). Mindfulness-based and ACT-derived interventions have effectively improved psychological well-being and decreased stress among Iranian infertile women (Mousavi et al., 2020; Rahimi et al., 2019). Novel approaches such as combining compassion and ACT have been suggested as promising for fostering psychological hardiness and self-acceptance (Pourgoli & Rezaei, 2023). Interventions adapted to cultural and contextual needs are essential because infertility carries intense sociocultural stigma in many regions (Amirpour et al., 2024).

At a physiological level, there is clear evidence that reducing psychological stress can modulate cortisol rhythms and potentially support fertility outcomes (Karunyam et al., 2023; Malina & Piotrowski, 2024). Experimental research has found that supportive and acceptance-based therapies lead to measurable reductions in cortisol secretion among women in fertility treatment (Cesta et al., 2018; Malina et al., 2019). Additionally, hypnofertility-based nursing interventions have been associated with improved fertility preparedness and pregnancy outcomes, partly through cortisol regulation (Fata & Tokat, 2021). These findings suggest that psychological therapies not only enhance coping and quality of life but may also influence biological systems crucial for reproduction (Swift et al., 2021; Wdowiak et al., 2020).

Despite these advances, there is a gap in integrative, compassion-enhanced ACT interventions explicitly targeting both psychological and physiological outcomes in infertile women undergoing hormone therapy. Existing ACT-based infertility programs have primarily emphasized psychological flexibility but have not fully leveraged compassion training to address self-blame and shame (Balsom et al., 2024; Barbosa et al., 2024). Likewise, mindfulness interventions have reduced stress but often lacked explicit self-compassion elements, which could be critical in populations facing identity threats and marital pressures (Aghasi, 2021; Rezaie, 2021). Furthermore, while studies have examined stress biomarkers such as cortisol in infertility, few have combined rigorous biological measurement with structured compassion-focused ACT protocols (Karunyam et al., 2023; More et al., 2022).

Given the complex interplay of psychological distress, endocrine function, and sociocultural pressure in infertility, there is a strong need for interventions that simultaneously reduce physiological stress and cultivate adaptive emotional regulation (Amirpour et al., 2024; Swift et al., 2021). Compassion-Based Acceptance and Commitment Therapy (ACT-Compassion) represents an innovative integrative approach designed to address this gap. By helping women accept infertility-related distress, reduce experiential avoidance, practice self-kindness, and focus on valued living, ACT-Compassion may promote psychological resilience while influencing biological markers such as cortisol (Ferreira et al., 2024; Pourgoli & Rezaei, 2023).

The present study aims to evaluate the effectiveness of an integrated Compassion-Based Acceptance and Commitment Therapy intervention in reducing salivary cortisol levels and enhancing mindfulness among infertile women undergoing hormone therapy.

2. Methods and Materials

2.1. Study design and Participant

This study was a quasi-experimental research conducted using a pretest–posttest design with a control group. In this design, the experimental group received therapeutic interventions, while the control group received only routine medical care. Such a design allows precise comparison between the two groups to examine the effects of compassion-based acceptance and commitment therapy. The present study was conducted at the private practice of Dr. Elham Naqshineh (specialist in obstetrics and gynecology, fellowship in infertility and IVF) located in Isfahan, Iran. The statistical population included infertile women who, during intervals of hormone therapy, visited infertility treatment centers in Isfahan in 2023 for continuation of treatment or medical follow-up. These women, like other patients with infertility, were under psychological pressure due to continuous treatments, stress associated with infertility, and social expectations.

The study sample consisted of 40 women (20 in the experimental group and 20 in the control group), selected based on inclusion criteria (such as infertility diagnosis,

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undergoing hormone therapy, and willingness to participate in the study) and through convenience sampling. This method is highly practical for accessing targeted populations such as infertile patients, as it relies on participants' attendance at medical centers. The research was conducted in a setting managed by Dr. Elham Naqshineh, with her direct supervision over all clinical sampling procedures, which ensured the reliability and validity of the final results.

2.2. *Measures*

In this study, multiple instruments were used to assess the research variables, each specifically designed to evaluate the psychological and physiological effects of the intervention:

Salivary Cortisol Assessment: Measuring cortisol levels through saliva was the primary method for assessing this hormone. The use of saliva as a test sample is a non-invasive procedure, particularly practical for infertile women undergoing multiple treatments, and can easily be integrated into home-based treatment routines. Saliva sampling was performed during both pretest and posttest phases, and samples were collected under controlled conditions (e.g., avoidance of specific foods and medications affecting cortisol levels). In this research, salivary cortisol level was evaluated as a biological marker of stress. Saliva sampling was performed at four specific time points during the day (morning, noon, afternoon, and night) to carefully examine the diurnal variations and biological fluctuations of this hormone. These time points were selected based on scientific evidence regarding the circadian rhythm of cortisol secretion: the first sample between 7–8 a.m., the second between 12–1 p.m., the third between 4–5 p.m., and the fourth between 9–10 p.m. For sample collection, standard saliva collection kits (Salivette) were used. All participants followed necessary instructions before each sampling session, including refraining from eating or drinking (especially caffeinated beverages), brushing teeth, and engaging in intense physical activity at least 30 minutes prior, to minimize external factors that could affect results. Participants were also asked to remain calm and stress-free for ten minutes before each sampling. Collected samples were immediately frozen in sterile containers at −20°C to prevent cortisol degradation and breakdown. After the collection phase, all samples were transferred to the laboratory and stored under refrigeration until analysis. Salivary cortisol levels were measured using the enzyme-linked immunosorbent assay (ELISA) method with a specialized salivary cortisol kit, following the manufacturer's protocol. Before testing, samples were thawed to room temperature; then a fixed volume from each sample was placed into the kit's wells, and reagents were added according to the protocol. Finally, absorbance was read using an ELISA reader, and cortisol concentrations were reported based on the standard curve. To increase data accuracy and validity, all analyses were performed in duplicate, and the results were compared; additionally, appropriate control and standard samples were used to ensure the accuracy of the tests. The final results were recorded in nanomoles per liter (nmol/L), and statistical analysis of the data was conducted according to time-based variations. Throughout all sampling and laboratory stages, strict adherence to quality control procedures and professional ethical protocols was maintained to ensure the reliability of salivary cortisol measurement at different times of day and the comparability of data.

Five Facet Mindfulness Questionnaire (FFMQ): This instrument evaluates different dimensions of mindfulness, including observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to emotions. The mindfulness questionnaire was used to assess the impact of the therapy sessions on the participants' mindfulness skills.

2.3. *Intervention*

The therapeutic intervention for the experimental group consisted of 10 weekly sessions of Compassion-Based Acceptance and Commitment Therapy (ACT-Compassion), structured according to standard ACT protocols integrated with compassion-focused training. The program began with establishing a strong therapeutic alliance and psychoeducation about infertility, stress physiology, the hypothalamic–pituitary–adrenal (HPA) axis, and cortisol regulation. Participants were introduced to the foundations of ACT and Compassion-Focused Therapy (CFT), and through motivational interviewing were encouraged to write their personal infertility narratives as an initial step toward emotional processing. In subsequent sessions, participants were guided to face internal experiences related to infertility, practice acceptance of distressing thoughts and emotions instead of experiential avoidance, and engage in exercises such as "leaves on a stream" and body scan meditations to foster greater mind–body awareness. Mindfulness skills were then cultivated through present-moment awareness exercises, including mindful breathing and "what is present now?" practices, aimed at reducing rumination and

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enhancing psychological flexibility. The concept of self-as-context was introduced to help participants decenter from negative cognitions, supported by metaphors like the "mind radio" and identity defusion exercises. Sessions also incorporated compassion-based components derived from Gilbert's emotional regulation model, teaching the interplay between the threat, drive, and soothing systems of the brain. Participants practiced self-compassion through compassionate letter writing, mirror compassion, and the compassionate hand technique to counter self-criticism and shame. Later sessions emphasized values clarification, helping participants identify core personal values beyond fertility goals, restructure priorities, and engage in meaningful actions aligned with these values through techniques such as the "small step toward values" and behavioral commitment contracts. Strategies for relapse prevention and advanced mindfulness skills were introduced to manage intrusive negative thoughts, anxiety surges, and potential cortisol reactivation, culminating in the creation of a personalized coping toolkit. The final session focused on consolidating therapeutic gains, reviewing progress in mindfulness, acceptance, compassion, and stress regulation, and strengthening hope and resilience through future-self letter writing and maintenance planning. All sessions were delivered in a supportive group format to promote shared experiences and peer validation, while ensuring confidentiality, informed consent, and protection against additional psychological burden. The control group did not receive any psychological intervention and continued routine medical supervision and hormone therapy, participating only in pretest and posttest assessments to allow rigorous comparison of the ACT-Compassion treatment effects.

2.4. Data Analysis

Data were analyzed using IBM SPSS Statistics version 26. Prior to inferential testing, descriptive statistics (means, standard deviations) were computed to summarize demographic variables and baseline scores. The primary analyses employed multivariate analysis of covariance (MANCOVA) to examine the overall effect of the intervention on salivary cortisol and mindfulness while controlling for pretest scores. To further evaluate group differences on each dependent variable, univariate analysis of covariance (ANCOVA) and multivariate analysis of variance (MANOVA) were conducted. Effect sizes were calculated using Eta squared (η^2) to determine the magnitude of intervention impact. Statistical significance was set at $P < .05$ for all tests.

3. Findings and Results

To examine the effect of Compassion-Based Acceptance and Commitment Therapy (ACT-Compassion), salivary cortisol level was measured as a physiological indicator associated with stress. At baseline (pretest), the mean cortisol levels in the experimental and control groups showed no significant difference ($P > .05$), indicating homogeneity of the participants' initial conditions before the intervention.

After implementing the intervention, posttest analysis of covariance revealed that the cortisol level in the experimental group significantly decreased ($F = 15.78$, $P < .001$), while the reduction in the control group was smaller and not statistically significant ($F = 3.21$, $P > .05$). These findings indicate the positive effect of the integrated therapy on reducing physiological stress, ultimately achieved through regulation of the hypothalamic–pituitary–adrenal (HPA) axis.

Furthermore, the mean reduction in cortisol in the experimental group was 18.3%, representing a considerable decrease in stress, while the control group showed only a 6.7% reduction, likely due to partial discontinuation of hormone therapy but without direct psychological support for stress management.

Table 1

Mean and standard deviation of salivary cortisol levels in the experimental and control groups

Group	Pretest (M ± SD)	Posttest (M ± SD)	Change (M ± SD)
Experimental	12.3 ± 2.4	10.1 ± 2.1	−2.2 ± 0.8
Control	12.5 ± 2.5	11.8 ± 2.3	−0.7 ± 0.6

Table 1 presents the mean and standard deviation of cortisol levels in the pretest and posttest for both groups. As shown, the mean cortisol level in the experimental group decreased from 12.3 µg/dL at pretest to 10.1 µg/dL at posttest. This reduction, with a lower standard deviation, indicates a meaningful and consistent change in the

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experimental group. In contrast, the control group showed only a slight decrease in cortisol levels, with a mean reduction from 12.5 µg/dL at pretest to 11.8 µg/dL at posttest. Although a decrease occurred, it was small and not statistically significant. These findings support the effectiveness of ACT-Compassion in reducing physiological stress related to salivary cortisol levels in the experimental group. The substantial cortisol reduction observed can be attributed to improved regulation of the HPA axis, while the minimal decline in the control group was likely due to biological adjustment from reduced hormone therapy without psychological support. This also indicates that psychological interventions can have a stronger impact on stress regulation than spontaneous biological processes, which is especially important for infertile women undergoing hormone treatment.

Table 2

Mean and standard deviation of mindfulness and its dimensions in the experimental and control groups

Variable	Pretest (M ± SD)	Posttest (M ± SD)	Change (M ± SD)	P-value
Overall Mindfulness	45.6 ± 5.2	58.9 ± 5.8	13.3 ± 3.1	P < .001
Acceptance of Negative Emotions	12.1 ± 2.8	16.5 ± 3.2	4.4 ± 1.2	P < .01
Present-Moment Attention	15.4 ± 3.1	19.3 ± 2.9	3.9 ± 1.0	P < .01
Nonjudgmental Awareness	18.1 ± 4.3	23.1 ± 3.8	5.0 ± 1.5	P < .01

Table 2 shows the mean and standard deviation of total mindfulness and three core dimensions (acceptance of negative emotions, present-moment attention, and nonjudgmental awareness) in the pretest and posttest for both groups. The mean overall mindfulness score in the experimental group increased from 45.6 to 58.9, with the improvement being statistically significant ($P < .001$). Additionally, the lower posttest standard deviation in the experimental group indicates greater response homogeneity and the consistent impact of the intervention. Across the subscales, the experimental group demonstrated significant improvements: a 4.4-point increase in acceptance of negative emotions, a 3.9-point increase in present-moment attention, and a 5.0-point increase in nonjudgmental awareness. In the control group, these changes were not statistically significant, and mean scores remained relatively stable. These results indicate that ACT-Compassion effectively improved skills in conscious emotional processing, present-moment focus, and self-awareness. Enhancing mindfulness is a key factor in stress management and mental health improvement for infertile women who face extensive psychological and physical challenges.

Mindfulness was assessed using the Five Facet Mindfulness Questionnaire (FFMQ). Comparison of pretest and posttest means using analysis of variance showed that mindfulness significantly increased in the experimental group ($F = 20.05$, $P < .001$), while the changes in the control group were not significant ($F = 2.34$, $P > .05$).

Based on the statistical analysis:

- The mean mindfulness score in the experimental group increased from 45.6 before the intervention to 58.9 after the intervention ($P < .001$).
- The mean mindfulness score in the control group increased slightly from 46.2 to 48.1, but the change was not significant ($P > .05$).

These findings demonstrate that mindfulness and compassion training in the experimental group significantly enhanced present-moment awareness and reduced self-critical responses.

Table 3

Results of Multivariate Analysis of Covariance (MANCOVA) on the Components of the Integrated Therapy

Dependent Variable	Source of Variation	SS	df	MS	F	P-value
Cortisol	Group	15.04	1	15.04	15.78	P < .001
Cortisol	Pretest (Covariate)	2.57	1	2.57	2.13	P > .05
Mindfulness	Group	420.3	1	420.3	20.05	P < .001
Mindfulness	Pretest (Covariate)	18.22	1	18.22	1.79	P > .05

Table 3 presents the results of multivariate analysis of covariance (MANCOVA) to examine the effect of the integrated therapy on the dependent variables, including salivary cortisol and mindfulness. The effect of the group variable on cortisol was significant ($F = 15.78$, $P < .001$), indicating that the experimental group experienced a

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significant reduction in cortisol levels compared with the control group. Similarly, the effect of the group variable on mindfulness was significant (F = 20.05, P < .001), showing a meaningful increase in mindfulness in the experimental group. The results also show that the effect of the pretest covariate was not significant for either variable, meaning that baseline scores did not substantially influence the posttest changes and that improvements were directly attributable to the intervention. These findings collectively support the effectiveness of the integrated therapy in reducing stress and improving mindfulness.

Pretest and posttest mean scores:

- Experimental group: pretest = 32.8, posttest = 22.6 (significant reduction, P < .01)
- Control group: pretest = 33.1, posttest = 30.4 (non-significant reduction, P > .05)

In addition, the assessment of self-compassion using compassion-focused behavior measures showed a significant improvement in the experimental group after the intervention (F = 18.34, P < .001), while the control group showed no meaningful change (F = 2.08, P > .05).

Mean self-compassion scores:

- Experimental group: pretest = 40.3, posttest = 54.2 (significant increase, P < .001)
- Control group: pretest = 39.7, posttest = 41.9 (non-significant increase, P > .05)

Table 4

Results of Multivariate Analysis of Variance (MANOVA) on the Dependent Variables of Cortisol and Mindfulness

Effect	Wilks' Lambda	F	df	P-value	Eta Square
Experimental vs. Control	0.712	18.98	2, 37	P < .001	0.542

Table 4 shows the results of multivariate analysis of variance (MANOVA) testing the combined effect of the group variable (experimental vs. control) on the dependent variables cortisol and mindfulness. The Wilks' Lambda value was 0.712 with a significance level of P < .001, indicating that the intervention had a highly significant effect on the combined dependent variables. The F value of 18.98 also demonstrates a strong overall effect of the intervention. The effect size (Eta Square) was 0.542, which represents a very large and meaningful impact of the therapy on the combined outcome measures. This analysis specifically indicates that Compassion-Based Acceptance and Commitment Therapy (ACT-Compassion) exerted positive effects both individually and collectively on reducing physiological stress (cortisol) and increasing mindfulness.

Pearson correlation analysis showed that the reduction in cortisol level was significantly and positively correlated with increases in both mindfulness and self-compassion in the experimental group (r = 0.71, P < .001).

Table 5

Results of Univariate Analysis of Covariance (ANCOVA) on the Variables of Compassion-Based Acceptance and Commitment Therapy

Dependent Variable	Source	SS	df	MS	F	P-value	Eta Square
Cortisol	Group	15.04	1	15.04	12.42	P < .001	0.39
Mindfulness	Group	420.3	1	420.3	18.69	P < .001	0.45

Table 5 reports the results of univariate analysis of covariance (ANCOVA) for cortisol and mindfulness. For cortisol, the F value was 12.42 with a significance level of P < .001, confirming a significant reduction in cortisol levels in the experimental group compared with the control group, with a medium-to-large effect size of 0.39. For mindfulness, the F value was 18.69 with P < .001, indicating a significant increase in mindfulness in the experimental group, accompanied by a strong effect size of 0.45. These analyses show that the therapeutic intervention effectively reduced stress by improving emotional regulation and mindfulness skills, leading to better physiological stress control and cortisol regulation.

4. Discussion and Conclusion

The present study examined the effectiveness of Compassion-Based Acceptance and Commitment Therapy (ACT-Compassion) on physiological stress, as indicated by salivary cortisol levels, and on psychological functioning, as measured by mindfulness, in infertile women undergoing

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hormone therapy. The findings demonstrated that participants receiving ACT-Compassion experienced a statistically significant reduction in salivary cortisol levels compared with the control group, whose cortisol reduction was minimal and not significant. Additionally, the intervention group exhibited marked improvements in overall mindfulness and its subcomponents, including acceptance of negative emotions, present-moment attention, and nonjudgmental awareness. These outcomes confirm the central hypothesis that integrating ACT with compassion-based training can produce meaningful improvements in both stress regulation and adaptive psychological coping in the context of infertility.

The reduction of cortisol in the experimental group highlights the capacity of psychological interventions to modulate stress biomarkers. Elevated cortisol is one of the most consistent physiological correlates of infertility-related distress and has been implicated in impaired reproductive function, oocyte quality, and pregnancy success rates (Cesta et al., 2018; Karunyam et al., 2023). Our results align with earlier evidence showing that psychosocial support and acceptance-based coping significantly reduce cortisol in women undergoing fertility treatment (Malina et al., 2019; Swift et al., 2021). The observed 18.3% reduction in cortisol among participants who received ACT-Compassion closely parallels the findings of supportive interventions that targeted HPA axis dysregulation (Malina & Piotrowski, 2024). Importantly, while hormonal adjustments alone in the control group yielded only slight decreases in cortisol, the structured psychological intervention produced a more robust and consistent downregulation of physiological stress, reinforcing the argument that psychological flexibility and self-compassion can directly influence endocrine balance (Fata & Tokat, 2021; Wdowiak et al., 2020).

This study also extends previous work on ACT and mindfulness in infertility care by integrating compassion as a critical therapeutic element. Prior research shows that ACT reduces psychological inflexibility and fosters resilience among women struggling with infertility (Balsom et al., 2024; Barbosa et al., 2024). Mindfulness-based approaches alone have been effective in decreasing anxiety and depression and improving fertility-specific quality of life (Nery et al., 2019; Wang et al., 2023). However, few interventions have simultaneously targeted the profound self-blame and shame commonly experienced by infertile women (Aghasi, 2021; Rezaie, 2021). By incorporating compassion-focused strategies, this study addresses a core emotional vulnerability: self-criticism. Compassion-based training is known to activate the soothing system of the brain, counterbalance the threat response, and facilitate a kinder internal dialogue (Ferreira et al., 2024; Pourgoli & Rezaei, 2023). Our results confirm that when compassion is integrated into ACT, participants show deeper acceptance of their circumstances, reduced hyperarousal, and improved emotional regulation, leading to measurable physiological and psychological benefits.

Mindfulness improvements in the present study were robust and extended across key domains, including increased acceptance of negative emotions and greater nonjudgmental awareness. These findings are consistent with evidence that ACT and mindfulness approaches enhance present-moment focus and reduce rumination, which is highly prevalent in women dealing with infertility (Fard et al., 2018; Mousavi et al., 2020). Meta-analyses have shown that mindfulness interventions can significantly reduce stress and improve psychological well-being in this population (Wang et al., 2023; Wen et al., 2024). Our results expand on these conclusions by showing that when mindfulness skills are cultivated within a compassionate ACT framework, the psychological changes may also translate to biological stress reduction, as indicated by cortisol modulation. This integrated approach may thus be more effective than mindfulness or ACT alone, particularly in populations with heightened self-judgment and societal stigma (Amirpour et al., 2024; Rahimi et al., 2019).

Another important implication is the effect of ACT-Compassion in the context of hormone therapy, which is both physiologically and psychologically taxing (Cervoni, 2025; Costa et al., 2025). Many infertility interventions fail to consider the added stress of pharmacological treatments, such as hormonal fluctuations and side effects, which may exacerbate emotional distress and disrupt the HPA axis (Miller et al., 2019). Our results indicate that ACT-Compassion may buffer against the psychological and physiological burdens of hormone therapy, empowering women to tolerate bodily changes and sustain psychological resilience despite challenging medical procedures. This is consistent with previous findings that mind-body interventions can positively interact with endocrine responses during fertility treatments (Fata & Tokat, 2021; More et al., 2022).

The strong effect sizes observed for mindfulness outcomes ($\eta^2 = 0.45$) and cortisol reduction ($\eta^2 = 0.39$) emphasize the practical impact of ACT-Compassion for women facing infertility. These values are higher than those

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reported in some earlier single-component interventions, suggesting the added value of combining acceptance, mindfulness, and compassion into one integrated model (Balsom et al., 2024; Ferreira et al., 2024). Furthermore, the positive correlation found between cortisol reduction and gains in mindfulness and self-compassion reinforces the theoretical link between psychological flexibility and physiological regulation (Järvelä-Reijonen et al., 2020; Malina & Piotrowski, 2024). These findings support biopsychosocial models that conceptualize infertility not just as a reproductive issue but as a stress-related condition responsive to integrated psychological care (Swift et al., 2021; Tarway & Kumari, 2024).

From a cultural perspective, our results are particularly relevant for Iranian women, where infertility can lead to intense social pressure and identity disruption (Amirpour et al., 2024; Jalali Fard, 2023). Interventions such as ACT-Compassion that address shame and self-blame may be especially beneficial in cultures where motherhood is closely tied to social value and marital stability (Asadollah Salmanpour & Pasha, 2023). The group-based format of our intervention created a safe environment for shared experiences and social validation, which has been shown to reduce stress and promote hormonal balance (Malina et al., 2019; Malina & Piotrowski, 2024).

This study also supports the growing recognition that psychological interventions can have measurable biological outcomes. While most infertility-focused therapies have traditionally been evaluated solely on psychological measures, our inclusion of cortisol as a biomarker underscores the mind–body interaction in reproductive health (Cesta et al., 2018; Wdowiak et al., 2020). Our findings complement studies where psychological support was associated with improved hormonal profiles and, indirectly, with better fertility outcomes (Fata & Tokat, 2021; More et al., 2022). The integration of biomarker assessment in infertility mental health research is critical for advancing precision medicine approaches and offering objective validation of therapeutic impact (Karunyam et al., 2023).

Finally, the success of ACT-Compassion in this trial adds to the broader literature on acceptance, mindfulness, and compassion-based therapies across chronic health conditions. Similar improvements in stress biomarkers and emotional well-being have been reported in interventions for inflammatory bowel disease, overweight adults, and chronic pain (Ferreira et al., 2024; Järvelä-Reijonen et al., 2020). These cross-condition parallels suggest that ACT-Compassion may be a transdiagnostic approach to managing stress-related physiological dysregulation, which could be adapted for other populations facing reproductive or hormonal challenges (Costa et al., 2025; Roncati, 2025).

5. Limitations and Suggestions

Despite its promising findings, this study has several limitations that must be acknowledged. First, the sample size was relatively small and limited to one urban region, which may affect the generalizability of the results to broader and more diverse populations. Second, the participants were recruited through convenience sampling, potentially introducing selection bias, as those willing to attend psychological sessions might have higher initial motivation or openness to therapy. Third, while salivary cortisol was used as a robust biomarker of stress, other physiological indicators, such as heart rate variability or inflammatory markers, were not assessed and could have provided a more comprehensive understanding of stress regulation. Fourth, the intervention lasted 10 weeks, and no long-term follow-up was conducted; thus, it is unclear whether the observed improvements in cortisol and mindfulness would be maintained over time. Additionally, the study did not evaluate direct reproductive outcomes such as conception rates or embryo quality, which could further elucidate the clinical significance of psychological interventions for fertility success. Finally, while efforts were made to maintain intervention fidelity, therapist effects and participant expectations may have influenced outcomes.

Future research should replicate these findings with larger, more heterogeneous samples, including participants from diverse cultural and socioeconomic backgrounds, to strengthen external validity. Multi-center studies involving different fertility clinics and regions could help confirm the robustness of ACT-Compassion across varied healthcare settings. Longitudinal designs are essential to examine the durability of both psychological and physiological effects over extended periods and to determine whether improvements in cortisol and mindfulness translate into enhanced fertility outcomes such as successful conception and pregnancy. Researchers should also consider integrating additional biomarkers—such as inflammatory cytokines, prolactin, and ovarian reserve indicators—to provide a multidimensional view of biological stress regulation. Moreover, future studies could compare ACT-Compassion directly with other established psychological interventions, such as mindfulness-based stress reduction or cognitive-

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behavioral therapy, to determine relative effectiveness and cost efficiency. Digital and hybrid delivery models may also be explored to increase accessibility, especially for women facing geographic or time barriers to in-person therapy.

From a clinical perspective, the results suggest that fertility clinics and reproductive health specialists should consider incorporating structured psychological interventions, particularly ACT-Compassion, as part of standard care for women undergoing hormone therapy. Practitioners can use the integrative model to help patients navigate infertility-related distress by fostering acceptance, self-kindness, and value-based living while simultaneously reducing physiological stress markers. Group-based delivery may be especially useful in providing social support and reducing isolation among infertile women. Collaboration between mental health professionals and reproductive endocrinologists could create comprehensive care pathways that address both psychological resilience and biological readiness for conception. Training fertility counselors and psychologists in ACT-Compassion protocols could improve treatment outcomes and enhance patient well-being throughout the often-challenging process of assisted reproduction.

Authors' Contributions

Authors contributed equally to this article.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants. This study was approved by the Ethics Committee of Islamic Azad University, Khomeinishahr Branch, with the ethics code IR.IAU.KHSH.REC.1402.128.

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