

Original Article

Effectiveness of Acceptance and Commitment Therapy on Physiological Measures in Patients with Type 2 Diabetes in Iran: A Systematic Review and Meta-Analysis

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Abstract

Background and Aim: This systematic review and meta-analysis summarized the studies that evaluated the effects of acceptance and commitment therapy on biological measures in Iranians with type 2 diabetes. In addition, the study determined the combined effect size of the varying effect sizes observed in various studies.

Materials and Methods: A systematic search of Iranian scientific databases, including insane.ir, Magiran, SID, Noormags, and ISC, from 2013 to 2023, retrieved randomized controlled trials that evaluated the effects of acceptance and commitment therapy on biological measures in type 2 diabetes. The study was conducted based on the main PRISMA reporting guideline (the PRISMA 2020 statement), and a meta-analysis report was generated by reviewing the studies that met the inclusion criteria.

Results: Among the 26 studies, 10 were deemed suitable for inclusion based on the PRISMA statement, while the remaining 16 were excluded. The effect size of acceptance and commitment therapy on the biological markers in type 2 diabetes was 0.767, indicating a significant effect. The average effect sizes for fasting blood glucose (FBS), 2-hour postprandial glucose (2HPP), and glycosylated hemoglobin (HbA1c) were 0.798, 0.586, and 0.711, respectively. These effect sizes suggest a significant effect for FBS, a relatively strong impact for 2HPP, and a strong effect for HbA1c.

Conclusion: Acceptance and commitment therapy significantly improve the biological measures of patients with type 2 diabetes. Furthermore, its impact on FBS and HbA1c indices exceeds that of HPP2.

Keywords: Acceptance, Commitment, Psychotherapy, Biomarkers, Type 2 diabetes, Glycosylated hemoglobin

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Introduction

Type 2 diabetes, classified as the main type of diabetes mellitus, is characterized by a gradual decline in metabolic function. This condition arises from a continuous elevation of blood glucose levels and accounts for 90% of all diabetes cases (1). The primary cause of T2D is the resistance of pancreatic beta cells to insulin, resulting in its deficiency. This resistance occurs when autoimmune attacks lead to the destruction of pancreatic beta cells (2). According to the International Diabetes Federation, the global prevalence of diabetes is concerning, affecting 10.5% of the population. It means that one in ten people worldwide is affected by diabetes. Even more concerning is the fact that nearly half of these individuals with diabetes, about 44.7%, are unaware of their condition (3). This lack of diagnosis can lead to severe and life-threatening complications in the long term, such as partial or complete blindness, kidney failure, heart disease, stroke, and lower limb amputations (1).

Type 2 diabetes is characterized by a combination of various risk factors, including behavioral and genetic. A sedentary lifestyle, which involves a poor diet, a lack of physical activity, and smoking, contributes significantly to its development. Additionally, genetic and environmental factors also have a significant impact on the onset of this condition (4). The signs and symptoms of type 2 Diabetes (T2D) encompass various indications such as frequent thirst, excessive hunger, overall fatigue, frequent urination, sudden weight loss, slow wound healing, and others. These manifestations may either be vaguely present or potentially absent (5). Currently, the confirmation of T2D in a clinical setting relies on blood glucose tests, including the Fasting Plasma Glucose (FPG), Oral Glucose Tolerance Test (OGTT), or glycosylated hemoglobin (HbA1c) test. These tests are prohibitively expensive and not affordable in resource-limited settings, particularly in low- and middle-income countries (6).

Regular health check-ups, including tests like FPG, OGTT, and HbA1c, along with routine examinations by doctors, provide the chance for early intervention and identification of risk factors for chronic ailments like type 2 diabetes (7). Even with medication, type 2

diabetes can reduce lifespan, impair the individual, and raise complications, underscoring the significance of psychosocial interventions (8).

Diabetes is a multifaceted and long-term condition that necessitates continuous medical attention involving diverse risk reduction approaches beyond simply managing blood sugar levels. Ongoing education and support for self-management in diabetes play a vital role in empowering individuals, averting sudden complications, and decreasing the likelihood of enduring complications (9). Cultivating constructive health habits and preserving mental well-being are fundamental for attaining diabetes management objectives and enhancing overall quality of life (10). Psychological therapies play a crucial role for individuals dealing with type 2 diabetes (11). A key therapy in this context is acceptance and commitment therapy (ACT), which combines acceptance and self-awareness techniques to modify behavior and address the challenges faced by those with chronic conditions (12,13). A primary objective of ACT is to enhance psychological flexibility (11).

ACT is one of the therapies that have gained popularity among therapists in recent years in the form of third-wave therapies and can be effective in the treatment of chronic patients. Instead of altering and changing one's cognitions, this treatment seeks to strengthen one's psychological connection with one's thoughts and feelings (14). ACT has a philosophical root in Relational Frame Theory (RFT) and has six central processes, including acceptance, diffusion, self-context, communication with the present, values, and committed actions that lead to greater individual flexibility (15). According to this theory, no thought, feeling, or memory is inherently problematic, dysfunctional, or incompatible, which is context-dependent (16). Clients choose those behavioral goals that are of most importance or value to them (15).

Acceptance and commitment therapy encourages individuals to accept and integrate into their life experiences to challenge emotional responses and to identify the controlling dimensions to which specific contextual situations apply. Acceptance and commitment therapy is influenced by functional contextualism, a practical philosophical situation that recognizes psychological events, including cognition, emotional responses, and behavior, which are

influenced by antecedents in a particular context (14). Acceptance and Commitment Therapy entails embracing or being open to facing pain, challenging situations, and difficulties without attempting to manage them and taking actions aligned with values and objectives. This involves choosing to act on personal aspirations rather than solely focusing on eradicating undesirable encounters (17).

The application of Acceptance and Commitment Therapy (ACT) has demonstrated positive outcomes in various diabetes-related issues, such as reducing glycated hemoglobin levels, enhancing self-care capabilities, and fostering illness acceptance in individuals with type 2 diabetes (8, 18). This study focuses on conducting a meta-analysis and systematic review of clinical trials to assess the impact of acceptance and commitment therapy on the biological aspects of diabetes. In this research, the articles whose therapeutic protocol was based on six central processes: acceptance, diffusion, self-context, and communication with the present, values, and committed action, were used. The primary aim of this research was to determine the effect size of acceptance and commitment therapy on the biological markers of patients with type 2 diabetes.

Methods

This systematic review and meta-analysis was conducted according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) (19). In this meta-analysis, effect sizes were calculated for each randomized controlled trial in the first step, standardized in a common matrix in the second step, and pooled in the final step to determine the average effect. Cohen (20) categorized effect sizes as small (0.0 to 0.2), medium (0.2 to 0.5), large (0.5 to 0.8), and very large (greater than 0.8). Due to the increasing prevalence of diabetes in recent years and the confirmation of the effect of ACT in various studies, the time from 2013 to 2023 was chosen for this study. The present study included clinical trials, regardless of the number of sessions, timing, and executors. Finally, the study comprised 26 studies conducted in Iran between March 21, 2013, and December 22, 2023, on the impact of acceptance and commitment therapy on biological measures in

patients with type 2 diabetes. This study is based on a research project approved by the Ethics Committee of Semnan University of Medical Sciences and Health Services on 11/3/2024 (ID: IR.SEMUMS.REC.1402.319). All procedures performed in this study were under the ethical standards of the institutional or national research committee and were consistent with the 1964 Helsinki Declaration and its later amendments or comparable.

Search strategy

A systematic search using Iranian scientific databases, including insane.ir, Magiran, SID, Noormags, and ISC, was performed to find the eligible studies. Language (only Persian language sources from Iranian databases) and time (time range between 2013 and 2023) restrictions were applied. Manual searches were based on reference lists of previously published scientific articles and meta-analyses. For the search purpose, MeSH (Medical Subject Heading) and non-MeSH keywords were used. The search terms focused on acceptance and commitment therapy (ACT), type 2 diabetes, biological measures, blood sugar control, fasting plasma glucose (FPG), oral glucose tolerance tests (OGTT), and glycosylated hemoglobin (HbA1c).

Eligibility criteria

The study's inclusion criteria encompassed randomized controlled trials focusing on the effectiveness of acceptance and commitment therapy in addressing biological aspects of type 2 diabetes in patients. The research design needed to be experimental or semi-experimental, with available mean and standard deviation data in assessment phases and using instruments with reliable psychometrics, valid scales, good sensitivity, and specificity. In addition, the studies needed to be published in Persian and conducted in Iran within the specified timeframe. Exclusion criteria involved descriptive, case, and qualitative studies, research presented in low-profile conferences or journals, repetitive studies without necessary statistical information, and studies lacking specificity regarding diabetes type in the diabetic samples.

Qualitative synthesis

A qualitative synthesis as an essential component of systematic reviews and a narrative and textual approach to summarize, analyze, and evaluate the selected articles before analyzing the quantitative data in a meta-

analysis was carried out by three competent experts. The qualitative composition in this study included the following: (1) a general summary of the characteristics and findings of the included studies was presented; (2) relationships between studies, patterns, and heterogeneity were explored, examined, and analyzed; (3) discussed the applicability of the selected collection of articles to the review question according to the Population, Intervention, Comparison, and Outcome (PICO) structure; (4) the use of qualitative findings in the meta-analysis was explained and the strength of its results was interpreted and analyzed; (5) strengths and weaknesses of the reviewed articles were critiqued as a whole, including a cumulative assessment of the risk of bias across studies; (6) any gap in the studies, such as insufficiently studied patient populations or different and inconsistent results were discussed; and finally (7) review findings were compared with current conventional wisdom.

Quality evaluation

A qualitative assessment of the inclusion of randomized controlled trials (RCTs) was carried out using Jadad's (1996) quality scale for randomized clinical trial reports (21). The highest possible score on the scale is 13, with articles scoring 9 or more considered good (22). In this review, articles were assessed by experts in health psychology, and the trials scoring 9 or more were included.

Study selection

In this current systematic review and meta-analysis, the selection process is progressed according to the PRISMA checklist. Out of the numerous available studies, only 15 articles met the inclusion criteria of research. The study followed the meta-analysis steps outlined by Howitt and Cramer (23): (1) identifying the subject and variables for the meta-analysis; (2) searching scientific databases; (3) reviewing and categorizing studies and variables; (4) calculating the effect size for variables in each study; (5) aggregating the effect size across studies; and (6) contrasting the effect sizes of studies with diverse characteristics and variables. At first, the retrieved references were merged, and redundant and unnecessary items were removed to facilitate the review process. Titles and

abstracts of all articles were evaluated independently by three reviewers and full texts of relevant articles were retrieved if eligible according to the criteria and then re-evaluated. Any disagreement between the reviewers was discussed and resolved by consensus. Finally, data were collected in a standard extraction format. The following information was extracted from each study: (1) author name(s) (reference); (2) publication year; (3) Intervention(s) and participants; (4) age range and/or mean; (5) sample size; (6) number of sessions; (7) number of cases and controls; (8) assessment tools; (9) outcome values. Figure 1 depicts the PRISMA 2020 flow diagram through the different phases of this systematic review and meta-analysis.

Out of 26 studies analyzed in Chart 1, 10 articles met the criteria for inclusion in this systematic review and meta-analysis following thorough scrutiny for duplicates and statistical accuracy.

Data synthesis and analysis

Data synthesis and analysis in this systematic review and meta-analysis were performed as follows: measurement of the unstandardized mean differences as the effect size calculated by the pooled estimate of weighted mean difference (WMD) with a 95% confidence interval and measurement of the fixed effects and random effects models according to heterogeneity levels.

Measuring the unstandardized mean differences as the effect size calculated by a pooled estimate of weighted mean difference (WMD) with a 95% confidence interval (CI) and the fixed effects and random effects models according to the level of heterogeneity. For effect size calculation, Cohen's effect size was computed based on the methodology established by Lakens's study (24). The effect size was calculated by subtracting the mean of the experimental group from the mean of the control group and then dividing it by the standard deviation of the composite scores. The mean and standard deviation values of both experimental and control groups were necessary for these computations, as outlined in the study. After calculating the effect size for each study, the average effect size was then estimated individually using the formula $d = \sum d_i / n$. $\sum d_i$ is equal to the sum of the effect sizes of all studies divided by the number of studies.

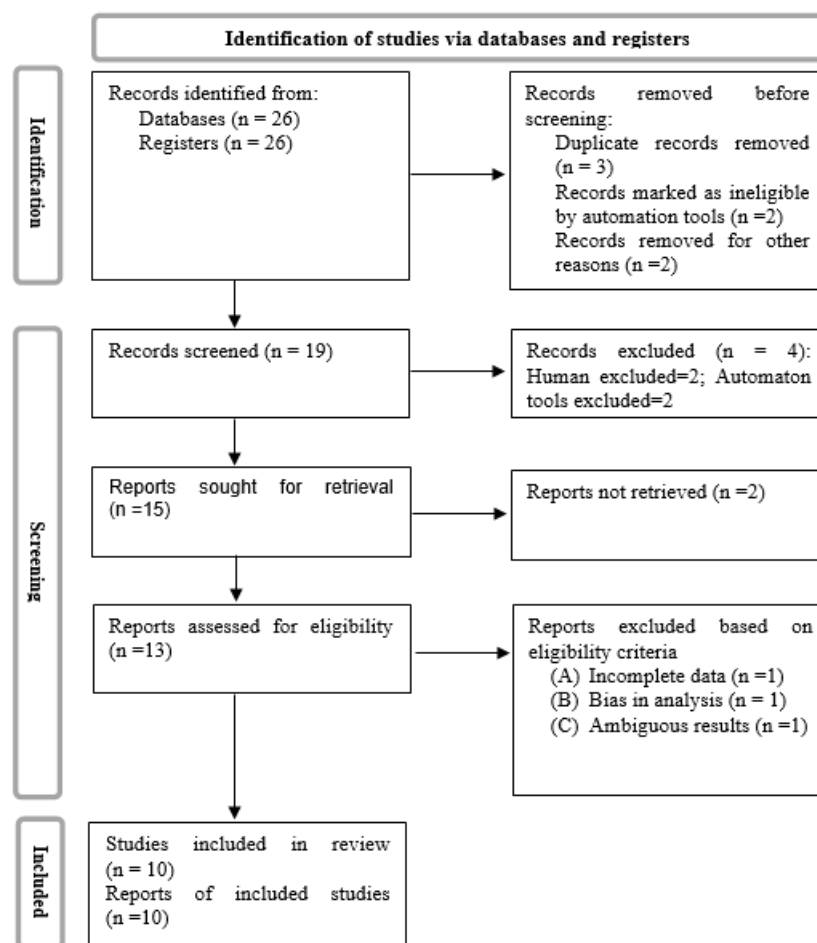


Figure 1. PRISMA 2020 flow diagram for systematic review and meta-analysis

Results

According to PRISMA, the results of the systematic review showed that during study selection, four studies out of all the reviewed studies were not eligible for screening and were not included in the meta-analysis because of incomplete data. In the systematic review, the characteristics necessary for the meta-analysis of the data, such as study size, sample size, and physiological measurements, were extracted for each study. The risk of bias in the trials was assessed, and data from three trials at risk of bias were initially excluded from the systematic review and meta-analysis. In the systematic review, the results of individual and case-based studies were assessed according to the strengths and weaknesses of each study, and summary data for each intervention, effect estimates, and confidence intervals were extracted and reported by qualitative assessment of the articles. A

systematic review synthesized the results of previous studies by presenting the results of each meta-analysis, including confidence intervals, measures of consistency, sensitivity, and subgroup analyses. Table 1 provides details of the studies reviewed, such as intervention(s) and participants, authors, year of publication, sample size, number of sessions, and outcome variables.

The risk of bias assessment for systematic reviews with meta-analysis of randomised controlled trials (RCTs) are presented in Figure 2. Table 2 presents the significance level, mean, and standard deviation of experimental and control groups, along with the effect size of each study and the overall average effect size. Absolute values were utilized to assess the effect size.

In Table 2, the effect size of individual variables and the effect size of each study has been computed. Furthermore, the overall effect size of the effectiveness

of acceptance and commitment therapy in this meta-analysis is 0.767, indicating a significant impact. Essentially, acceptance and commitment therapy proves highly effective in enhancing the physiological aspects of type 2 diabetes. For a more thorough

interpretation, the average effect size of the different biological measures was calculated separately, as shown in Table 3. Based on Table 3, acceptance and commitment therapy shows a strong effect on FBS ($d = 0.798$), HbA1c ($d = 0.711$), and an above-average effect on 2HPP ($d = 0.586$) in patients with type 2 diabetes.

Table 1. The studies included in the meta-analysis

Number of study	Intervention(s) and participants	Authors name(s)	Publication year	Sample size	Number of sessions	Outcomes
1	Acceptance and Commitment Group Therapy; Type II diabetes	Shayeghian, Amiri, Aguilar-Vafaie&Besharat (25)	2016	100	10	Glycosylated Hemoglobin (HbA1c)
2	Acceptance and Commitment Therapy; Type II diabetes	Rahimi, Aghayosefi&Abaspour (26)	2019	40	8	Biological Markers (2HPP, HbA1c, FBS)
3	Acceptance and Commitment Therapy; Women with type II diabetes	MohaddesShakouriGanjavi, Ahadi, Jomehri&Khalatbari (27)	2021	30	8	Fasting Plasma sugar
4	Group Acceptance and Commitment Therapy (GACT); Type II diabetes	Nasiri, Omid, Mozaffari, Mousavi &Joekar (28)	2020	60	8	HbA1c
5	Acceptance and Commitment Group Therapy; Group Intervention of Emotional Regulation; Type II diabetes	Eghrari, Bayazi&Rajayi (29)	2021	45	15	Glycosylated Hemoglobin (HbA1c)
6	Acceptance and Commitment Therapy Type II diabetes; Type II diabetes	Sadr-Hashemi, Asgari, Makvandi&Seraj-Khorami (30)	2021	60	9	Glycemic Control
7	Acceptance and Commitment Therapy; Stress Management Intervention; Type II diabetes	GhafarzadehAlmasi, Hajializadeh&Tajeri (31)	2021	45	15	Blood Sugar Control
8	Acceptance and Commitment Therapy; Mindfulness-Based Therapy; Type II diabetes	Hosseini, Ahadi, Hatami&Khalatbari (32)	2021	45	15	Blood Sugar levels
9	Acceptance and Commitment Therapy (ACT); Type II diabetes	Fanayi, Zare, Rahmanian &Safariniya (33)	2022	30	8	A1C
10	Acceptance and Commitment-Based Therapy; Type II diabetes	Ahmadi, Hamel, Zarinpeikar&RafieiGoligan (34)	2023	30	15	Glycosylated Hemoglobin

HbA1c, glycosylated hemoglobin; 2HPP, 2 hour postprandial glucose; FBS, fasting blood glucose

Table 2. Effect size of each study and their average

Number of study	Outcomes	Component	Experimental Group			Control Group			Effect size of each Outcome (d)	The average effect size of each study (d)	The average effect size of all studies
			N	M _E	S _E	N	M _c	S _c			
1	Glycosylated Hemoglobin	-	50	7.33	.935	50	7.63	.805	.344	.344	
2	Biological	FBS	20	166.605	41.475	20	195.95	43.845	.688		

	Measures	HbA1c	20	7.735	1.775	20	8.27	1.28	.346	.54	
		2HPP	20	208.725	44.015	20	235.025	45.755	.586		
3	Fasting Plasma sugar	-	15	143.37	16.78	15	166.65	18.77	1.28	1.28	
4	Glycosylated Haemoglobin	-	30	7	.325	30	7.6	.195	2.239	2.239	
5	Glycosylated Haemoglobin	-	15	8.13	1.73	15	8.895	1.725	.443	.443	.767
6	Glycemic Control	HbA1c	30	6.7	1.15	30	7.1	.8	.404	.404	
7	Blood Sugar Control	FBS	15	165.8	13.25	15	173.735	11.695	.635	.635	
8	Blood Sugar levels	FBS	15	162.8	21.385	15	174.835	19.345	.59	.59	
9	A1C	-	15	6.76	1.265	15	7.64	1.915	.542	.542	
10	Glycosylated Hemoglobin	-	15	7.693	.874	15	8.28	.907	.659	.659	7.676 = sd

Me: Mean of the experimental group in the pre-test and post-test; Mc: Mean of the control group in the pre-test and post-test; Se: Mean standard deviation of the experimental group in the pre-test and post-test; Sc: Mean standard deviation of the control group in the pre-test and post-test

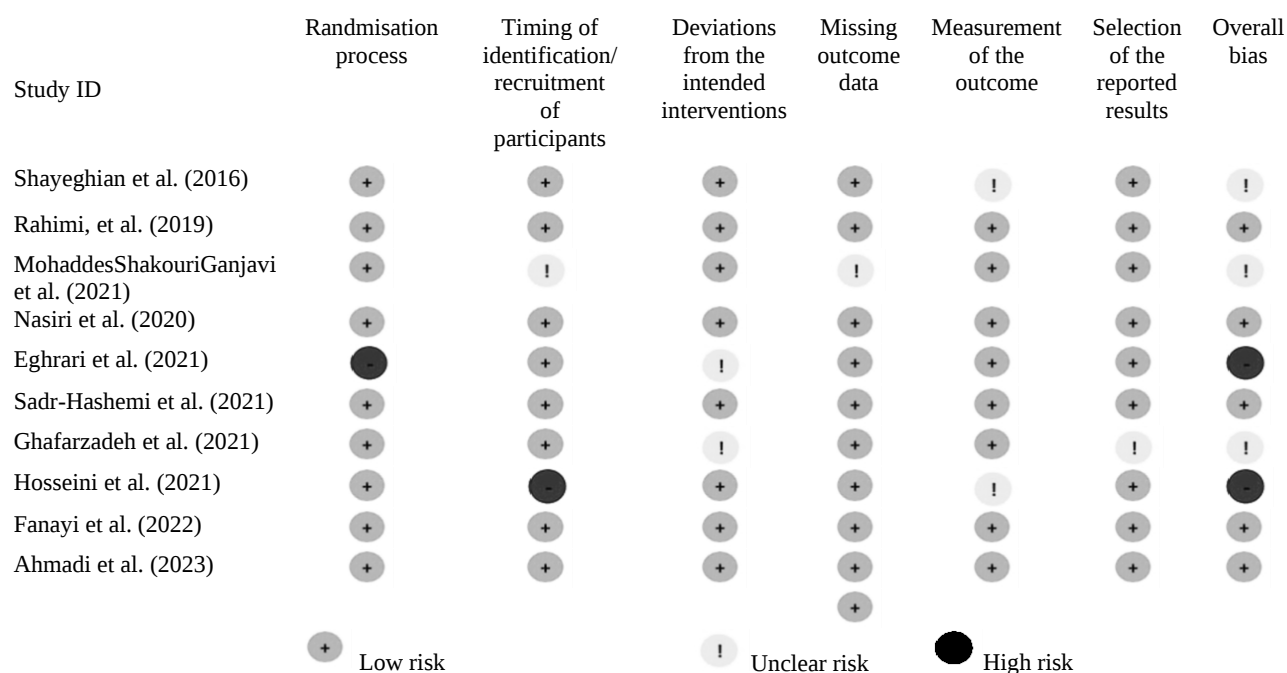


Figure 2. Risk of bias summary

Table 3. Average effect size of each biological measures

Biological measures	Code	Variable effect size	The average size of each measure
FBS	2	.688	
	3	1.28	.798
	8	.59	
	7	.635	sd=3.193
2HPP	2	.586	.586
	1	.344	
	2	.346	
HbA1c	4	2.239	sd=3.221
	5	.443	.711
	6	.404	
	9	.542	
	10	.659	sd=4.977

Discussion

This study aimed to consolidate research on the impact of acceptance and commitment therapy on the biological measures of individuals with type 2 diabetes. The systematic review and meta-analysis revealed that acceptance and commitment therapy (ACT) has a significant effect on improving biological measures (FBS, HbA1c, and 2HPP) in type 2 diabetes. Furthermore, the findings suggest that ACT is particularly effective in improving FBS and HbA1c compared to 2HPP.

According to recent research, ACT has been shown to reduce glycated hemoglobin levels and improve self-management self-efficacy, and disease acceptance in people with type 2 diabetes (8). Another meta-analysis by Wang et al. (35) showed that ACT could improve glycaemic control, disease acceptance, and self-efficacy and reduce distress in people with type 2 diabetes. We can argue that ACT may reduce glycosylated hemoglobin levels and improve symptoms through behavioral mechanisms such as improving self-management, strengthening self-care behaviors, and increasing adaptation to psychological disturbances associated with diabetes.

Furthermore, in another meta-analysis, Konstantinou et al. (12) found that ACT is an effective approach for improving quality of life and reducing symptoms in several chronic diseases. Additionally, Winkley et al. (36) discovered in a systematic review and meta-analysis of RCTs that psychological interventions effectively improve blood sugar control in individuals with type 1 diabetes, both children and adults, by reducing HbA1c levels. A meta-analysis by Ma et al. (37) on the efficacy of acceptance and commitment-based therapy for chronic pain revealed that this therapy is beneficial and effective for reducing chronic pain.

It is worth mentioning that psychological consequences such as anger, anxiety, fear, and depression due to a chronic disease such as diabetes are inevitable, and these factors during the disease can cause erosion of physical and mental reserves, which in turn weakens the immune system and low body resistance (35). All these factors can negatively affect the treatment period of the disease and cause the person to be disappointed with the treatment and

ignore the prescribed recommendations (16). The present meta-analysis highlights the effectiveness of acceptance and commitment therapy (ACT) in improving diabetes. During ACT, patients learn to accept their feelings without avoidance and focus on their thinking process, which helps them take action based on their goals. This therapy promotes illness acceptance among patients with diabetes, leading to better self-management and self-care behaviors (28, 38).

In Acceptance and Commitment Therapy, individuals' desire for internal experiences was emphasized, and trying to help patients experience their maladaptive thoughts as a single thought and become aware of the ineffective nature of their current plan. Instead of reacting, they do what is necessary in their lives and under their values. Also, in ACT, accepting these uncomfortable thoughts and feelings and allowing them to be present, rather than controlling or repressing them, can reduce the experience for these people. It creates flexibility in individuals by using exercises and metaphors (14). Commitment and acceptance therapy also teach people to accept all thoughts and feelings instead of challenging thoughts and trying to control emotions. This change in attitude towards private experiences seems very important in chronic conditions, where there is evidence of painful private experiences (15).

Patients who undergo ACT are more likely to adhere to prescribed medications and insulin, follow recommended diets, engage in physical activity, and regularly monitor their blood sugar levels (29). These improvements in self-care behaviors contribute to enhanced metabolism and increased glucose transporters in muscle cell membranes. As a result, the body's sensitivity to insulin improves, leading to decreased glycosylated hemoglobin levels (18). In support of this result, we can argue that by focusing on two vital factors, i.e., acceptance and commitment, ACT helps to improve adherence to treatment and adherence to a diet plan, and adherence to drug treatment and a healthy lifestyle plays an essential role in reducing blood sugar levels and improving other harmful biological indicators in type 2 diabetes.

Furthermore, ACT positively impacts blood sugar control by reducing negative emotions like distress and hopelessness while increasing positive emotions such

as hope and happiness (17, 39-40). Increased psychosocial stress is associated with elevated blood sugar levels, as stress hormones released during tense situations inhibit sugar consumption by the body's cells and reduce insulin sensitivity (30, 31). We can say that ACT positively affects the reduction of excitability of the hypothalamus-pituitary-adrenal axis by reducing involvement in negative thoughts and feelings or creating defusion with psychological worries and distress, ultimately reducing blood sugar and controlling diabetes.

The impact of stress on blood sugar levels is mediated by the activation of the hypothalamus-pituitary-adrenal axis and the decrease in health-promoting behaviors (32). Stress hormones such as adrenaline, noradrenaline, and cortisol, released during periods of nervous tension, elevate blood sugar levels by mobilizing the body's reserves and inducing insulin resistance. It hinders sugar consumption by cells, exacerbating diabetes symptoms. In addition, glucagon, growth hormone, and cortisol are also released during stress, contributing to sugar elevation through a similar mechanism (33). Consequently, under stress, cells become less responsive to insulin, causing elevated blood sugar levels and increased glycosylated hemoglobin. Nonetheless, acceptance and Commitment Therapy (ACT) can mitigate negative emotions, including stress, through practices like mindfulness, thereby aiding in regulating blood sugar and glycosylated hemoglobin (17).

The current systematic review and meta-analysis focused on measuring the effect size of acceptance and adherence therapy on biomarker measures in type 2 diabetes as a strength. Due to the occurrence of many complications caused by the elevation of biological measures in patients with diabetes, the determination of psychosocial interventions with appropriate effect sizes is vital in controlling diabetes and its complications. However, there are several limitations of the current systematic review and meta-analysis. First, using a variety of databases in a specific population to derive a theme is biased because self-reported information is particular to that population and may not be generalizable to other populations. Different structures and definitions of variables between different studies affect the results of meta-analysis. In addition, different studies have reported

the investigated outcome variable with different units, and these differences may be the reason for the error in estimating the desired effect size. There were also different confounding factors in the different trials, which could have affected the results.

Conclusion

The current systematic review and meta-analysis indicated that the ACT model improves self-care behaviors and biological measures such as fasting blood sugar, glycosylated hemoglobin, and 2-hour postprandial plasma glucose levels in patients with type 2 diabetes. It is concluded that acceptance is crucial when faced with experiences that cannot be changed, such as living with diabetes. By acknowledging personal thoughts, emotions, and feelings in ACT, individuals can engage in value-driven committed action and accept negative emotions as a part of life. ACT empowers patients to avoid futile struggles with negative emotions and instead focus on pursuing values and engaging in values-based actions. Although more large prospective studies and well-designed interventional studies are recommended to confirm the obtained results, the results of the present study support the recommendations for using an acceptance and commitment therapy approach for the prevention and control of diabetes and its complications. The development of strategic plans based on this treatment model to control and reduce the complications of diabetes, especially in outpatient clinical settings, is suggested to reduce the disease burden in this population.

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Ethical Approval

This study is based on a research project approved by the Ethics Committees of Semnan University of Medical Sciences and Health Services (ID: IR.SEMUMS.REC.1402.319) at 11.3.2024. All

procedures performed in this study were in accordance with the ethical standards of the institutional or national research committee and were consistent with the 1964 Helsinki Declaration and its later amendments or comparable.

Conflict of Interest

The authors declare no conflict of interest.

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