International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 7 | Issue: 1 | Jan – Feb 2026 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v7i1.13

Effect of Chronic Stress on Insulin Resistance and Hba1c Levels: Literature Review

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ABSTRACT

Chronic psychological stress has been increasingly recognized as a major factor influencing glycemic control in diabetes mellitus, particularly type 2 diabetes (T2DM). This literature review explores the physiological and behavioral mechanisms linking chronic emotional stress with insulin resistance and elevated HbA1c levels. Activation of the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system during prolonged stress leads to increased secretion of cortisol and catecholamines, promoting hepatic gluconeogenesis, lipolysis, and insulin resistance. Concurrently, chronic stress triggers inflammatory cytokines such as IL-6, which further disrupt insulin signaling pathways. Behavioral consequences, including poor medication adherence, unhealthy dietary habits, reduced physical activity, and sleep disturbances, exacerbate glycemic dysregulation. Evidence from observational and interventional studies consistently demonstrates that higher psychological distress correlates with poor glycemic control, while psychological interventions such as Cognitive Behavioral Therapy (CBT), Mindfulness-Based Stress Reduction (MBSR), and resilience training can improve HbA1c and overall well-being. The integration of stress screening and management into diabetes care, as recommended by major international guidelines, may optimize metabolic outcomes and enhance quality of life for patients. This review underscores the necessity of a holistic biopsychosocial approach in diabetes management.

Keywords: chronic stress; insulin resistance; HbA1c; diabetes mellitus; HPA axis; psychological intervention; glycemic control

INTRODUCTION

Diabetes mellitus (DM), particularly type 2 DM, is a metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Effective glycemic control is fundamental in preventing microvascular and macrovascular complications associated with diabetes. Glycosylated hemoglobin or HbA1c serves as a key biomarker that reflects the average blood glucose levels over the preceding two to three months, providing a standard measure to guide diabetes management and evaluate long-term glycemic control [1,2].

Recent studies indicate that psychological stress significantly affects glycemic control in individuals with diabetes. Both acute and chronic psychological stress can disrupt glucose metabolism, leading to elevated blood glucose levels and HbA1c. Acute stress conditions (hours to days), whether unrelated or related to the disease or its treatment, such as initiating insulin therapy or using new technologies like insulin pumps or continuous glucose monitoring devices can serve as sources of stress. However, acute stress only temporarily increases glucose levels, so short-term stress episodes do not significantly impact HbA1c levels [2,3].

Chronic emotional stress (weeks to years) related to diabetes, such as the anxiety experienced by individuals living with diabetes while managing their condition, is also commonly observed. The prevalence of this chronic stress is reported to range from 20 to 40% in people with type 1 DM and type 2 DM. Studies have consistently shown an association between severe chronic stress levels and poorer glycemic control in adults with diabetes [1-3].

This literature review will discuss the role of chronic emotional stress factors in the care of diabetes patients and is expected to encourage the implementation of a more holistic management approach for diabetes patients.

PATHOPHYSIOLOGY OF STRESS EFFECTS ON INSULIN RESISTANCE AND HbA1C LEVELS

Psychological stress influences HbA1c levels and insulin resistance through complex neuroendocrine and molecular mechanisms that disrupt glucose metabolism and insulin signaling. The hippocampus-pituitary-adrenal (HPA) axis and activation of the autonomic nervous system (ANS) are the primary pathways that transform the stress response into metabolic disturbances, contributing to insulin resistance and diminished glycemic control, as reflected by elevated HbA1c levels [2,4].

Psychological stress triggers activation of the HPA axis, resulting in increased secretion of glucocorticoids such as cortisol. Elevated cortisol levels stimulate gluconeogenesis in the liver and inhibit insulin action, thereby impairing glucose uptake into skeletal muscle and adipose tissue. Chronically high cortisol can desensitize insulin receptors, reduce insulin signaling efficacy, and promote systemic insulin resistance. Stress also activates the sympathetic nervous system, increasing circulating catecholamine levels (epinephrine and norepinephrine), which further inhibit insulin-mediated glucose uptake by promoting glycogenolysis and lipolysis, releasing glucose and free fatty acids that additionally disrupt insulin signaling pathways [4,5].

Hyperactivation of the autonomic nervous system due to chronic stress disrupts peripheral glucose homeostasis by altering adipokine secretion and inflammatory cytokine production. Inflammatory mediators such as IL-6 contribute to insulin resistance by interfering with insulin receptor substrate signaling pathways, such as PI3K–Akt. These processes ultimately result in insulin resistance and poor glucose control, which manifest as elevated HbA1c levels [2,4,5].

Stress also indirectly affects glucose control by disrupting diabetes self-management behaviors. High levels of psychological stress often lead to patient behavioral changes, such as poor adherence to medication regimens, diet, and exercise; depressive symptoms that reduce motivation and self-care capacity; and sleep disturbances that affect metabolic regulation and insulin sensitivity [2,6].

Thus, the impact of psychological stress on poor glucose control and elevated HbA1c in diabetes occurs through direct physiological effects and indirect behavioral changes. These two pathways often coexist and reinforce each other. For example, hyperglycemia induced by stress can exacerbate emotional distress, which further impairs self-management, creating a negative cycle (Figure 1) [2,4,6].

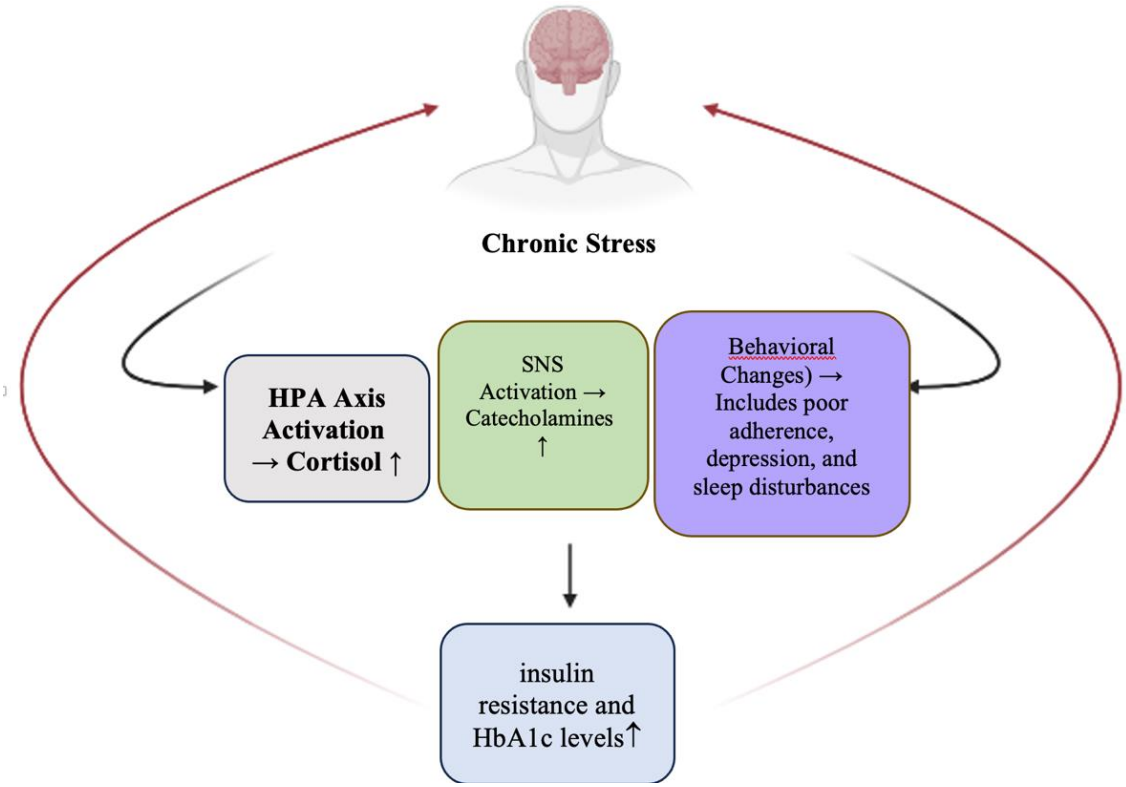

FIGURE 1: Relationship between Chronic Stress and Insulin Resistance.

STUDIES LINKING STRESS TO GLYCEMIC CONTROL

Recent studies have confirmed the relationship between psychological disorders and poor glycemic control. A 2025 observational study in Pakistan found that moderate to severe psychological disorders significantly worsened HbA1c levels by negatively affecting diabetes self-management and patients' mental health [7]. Similarly, a study in Ethiopia reported that high stress levels in newly diagnosed type 2 diabetes mellitus (DM) patients correlated with elevated HbA1c levels and suboptimal glycemic control [1].

Epidemiological data from Denmark also indicate that diabetic patients experiencing depression and diabetes-related psychological disorders are more likely to have poor glycemic control, increasing the risk of complications [8]. Zheng et al. analyzed data from over 30,000 participants in the United States and found that more severe depression levels were significantly associated with increased diabetes incidence, higher HbA1c, fasting glucose, and insulin levels. These mechanisms involve behavioral disruptions (reduced self-care and adherence) as well as biological factors such as increased insulin resistance through chronic inflammation and neuroendocrine dysregulation [9].

Intervention clinical trials have also shown that psychological interventions can lead to significant reductions in HbA1c levels and improve mental health outcomes in diabetic patients. Digital health technologies and education programs have demonstrated potential in reducing psychological disorders and enhancing glycemic control, as reflected in HbA1c levels [10,11].

Patient personality traits have also been linked to glycemic control in diabetic patients in several studies. The personality traits most strongly predicting poor glycemic control in DM patients are neuroticism and Type D personality. Neuroticism, characterized by negative emotions such as dysphoria, worry, and tension, increases the likelihood of higher HbA1c levels by approximately threefold compared to traits like openness or extraversion. Type D personality, which encompasses negative affectivity and social inhibition, also predicts poor glycemic control, poor medication adherence, and unhealthy behaviors. In contrast, traits such as self-awareness and openness are associated with better glycemic control due to healthier behaviors and higher treatment adherence [12,13,14].

Additionally, studies on resilience traits show that higher psychological resilience predicts better self-care behaviors, lower HbA1c levels, and improved mental health. This suggests that resilience-building interventions can counteract the adverse effects of stress on glucose control and limit HbA1c elevations [15].

STRATEGIES FOR MANAGING EMOTIONAL STRESS IN DIABETES MELLITUS PATIENTS

The studies above highlight the importance of effective stress management in diabetes care aimed at improving metabolic control and quality of life. Several psychological approaches have been evaluated for their benefits in diabetes management. Cognitive Behavioral Therapy (CBT) helps patients recognize and change negative thought patterns while enhancing emotional coping skills. Clinical evidence shows that CBT can lower HbA1c by improving self-care adherence and reducing stress [1,16].

Mindfulness-Based Stress Reduction (MBSR) involves meditation and relaxation techniques that lower cortisol levels and regulate autonomic nervous system activity, thereby stabilizing glucose levels. This program has been shown to improve glycemic control outcomes. Exercise also releases endorphins, enhances insulin sensitivity, reduces stress, and lowers HbA1c.[10,17] In recent years, technology-based psychological support such as telehealth has expanded access to stress management interventions and proven effective in improving glycemic control.[11] In certain cases, short-term anxiolytics like benzodiazepines may be used adjunctively to reduce the effects of acute stress on glucose metabolism, though this requires monitoring [10,18].

Screening for psychological stress and mental health disorders is increasingly used in diabetes care. Early identification of psychological disorders or psychiatric comorbidities enables timely interventions, which can improve HbA1c outcomes and quality of life. Based on expert consensus guidelines from organizations such as the American Diabetes Association (ADA), Diabetes UK, and the National Institute for Health and Care Excellence (NICE), screening can be conducted in several situations: (1) at initial diagnosis to identify pre-existing psychological issues, (2) annually as part of routine diabetes management, (3) when there is a change in disease status, such as new complications or poor glycemic control despite treatment efforts, (4) during major life changes or psychosocial stress (e.g., death of a loved one, job loss).[19,20]. Several screening instruments can be used, such as the Diabetes Distress Scale (DDS-17), Patient Health Questionnaire-9 (PHQ-9), and Shatri Sinulingga Psychosomatic Test (SSPT) for detecting psychosomatic disorders in patients [19,21].

CONCLUSION

Chronic psychological stress plays a significant role in worsening glycemic control in diabetes mellitus patients through interconnected physiological and behavioral mechanisms. Prolonged stress activates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system, increasing cortisol and catecholamine secretion, which impairs insulin action, stimulates gluconeogenesis, and causes insulin resistance. Additionally, chronic stress triggers an inflammatory response via elevated cytokines like IL-6, further disrupting insulin signaling pathways. From a behavioral perspective, emotional stress reduces treatment adherence, lowers

exercise motivation, disrupts eating and sleep patterns, thereby exacerbating blood glucose control and elevating HbA1c levels.

Various studies demonstrate a consistent association between chronic stress levels and higher HbA1c, as well as the effectiveness of psychological interventions such as CBT, MBSR, and technology-based therapies in reducing stress and improving glycemic control. Therefore, diabetes patient management should adopt a holistic approach that targets not only medical aspects but also patients' mental and social health. Routine stress screening and timely psychological support can serve as effective strategies to enhance overall metabolic outcomes and quality of life in diabetic patients.

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