Association between Stress, Cortisol, and Blood Glucose Levels in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Type 2 diabetes mellitus (T2DM) is a chronic degenerative disease that represents one of the leading causes of morbidity and mortality worldwide. Its complications significantly affect patients' quality of life, posing a constant challenge for public health systems. On the other hand, stress has been considered a relevant factor due to its impact on body homeostasis, mainly through activation of the hypothalamic–pituitary–adrenal (HPA) axis and the consequent release of cortisol, a hormone closely related to glucose metabolism.

Objective: To analyze the association between stress levels, cortisol concentrations, and blood glucose levels in patients with T2DM treated at a healthcare center in Puebla, Mexico.

Methods: An observational, cross-sectional, and descriptive study was conducted. The sample included 90 patients with T2DM, aged between 30 and 70 years, selected through non-probabilistic convenience sampling. Stress levels were assessed using the PAID (Problem Areas in Diabetes) scale, which consists of 20 items designed to identify areas of diabetes-related psychosocial distress. Cortisol concentrations were determined using the ELISA technique, and fasting glucose levels were measured by spectrophotometry.

Results: A total of 71.1% of participants presented moderate stress levels, while 28.9% had severe stress. Elevated cortisol levels were observed in 50% of patients, and 30% presented hyperglycemia. No statistically significant correlation was found between stress and cortisol levels ($p > 0.9999$); however, a statistically significant association was observed between stress levels and blood glucose concentrations ($p = 0.0001$). These findings suggest that emotional stress may directly influence glucose metabolism in patients with T2DM.

Conclusions: The results highlight the importance of integrating psychological approaches into the comprehensive management of T2DM, especially in contexts where socioeconomic and cultural factors may increase patient vulnerability. Considering stress as a modulator of metabolic status could contribute to improving clinical management and patients' biopsychosocial well-being.

Keywords: stress; cortisol; type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic degenerative disease characterized by hyperglycemia resulting from alterations in insulin secretion and action. It represents the most common form of diabetes and constitutes one of the leading public health problems worldwide. In Mexico, its prevalence has shown a sustained increase in recent decades; according to the National Health and Nutrition Survey (ENSANUT 2021), approximately 12.4 million people are living with this condition (1,2).

The pathophysiology of T2DM is associated with genetic–environmental interactions, as well as insulin resistance and progressive pancreatic β-cell dysfunction, leading to chronic hyperglycemia. This condition promotes the development of long-term complications affecting target organs such as the retina, kidneys, nervous system, heart, and blood vessels, thereby impacting patients' quality of life (3,4).

Insulin resistance is defined as a diminished response of insulin-sensitive tissues, particularly the liver, muscle, and adipose tissue. Several mechanisms are involved in alterations of the insulin signaling pathway, including downregulation of insulin receptors, decreased catalytic activity, abnormal activation of kinases such as PI3K and Akt, and defects in the expression and function of GLUT-4. Additionally, endoplasmic reticulum stress and mitochondrial dysfunction have been implicated (5–7).

In individuals with obesity, increased adipose tissue enhances the production of proinflammatory adipokines such as TNF-α and IL-6, which contribute to insulin resistance through mechanisms including increased lipolysis, altered phosphorylation of IRS-1, and reduced GLUT-4 expression (8,9). Excess free fatty acids promote lipotoxicity, leading to the accumulation of lipid intermediates that impair insulin signaling and prevent proper GLUT-4 translocation to the cell membrane (8,10,11). Furthermore, ceramide formation activates apoptotic pathways that contribute to β-cell destruction and reduced insulin secretion (12).

On the other hand, glucotoxicity refers to the state of sustained hyperglycemia that impairs pancreatic β-cell function, decreasing insulin synthesis and secretion while promoting the production of free radicals and protein glycation (13,14).

The diagnosis of diabetes mellitus is based on established analytical criteria, including random plasma glucose ≥200 mg/dL in the presence of classic symptoms, fasting plasma glucose ≥126 mg/dL, or values ≥200 mg/dL two hours after an oral glucose tolerance test (15). Treatment should include diabetes education, appropriate nutrition, physical activity, and the use of oral hypoglycemic agents and/or insulin (18).

In recent decades, stress has been recognized as an important factor in metabolic regulation. Evidence suggests that it may contribute to the development of T2DM in genetically predisposed individuals and affect glycemic control in patients already diagnosed (19). Stress is defined as the body's response to physical, mental, or emotional stimuli that exceed coping capacity, leading to alterations in cognition, emotion, and behavior, largely mediated by cortisol (20).

In situations of acute physiological stress, such as surgery, trauma, or severe infections, transient hyperglycemia may occur in the absence of prior diabetes, a phenomenon known as stress-induced hyperglycemia. When this condition becomes chronic, it is associated with a higher likelihood of developing T2DM, suggesting underlying β-cell dysfunction (15). Moreover, chronic psychological stress is associated with persistent activation of the hypothalamic–pituitary–adrenal (HPA) axis, sustained elevation of cortisol, increased gluconeogenesis, abdominal obesity, and impaired glycemic regulation (5).

The physiological response to stress is mediated by the sympathetic–adrenomedullary system and the hypothalamic–pituitary–adrenocortical axis, which regulate the release of catecholamines and cortisol. When stress is prolonged, these mechanisms may contribute to the development of metabolic disturbances, hypertension, and immune dysfunction (21,22,28).

In recent years, the importance of psychoemotional factors in the management of chronic diseases has been increasingly recognized. However, the relationship between stress levels, cortisol concentrations, and glycemic control has not been sufficiently studied in local contexts with specific socioeconomic characteristics. In communities such as Tepeaca, Puebla, where there are limitations in access to healthcare services and variability in treatment adherence, the impact of stress may be greater.

T2DM represents not only a clinical problem but also an economic and social burden due to its chronic course and complications. In this context, stress may act as a factor that exacerbates metabolic status and contributes to progressive health deterioration. Therefore, there is a need to analyze the association between stress levels, cortisol concentrations, and their effect on blood glucose levels in patients with T2DM treated at a healthcare center in the state of Puebla.

Methodology

An observational, cross-sectional, and analytical study with a quantitative approach was conducted. The study population consisted of patients attending the Center for Health Services with Extended Capacity (CESSA) in Tepeaca, Puebla.

The sample included 90 patients diagnosed with type 2 diabetes mellitus (n = 90), selected through non-probabilistic convenience sampling. Data collection was carried out between July and August 2023.

After obtaining informed consent, stress levels were assessed using the Problem Areas in Diabetes (PAID) scale, developed by William H. Polonsky. This instrument consists of 20 items evaluating emotional distress related to diabetes. The total score is calculated by summing item scores and multiplying by 1.25, with a range from 0 to 100; scores ≥40 were considered indicative of high stress. The scale has high internal consistency, with a Cronbach's alpha of approximately 0.90.

Venous blood samples were collected under aseptic conditions by trained personnel to measure serum cortisol and glucose levels. Cortisol was determined using enzyme-linked immunosorbent assay (ELISA), with reference values ranging from 5 to 23 µg/dL in adults. Fasting serum glucose was measured by spectrophotometry, with values ≥126 mg/dL considered elevated.

Data were analyzed using GraphPad version 7.0. Descriptive statistics (frequencies and percentages) were used, and factorial ANOVA was applied to evaluate associations between variables, considering $p < 0.05$ as statistically significant.

Results

The sample consisted of 90 patients with type 2 diabetes mellitus, aged between 30 and 70 years (mean: 57 years); 65.5% were female.

Regarding stress levels, assessed using the PAID scale, 71.11% of participants presented moderate stress, while 28.89% showed severe levels.

In terms of biochemical parameters, 50% of patients had elevated serum cortisol levels (>24 µg/dL). Concerning fasting glucose, 30% of participants presented hyperglycemia (≥126 mg/dL), while the remainder were within normal or intermediate ranges (Table 1).

Table 1. Cortisol levels (ELISA test)

Values	Frequency	Percentage
Low 4 µg/dL	5	5.55%
Normal 5 - 23 µg/dL	40	44.44%
High 24 µg/dL	45	50%
Total	90	100%

Source: Own elaboration based on the results obtained using the GraphPad statistical package version 10.

30% showed elevated glucose levels (>130 mg/dL) (Table 2).

Table 2. Fasting glucose levels

Glucosa	Frequency	Blood sugar percentage
Normal 70-130 mg/dL	63	70%
High 131 mg/dL	27	30%
Total	90	100%

Source: Own elaboration based on the results obtained using the GraphPad statistical package version 10.

The average glucose level was 192.4 mg/dL, indicating that a significant proportion of patients present glycemic imbalance. When analyzing the relationship between perceived stress level and serum cortisol level, no statistical significance was found ($p > 0.9999$) (Table 3).

Table 3. Stress and cortisol

P value and statistical significance	
Test	Fisher's exact test
P value	>0.9999
P value summary	Ns
One- or two-sided	Two-sided
Statistically significant (P < 0.05)?	No

Source: Own elaboration based on the results obtained using the statistical package GraphPad version 10.

However, when evaluating the association between stress and cortisol on glucose levels through a factorial analysis of variance (ANOVA), a statistically significant result ($p < 0.0001$) was obtained for the glucose factor (Table 4).

Table 4. Stress and cortisol on glucose

Two-way ANOVA	Ordinary			
Alpha	0.05			
Source of Variation	% of total variation	P value	P value summary	Significant?
Row Factor (CORTISOL)	12.08	0.1197	ns	No
Column Factor (GLUCOSA)	68.40	<0.0001	****	Yes

Source: Own elaboration based on the results obtained using the GraphPad statistical package version 10.

Discussion

The mean age of the participants was 57 years, which is higher than that reported in other studies, where a mean age of 48 years has been observed in patients with type 2 diabetes mellitus (31). Regarding gender, this study reports that 65.5% of participants were female, a figure similar to that described in the literature, where 63.58% female prevalence has been reported (32).

In relation to stress, it has been documented that levels in diabetic patients tend to be moderate (31), which is consistent with the findings of the present study, where 71.11% of participants exhibited a moderate level of stress. Regarding cortisol, it has been reported that patients with diabetes may present elevated levels (32), which aligns with the results obtained, where 50% of patients showed high levels.

With respect to glucose levels, a mean of 176 mg/dL has been reported in previous studies, which is comparable to the findings of this research, where a mean of 192 mg/dL was observed. Additionally, a statistically significant association between cortisol levels and metabolic alterations in diabetic patients has been described (33), which partially agrees with the results of this study. Specifically, statistical significance was found in the interaction between stress and cortisol on glucose levels ($p < 0.0001$), although no direct association between stress and cortisol was observed when analyzed independently.

These findings suggest that, although stress and cortisol do not act independently in a statistically significant manner, their combined effect may influence glucose metabolism. This is consistent with the literature, where chronic exposure to elevated cortisol levels promotes progressive deterioration of pancreatic β-cells, reducing the ability to compensate for hyperglycemia and contributing to the development or worsening of diabetes mellitus (34).

The fact that 50% of patients presented elevated cortisol levels and that 30% had glucose levels above normal values indicates that a substantial proportion of the studied population is at risk of developing complications. Although stress levels were predominantly moderate, their clinical impact remains relevant, as stress may influence treatment adherence, diet, sleep, and physical activity.

Several studies have indicated that factors such as low psychosocial support, educational level, and limited access to healthcare services may intensify the emotional impact of diagnosis, impair self-care, and contribute to poor glycemic control (22,31).

Likewise, the importance of the sociocultural context of the health center in the state of Puebla is highlighted, as it is located in a semi-urban community with rural influence, where factors such as limited psychological support coverage and economic constraints may exacerbate the condition, positioning stress as a relevant factor in the health of this population.

Finally, this study highlights that the control of type 2 diabetes mellitus depends not only on clinical factors but also on the emotional and neuroendocrine status of the patient. It is important to acknowledge that there are variables not addressed in this study, such as sociodemographic factors and lifestyle, which may influence stress, cortisol, and glucose levels, opening avenues for future research.

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