

EDITORIAL

Unmasking the Mysteries of Uncontrolled Diabetes Mellitus: “Why the Pharmacotherapeutic Advances are Not Competently Enough?”

Asim Zulfiqar

Since the IDF's most recent figures were released in 2019, the prevalence of diabetes in Pakistan has dramatically increased. 33 million adults in Pakistan had diabetes in 2021, a 70% rise from 2019. After China (141 million) and India (74 million), Pakistan presently has the third-highest number of persons with diabetes worldwide. Diabetes caused 400,000 fatalities in the nation in 2021, more than any other disease in the Middle East and North Africa. In Pakistan, an extra 11 million persons have impaired glucose tolerance (IGT), putting them at a high risk of getting type 2 diabetes. Pakistan has the highest national prevalence of diabetes in the world, with a frequency of one in four persons (26.7%) almost a quarter.¹

Diabetes is a chronic illness with several underlying factors: insulin resistance, beta cell failure, incretin deficiency/resistance and inadequate renal tubular handling of filtered glucose are few of them.² Number of pharmaco therapeutic agents like metformin, TZD, Sulphonylurea, glinides, DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors along with various types of exogenous insulins are available to tackle these various pathogenic mechanisms.³ Even in the presence of so many advanced therapeutic options, achievement of glycemic/metabolic targets along with improving quality of life of our diabetic patients seems to be very difficult. There is something somewhere that is not working for our diabetic patients. Control over the disease still seems remote and very challenging. This fact leads to the search of various non-pharmacological factors that can contribute to poor disease control. One of them can be allostatic load. Allostatic load refers to the cumulative burden of chronic stress and life events. It involves the interaction of different physiological systems with

Department of Medicine

Pakistan Railway General Hospital, Rawalpindi

Correspondence:

Dr. Asim Zulfiqar

Department of Medicine

Pakistan Railway General Hospital, Rawalpindi

E-mail: asimzulfiqar786@gmail.com

Received: May 10, 2023; Accepted: June 01, 2023

<https://doi.org/10.57234/jiimc.june23.1738>

environmental stress. When environmental challenges exceed the individual's ability to cope then the allostatic overload ensues.⁴ Stress has an important role in the glycemic control of a diabetic patients. Diabetic patients not only have to face the stressors regarding their disease like frequent blood sugar checks, diet restrictions, strict exercise routine but have also to face anxiety regarding glycemic variations as well as must live with continuous fear of having acute or chronic complications of the disease.^{5,6} This is in addition to concerns regarding their work, family or finances that are not directly related to their illness. In a number of studies this has been documented that stress or allostatic load leads to increased inflammatory/oxidative damage thus contributing to poor glycemic control and increased incidence of complications in diabetic patients.^{7,8} So health care providers must address the allostatic load management like provision of the services of psychotherapists/support groups for the holistic care of our diabetic patients. There is a significant link between psychological stress and glycemic control. Psychological stress affects the action of the pituitary gland and the sympathetic nervous system, which causes an increase in the levels of circulating catabolic hormones and a suppression of the anabolic hormones. People with Type 1 diabetes experience elevated blood glucose levels because of this. Stress results in behavioral modifications that can interfere with self-care. For instance, time constraints make it impossible to monitor blood glucose, which disrupts metabolic control. Additionally, comfort-seeking, or coping behaviors, such as increased food consumption and decreased physical activity, may be brought on by stress. People with diabetes who engage in these behaviors run the risk of having their metabolic regulation disturbed. Another factor that can play a limiting role in the control of disease of a diabetic patients is a dysbiosis of gut microbiota. Insufficient glycemic control has been attributed to dysbiosis of gut microbiota that has significant impact on host metabolism specially glucose hemostasis. Dysbiosis has been revealed to affect short chain fatty acid synthesis and result in

alteration of insulin signaling pathways, consequently developing inadequate glycemic control.¹⁰

The potential risk factors for type 2 diabetes include obesity, an unhealthy lifestyle, and gut microbial dysbiosis. Low intake of dietary fibers and consumption of meals high in fat and sugar have both been linked to a decrease in the diversity and abundance of the gut microbial community. The metabolic and functional pathways in the gut that are implicated in the onset of type 2 diabetes may be impacted by gut microbial dysbiosis. The production of short-chain fatty acids (SCFAs) and the composition of the gut microbiota are both significantly influenced by diet. The colony of commensal bacteria in the colon performs fermentation on the carbohydrates that are not digested and absorbed in the small intestine.¹¹ So for achieving metabolic/glycemic targets, minimizing acute/chronic complications, improving quality of life of our diabetic patients, health care providers will have not only to prescribe appropriate pharmacotherapeutic agent but also need to address some other less considered but important non pharmacological contributing factors like allostatic load, dysbiosis etc. This fact necessitates a multidisciplinary approach that not only involve physicians, nurses but also psychotherapist, counsellors, dieticians, and patient support group. This holistic approach by recognizing the non-pharmacological missing links, is the need of the time for achieving control of our diabetic patients.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional, and

country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes research and clinical practice.* 2022;183:109119.

2. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus. *Nature reviews Disease primers.* 2015;1(1):1-22.

3. Esposito K, Chiodini P, Bellastella G, Maiorino M, Giugliano D. Proportion of patients at HbA1c target< 7% with eight classes of antidiabetic drugs in type 2 diabetes: systematic review of 218 randomized controlled trials with 78 945 patients. *Diabetes, Obesity and Metabolism.* 2012;14(3):228-33.

4. Kolesnikova VA, Clarke PJ, Mukherjee B, Sen S, Mezuk B. Psychosocial Stress and Hypothalamic-Pituitary-Adrenal Axis Stress Reactivity: Variations by Race and Socioeconomic Status Among Adults at Risk of Diabetes. *Psychosomatic Medicine.* 2022;84(7):813-21.

5. Juanamasta IG, Aunguroch Y, Gunawan J, Suniyadewi NW, Wati NMN. Holistic care management of diabetes mellitus: An integrative review. *International Journal of Preventive Medicine.* 2021;12.

6. Mustafa M, Jahan S, Waseem M, Ramzan T, Latif D. Comparing Fasting Homocysteine Levels Among Healthy Adults, Diabetic and Non-Diabetic Cardiac Patients: JRCRS. 2018; 6 (2): 63-66.

7. Sharma VK, Singh TG. Chronic stress and diabetes mellitus: interwoven pathologies. *Current diabetes reviews.* 2020;16(6):546-56.

8. Jahan S, Parveen S, Barnabas S, Mehreen A. Restless Leg Syndrome and Sleep Quality in Diabetic Patients with and without Neuropathy.

9. Riazi A, Pickup J, Bradley C. Daily stress, and glycaemic control in Type 1 diabetes: individual differences in magnitude, direction, and timing of stress-reactivity. *Diabetes Research and Clinical Practice.* 2004 Dec 1;66(3):237-44.

10. Bielka W, Przekazak A, Pawlik A. The role of the gut microbiota in the pathogenesis of diabetes. *International journal of molecular sciences.* 2022;23(1):480.

11. Ojo O, Feng QQ, Ojo OO, Wang XH. The role of dietary fibre in modulating gut microbiota dysbiosis in patients with type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. *Nutrients.* 2020 Oct 23;12(11):3239.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

This is an Open Access article distributed under the terms of the Creative Commons Attribution- Non-Commercial 2.0 Generic License.