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.

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. 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. 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 environmental stress. When environmental challenges exceed the individual's ability to cope then the allostatic overload ensues. 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. 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. 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

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Received: May 10, 2023; Accepted: June 01, 2023
https://doi.org/10.57234/jiimc.june23.1738
alteration of insulin signaling pathways, consequently developing inadequate glycemic control.\textsuperscript{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.\textsuperscript{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.

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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.

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