Can Yoga-Based Diabetes Management Studies Facilitate Integrative Medicine in India? Current Status and Future Directions

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Keywords
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Abstract
Background: India is fast becoming the diabetic capital in the world according to a recent report. Patients with diabetes are at increased risk of mortality due to diabetic complications, which has enormous implications for the health budget. Objectives: The main objective of this review is to provide an overview of the work carried out in the world, including modern and traditional approaches for the prevention and management of diabetes and reducing the
chances of onset of further complications via cost-effective lifestyle interventions and integrative medicine. **Material and Methods:** We performed a literature search from various databases like PubMed, Scopus, Google scholar, etc., using the keywords diabetes, prediabetes, MCI and prediabetes, diabetes and yoga, diabetes. **Results:** Upon reviewing the published articles, it was noticed that one of the most neglected complications of diabetes, namely cognitive dysfunction, which is characterized by a pattern of vascular dementia and Alzheimer disease (AD), has been largely ignored, and there has been no large study investigating the role of yoga intervention in diabetes and/or associated cognitive impairment. **Conclusion:** The review article opens new paradigms for researchers to evaluate the connection between diabetes and AD through a yoga-based national campaign on diabetes. This paves the way towards the goal of integrative medicine.

**Introduction**

Diabetes mellitus (DM) is a metabolic disorder which affects and alters carbohydrate metabolism leading to hyperglycemia. In the hyperglycemic condition, there is deficiency of insulin production (type 1 diabetes, T1DM) or improper action of insulin (type 2 diabetes, T2DM) from islets of Langerhans (β-cells) of the pancreas along with the altered counter mechanism in response to insulin secretion. The risk for developing DM increases with age, sedentary lifestyle, obesity-promoting environment, energy imbalance, and also with the onset of obesity that may impact brain health during the progression of the disease; its onset may convert a healthy (normal) person to the intermediate stage, i.e. prediabetes mellitus (PreDM) with the propensity to develop DM. PreDM is one of the leading causes of the increased prevalence of DM around the world. The PreDM condition is the reflection of impaired glucose tolerance (IGT) measured as postprandial blood sugar (PPBS [140–199 mg/dL]). Another parameter, which also signifies PreDM, is impaired fasting glucose (IFG) measured as fasting blood sugar (FBS [100 to 125 mg/dL]). PPBS, fasting blood glucose (FBG), or both are considered as markers in the screening for PreDM in a healthy population [1]. There is a 70% transition rate of PreDM to DM, if not detected earlier [2]. PreDM is characterized by insulin resistance (IR), impaired insulin secretion [3, 4], and low-grade inflammation associated with progression of PreDM to T2DM [5], micro- and macrovascular complications [6], and poor cardiovascular outcomes [7]. Blood HbA1c level, ranging from 5.7 to 6.4% (according to the 2010 ADA suggestion), is another potent marker in testing for PreDM. The prevalence of T2DM is increasing at an alarming rate and will affect 592 million individuals (according to the International Diabetes Federation) by the year 2035 globally [8]. The genetic factors that participate in the pathway for maintenance of glucose homeostasis and insulin control play a pivotal role in the stimulation of increased risk of diabetes, and some of them may be common to brain metabolism. Several genome-wide association studies put forward some candidate genes like INSR, IRS1, CDKN2A, TCF7L2, and FTO [9, 10]. Treatment of DM includes insulin administration (type 1 or type 2) via various methods (like use of syringe, insulin pen, external insulin pumps, injection port, injection aids, and the artificial pancreas). The enthusiasm for and utilization of complementary and alternative medicine has recently increased in many nations around the globe. Therefore, this review provides an insight of assessing the effectiveness of yoga in the community-based management of DM via cost-effective lifestyle interventions. A supplement was published by *Integrative Medicine International* highlighting the importance of yoga and its effect on naive healthy volunteers and experienced yoga trainers [11, 12].
Cognitive Dysfunction and Diabetes

The onset of a cognitive deficit manifests during 2 phases of the lifespan; first, early years (5–7 years) which signify the period of development of the brain systems; and the second, late years (>60 years), the most vulnerable period denoting neurodegeneration which characterizes the process of aging. Across the world, cognitive dysfunction affects most of the elderly population [13]. Cognitive dysfunction, thought to be a complication of diabetes, makes it a risk factor for developing dementia and Alzheimer disease (AD). The cognitive dysfunction results from decline in cognitive function of amygdala and hippocampus that are affected as a result of neurodegeneration, as seen in the case of dementia and AD. Most of the problems associated with increasing age are linked to the decline in cognitive abilities. HbA1c, as the gold standard diagnostic method from ADA, is used to diagnose the prediabetes state and is inversely related to cognitive function [14–17]. Cognitive functions are the outcomes of different anatomical structures that are involved in various cognitive domains accessed by various standard test batteries used for measuring intelligence, learning and memory, executive functioning, and psychomotor functioning [18–26]. Since glycemic control is neuroprotective, as found in a study in T2DM patients [27], alterations in insulin and glucose metabolism are critical in the progression of AD pathology (tau and amyloid-β [Aβ]) [28]. A post-mortem change that contains large amounts of Aβ and NT in T2DM confirms the association of diabetes with AD [23]. Other psychological domains that affect the cognitive action are stress, anxiety, and depression [29]. These domains enhance the cognitive functioning when they are in equilibrium, but when they are not in equilibrium, they accelerate the decline in cognitive function. It is, therefore, attractive to examine the correlation between biochemical, epigenetic, molecular, and neuropsychological markers that mediate or are associated with the transition of PreDM to T2DM and the rate of change of clinical transition between “pre-T2DM/T2DM with comorbidities” and “pre-T2DM/T2DM without comorbidities” by yoga intervention.

Detecting It Earlier in Communities Rather Than Hospitals: PreDM

PreDM is defined as a borderline demarcation between diabetes and normal individuals having high blood glucose level but not as significantly high that they would fall into the range of diagnostic criteria for DM as per clinical recommendations. Both of the parameters (FBS and PPBS) are considered to be effective biomarkers that have been used for the screening of PreDM in the population [1]. There is a possibility of misinterpretation of the results based on the values of blood glucose before (FBS) and after (PPBS) the intake of a meal even if this is done through camps in communities. In 2010, the Diabetic Association of America recommended another parameter, i.e. glycated hemoglobin (HbA1c), which is estimated through HPLC and the screening rate for PreDM ranges between 5.7 and 6.4%. The earlier detection and treatment of prediabetes reduces the risk of cardiovascular changes associated with macroangiopathy in patients showing both IGT and IFG [30] and also reduces the chances of developing DM. There is also a concomitant need to examine experimental biomarkers which probe the causes that underlie this conversion. Whether yoga can alter it will only be tested if Integrative Medicine Centers are installed in premier medical institutes to generate comparative data between modern medicine and yoga intervention. Different guidelines or recommendations of various organizations around the world, like Diabetic Association (DA) and Association of Clinical Endocrinologists (ACE) in America, Health Services (IHS) in India, Diabetes Association of Canada (CDA), and Diabetic Society (ADS) of Australia, suggest the treatment regime to follow and get rid of PreDM at various time points. The ADA and AACE
recommend lifestyle modifications along with metformin [31]. The organizations like IHS, CDA, and ADS strongly recommend the use of certain oral antidiabetes drugs (OADs) as a therapeutic approach (thiazolidinedione, alpha glucosidase inhibitor, etc.) and also advocate the utility of lifestyle modification as a preventive approach for managing and reducing the chances of progression of PreDM to DM [32]. In the context of several randomized clinical trial studies, a well-established fact is that lifestyle modification plays an important role in delaying the abnormal parameters (FBS/PPBS/HbA1c) in blood for screening and detection of DM. Lifestyle modification is effective and devoid of side effects (vomiting, nausea, diarrhea, gastritis, hypoglycemia, etc.) as shown by OADs. It is also proven to be effective in those on various combinations of OADs (metformin, acarbose, voglibose, and troglitazone) [27, 33, 34]. There are several changes at the cellular level that form the main characteristics: impaired insulin secretion and IR [3, 4], onset of low inflammation that represents the progression of PreDM to T2DM [5], complications in the vasculature at the micro- and macrolevel [6], and also a poor output of the cardiovascular system [7] in PreDM. The clinical diagnostic criteria for differentiation between normal, PreDM, and DM individuals [35] based on parameters like IGT, IFG, and HbA1c according to ADA recommendations are summarized in Table 1.

### Are There Cases of Undetected DM in the Communities in India?

DM is not a disease but a combined effect of disturbed metabolic functions (altered metabolism of carbohydrates, proteins, fats, etc.) required for carrying out vital body processes. Disturbances in metabolic functions are characterized by various conditions such as dyslipidemia, hyperglycemia (disturbed glucose metabolism), etc. Hyperglycemia arises from a disturbed functioning of β-cells (insulin production/insulin action or sometimes both). A prolonged hyperglycemic condition results in changes in the micro- and macroenvironment of blood vessels and impaired functioning of various tissues, which ultimately leads to failure of various organ systems like eyes (retinopathy), kidney (nephropathy), nerves (neuropathy), and heart (cardiomyopathies). Hence, an early detection of T2DM program focuses on taking the blood tests to households and proposing them a lifestyle intervention program consisting of Yoga and conventional medication.

### What Is the Burden of DM?

As the number of deaths from DM and associated complications increases, it may compel WHO to declare DM as the 7th mortality factor when we enter into the year 2030 [36, 37]. The main concerning noncommunicable disease of the world is DM. India is ranked as one of the countries (China, USA, etc) vying for the top spot as the diabetic capital. It contributes the...
majority of increased cases of morbidity and mortality, poor quality of life along with the economic burden on the existing healthcare systems independently for management and preventive approaches. The highly susceptible populations which show differences in the diagnostic criteria for DM are Mexican American [38], Pacific Islanders [39], South African Indians [40], Egyptians [41], Malaysians [42], and Americans in the United States [43]. Asian Indian phenotypes (abnormal clinical and biochemical disturbances seen in Indians) include IR, greater abdominal adiposity (waist circumference, WC), low body mass index (BMI) and occurrence of T2DM onset at an earlier age compared with Caucasians [44, 45]. The Asian Indians show IR (adolescence [46]) and hyperinsulinemia (at birth). A study on the South Asian population shows an increased prevalence rate of diabetes [47], higher level of blood insulin [48], more cases of IR [49], and early signs of decreased activity of pancreatic β-cells [45, 50, 51].

Genes That Predispose to Higher Risk of Diabetes

Genome-wide association studies have revealed several candidate genes (INSR, IRS1, CDKN2A, TCF7L2 and FTO) [9, 10] that help in the maintenance of glucose homeostasis, and the polymorphic forms of those genes play an important role in increasing the risk of diabetes. Similarly, SLC16A8 is a transmembrane protein that can regulate the transportation of monocarboxylic acids like pyruvate, lactate, etc. A study in SLC16A8 knockout mice has shown altered visual response due to changes in alpha waves and histology of the retinal layer. Recently, Sharma et al. [46] have also demonstrated the increased serum levels of SLC16A8 AMD in comparison to control, suggesting the importance of this regulatory molecule for cellular function and in maintenance of pH in the cell. Therefore, protein expression in diabetes and AD (age-related disease) can bridge the genetic gap between 2 genetically and/or phenotypically different diseases.

It is difficult to ascertain whether certain genotypes are resistant to yoga-based lifestyle intervention. Such studies are impossible without establishment of Integrative Medicine Centers in premier medical institutes.

Factors Promoting Risk of Diabetes

Environmental/Epigenetic Contributors

There are several factors other than genes (epigenetic) which are directly under the influence of the environment. The surrounding of an individual is known as its environment, which includes habits (smoking, drinking, etc.), quality of nutrients, food intake timing (disturbed routine due to heavy work load), quality of sleep, being more inclined to consume fast food, lack of physical activity, age, increased blood pressure, abnormal changes in the lipid profile, but also overweight and obesity (metabolic disturbances), i.e. these are the major contributors to the increased risk of developing PreDM and progression to T2DM [52, 53]. Future studies should focus on the effect of yoga intervention on other factors.

Obesity

Obesity is an indicator of T2DM progression [54, 55] that results from the interaction of genetic and environmental factors that show a particular type of metabolic characteristics, physical inactivity, and intake of high-calorie diet [54]. A study shows the interconnection of one of anthropometric variables, i.e. BMI, with the occurrence of T2DM in the population. Individuals with a high BMI have a greater T2DM incidence in their early age as compared to individuals with a low BMI who may develop the disease late in their life. Children with a
greater BMI have higher chances of late onset of DM or metabolic syndrome than their counterparts with a lower BMI [56]. There are several other studies which compared various anthropometric variables, like WC or WHR, and BMI, and found WC/WHR a better option for predicting diabetic risk in the population [57, 58].

**Lack of Physical Activity**

Individuals living in the postmodern era are prone to diabetes due to the lack of physical activity. Lack of physical activity promotes the initiation and progression of diabetes, which is associated with increased morbidity and mortality. The incidence rate of prediabetes and diabetes is increased in children and adolescents due to their zest for spending more time in front of TV, laptops, video games rather adopting a habit of regular physical activity. A study showed a comparative risk assessment for diabetes between individuals who prefer a sedentary lifestyle versus individuals who perform heavy workouts (physical activity). The study found that sedentary lifestyle individuals have a 3 times greater risk than physically active group [59]. The various protocols of physical activity have to be documented in the future studies on diabetes which is also the basis of the Indian Diabetes Risk Score criteria.

**Composition of Dietary Intake**

Dietary intake is an important aspect that brings the vital force, i.e. energy for carrying out various metabolic processes. A good composition of diet consists of all the nutrients in proper amounts and proportion that constitutes a balance diet. A balance diet contains basic constituents like carbohydrates, protein, fat, vitamins and minerals in a quantity which is necessary for proper functioning and maintaining energy homeostasis. The amount and quality of the fat content in a diet is a decisive factor that plays an important role in modifying the conditions like glucose tolerance and insulin sensitivity pertaining to an individual [60, 61]. Increased dietary fat content leads to the impairment of glucose tolerance via various mechanisms like reduced affinity of insulin for its receptor; it also hampers glucose transport via glucose transporter (less uptake), reducing enzymatic (glycogen synthase) conversion of glucose to glycogen, thus promoting the accumulation of triglycerides in the skeletal system (muscles) [62]. Moreover, there are very few prospective studies examining the effect of yoga-based diet on the development of diabetes.

**Adaptation to Stress**

Stress is considered as a stimulus that brings the physiological processes into disequilibrium state due to the action of various agents of stress. Stress is also associated with changes in the functioning of neuroendocrine glands which reads the signals and is converted into signals, i.e. easily detected through pathophysiology of affected tissue or cells involved in the disease [63]. Human body has a unique feature for maintaining the homeostasis and coping with the stressful environment. During stress, the main hormone adrenalin comes into play. The oversecretion of adrenalin is controlled by the hypothalamus. There are 2 systems which take care of coping strategies in response to stress. One forming an axis that includes the series of different interrelated organs (hypothalamus, pituitary, and adrenal glands) called the hypothalamic-pituitary-adrenal (HPA) axis. The nervous system is another modality that controls our body and other physiological activities through the action of nerve conduction. The nervous system is divided into 3 parts, the first part is the central nervous system (the brain and spinal cord), the second is the peripheral nervous system (cranial and spinal nerves), and the third, autonomic nervous system (sympathetic and parasympathetic). The sympathetic nervous system (SNS) is another stress coping modality that comes into play when cells or tissues or individuals are in a stressful situation. Stress triggers a series of spontaneous events that lead to changes in physiological, behavioral, and psychological aspects.
due to imbalance in cortisol and catecholamine levels (epinephrine or nor epinephrine) during the onset of disease. When both modalities (HPA and SNS) work in a regulated manner there is balance with stress, coping strategies, and normal psychophysiological activities, but when they work in an unregulated manner, this results in a variety of diseases like autoimmune diseases, disturbed metabolism, which leads to obesity, depression, risk of drug abuse for relief from stress, and it also increases the risk of developing various cardiovascular diseases in susceptible persons [29]. A study demonstrates the involvement of anxiety and/or depression as a major risk factor which contributes to the progression of diabetes [61, 64, 86, 87] and vice versa [65, 66]. The HPA axis is the first modality that senses and encounters a stress condition for a cell or tissue; then, it triggers a series of hormones to counteract the stress condition. During a hyperglycemic condition, a hallmark of T2DM, the HPA axis fails to control the secretion, and a study demonstrated an increase in the level of certain releasing hormones from the hypothalamus like corticotropin-releasing hormone, growth hormone, cortisol, epinephrine, norepinephrine, insulin, glucagon, and neuropeptide Y, which contributes to a great extent to T2DM development. The second modality, SNS, also triggers a disturbed HPA axis during a stress condition leading to impaired eating habits, which results in obesity and thus increases the risk of developing DM. A study shows the relationship between chronic stress and development of visceral obesity, which provides a positive correlation with the prevalence of T2DM. Another study validates the association of stressful events with new cases of DM [67]. How this can be alleviated by yoga intervention has to be investigated in the future studies.

**Circadian Rhythms**

There are several studies which advocate the doctrine of circadian rhythms as major contributors of risk factors associated with diabetes [68] due to the altered CLOCK gene which causes disturbed pattern of glucose tolerance and insulin sensitivity. The suprachiasmatic nucleus (generator of circadian rhythms) and melatonin (hormone) play a pivotal role in the regulation of circadian rhythms. A study demonstrates the low level of circulating levels of melatonin [69] and upregulated expression of melatonin membrane receptors [70]. There is an association of the allelic variants of melatonin membrane receptor with the level of FBG that shows an increased risk of T2DM. This shows the role of melatonin in glucose homeostasis in blood [71–73]. Whether these are impacted by yoga intervention has not been investigated; however, the data from future studies may provide new clues about the impact of sleeping patterns.

**Age-Related Cognitive Decline**

The most neglected complication of DM is the occurrence of cognitive deficit, mainly in early years of life (5–7 years) that corresponds to the development of the brain system and also in later years of life (>60 years), which corresponds to the neurodegenerative phase due to aging. The scientific community has shifted its attention towards the investigation of the most neglected part of diabetic complications (cognitive dysfunction and dementia). Cognitive dysfunction represents a highly prevalent and very serious problem faced by the majority of the elderly population worldwide [13]. DM is proving to be a potent risk factor for the development of dementia (vascular) and neurodegenerative disease (AD). Several studies show structural changes in the brains [74–79] of patients with T1DM and T2DM, and also show a decline in multiple domains of cognitive functioning. These cognitive functions show a decline in specific cognitive domains like intelligence, attention, memory, executive functioning, and processing speed. The main domain of cognitive deficits lies mainly in psychomotor and
processing speed [21–26]. A study shows the role of glycemic control in preserving cognitive performance in patients with T2DM. Another study shows an inverse relationship between serum HbA1c and cognitive functioning [learning [14], executive functioning [15], working memory [15, 16], and complex psychomotor performances [17, 80]]. An MRI-based comparative study showed alteration of the amygdala and hippocampal regions in T2DM patients as compared with control subjects. These 2 areas play an important role in memory and behavior, and were found to deteriorate in neurodegenerative disease (AD) [28]. The emerging yoga intervention studies should probe the cognitive dysfunction and its presentation in diabetes.

**Diabetes Mellitus and AD**

The main connecting domains of cognitive dysfunction in DM correspond to hyperglycemia, vascular disease, IR, and hypoglycemia [81]. DM promotes the atrophy in the cerebral structures and interferes with cognitive reserves and threshold parameters (cerebral amyloid and tau metabolism [82]) that reflect the symptoms of AD. Altered insulin and glucose metabolism affects insulin receptors in the brain and its functioning that promotes the oligomerization of β-amyloid and stimulates hyperphosphorylation of the tau protein. Another component that accelerates biological aging is IR through formation of advanced glycation end-products and reactive oxygen species [83]. A study shows heavy deposition of β-amyloid and neurofibrillary tangles in the brain sections of T2DM patients. Another study shows an increased amyloid deposition of patients having both (APOE-4 genotype and DM) [79, 82].

**Treatments and Lifestyle Interventions**

The HIS, CDA, and ADS strongly recommend the use of certain OADs like thiazolidinedione and alpha glucosidase inhibitors. The use of OADs provides relief to an extent, but its side effects may include gastrointestinal disturbance which includes vomiting, nausea, diarrhea, gastritis, hypoglycemia, and accumulation of gas in the alimentary canal. The onset of DM may be delayed by adopting the lifestyle modifications with or without the use of various drugs in combination like metformin, acarbose, voglibose, and troglitazone [27, 33, 34]. Lifestyle interventions associated with increased physical activity followed by adapting healthy eating habits (dietary advices) have proven to be effective in preventing diabetes [14, 15, 85]; however, they seem to be a failure due to the rising numbers of PreDM individuals, which are contributing to the increase in the cases of T2DM. One of the most popular and economic lifestyle intervention tools is yoga. The description of word yoga is found in Sanskrit. In Sanskrit, *yuj* means to unite one’s body breath and mind [80] to the universal power. Yoga is an ancient practice that emphasizes balancing of various aspects (like physical, mental, emotional, and spiritual) of an individual. Yoga focuses on the general well-being of an individual by following the path of physical postures (asanas), breathing exercises (pranayamas), and meditation (dhyana) [85]. Yoga therapy consists of a specialized set of asanas, pranayamas along with meditation depending on different health problems. Certain sets of asana that have proven to be beneficial for the abdominal area cause rejuvenation/ regeneration of the pancreas, which promotes glucose metabolism along with its utilization through several tissues like peripheral tissues, liver, and adipose tissue via enzymatic activity [86–88]. A case-control study showed the effect of yoga in T2DM patients reducing the requirement of insulin and also a significant decrease in various parameters (FBS, PPBS, HbA1c) [89]. Several studies show an association of altered autonomic function with diabetes and obesity [25, 26]. Studies also show improved cardiac autonomic functions of patients between the groups (yoga
breathing group and standard therapeutic group) [90, 91]. Another randomized control trial by McDermott et al. [25] demonstrated the effectiveness of yoga in reducing weight validated by reduced WC, reduction in systolic and diastolic blood pressure, and reduced level of total cholesterol in lipid profiling. There is also a significant decrease in the levels of anxiety, depression, and stress perception in both groups (yoga and walking intervention) [92]. Yoga plays a pivotal role in reducing the expression of the inflammatory marker C-reactive protein and cytokines (interleukin-6 and lymphocyte-1B) [93, 94]. Another study has shown an increased level of the anti-inflammatory marker adiponectin in yoga practitioners [95]. There are several studies which emphasize the role of yoga in reducing the risk factors for T2DM development through reduction in weight, and also promoting mental and holistic well-being, i.e. required for happy and healthy living of an individual [92]. Many other studies favor yoga as an effective tool for reduction of stress, facilitated by the regulation of SNS-HPA. Another study has reported the usefulness of yoga in reducing cortisol level, glucose level (in blood), level of rennin (in plasma) and also reduced level of catecholamines (norepinephrine and epinephrine) in urine within 24 h [96].

**Guidelines, Organizations, and Management**

The guidelines issued by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) describe treatment of diabetes in different ways. The individuals who suffer from diabetes will be required to take insulin through different methods like injecting subdermally (with the help of a syringe, pen, injection aid, and injection port), external insulin pumps, and the last method is artificial pancreas. Other organizations like HIS, CDA, ADS that work for the eradication of diabetes, in their guidelines refer to the clinician for prescribing OADs (thiazolidinedione, alpha glucosidase inhibitors, etc.). The onset of DM is delayed by adopting lifestyle modifications alone or with the use of various combinations of metformin, acarbose, voglibose, and troglitazone [10, 52, 53]. Another aspect of management is a preventive aspect that concerns regular monitoring of cholesterol level and blood pressure, blood glucose, etc. The report published by the WHO advocates the use and promotion of healthy habits like healthy food (less fast food), not smoking, and regular physical activity to maintain normal body weight, and also advises to screen early for diabetes-associated retinopathy, neuropathy and kidney disease [97].

**Yoga as a Lifestyle Modification Tool**

The comfort zone of an individual is his/her lifestyle, and it follows a particular pattern during his/her lifespan. Therefore, lifestyle is a way of doing things in a way that is comfortable for an individual. Today, teenagers are used to spending luxurious life pertaining to outing with friends late at night, consuming fast food very often, developing irregular dietary habits and, most importantly, neglecting physical activity required for proper physiological and metabolic functioning. The central target for any lifestyle modification strategy is to motivate individuals to take up physical activity, directing them to avoid fast food on a regular basis as suited to one’s lifestyle and energy consumption. The main cause of the increase in the prevalence of diabetes is partly because PreDM remains undetected due to asymptomatic features even though the lifestyle modifications appear to be ineffective in prevention and development of diabetes. Lifestyle modification seems to be effective through promotion of physical activity followed by dietary suggestions from clinicians as a preventive tool for management of diabetes [98–101]. There are several studies on lifestyle modification programs which show its worth and support prevention of diabetes, i.e. Diabetes Prevention Study (DPS) [102], US Diabetes Prevention Program (UDPP) [103], Indian Diabetes Prevention Programme
(IDPP) [104, 105], and Da Qing IGT and Diabetes Study (DQS) [106] from Finland, USA, India, and China, respectively. Lifestyle modification seems to be the most effective way for preventing and managing the rate of progression from PreDM to DM in high-risk individuals [98]. This is why the Indian PM has advocated the yoga intervention in the lives of Indian diabetics.

**Yoga as a Possible Solution for Prevention and Management**

One of the most popular and economic lifestyle intervention tools in the management of diabetes and its complications is yoga. In the ancient sacred scriptures like patanjali yogasutra or hatyogpradipika entitled *Yogaschittavritti Nirodaha*, the main body of the text signifies the importance of yoga as a union of healthy mind, body, and soul to the supreme soul of the universe. Yoga focuses on the general well-being of all the individuals via following the 8-fold path as described in hatyoga practitioners which puts emphasis on various aspects; some of them include physical postures (asanas), breathing exercises (pranayamas), and meditation (dhyana) [85]. In our modern era, the scriptures that advocate the usefulness of yoga as a remedy for various ailments now reveal its medical importance in terms of its therapeutic application which comprises of various standardized techniques like panchkarma therapy, Sherodhara, vanama, nauli, accupressure, etc. So, yoga therapy [107, 108] comprises a set of yogic exercises that an individual performs on his/her own after an orientation class. An individual may attend a yoga module regardless of his/her previous experience. A yoga module ranges from gentle warming exercises to complex practices of asanas and pranayama. An important component of yoga is asanas, which provide strength for the musculoskeletal system through the balance between the relaxing and stretching components of muscular tissue. It helps in the mobilization of skeletal joints and postural stability required for the stability and equilibrium of the physiological and psychological components of an individual. Another important component of yoga is pranayama. It is believed that when practicing hatyoga, if a person controls the breathing rhythm, they will control their own mind and body. Controlling breathing seems to be difficult because one has to connect one’s unconsciousness to consciousness for maintaining a uniform flow of energy which is regulated by different energy chakras in our body that help to maintain a homeostasis and promote a holistic, healthy, and happy living.

**Effect of Yoga on the Biochemical Profile**

Asanas focus on stretching exercises which promote balanced glucose metabolism along with effective enzymatic activities in peripheral organs (liver, adipose tissue, etc.) [85–87]. A study has shown a reduction in the level of blood sugar (a biochemical parameter) [109] and improved metabolic activity (measured as triglyceride uptake by adipose tissues) [110, 111]. Yoga postures (asana and pranayama) also improve β-cell sensitivity to glucose signaling and insulin secretion [112] and help in the regulation of body homeostasis [113]. Another study compared the baseline biochemical parameters (FBG, serum total cholesterol, LDL, VLDL, and their ratios) before and after assessment of an 8-day yoga practice and found them to be significantly reduced [114]. Another case-control study shows its effectiveness in lowering biochemical parameters (FBG, PPBS, HbA1c) along with reducing the need of insulin in T2DM [115]. The limitation of the study was small sample size (n = 44) and short duration of intervention (3 months). Another study has shown the effectiveness of yoga practice (40 days) and found a significant reduction in some of the biochemical parameters (insulin and FBG level), and taking into consideration WHR as one of the anthropometric variables [116]. Yoga practice also significantly improved biochemical parameters (adiponectin, lipid levels [serum]) along with a reduced risk of the metabolic syndrome in obese individuals (post-menopausal women) [117].
Effect of Yoga on Cognitive Functions

Current studies provide evidence for the involvement of T2DM in cognitive dysfunction and structural changes that take place in the brain [118]. Brain is considered as the master of the body owing to its role in the regulation of the normal glucose level in the body and the development of T2DM. Certain studies show the involvement of higher centers of the brain in lowering blood glucose in an insulin- and non-insulin-dependent manner [119]. There are several cohort studies which demonstrate the progression of PreDM cases to T2DM around the world [120–125]. A study showed a close relationship between brain insulin sensitivity and visceral adipose tissue changes brought about during lifestyle intervention [125]. Another study showed the effectiveness of yoga in improving the cognitive function of T2DM patients. The main lacunae in the study is its small sample size (n = 60) and short duration (45 days) [126].

Yoga and Neurophysiology

The micro- and macrovascular complications are considered as a hallmark of diabetes and other associated complications. A study by Dunstan et al. [127] showed the appearance of these complications (micro- and macrovascular) in PreDM. The risk of IFG and IGT along with cardiovascular complications differs between individuals [128–130]. A number of studies show an association of altered autonomic function with diabetes and obesity [131, 132]. Early detection of altered cardiac autonomic function acts as a diagnostic marker for screening of cardiovascular risk in PreDM and has been laid down as the foundation of preventive measures against the progression to DM. Another cross-sectional study found a combination of various factors (altered cardiac autonomic function, hyperinsulinemia, IR, oxidative stress, inflammatory response, and IFG) that contributes and ultimately leads to the progression of diabetes [133]. A study compared the level of cardiac autonomic functions and found it to be improved in patients of the yoga breathing group [90, 91]. Another study showed yoga as effective in reducing the heart rate, and systolic and diastolic blood pressure [134]. A recent study put emphasis on disturbances in autonomic function which were positively correlated with poor control of glucose metabolism, an increase in lipid peroxidation, and a decrease in NOx− levels, which signifies greater chances for development of vascular dysfunction and cardiac disease in T1DM patients. The major limitation of the study was its small sample size (n = 19, CT = 10 and T1DM = 9), and only males participated in the study. Another randomized control study showed the effect of yoga on various parameters, i.e. anthropometric (weight, WC, systolic blood pressure, diastolic blood pressure), biochemical (total cholesterol), and some psychological parameters (stress, anxiety, and depression), and found yoga to reduce them significantly [92]. Imaging can be included in future studies and campaigns against diabetes.

Yoga and the Immune System

A study showed an immunomodulatory effect of yoga on stress through the increased level of immunoglobulin A along with natural killer cells. Another study demonstrated a pivotal role of yoga in reducing the inflammatory marker C-reactive protein and cytokine (interleukin-6 and lymphocyte-1B) expression [93, 94], and an increased level of the anti-inflammatory marker adiponectin [95]. Yoga has also been shown to be effective in reducing weight in relation to obesity, which is associated with the risk of developing T2DM, and also provide a feeling of wellbeing in an individual from the psychological point of view. The limitations of the study is its small sample size (n = 41, yoga = 21 and walking control = 20) and its short duration (8 weeks) [92]. A study found the usefulness of yoga in reducing cortisol (examined through saliva), glucose (in blood), rennin (in plasma), and catecholamine (norepinephrine and epinephrine) in urine within 24 h [96]. There are about 25 studies which
advocate the association of decreased blood glucose, HbA1c, and IR, and improved insulin sensitivity [132, 136] along with improved values for oral glucose tolerance test through a yoga intervention lasting 8–12 months. A study showed how yoga affects the physiological and psychological aspects by assessing various anthropometric (weight, BMI, WHR) and psychological parameters (mood, self-esteem, and QOL) [115] and found yoga to reduce the anthropometric variables and improve the psychological variables. Yoga shows its benefits for improving nerve conduction and cognitive functions in diabetic patients leading to effective management of diabetic complications [137]. Yoga has been gaining in popularity in recent years as an intervention with the potential of preventing the occurrence and progression of metabolic deterioration and comorbidities. On the basis of the cited literature, the major focus is on prevention for the reduction of healthcare costs that can be borne by an individual for the treatment of the disease. According to the study conducted by ICMR, the prevalence of diabetes and prediabetes is 11.1 and 13.2%, respectively, in Chandigarh. Yoga has the potential for managing DM in an effective manner as proven by the cited literature so far, but the greatest lacunae of the cited literature is that no one has attempted to investigate the effect of yoga on the prevention and management of PreDM and its progression to further diabetic complications (especially cognitive decline as a hallmark of neurodegenerative disease) with cognitive changes.

**National Campaign for Yoga-Based Diabetes Management**

The current review has highlighted the potential benefits of yoga-based lifestyle modification for the management of diabetes, which has to be explored further in future studies. A systematic population-based multicenter study evaluating yoga-based lifestyle modification would provide future directions. The need of the hour is a national campaign targeting various regions of India and identifying the population at risk. Further, the risk factors such as dietary habits, addictions, lifestyle, physical activity level, sleep quality and stress level would need to be assessed. The anthropometric parameters, cognitive functions, and biochemical indices such as fasting glucose, postprandial glucose levels, HbA1c, and lipid profile would also provide valuable insight in more objective assessments. The campaign would help in validating a yoga-based lifestyle program and provide policy makers with directions.

**Conclusions**

It is expected that this systematic review will attract many researchers across the world, especially in developing countries, to perform further studies on yoga-based lifestyle management in diabetes. Multicenter studies will be useful in establishing centers of integrative medicine as these will be cost effective.

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