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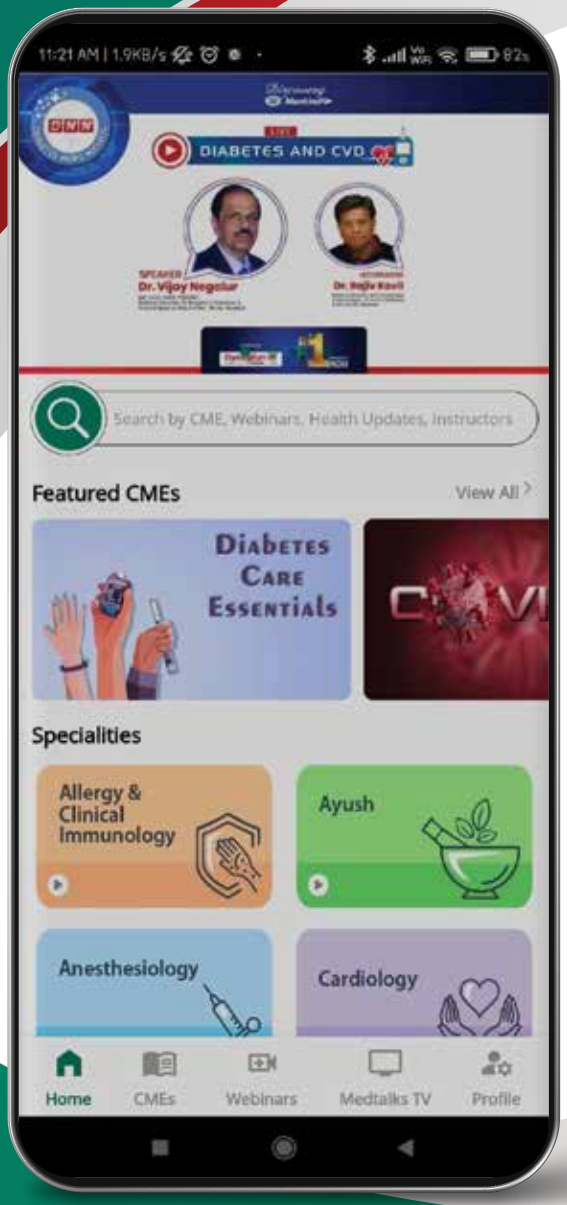

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CLINICAL STUDY

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Prediabetes: A Platform for Prevention of Diabetes

The diabetes pandemic has created a major clinical as well as public health challenge for the world. This has led to a mammoth infrastructural and financial burden, threatening national economies. While diabetes is a major issue, the worsening prediabetes epidemic is even more worrisome. The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB)-17 report highlights that prediabetes is more prevalent than diabetes in every Indian state.[1] The high diabetes epidemicity index means the worst is yet to come.[2]

Prevention of Diabetes

The best way of managing diabetes is to prevent it. This can be done by intervening actively at the prediabetes stage. Prediabetes is a well-defined clinical condition. There are clearly delineated diagnostic criteria endorsed by the World Health Organization (WHO) and American Diabetes Association (ADA).[3,4] As prediabetes is usually asymptomatic, proactive screening is required to identify it on time. The screening methods and the high-risk populations that need to be targeted are well-defined. Screening is simple: a plasma glucose estimation is required to diagnose dysglycemia using WHO cut-offs.[4]

Diagnosis of Prediabetes

It makes sense, therefore, to promote timely screening, diagnosis and management of prediabetes. This should be made a public health priority and be practiced at all levels of health care, whether primary, secondary, or tertiary. Various national health care programs, e.g., human immunodeficiency virus (HIV) and tuberculosis (TB), integrate screening for diabetes and prediabetes in their protocols.[5-7] Such activities can be strengthened and expanded to include a wider population segment in their ambit.

At the clinical level, too, one must practice screening for prediabetes. This can be done cost-effectively in high-risk persons who access the health care system with clinical features, comorbidities, complications or concerns suggestive of dysglycemia. It should also be carried out in asymptomatic persons from high-risk ethnicities.

Caveats and Care

One should be aware of and respect the caveats that accompany any screening intervention. Appropriate tools should be used: glucometers should be Federal Drug Administration (FDA) or International Standard Institute approved; glycated hemoglobin (HbA1c) should be measured in accredited laboratories or by accredited point-of-care testing machines. The right technique should be followed, as reinforced by the principles of glucometric guardianship.[8]

Clinical Responsibility

Screening should not be limited to just sharing a biochemical number or diagnosis with the patient.

It should include counseling about the interpretation and impact of these numbers and the interventions needed to optimize them.

It is not necessary that pharmacological interventions have to be offered to everyone with prediabetes. Lifestyle modification remains the treatment of choice. It can be supplemented with functional foods, nutraceuticals, and drugs to optimize metabolic dysfunction such as obesity, hypertension and dyslipidemia. In selected persons, medication may be indicated. These include persons with established (or at high-risk of) atherosclerotic cardiovascular disease, those at high-risk of developing diabetes, as well as those who are concerned about their health.[9]

Advocacy and Activism

While action is required at both public health and clinical levels, collaborative and concerted activism, and advocacy is necessary to tackle prediabetes and prevent diabetes. Keeping this in mind, the Endocrine Society of India observed the first International Prediabetes Day in 2021. The date 14th August was chosen, as it falls 90 days before World Diabetes Day on 14th November the usual time required to reverse prediabetes and observe a meaningful change in HbA1c levels. Multiple partners added their voices to this initiative. Within 2 years, Prediabetes Day has become a truly international event endorsed by the South Asian Federation of Endocrine Societies (SAFES) and International Diabetes Federation (IDF). While the 2021 theme was Fight Prediabetes, 2023 takes inspiration from the IDF's theme for World Diabetes Day, "Access to Diabetes Care".

Showing solidarity the Asian Journal of Diabetes also lends its voice to advocate for "Access to Prediabetes Care". By this, we mean facilities for regular, timely screening, lifestyle counseling, testing for possible complications and comorbidities, as well as the institution of pharmacological therapy if necessary.

The Way Ahead

To do so, we all need to work together at a mass level. Policymakers, planners, physicians, paramedical personnel, popular personalities, members of the public, and patients, all need to understand the importance of detecting and dealing with prediabetes. It is not that a new 'disease' is being created by us; rather, we wish to prevent disease from taking root in our society.

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Sapiotypes and Diabetes Care

Introduction

Diabetes care is a complex affair. The vast diversity of the causative factors, clinical features and concerns that a person presents with, along with the equally diverse complications, comorbidities and concomitant medications that may coexist with diabetes, make management challenging. One way of meeting this is to classify diabetes in a manner which helps in therapeutic planning.

Rubrics of Classification

Various rubrics have been proposed by expert clinicians and researchers to assist in this endeavor. The simplest, perhaps, is the metabolic fulcrum, which divides persons with diabetes into those who are catabolic 'eubolic', and those who are 'maladaptively anabolic.[1] This is concordant with the tridoshic concept of Ayurveda, which lists vata, pitta and kapha as the three doshas.[2] Catabolism can be viewed as an equivalent of vata, embolism as pitta, while maladaptive anabolism can be viewed as kapha. While the metabolic fulcrum is based upon phenotype and physiology, it is backed by biochemistry, and promotes person-centred choice of pharmacotherapy as well.

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Recently, researchers have suggested five clusters of diabetes: severe autoimmune diabetes, severe insulin deficient diabetes, severe insulin resistant diabetes, mild obesity related diabetes and mild age-related diabetes.[3] Insulin resistant obese diabetes is also reported from India, as is combined insulin resistant and deficient diabetes.[4]

Advantages of Phenotyping

These phenotypes assist in not only classifying, but also managing diabetes. Identifying the specific phenotype allows the clinician to anticipate the natural trajectory of the syndrome, counsel the patient and advise appropriate screening, monitoring and therapeutic interventions. There is much more to diabetes than mere biochemistry, however. The individual's attitude towards the health care system influences the natural history of diabetes as much as biomedical factors do. Health care seeking, and health care accepting behaviors contribute to the success, or otherwise, of any diabetes care strategy. Accepting the diagnosis of diabetes, and prescribed treatments, are the rate-limiting step of the diabetes care pathway. Emotional and social factors play an important role in this process.[5]

Sapiotyping

We propose the term 'Sapiotype', based on the Latin root 'sapiens' (wise) to describe the various attitudes that persons with diabetes may have towards their disease, their doctor or health care providers, a specific

diagnostic procedure, drug or delivery device, and the health care system at large.

Understanding the sapiotype assists the diabetes care professional in understanding the mental makeup of the individual being treated, in crafting effective communication and counseling strategies and in planning person-centric therapeutic interventions. We list these sapiotypes in Table 1, providing an alliterative rubric that can be used in the clinic.

Just as we compare the metabolic triad with the Ayurvedic tridoshic model, we attempt to link sapiotypes to the three mental and emotional phenotypes of Indian philosophy: Rajsik, sativik and tamsik.[6] While rajsik conveys an action-oriented, androgenic and adrenergic mindset; tamsik describes the opposite-complacence, casualness and callousness. Sativik is a balanced state, characterized by equanimity and equipoise.

Table 1. Sapiotypes Encountered in Health Care

Sapiotype	Equivalent in Indian philosophy
Avowed denial	Tamsik
Annoyed/angry Aggressive/argumentative	Rajsik
Accepting/aware/ Action oriented	Sativik
Anxious/afraid (diabetes distress, insulin distress)/alarmed	Rajsik
Apathic/acquiescent (fatalistic)	Tamsik

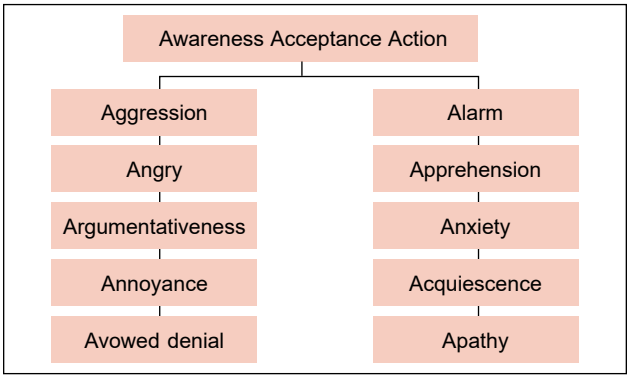

Figure 1. The spectrum of sapiotypes.

Sapiotypic Spectrum

The sapiotype may be viewed as a spectrum of emotions (Figure 1), ranging from extreme denial and anger on one hand, to extreme apathy and fatalism on the other. The zone in the middle-acceptance, affirmative assertion and action, in anticipation of better health, is the ideal state of mind for health care.

Sapiotypic Fluidity

No single emotion can exist in isolation and neither can it be sustained lifelong. The same person may exhibit varied emotions to different targets (e.g., members of the health care team; specific investigations and medications) at various times during the journey of diabetes. These variations should be accepted as a part of emotional fluidity. However, there will always be a single emotion that will predominate at the start of any clinical encounter. This is the sapiotype of the individual at that point of time.

The sapiotype is malleable, and can be molded and modified to optimize therapeutic outcomes. Knowing where one starts from can help the astute clinician guide the patient, using a process of informed and shared decision making, towards optimal health. This is the process of responsible person centered care.

The Way Forward

We suggest the use of sapiotypes in clinical practice, as well as in research, to create person-centered therapeutic counseling and education interventions, The sapiotypic model also allows for institution of appropriate pharmacological therapy, as it includes the clinical constructs of diabetes distress and insulin distress. The first step, however, would be to create and validate screening and diagnostic tools to help identify sapiotypes. Once this is done, sapiotypic characterization will become part of evidence-based medicine.

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REVIEW ARTICLE

Knowledge, Attitude and Practice in Managing Chronic Kidney Disease with SGLT2 Inhibitors

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ABSTRACT

Background and objective: Chronic kidney disease (CKD), and its increasing global burden, is associated with significant morbidity and mortality. This survey-based study aims to capture the knowledge, attitude and practices (KAP) amongst practicing physicians in considering sodium-glucose cotransporter 2 inhibitors (SGLT2i) for the prevention and progression of CKD in diabetic or nondiabetic individuals. **Methodology**: An online questionnaire-based survey was conducted among 262 health care practitioners (HCPs) who manage people with CKD with or without diabetes. The survey was prepared as a Google form and circulated through email to different HCPs. The survey consisted of 6 knowledge-based questions, 4 attitude-based questions and 4 practice-based questions. The forms were filled up voluntarily by the participants and the authors had no control over the response provided. All the responses were consolidated using Microsoft Excel and analyzed. **Results**: A total of 262 HCPs from different regions of the country participated in the survey. About 87% to 94% of the participants were aware that SGLT2i, specifically dapagliflozin, is approved for use in CKD patients with or without diabetes. About three-fourths of the HCPs accepted that an initial drop in estimated glomerular filtration rate (eGFR) occurs upon initiation of dapagliflozin treatment. Almost 90% of them acknowledged the importance of screening for CKD in diabetic patients, and the majority were aware of the renal benefits of SGLT2i. Almost 96% of HCPs consider that dapagliflozin could be used in all patients with CKD irrespective of their diabetes status. Major determining factors with respect to a setback in practice are fear of side effects (54%) and hesitation in switching to newer medications when older medications work fine (34%). **Conclusion**: SGLT2i have demonstrated significant clinical benefits in patients with CKD with or without diabetes. This survey has shown good awareness among clinicians of the beneficial role of SGLT2i in CKD.

Keywords: KAP, health care practitioners, survey, diabetic kidney disease, SGLT2i, diabetes, dapagliflozin

Introduction

Chronic kidney disease (CKD), and its increasing global burden, is associated with significant morbidity and mortality.[1] In addition to the distressing effects of decreased renal function, the treatment burden also severely impaired the quality of life of affected individuals.[2,3] With the alarming global prevalence of comorbidities, including diabetes, hypertension and obesity, there is a corresponding significant surge in the prevalence of CKD.[4,5] Diabetic kidney disease coexisting in 30% and 40% of individuals with type 1 and type 2 diabetes (T2DM) remains a grave concern, highlighting the need to prevent CKD and its progression.[6]

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There are no new medicines that have shown to decelerate the progression of CKD to kidney failure in the last two decades. Surprisingly, sodium-glucose cotransporter 2 inhibitors (SGLT2i) came out as reno-protective agents due to their potential to treat diabetes and kidney dysfunction.[7,8] Various clinical trials and consensus guidelines have recommended the use of SGLT2i in individuals with T2DM to reduce risks for CKD and cardiovascular disease (CVD).[9-12] The mechanisms of nephroprotective action of SGLT2i extend beyond glucose-lowering, weight-lowering and blood pressure-lowering effects that accompany their glucosuric action in people with diabetes. They protect the glomeruli by reducing intraglomerular pressure, improving tubular oxygenation and metabolism and reduction in renal inflammation and fibrosis.

Among the class of SGLT2i, dapagliflozin is the first drug to be approved by the Food and Drug Administration (FDA) in April 2021 for use in CKD patients irrespective of their diabetes status.[13]

The results of DECLARE-TIMI 58 suggested a role for SGLT2i in the prevention of diabetic kidney disease. Dapagliflozin had demonstrated a favorable effect on urinary albumin-to-creatinine ratio (UACR) and renal-specific outcome across baseline UACR categories, including patients with normal albumin excretion.[14] In 2020, generic and affordable versions of dapagliflozin were made available by various manufacturers. Despite supporting evidence and improved affordability, the usage of dapagliflozin is still inadequate by the Indian practitioners who manage CKD based on treatment audit.[9]

Experts certainly follow guidelines based on high-quality evidence from landmark studies. However, when it comes to the practical application of the guidance, they must go through certain adaptations that consider the newer evidence and clinical practice guidelines and patient's context, such as comorbidities, economic status, education status and ability to comply with the proposed management. So, the real-world usage or complete adherence to guidelines may not be exactly reflective of a randomized clinical trial setting. Ultimately, real-world usage is based on evidence, expert guidelines and experience-based applications.

Despite all the affirmative findings and guideline statements and regulatory approvals, continuing medical education (CME) programs, the question remains to what extent the physicians are really applying this knowledge. If this knowledge does not translate into practice, it undermines all the efforts and the actual benefits are never reaped. Therefore, the current survey was conducted to capture the knowledge, attitude and practices (KAP) amongst practicing physicians in considering SGLT2i for the prevention and progression of CKD in diabetic or nondiabetic individuals. Through this study, the authors sought to identify and highlight the gaps and eventually hope that the practitioners would reduce these gaps and pass on the benefits of SGLT2i based on recent evidence and guideline recommendations in the management of CKD.

Materials and Methods

An online questionnaire-based survey was conducted among 262 health care practitioners (HCPs) who manage people with CKD with or without diabetes. The HCPs practicing in different geographical locations were selected based on random sampling method. The survey was prepared as a Google form and circulated through email to different HCPs. The survey consisted of 6 knowledge-based questions, 4 attitude-based questions and 4 practice-based questions.

The forms were filled out voluntarily by the participants who had no control over the responses provided. All the responses were consolidated using Microsoft Excel and analyzed.

Results

A total of 262 HCPs from different regions of the country participated in the survey.

Two-third of the HCPs were correct in their responses of the patient group included in the DECLARE-TIMI trial (Fig. 1A) and almost 90% were aware that dapagliflozin was the drug studied in the clinical trial including patients with CKD and heart failure with reduced ejection fraction (HFrEF) (Fig. 1B).

About 87% to 94% of the participants were aware that SGLT2i, specifically dapagliflozin, is approved for use in CKD patients with or without diabetes and is considered a first-line treatment choice for diabetes in patients with diabetes and CKD (Table 1). About three-fourths of the HCP accepted the initial drop of estimated glomerular filtration rate (eGFR) upon initiation of dapagliflozin treatment.

Almost 90% of the HCPs acknowledged the importance of screening for CKD in diabetic patients, and the majority were aware of the renal benefits of SGLT2i. Three-fourths of the respondents were aware about the use of dapagliflozin in CKD patients irrespective of the glycated hemoglobin (HbA1c) status.

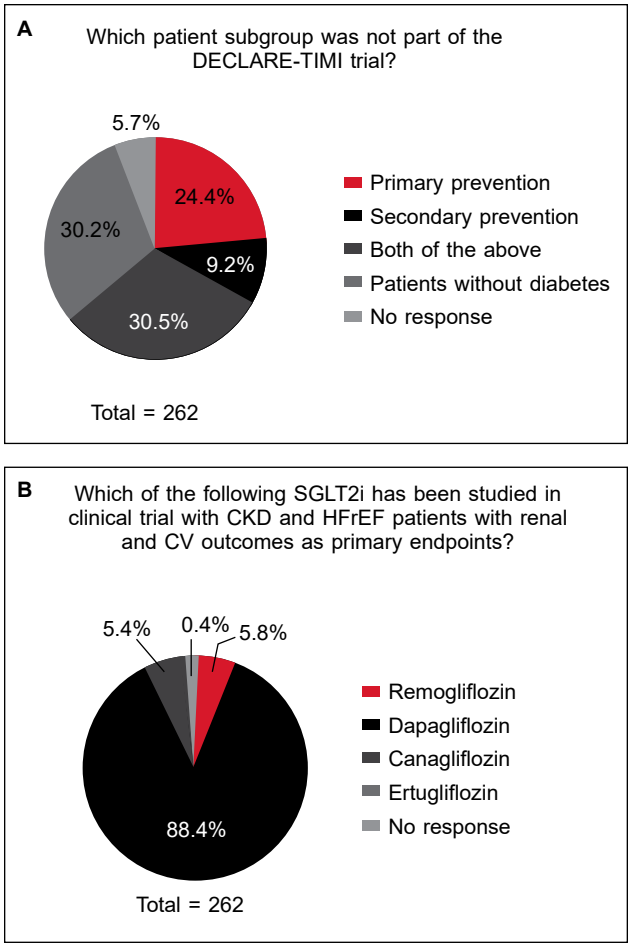

Figure 1. Knowledge-based responses to questions on clinical trials.

Table 1. Responses to Knowledge-based Questions

Questions to map the knowledge gaps	No. of responses	True/Yes
SGLT2i are recently approved for the management of CKD with or without diabetes.	245	94.3%
Dapagliflozin reduced the long-term decline of eGFR?	245	92.2%
In patients with CKD, SGLT2i is indicated as first-line agent of T2DM with CKD.	241	87.1%
There will be an initial drop of eGFR upon initiation of dapagliflozin. Is it acceptable?	242	74%

Majority of the HCPs opined that people with diabetes must be screened for CKD and consider SGLT2i for management (Fig. 2A and 2B). Almost 96% of HCPs consider that dapagliflozin could be used for management in all patients with CKD irrespective of their diabetes status (Fig. 2C and 2D).

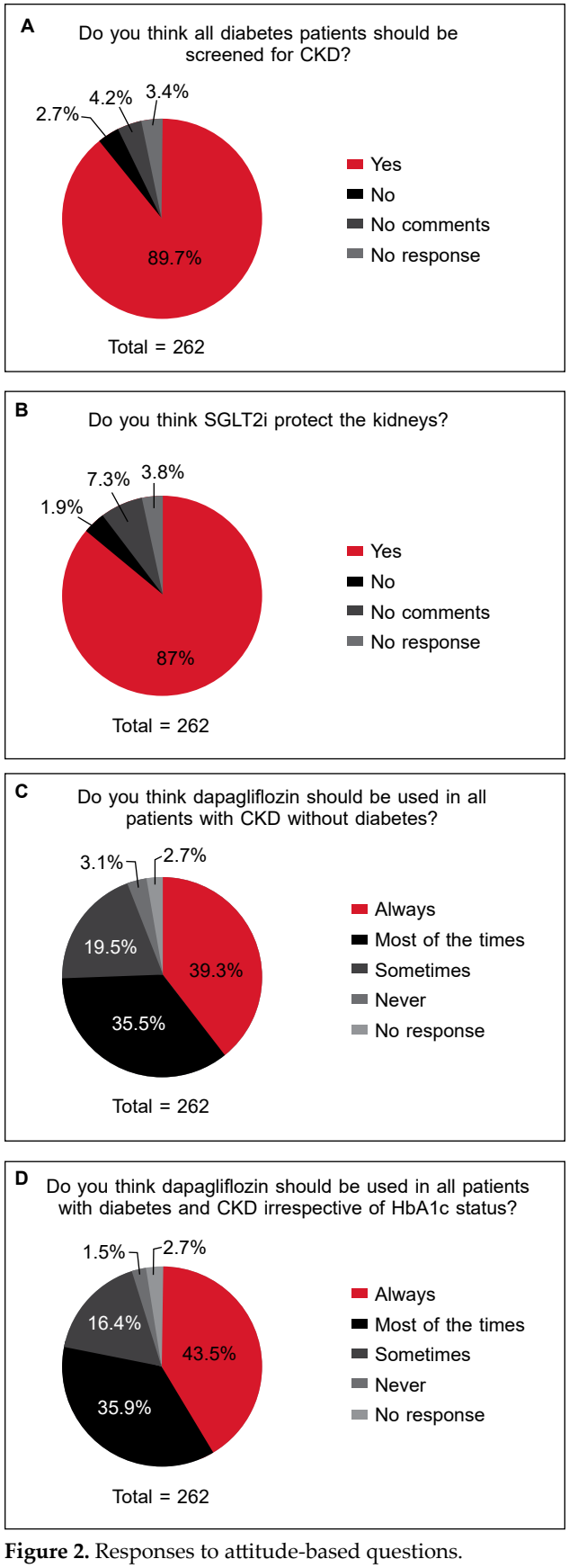

Figure 2. Responses to attitude-based questions.

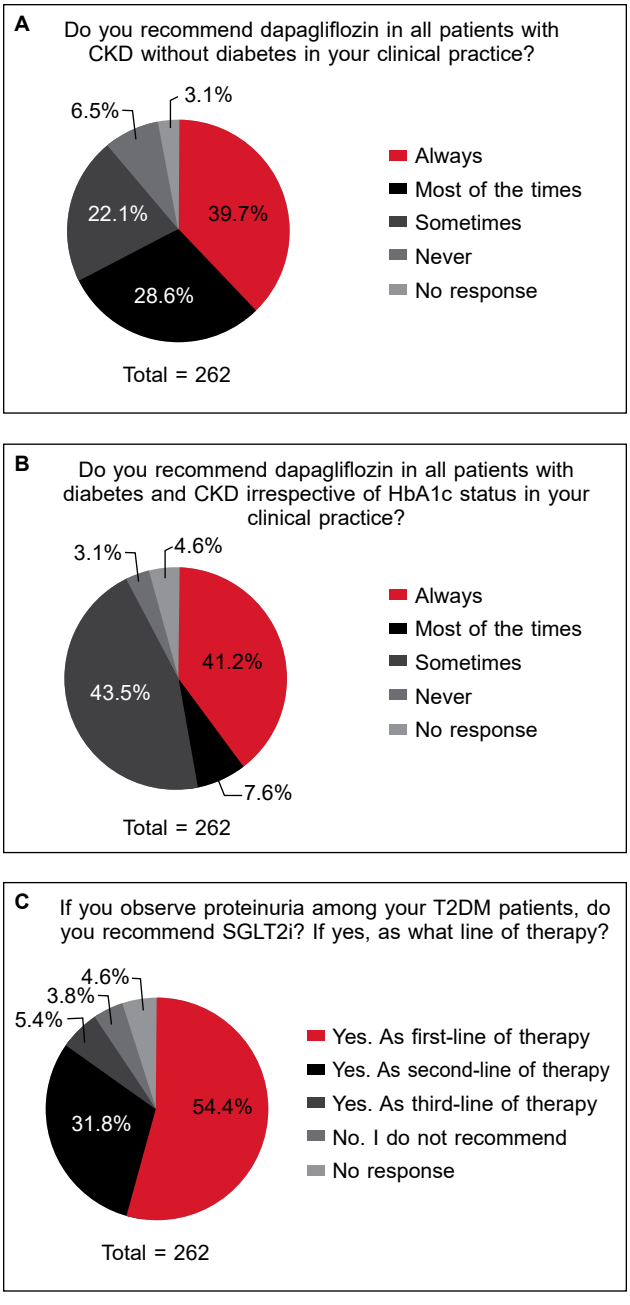

Figure 3. Extent of recommendation of dapagliflozin **A**) in patients with CKD with or without diabetes, **B**) All patients with diabetes, CKD and **C**) T2DM patients with proteinuria.

Practice-based Questions

Only about 40% to 50% of the respondents always recommended the use of SGLT2i in patients with proteinuria or dapagliflozin for CKD patients with or without diabetes (Fig. 3A-3C). Major determining factors with respect to a setback in practice are fear of side effects (54%) and hesitation in switching to newer medications when older medications work fine (34%) (Fig. 4).

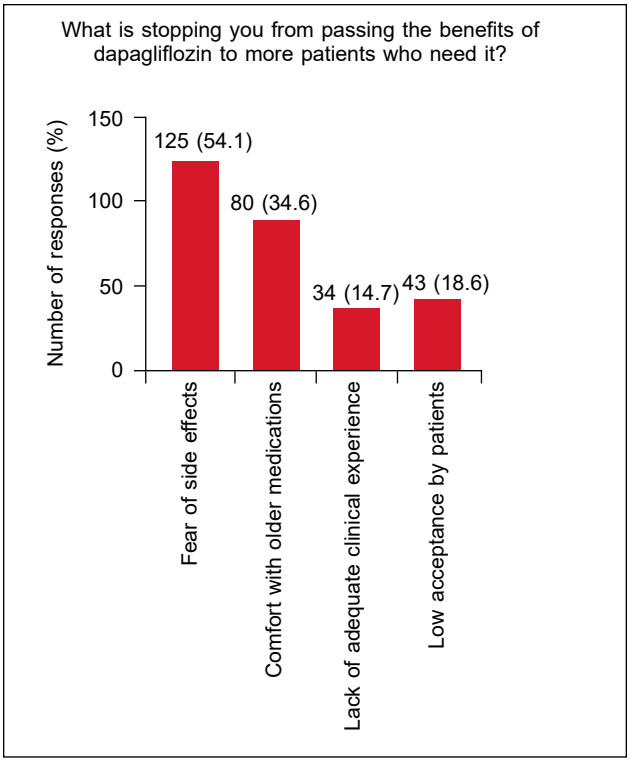

Figure 4. Factors affecting practice of passing the benefits of dapagliflozin to more patients.

Discussion

Knowledge among HCPs about SGLT2i and the efficacy of dapagliflozin to prevent the decline of eGFR is noteworthy (Fig. 1). Based on the responses to different types of questions, it was seen that there is a high level of awareness on the pertinent aspects on the usage of SGLT2i for the management of people with CKD. Various clinical trials and consensus guidelines have recommended the use of SGLT2i in individuals with T2DM to reduce the risks of CKD and CVD.[9] The KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease recommends the administration of SGLT2i in patients with T2DM and CKD with an eGFR ≥20 mL/min/1.73 m^2.[10] However, for people with type 2 diabetes and diabetic kidney disease, use of an SGLT2i in individuals with eGFR ≥20 mL/min/1.73 m^2 and UACR ≥200 mg/g creatinine is recommended to reduce CKD progression and cardiovascular events. This is a change in eGFR from previous recommendations that suggested an eGFR level ≥25 mL/min/1.73 m^2.[11] Among SGLT2i, dapagliflozin was the first drug to be approved by the FDA in April 2021 for use in CKD patients irrespective of their diabetes status based on the findings of the DAPA-CKD trial.[12] NICE has also recommended dapagliflozin as a treatment option for certain people

with CKD in adults.[13] Dapagliflozin was found to reduce the progression of kidney disease in the DECLARE-TIMI 58 trial, which included patients with T2DM and either known CVD (secondary prevention cohort) or at least two risk factors for CVD (primary prevention cohort). Most of the patients in DECLARE-TIMI 58 had preserved renal function.[14]

More than 90% of the HCP could recognize dapagliflozin as the SGLT2i with approved usage. A critical observation from various trials is an initial decline in eGFR upon initiation of treatment with SGLT2i. These drugs inhibit sodium and glucose reabsorption in the proximal tubule increasing sodium and chloride delivery to the macula densa. This results in afferent arteriolar vasoconstriction, causing a reduction in the intraglomerular pressure and the GFR.[15,16] The question pertaining to the decline in initial eGFR rate upon initiation of SLGT2i was correctly answered by three-fourths of the practitioners. Hence, the knowledge about SGLT2i in cardiovascular outcome trial (CVOT) and renal outcomes are considered to be very good. Aligning with the knowledge-based responses, the attitude of the doctors towards considering SGLT2i, especially the approved dapagliflozin for CKD patients with or without diabetes, is gratifying (Fig. 2). The majority of practitioners believe that dapagliflozin may help in preventing the long-term decline in eGFR.

When it comes to practice, only less than 50% always consider SGLT2i or dapagliflozin as a choice of treatment in CKD individuals or those with proteinuria (Fig. 3). This is concerning despite the fact that several clinical trials and regulatory agencies have approved the drug as a first-line treatment option in CKD patients.[8,13] Fear of side effects was the first major concern (Fig. 4). SGLT2i are known for their side effects of urinary tract infections, among others.[17,18] The answers have two limitations: 1) Did the responders have major concerns regarding the incidence of genital mycotic infections (GMI) and other potential side effects like increased hypoglycemia, among others? 2) The questionnaire itself does not lend any scope to understanding the specific concern of side effects. Further, we also cannot infer whether this fear of side effects is fully qualified or is it more of a perception issue. Future studies with specific questions may throw clarity on this aspect.

The other point that stops the prescribers from passing on the benefits of dapagliflozin to more patients, as conveyed by 34.6% of respondents, is comfort with old medications (Fig. 4). This response also has a few limitations as regards which medication and what do they mean by discomfort. We do not know whether this is due to fear of hypoglycemia or any possible drug interactions with other medicines.[19,20] These two aspects, i.e., fear of side effects and comfort with old medications, are eminently addressable with data and studies and concerted education efforts.

Summary

SGLT2i have demonstrated significant clinical benefits in patients with CKD with or without diabetes. This survey has shown good awareness among clinicians of the beneficial role of SGLT2i in CKD. However, the usage and attitude towards SGLT2 in the management of patients with CKD are low, and there could be several reasons for this. Overcoming these challenges will help in the broader usage of SGLT2i in people with CKD, which may help in improving outcomes in such patients.

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REVIEW ARTICLE

Glucometric Guardianship

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ABSTRACT

It is a well-known fact that the knowledge of their current glucose readings empowers people with diabetes to evaluate and monitor the trends in glucose fluctuations and take informed decisions on adjusting their medicines, food intake, and physical activity. Glucose monitoring technology has undergone a technological evolution and has improved diabetes care in patients living with type 2 diabetes. This has also made the need to efficiently and effectively utilize blood glucose monitoring tools. Glucometric checklists offer a standardized approach to glucometric guardianship which is necessary to improve the process of drug choice and dose titration. The stepwise factors included in the glucometric guardianship checklist include procurement, distribution, pre-testing hygiene, testing, recording, action, disposal, quality control, and procedure safety. This article has reviewed the significance of glucometric guardianship and has also developed checklists for efficient glycemic management.

Keywords: Type 2 diabetes, glucometric guardianship, checklist, glucose meters, glycemic triad.

Introduction

Introduced in the late 1970s and regulatory clearance received for the first time in 1980, blood glucose monitoring (BGM) has revolutionized the self-care of people with diabetes. A knowledge of their current glucose readings empowers people with diabetes to assess and better understand their glucose patterns to adjust their food intake, activity and medications to achieve their glycemic goals.[1]

BGM is an essential part of case management in patients with diabetes. Having very high or very low blood glucose levels may affect cellular function and could be life-threatening, including direct health care costs and reduced productivity; if not managed appropriately. It serves as a critical measure in individuals with ongoing diabetes management.[2]

The American Diabetes Association (ADA) 2017 reported that the total estimated cost of diagnosed diabetes in 2017 was $327 billion;[3] however, the direct cost of treating complications, including hospitalizations, emergency room visits and nondiabetes prescriptions, along with indirect costs related to lost/reduced productivity and human costs account for almost 73% of the total diabetes cost.[4]

The need to effectively and efficiently utilize BGM tools and resources to improve diabetes outcomes is indisputable. Continuous glucose monitoring is set to bring a fundamental change in the treatment of diabetes and patient engagement of those affected with this disease.[5] Over the years, diabetes practice has become more and more algorithm-based and statistic oriented, which facilitates the patient-centric treatment approach.

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Glucocentric screening and monitoring, added to this, have led to the neglect of a holistic medicine approach.[6] Hence, in this review, we have reviewed the significance and value of glucometric guardianship. We have also attempted to design checklists to facilitate routine clinical practice and impact decision-making.

Glycemic Guardianship

Kalra et al proposed the concept of glycemic guardianship, which was defined as "*activities carried out by the health care team and health care system to ensure optimal care of the person, or group of peoples, living with diabetes.*" Glycemic guardianship is a novel concept that can be functional at the national/regional level as well as the individual level and is ideally considered in partnership with individuals living with diabetes. The World Health Organization's Global Diabetes Compact (GDC) targets provide an umbrella for all activities related to glycemic guardianship.[7]

GDC emphasizes five targets comprising diagnosis of diabetes in 80% of individuals living with diabetes, achieving glucometric optimization in 80% of individuals diagnosed with diabetes, blood pressure control in 80% of individuals diagnosed with diabetes, ensuring statin prescription in 60% of individuals with diabetes who are 40 years or more in age, availability of affordable insulin, and blood glucose self-monitoring for all the people with type 1 diabetes. With the second-largest population of diabetes individuals living in India, the country's health care system and providers must strive to screen, diagnose, manage and prevent diabetes and related complications. While the prevalence of diabetes has increased, so has the proportion of those living with undiagnosed diabetes, thereby diminishing or counterbalancing the advances in diabetes care and delivery.[7]

With the Indian pharmaceutical industry being the world leader in manufacturing good quality drugs and devices, the easy availability of good quality and reasonably priced glucose monitoring devices and ancillaries has also been facilitated. With this, glucovigilance and personalized diabetes management have become integral to diabetes management and care.[8]

The Domains of Glucometric Guardianship

The benefits of glucometric guardianship are that it encompasses the physical and electronic infrastructure and further delineates the roles and responsibilities of various health care team members. The infrastructural requirements of glucometric guardianship include hardware (glucose measuring devices and ancillary supplies) and software (data recording and analysis). Table 1 shows the domains of glucometric guardianship.

Procurement
- Glucometer
- Ancillaries, i.e., lancets, strips, swabs
- Indented by; at time of admission/later

Distribution
- Individual
- Shared/number of beds

Pre-Testing Hygiene
- Glucometer battery
- Sanitization; finger-tip sanitization

Testing
- Glucometer check
- Procedure of pricking
- Troubleshooting (e.g., poor circulation, lack of hygiene)
- Frequency

Recording
- On paper
- E-Enabled (Integrated personalized diabetes management)

Action
- Frequency of measurement
- Change of insulin dose
- Change in IV fluids
- Escalation to senior medical staff

Disposal
- Plastics
- Sharps
- Blood-stained swabs

Quality Control
- Calibration
- Audit

Procedure Safety
- What to do if there is needle stick injury/exposure to blood
- How to check BG of HIV/HBsAg+ve patient

Box 1. Stepwise factors for glucometric guardianship checklist.

Table 1. Infrastructure of Glucometric Guardianship

Equipment	• Choice of the glucose monitoring device, e.g., Glucose meters vs. flash glucose monitoring device; glucose meters/FGMS model
	• Individual device or common device: e.g., prefer individual glucose meters if expected hospital stay of >2-3 days or if the expected number of glucometer pricks is >20
	• Glucose sticks: available at bedside/central station
	• Lancets: available at bedside/central station
	• Alcohol swabs: available at bedside/central station
	• Meter calibration: needed/not needed: at what frequency
Roles and responsibilities	• Glucose monitoring: by-
	• Data entry: by-
	• Analysis: by-
	• Disposal of used ancillary supplies: by-, at-
	• Red flag range: e.g., call duty doctor if plasma glucose <70 mg/dL and >400 mg/dL; check urine/blood ketones if BG >400 mg/dL
	• Treatment/titration: by-
	• Meter calibration: by-
Patient-specific glucometric guardianship	• Frequency of monitoring
	• Site of prick; rotation of fingers
	• De-escalation of frequency of monitoring: e.g., if BG 100-200 mg/dL; <20% change in consecutive glucose values at the current frequency
	• Escalation of frequency of monitoring: e.g., if BG <100 or >200 mg/dL; >20% change in consecutive glucose values

The advantages of glucometric guardianship are given in Table 2 given below.

Table 2. Advantages of Glucometric Guardianship

- Accurate determination of glucose control
- Avoidance of hypo-/hyperglycemia
- Prevention of complications
- Facilitation of audit
- Comparison and research

Glucometric Guardianship Checklist

"You can't improve what you can't measure accurately" is an adage illustrating the dilemma facing attempts to optimize glycemic control. Glucometric guardianship ensures appropriate measurement and monitoring of glucose levels to ensure alertness in glycemic management and agility in anticipating and identifying suboptimal glycemic parameters and responding to them.[9] (Box 1)

In diabetes care, several well-developed algorithms are available for glycemic management in the inpatient and outpatient settings; however, they do not integrate the nuances of glucose monitoring. Thus, glucometric measurements act as a challenge as well as a facilitator to achieving optimal glucose control. Hence, a standardization of glucometrics and adopting a practice-based approach to glucometric guardianship is essential to improve the process of drug choice and dose titration.[9]

The objective of developing these checklists are: (i) to emphasize the need for accurate measurement, monitoring, of glucose levels to improve the management of diabetes; (ii) to facilitate the process of glucometric guardianship by outlining the steps and factors to consider when monitoring and analyzing blood glucose patterns in individuals with diabetes; (iii) standardize the process of glucose monitoring and ensure that health care providers have a systematic approach to managing blood glucose levels in different care settings.

Outpatient Glucose Monitoring

Glucose control is an imperative and essential component of outpatient deviations in blood glucose level care in diabetes. Clinical scenarios with better glucose control have been shown to improve patient outcomes. Glycated hemoglobin (HbA1c) can be used

to assess the quality of outpatient glycemic control. Glucometrics has been shown to allow comparison of inpatient glycemic control among hospitals and patient care units and will allow institutions to evaluate the success of their quality improvement initiatives.[10]

The availability of point-of-care meters capable of storing glucose measurements from many patients eases, to some degree, the burden of data collection.[11]

Inpatient Glucose Monitoring

Inpatient hyperglycemia and hypoglycemia are related to worse patient outcomes, such as additional wound infections, prolonged hospital stays and higher mortality rates, especially in ICU. In most cases, an inpatient target glucose range of 140-180 mg/dL may represent the optimal balance for avoiding complications associated with extraordinarily high- and low-glucose levels.[12]

Emergency/Casualty

Many patients reporting to emergency care could have hyperglycemia who may be undiagnosed. Uncontrolled hyperglycemia and iatrogenic hypoglycemia are associated with a broad range of adverse outcomes, with insulin commonly attributing to adverse drug events if the patient is a known case of diabetes on treatment. While insulin and hypoglycemia management protocols allow for managing patients in emergency care, there is a lack of glucometric standardization and limited resources acting as challenges in diabetes management.[13]

Checklists

Because of the challenges in managing outpatient, inpatient, and emergency patients, we have attempted to devise CHECKLISTS to test, monitor and analyze the blood glucose pattern in individuals with diabetes

Table 3. Checklist for Outpatients

Patient ID	**Visit 1**	**Visit 2**
Procurement: • if the patient using a glucometer (which brand) • of a meter (which brand if patient not using glucometer) • of ancillaries, i.e., lancets, strips, swabs (which brand)	**Procurement** • Which brand of glucometer • Recommended brand of glucometer • Recommended brand of ancillaries • Comments, if any	**Cross check availability of** • Glucometer • Ancillaries
Usage pattern and training: • Individual/shared/family Training of • How to use the glucometer • Testing: change of lancet after how many pricks • How to share readings with the HCP	Individual☐ Shared☐ Family☐ • Done – Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐ Comments, if any	Cross-check usage pattern and technique
Pre-testing hygiene: • Time/Date of calibration • Glucometer battery • Sanitization a) Fingertip sanitization b) Glucometer Disinfection • Needle	• Time/Date • Glucometer battery working Y☐ N☐ • Sanitization Y☐ N☐ Done Y☐ N☐ Done Y☐ N☐ • Needle Checked Y☐ N☐ Comments, if any	• Time/Date • Glucometer battery working Y☐ N☐ • Sanitization Y☐ N☐ Done Y☐ N☐ Done Y☐ N☐ • Needle Checked Y☐ N☐ Comments, if any
Testing: • Glucometer check • Confirm glucose units (mg or mmol) • Procedure of pricking/intensity of lancet prick	• Done – Y☐ N☐ • Done – Y☐ N☐ • Checked – Y☐ N☐	• Done – Y☐ N☐ • Done – Y☐ N☐ • Checked – Y☐ N☐

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Table 3. Checklist for Outpatients

Patient ID	Visit 1	Visit 2
• Troubleshooting frequency	• Done – Y☐ N☐ If Y, specify the reason Comments if any	• Done – Y☐ N☐ If Y, specify the reason Comments, if any
Frequency (Appendices 1 and 2)		
Recording: • Cross-checking glucometer data with the CBG log • E-enabled [Integrated personalized diabetes management (IPDM)] • On paper	• Done – Y☐ N☐ • Y☐ N☐ • Y☐ N☐	• Done – Y☐ N☐ • Y☐ N☐ • Y☐ N☐
Action: • Change in diet/physical activity • Change in OAD • Change in insulin dose	• Done – Y☐ N☐ If Y, Specify • Done – Y☐ N☐ If Y, Which OAD? • Done – Y☐ N☐ If Y Specify	• Done – Y☐ N☐ If Y, Specify. • Done – Y☐ N☐ If Y, which OAD? • Done – Y☐ N☐ If Y Specify
Storage of strips **Disposal: (home/hospital)** • Plastics • Sharps • Blood-stained swabs	**Storage done as per instruction Y☐ N☐** **Disposal: Home (Y) or Hospital (Y)** • Done – Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐	• Cross-check storage and disposal

Appendix 1: Glucose Monitoring Log (Outpatients)

Date/Time	BB	AB	BL	AL	BD	AD	3 am	Comments

Week: ….Date Onwards

Date/Time	BB	AB	BL	AL	BD	AD	3 am	Comments

BB, BL, BD: Before Breakfast, Lunch, Dinner

AB, AL, AD: After Breakfast, Lunch, Dinner

Appendix 2: Diet Log (Outpatients)

Day/Time	Diet log/changes in diet/activity/illness next to the blood glucose levels
Monday	
Tuesday	
Wednesday	
Thursday	
Friday	
Saturday	
Sunday	

BB, BL, BD: Before Breakfast, Lunch, Dinner

AB, AL, AD: After Breakfast, Lunch, Dinner

Table 4. Checklist for Ward Patients

Ward ID	Audit No. 1	Audit No. 2 onwards
Procurement: • of meter (which brand?) • of ancillaries, i.e., lancets, strips, swabs (e.g., which brand)	• Recommended brand of glucometer • Recommended brand of ancillaries • Comments, if any	CMEs and CNEs should be conducted regularly (monthly or quarterly). This should be accompanied/ followed by audits at frequent intervals. These audits are targeted at ward nurses/diabetes educators. It is expected that these health care providers will disseminate the right knowledge to all patients admitted to their ward as well as their caregivers.
Usage pattern: • Individual • shared/beds	• Individual☐ • Shared☐	
Pre-testing practices: • Glucometer battery • Sanitization a) Fingertip sanitization b) Glucometer disinfection • Setting intensity of lancet prick	• Glucometer battery working – Y☐ N☐ • Sanitization Done Y☐ N☐ Done Y☐ N☐ • Done as per skin thickness over the fingertip comments, if any	
Testing: • Glucometer check • Confirm glucose units (mg or mmol) Procedure of pricking • Loading the lancet • Rotating site of finger prick • Troubleshooting (poor circulation, lack of hygiene) • Check from the hand where the IV line is going on • Check from the limb in which no dextrose infusion going on • Care of finger prick site after checking glucose	• Done – Y☐ N☐ • Done – Y☐ N☐ • Checked- Y☐ N☐ • Checked– Y☐ N☐ • Checked– Y☐ N☐ Y☐ N☐ Comments, if any • Checked– Y☐ N☐ • Checked– Y☐ N☐	
Log (Appendix 3)		
Recording and analysis: • On paper	• Y☐ N☐	

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Table 4. Checklist for Ward Patients

Ward ID	Audit No. 1	Audit No. 2 onwards
• E-enabled (Integrated personalized diabetes management [IPDM]) • Escalation matrix in place	• Y☐ N☐ • Y☐ N☐	
Action: • Change in diet • Change in frequency and timing of glucose testing • **Change in OAD/ insulin type.** • Change in insulin dose • Use of dextrose or any other IV fluids	 • Done – Y☐ N☐ If Y, Specify • Done – Y☐ N☐ If Y, Specify • Done – Y☐ N☐ If Y, Which OAD? • Done – Y☐ N☐ If Y Specify	
Storage (e.g., strips) **Disposal: hospital** • Plastics • Sharps • Blood-stained swabs	• Storage Done as per instruction Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐	

Appendix 3: Glucose Monitoring and Insulin and/or OAD Log (Ward patients)

Day/Time		Fasting	AB	BL	AL	BD	AD	3 am	Comments (eg any change in diet, physical activity, illness, antibiotics)
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								
Date	Blood Glucose								
	Insulin Dose								

BB, BL, BD: Before Breakfast, Lunch, Dinner
AB, AL, AD: After Breakfast, Lunch, Dinner

Table 5. Checklist for Emergency/Casualty Patients

	Audit 1	Audit 2
Procurement: • Type of glucometer- glucose oxidase or glucosedehydrogenase (which brand) • of, ancillaries i.e., lancets, strips, (which brand)	**Procurement** • Recommended brand of glucometer • Recommended brand of ancillaries Comments, if any	CMEs and CNEs should be conducted regularly (monthly or quarterly). This should be accompanied/followed by audits at frequent intervals. These audits are targeted at emergency nurses. It is expected that they will follow good glucometric practices. They should be able to refer the patient as well as their caregivers to the right health care provider upon discharge.
Usage pattern: • Individual bed • Shared beds	• Individual☐ • Shared☐	
Pre-testing practices • Glucometer battery • Sanitization a) Fingertip sanitization b) Glucometer disinfection • Check from the hand where the IV line is going on • Check from the limb in which no dextrose infusiongoing on	• Glucometer battery working – Y☐ N☐ • Sanitizatiion Y☐ N☐ Done Y☐ N☐ Done Y☐ N☐ • Needle Checked Y☐ N☐ Comments, if any	
Testing: • Glucometer check • Confirm glucose units (mg or mmol) **Procedure of pricking** • Care of finger prick site after checking glucose • Rotating site of finger prick • Troubleshooting (poor circulation, lack of hygiene)	• Done – Y☐ N☐ • Done – Y☐ N☐ • Checked – Y☐ N☐ • Checked – Y☐ N☐ • Checked – Y☐ N☐ Comments, if any	
Log (Appendix 4)		
Recording: • E-enabled matrix/hospital information system	• Done – Y☐ N☐	
Action: • Change in insulin dose/insulin type • Last insulin dose and time before discharge • Escalation/De-escalation matrix	• Done – Y☐ N☐ If, Y Specify dose & type, • Last insulin dose……..... time before discharge……. • Specify	
Storage of strips disposal: hospital • Plastics • Sharps • Blood-stained swabs	• Storage done as per instruction – Y☐ N☐. • Done – Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐	

Appendix 4: Frequency of Monitoring and Insulin Log (Emergency/Casualty patients)

Date: .....

Type of Insulin.....

Day/Time	8 am	8:15 am	8:30 am	8:45 am	9:45 am	11:00 am	
GCS							
Plasma Glucose							
IV Infusion							
Oral Intake							
Insulin							

Date:

Table 6. Checklist for ICU Patients

Patient - Name	Audit 1	Audit 2
Procurement: • Type of glucometer- glucose oxidase or glucose dehydrogenase (which brand) • of ancillaries, i.e., lancets, strips, (which brand)	**Procurement** • Recommended brand of glucometer • Recommended brand of ancillaries • Comments, if any	CMEs and CNEs should be conducted regularly (monthly or quarterly). This should be accompanied/followed by audits at frequent intervals. This audit is targeted at ICU nurses. It is expected that they will follow good glucometric practices. They should be able to refer the patient as well as their caregivers to the right healthcare provider upon discharge.
Usage pattern of glucometer: (tick any) • Individual or • Shared	 • Individual☐ • Shared☐	
Pre-testing practices: • Glucometer battery (check after how much time) • Sanitization; a) Fingertip sanitization b) Glucometer disinfection • Check from the hand where the IV line is going on • Check from the limb in which no dextrose infusion going on	 • Glucometer battery working – Y☐ N☐ • Sanitization • Done Y☐ N☐ • Done Y☐ N☐ • Checked Y☐ N☐ Comments, if any	
Testing: • Glucometer check • Confirm glucose units (mg or mmol)	 • Done – Y☐ N☐ • Done – Y☐ N☐	
Procedure of pricking • Care of finger prick site after checking glucose • Rotating site of finger prick • Troubleshooting (poor circulation, lack of hygiene)	 • Checked – Y☐ N☐ • Checked – Y☐ N☐ • Y☐ N☐	
	Comments if any	
Log (Appendix 5)		
Recording: • E-enabled system (Hospital information system) • On paper (Structured Reports)	 • Done – Y☐ N☐ • Done – Y☐ N☐	

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Table 6. Checklist for ICU Patients

Patient - Name	Audit 1	Audit 2
Action: • Change in insulin dose/type • Escalation/De-escalation rules	• Done – Y☐ N☐ If Y Specify dose & type • Y☐ N☐ Comments, if any	
Storage (e.g., of strips) Disposal: hospital • Plastics • Sharps • Blood-stained swabs	• Storage Done as per instruction Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐ • Done – Y☐ N☐	

Appendix 5: Frequency of Monitoring and Insulin and/or OAD Log (ICU Patients)

Day/Time	Fasting	2 hours after breakfast	BL	2 hours after lunch	BD	2 hours after dinner	3 am	Random	
		BG/Insulin rate						Time	Glucose value
Monday									
Tuesday									
Wednesday									

Week:....Date Onwards

Day/Time	8 am	10 am	Noon	2 pm	4 pm	6 pm	8 pm	Random	
		BG/Insulin rate							
Monday									
Tuesday									
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presenting to the health care systems at different levels of point-of-care. Tables 3-6 and Appendices 1-5 describe the checklist and logs for outpatients, ward patients, Emergency/Casualty and ICU patients.

Conclusion

Glucometric guardianship aims to ensure optimal glycemic management. It is a process of allowing appropriate assessment, monitoring, and analysis of glucose levels regularly. The aim of glucometric guardianship is to (i) enable alertness in glycemic management; (ii) agility in anticipating and detecting suboptimal glycemic parameters, and (iii) response to glycemic variability. These checklists will enable health care providers to enhance glycemic management, anticipate and identify suboptimal glycemic parameters, and respond effectively to glycemic variability.

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CLINICAL STUDY

Association Between Triglyceride Glucose Index in Type 2 Diabetes Mellitus Patients and Acute Ischemic Stroke

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ABSTRACT

Background: Stroke is a leading cause of mortality and disability globally. Diabetes mellitus increases the risk of stroke. It has been observed that the risk of stroke is usually higher among the young diabetic patients. Prediabetic patients are also at risk of stroke as the presence of glucose in blood results in vascular endothelial dysfunction, increased early-age arterial stiffness, systemic inflammation and thickening of the capillary basal membrane. In this prospective observational study we aimed to determine the association between triglyceride glucose (TyG) index in type-2 diabetes mellitus patients and acute ischemic stroke. **Methods:** A total of 75 patients with acute ischemic stroke and history of diabetes mellitus during the period of study were included in the study. **Results:** The mean age of the patients was 58.74 ± 11.37 years and the majority of the patients were males (57%) with 43% females. The average National Institutes of Health Stroke Scale (NIHSS) score of study participants was 5. The mean fasting plasma glucose (FPG) value was as 6.13 ± 2.03 (mmol/L), mean total cholesterol (TC) was 5.76 ± 1.4 (mmol/L), mean triglyceride (TG) 1.98 ± 0.93 was (mmol/L) and mean TyG index was 8.76 ± 0.28. **Conclusion:** The present study concluded that the TyG index is an important risk factor of ischemic stroke as it was observed that the patients with higher TyG index has higher incidence of ischemic stroke.

Keywords: Diabetes, glucose level, triglycerides, ischemia and stroke.

Introduction

Diabetes is known as silent killer, which can start from early stages of life and can be asymptomatic. It is a chronic noncommunicable[1] disease characterized by a state of chronic hyperglycemia, resulting from diverse etiologies, the environment and genetic, acting jointly. The underlying cause of diabetes is the defective production or action of insulin, a hormone that controls glucose, fat and amino acid metabolism with variable clinical manifestations and progression.

Diabetes mellitus increases the risk of stroke. It was observed that the risk of stroke is usually higher among the young diabetic patients. According to the Greater

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Cincinnati/Northern Kentucky stroke study, diabetes mellitus increases the risk and incidence of ischemic stroke among all age groups, but this risk is most striking before the age of 55 years in African Americans and before the age of 65 years in whites.[2]

Prediabetic patients are also at risk of stroke as the presence of glucose in blood results in vascular endothelial dysfunction, increased early-age arterial stiffness, systemic inflammation and thickening of the capillary basal membrane.[3]

Stroke is a leading cause of mortality and disability globally.[4] There are multiple risk factors or associated conditions resulting in stroke. Literature suggests that insulin resistance enhances progression of stroke and is also associated with poor prognosis. Triglyceride glucose (TyG) index is used to measure insulin resistance and is derived from fasting blood glucose and triglycerides.[5]

Several studies have concluded that high triglyceride index is an important predictor of mortality and outcome of acute ischemic stroke.[6]

Thus, the present study was undertaken to elucidate the association between TyG index acute ischemic stroke in patients with type 2 diabetes.

Material and Methods

This prospective observational study was done in the Department of Medicine in Acharya Shri Chander College of Medical Sciences and Hospital, Jammu, from January 2022 to February 2023 after obtaining approval from the Institutional Ethics Committee.

A total of 75 patients with acute ischemic stroke and history of diabetes mellitus during the period of study were included in the study.

Detailed clinical examination followed by routine laboratory and radiographic investigations were carried out in all cases. A detailed history including demographic variables, medication history, past history of illness, etc. was collected.

Blood samples were collected for TyG index and fasting blood sugar (FBS).

Data was organized, tabulated, analyzed and interpreted in both descriptive and inferential statistics i.e. frequency and percentage distribution, mean by using statistical package for social sciences (SPSS) software version 21. Categorical variables were expressed as number and percentage.

Observations and results

In the present study, 75 cases with acute ischemic stroke and history of diabetes mellitus were evaluated.

The mean age of the patients was 58.74 ± 11.37 years and the majority of the patients were males (57%) followed by 43% females. The average NIHSS score of study participants was 5.

The observed mean systolic blood pressure (SBP) was 145 ± 26.3 mmHg and mean diastolic blood pressure (DBP) was 90.2 ± 18.6 mmHg as depicted in Table 1.

Fifty-two percent of the patients were smokers as shown in Figure 1.

In our study, 69.33% subjects were on antidiabetic drugs, followed by antihypertensives (61.33%), lipid lowering drugs (50.66%), anticoagulants (16%) and antiplatelets (14.66%) as depicted in Table 2.

Figure 2 represents that 59% patients had family history of diabetes mellitus and 5% patients had family history of stroke.

The mean fasting plasma glucose (FPG) value was 6.13 ± 2.03 (mmol/L), mean total cholesterol (TC) was

Table 1. Blood Pressure

Blood pressure	Mean ± SD
SBP (mmHg)	145 ± 26.3
DBP (mmHg)	90.2 ± 18.6

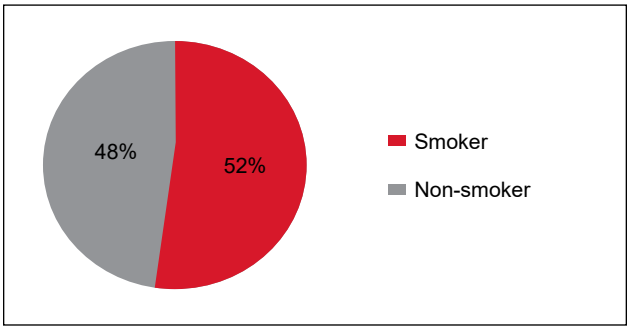

Figure 1. Smoking status.

Table 2. Drug History

Drug	No. of cases	Percentage
Antidiabetic	52	69.33
Anticoagulants	12	16
Antihypertensive	46	61.33
Lipid lowering drugs	38	50.66
Antiplatelets	11	14.66

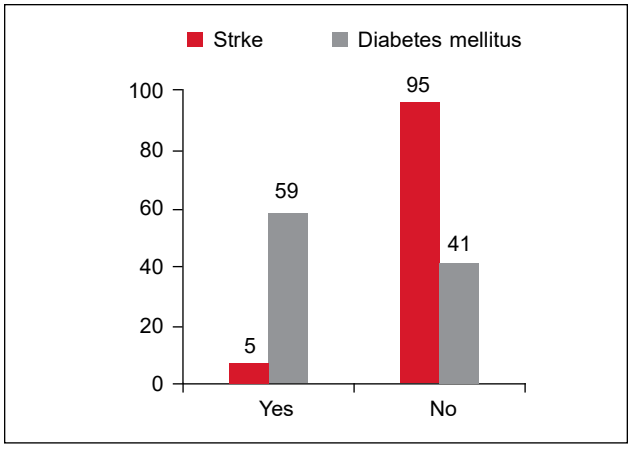

Figure 2. Family history of diabetes mellitus and stroke.

Table 3. Laboratory Findings

Parameters	Mean ± SD
FPG (mmol/L)	6.13 ± 2.03
TC (mmol/L)	5.76 ± 1.4
TG(mmol/L)	1.98 ± 0.93
TyG index	8.76 ± 0.28

Table 4. TyG Index vs. Stroke

TyG index	Incidence of stroke N (%)	P value
Q1 (4.31-5.48)	10 (13.33)	0.27
Q2 (5.48-5.81)	15 (20)	0.21
Q3 (5.81-6.22)	21 (28)	0.04
Q4 (6.22-8.17)	29 (38.66)	0.03

5.76 ± 1.4 (mmol/L), mean triglyceride (TG) 1.98 ± 0.93 was (mmol/L) and mean TyG index was 8.76 ± 0.28 as depicted in Table 3.

Table 4 shows that the patients with higher TyG index showed a higher incidence of stroke (p = 0.03).

Discussion

In our study the mean age of the patients was 58.74 ± 11.37 years and the majority of the patients were males (57%) followed by 43% females. The average NIHSS score of study participants was 5. It was reported that the most of the patients were smoker. These observations correlate with the study by Liu, et al (2022)[7] who found that the mean age of the study participants was 65.0 (57.0-73.0) years, most of the patients were males (59.2%) and the median NIHSS score was 4.0 (2.0-7.0). Toh, et al; (2022)[8] found that the most of the patients were males (61.5%), the median age of the patients was 65.00 (55.00, 76.00) years and the median NIHSS score was 6.0 (2.0, 15.0). Zhou, et al (2020) found that 44.4% subjects were smoker.[9]

The observed mean SBP was 145 ± 26.3 mmHg and mean DBP was 90.2 ± 18.6 mmHg. 59% patients had family history of diabetes mellitus and 5% patients had family history of stroke. These findings are consistent with the study by Zhou, et al (2020)[9] who reported that the mean SBP and DBP was 149.2 ± 23.0 mmHg and 87.44 ± 13.4 mmHg. Kourtidou, et al (2022) also observed that the mean SBP and DBP was 151 ± 27 mmHg and 81 ± 15 mmHg.[10]

Present study showed that 69.33% subjects were on antidiabetic drugs, followed by antihypertensive (61.33%), lipid-lowering drugs (50.66%), anticoagulants (16%) and antiplatelets (14.66%).

These findings are similar to the study conducted by Zhou, et al (2020)[9] who found that 19.6% subjects were on antiplatelet drug, 1% were on anticoagulants 44.9% were on antihypertensive drugs, 6.8% were on lipid-lowering drugs and 16.0% were on hypoglycemic agents.

The mean FPG value in the present study was 6.13 ± 2.03 (mmol/L), mean TC was 5.76 ± 1.4 (mmol/L), mean TG 1.98 ± 0.93 was (mmol/L) and mean TyG index was 8.76 ± 0.28. These results are in accordance with the study conducted by Guo, et al (2021)[11] who found that the mean fasting glucose value was 4.9, 5.1, 5.4 and 7.1 (mmol/L) among 4 groups, mean TC was 1.0, 1.2. 1.4 and 1.6 (mmol/L) among 4 groups, and mean TG was 2.5, 3.3, 4.0 and 4.6 (mmol/L) among 4 groups. Zhou, et al (2020)[9] found that the mean TG was 119.5 (mg/dL) and mean FBS was 114.1 ± 46.9 (mg/dL).

The present study showed that the patients with higher TyG index showed a higher incidence of stroke (p = 0.03). These findings correlate with the studies conducted by Liu, et al (2022)[7], Toh, et al (2022)[8], Hu, et al (2022)[12] and Zhou, et al (2020)[9] who reported significant association between TyG index in type 2 diabetes mellitus patients and acute ischemic stroke.

Conclusion

The present prospective study found that there was significant association between TyG index in type 2 diabetes mellitus patients and acute ischemic stroke. Thus, it is concluded that the TyG index is an important risk factor of ischemic stroke.

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BRIEF COMMUNICATION

Is Diabetes Pre-coded in the Brain? Role of Hypothalamus, Addiction Network and Social Cognition

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ABSTRACT

The hypothalamus, the master regulator of circadian rhythm, in association with peripheral clocks, plays crucial role in glucose metabolism. Impairment in cerebral sensing, uptake and processing of glucose has been suggested in various animal and human diabetic models. Diabetes mellitus (DM) has been largely superseded by the discovery of insulin and insulin resistance. Expanding horizons of knowledge of the roles of the hypothalamus in glucose metabolism and the overlapping neural pathways of sugar addiction with other classically described substance and behavioral addictions networks have again thrown some light on the cerebral theory of pathogenesis of DM.

Keywords: Diabetes mellitus, hypothalamus, brain, cognitive impairment

Introduction

Evidence in favor of multifaceted afflictions of diabetes mellitus (DM) on the brain has been burgeoning. Contemporary studies exhibited the definitive and deleterious impact of DM on the brain leading to premature brain aging and manifestations ranging from cognitive impairment, and behavioral alteration to focal neurological deficits.[1] Authors, herein, want to decode the inverse relationship. Although, the brain has been regarded as one of the key organs in the classic "ominous octet",[2] its exact role in the pathophysiology of DM is yet to be fully decrypted.[3] Further elucidation is needed regarding the mechanistic pathways through which psychoneurotic traits, an established risk factor for the development of diabetes mellitus and the maintenance of glycemic balance, operate.[4,5] Is there a possibility of the beta-cell failure to be prospectively orchestrated by altered glucose-sensing machinery residing in the brain? Are there certain pre-existing pre-destined frameworks in the brain responsible for the future development of DM? How can certain brain-behavior relationships lead to the development of DM in later life?

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Cerebral Pathogenesis of Diabetes – Role of Hypothalamus, Midbrain and Brainstem

Hypothalamus has long been considered the nodal player in the regulation of satiety, body weight and glycemic status since 1854 when Claude Bernard reported that a lesion in the floor of the fourth ventricle in dogs altered glucose levels, thereby presenting the first evidence of the brain's role in glycemic regulation.[3] Works in *Drosophila* have found that there are key glucose-sensing neurons, which orchestrate insulin and glucagon secretion downstream.[3,6] A case has been made regarding the common evolutionary

origin of beta cells and brain.[7] The key parameters of glycemic control viz. satiety, obesity, insulin secretion and insulin resistance, which predict the future risk of development of DM have now been proven to be governed by the hypothalamus.[3,8] The hypothalamus, the master regulator of circadian rhythm, in association with peripheral clocks, play crucial roles in glucose metabolism.[9,10] Impairment in cerebral sensing, uptake and processing of glucose has been suggested in various animal and human diabetic models.[11-14] One of the most recent additions to the understanding of cerebral pathogenesis of diabetes is "glucose effectiveness", the phenomenon through which glucose promotes its own disposal using central K_{ATP} channels (independent of insulin).[15] Analogous to the leptin resistance in obesity, DM which is also a closely related metabolic disease, can be viewed as a cerebral glucose-resistant state that uplifts the glycemic set-point to set in a new steady-state leading to the generation of a vicious cycle of glucotoxicity and progressive beta-cell failure.[3,16] The role of the brain in glucose metabolism is further strengthened by the evidence that intracerebroventricular administration of leptin ameliorates hyperglycemia by insulin-independent pathways.[17,18] Similarly, intracerebroventricular injection of the fibroblast growth factor (FGF) family of proteins, especially FGF-1, 19 and 21 is capable of reversing hyperglycemia in rodents.[19-21]

Addiction Circuitry and Diabetes

Smoking, alcohol and other substance abuse have been causally linked to the pathogenesis of DM based on epidemiological proofs and identifying downstream cascades of deleterious molecular mechanisms. Addictive behavior has a definitive role in the future development of DM, governed by brain networks (addiction and reward circuits) as they share a common genetic susceptibility region afflicting the cerebro-pancreatic network.[22] Food addiction has been linked to the development of type 2 DM independent of age, sex, body mass index and other comorbidities including obesity.[23]

Contextually, the concept of sugar addiction and its causative role in obesity, DM and other chronic metabolic diseases has already gained popularity in the public health arena.[24] Studies already have demonstrated that sugar addiction involves the ventral tegmental area (VTA) and nucleus accumbens (NAc), the same designated brain network involved in substance and behavioral addiction. Dopamine is the key neurotransmitter responsible for food (sugar) addiction with contributions of acetylcholine and opioid neurotransmitters as well.[24,25] Sugar addiction can cause glucotoxicity, rebound insulin release and beta-cell exhaustion in the long-term with an increased risk of developing insulin resistance and eventually DM in the future.[26] It has also been observed reciprocally during treatment of DM and subsequent counseling regarding the risk of development of hypoglycemia; patients often take sugar binge without any definitive evidence of hypoglycemia. This is an indirect reflector of addictive behavior (sugar addiction), which significantly interferes with the achievement of proper glycemic control.[27,28] Internet addiction, the most common modern form of behavioral addiction[29] has been associated with a sedentary lifestyle,[30] which is the harbinger of incident diabetes. In a reverse way, researchers have also untangled the intricate association of increased prevalence of addiction among diabetics compared to nondiabetic individuals further strengthening the role of an in-built "addiction network" in the brain much before the development of DM.[31]

Parenting, Personality Development and Risk of Developing Diabetes Mellitus

Personality is the supreme reflection of cognitive and behavioral excursion in a patterned way based on learning and experience in environmentally triggered situations and personal space issues.[32] Parental personality and parenting style have dominating effects on the lifestyle and food habits of their children.[33,34] Type A personality of parents and parental stress being transferred to their offspring lead to faulty food habits, altered sleeping patterns decreased play time, competitive attitudes and a sedentary lifestyle from a very early phase of life.[35] This prodiabetic personality, behavior and lifestyle of the child and that of the family, implant the seeds of a faulty metabolic milieu deeply inside the evolving nascent networks of the brain of these children, earlier in life much before the development of glycemic dysregulation.[36]

Conclusion

Although the discovery of neural control of glycemia dates back nearly 200 years, the concept that the brain is the central player in the pathogenesis of DM has been largely superseded by the discovery of insulin and insulin resistance. Expanding horizons of knowledge of the roles of the hypothalamus in glucose metabolism and the overlapping neural pathways of sugar addiction with other classically described substance and behavioral addictions networks have

again thrown some light on the cerebral theory of DM pathogenesis. Personality traits of children and their parents, parenting and lifestyles are crucially and intricately related to brain functions and may have the potential to cause DM in later life. Keeping in an analogy of purely neurological and psychiatric illness that occurs in an already compromised brain, the seeds of diabetes mellitus, obesity and metabolic syndrome per se are ingrained in the fertile soil of an already precarious brain.[37] Lastly, there has been a long-awaiting dearth of artillery in the therapeutic armamentarium of DM directed at the brain and the authors anticipate that this is an area for an Odysseus voyage in future research.[38,39]

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Diabetes India 2022: 12th World Congress of DiabetesIndia

Pharmacotherapy of Type 2 Diabetes: Getting The Basics Right to Improve Outcomes

Dr Mandeep Bajaj, USA

- Choose an agent after considering the condition of the patient and any underlined comorbidities that he may have. Consider the available data with all the drugs including a glucagon-like peptide 1 (GLP-1) receptor agonist, a diapeptidyl peptidase-4 (DPP-4) inhibitor, an SGLT2 (sodium-glucose co-transporter 2) inhibitor, pioglitazone and sulfonylurea.
- For instance – In a patient with heart failure, SGLT2 inhibitors are recommended; in a patient with nonalcoholic hepatitis, a GLP-1 receptor agonist or pioglitazone may be added.
- Base your clinical judgment on the overall condition of the patient (instead of just glycemic control), and underlying comorbidities, consider the options available and then reach a conclusion.

Obstructive Sleep Apnea and Diabetes – The Link

Dr Anil Bhoraskar, Mumbai

- Obstructive sleep apnea (OSA): Repeated partial or complete obstruction of the upper airway during sleep. The complications linked with OSA are metabolic, cardiovascular, behavioral and others such as excessive daytime sleepiness, headache and fatigue-related accidents.
- A number of studies have shown that OSA is a risk factor for type 2 diabetes (T2D) independent of obesity and other risk factors.
- Interestingly, both OSA and T2DM are associated with similar comorbidities such as hypertension, cardiovascular disease (CVD), dyslipidemia and chronic kidney disease.
- Several cross-sectional studies have demonstrated the link between OSA and poor glycemic measures. Continuous positive airway pressure (CPAP) is the gold standard treatment for OSA. Along with CPAP, lifestyle modification, sleep hygiene and weight loss should be advised in all patients with T2D with OSA.
- Some other treatment options for OSA include dental appliances, surgeries in a select group of patients, and conservative measures such as alcohol cessation, smoking cessation and mild nasal decongestants.
- CPAP reduces the risk of incident T2D. Treatment with CPAP improves HbA1c levels, fasting plasma insulin and insulin resistance. In T2DM, OSA treatment with CPAP has been shown to reduce the mean arterial pressure, systolic blood pressure (BP) and diastolic BP.
- CPAP has been shown to delay or prevent the occurrence of CVD in T2DM patients.
- Retinopathy, nephropathy and neuropathy are probably delayed by treatment with CPAP.

Hepatopancreatic Fat-Fetuin-A Based Axis for the Pathogenesis of Diabetes and its Reversal

Dr Anoop Misra, New Delhi

- A number of studies have demonstrated a link between pancreatic fat and impaired glucose metabolism, as well as between pancreatic fat and T2DM. In general, pancreatic volume decreases with age and in diabetes, while pancreatic fat increases with both.
- Ethnic differences in pancreatic volume have been reported, while research in India is negligible.
- Fetuin-A is a key metabolic regulator causing effects on the pancreas and multiple other tissues, and responsible for insulin resistance, hyperglycemia and (with palmitate) β-cell apoptosis.
- Different approaches, such as a hypocaloric diet, exercise, bariatric surgery and pharmacological interventions, can reduce pancreatic fat content.
- A decrease in pancreatic and hepatic fat and a decrease in fetuin-A (insulin resistance/inflammation) could lead to reversal of diabetes.

Promises and Pitfalls of Remission of Diabetes

Dr Sujoy Majumdar, Kolkata

- The term used to describe a sustained metabolic improvement in T2DM to nearly normal levels

should be remission of diabetes and not a reversal of diabetes mellitus.

- Remission should be defined as a return of HbA1c to <6.5% (<48 mmol/mol) that occurs spontaneously or following an intervention and that persists for at least 3 months in the absence of usual glucose-lowering pharmacotherapy.
- When HbA1c is determined to be an unreliable marker of chronic glycemic control, fasting plasma glucose (FPG) <126 mg/dL or estimated A1c <6.5% calculated from continuous glucose monitoring (CGM) values can be used as alternate criteria.
- Testing of HbA1c to document a remission should be performed just prior to an intervention and no sooner than 3 months after initiation of the intervention and withdrawal of any glucose-lowering pharmacotherapy.
- Subsequent testing to determine long-term maintenance of remission should be done at least yearly thereafter, together with the testing routinely recommended for potential complications of diabetes. Reversal of diabetes remains a distant goal to date.

Effects of Lipid-Lowering Drugs and Types of Statins on SARS-COV-2 Infection and Severity in Diabetes

Dr Michel P Hermans, UK

- Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, diabetes is considered a risk factor for severe COVID-19. There is no evidence that having diabetes increases the risk of contracting COVID-19.
- The two major risk factors for T2DM onset and severe COVID-19 are the same, i.e., age and obesity.
- Factors predisposing to infection and/or severe disease are subject to generalizations that do not take into account the type of diabetes.
- A study was conducted to document the phenotype before infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and with severe COVID-19 – In a T2DM-T1DM cohort; In T2DM and T1DM subgroups.
- The conclusions of the study were: Infected (T2DM + T1DM) patients less often on statins; Infected T2DM less often on statins (–10%) – [More often on atorvastatin (+39%), Less often on rosuvastatin (–24%)]; No difference in statins use between infected and noninfected T1DM – Nonsignificant higher use of atorvastatin among infected T1DM; Similar % of severe COVID-19 on statins compared to nonsevere – Same SED of statin in severe vs. nonsevere, Nondifferent % of HIS in severe vs. nonsevere; Severe COVID-19 >2 times more R/atorvastatin (+238%); Nonsevere forms >4 times more R/rosuvastatin (+434%); Ezetimibe ± statins much lower (–57%) in severe COVID-19, as was the combination of [any statin + ezetimibe] (–69%).

Multidisciplinary Management of Diabetic Foot Ulcers: Can We Do It Better?

Dr ZG Abbas, Tanzania

- There is an urgent need to reassess care pathways pertaining to diabetic foot ulcer (DFU) management in our health systems, as we sense the overall gravity of this diagnosis is underestimated.
- The concomitant lack of prevention, insufficient early detection and often inadequate management of ulcers often lead to eventually high morbidity and mortality.
- The multidisciplinary diabetic foot clinic has proven to be a unique forum to provide urgent treatment of infection and ischemia with rapid access to laboratory, radiological and inpatient facilities.
- The multidisciplinary team (MDT) especially those able to address glycemic control, local wound management, vascular disease and infection are associated with a reduction in the risk of major amputation for patients with severe diabetic foot.
- One-step, MDT-led diabetic foot clinic benefits patients and improves outcomes related to the avoidance of hospital admissions, limb salvage procedures and minor amputations, although, we recognize that time and education are needed to see its full effects.

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News and Views

Cognitive and Heart Benefits of Blueberries

Eating a handful of blueberries daily lowers blood pressure (BP) and improves vascular and cerebral blood flow leading to better cardiovascular and cognitive health, according to a recent study published in the *American Journal of Clinical Nutrition*.[1]

Researchers from the UK, Germany and Portugal collaborated in this randomized, double-blind, placebo-controlled trial to evaluate the beneficial effects of blueberries. For this, they enrolled 61 healthy older adults aged 65 to 80 years, who were randomly assigned to receive a drink constituted from 26 g of freeze-dried wild blueberry powder (equivalent of 178 g of whole blueberries containing 302 mg anthocyanins) or a matched placebo but with no anthocyanins for a duration of 12 weeks.

After 12 weeks, there was a substantial increase in the flow-mediated dilation (FMD), a measure to evaluate endothelial function, in the participants in the blueberry group compared to the placebo group (0.86%). The 24-hour ambulatory systolic BP also decreased by 3.59 mmHg. No difference was noted for arterial stiffness and blood lipids between the two groups. Participants who consumed blueberries showed enhanced "immediate recall on the auditory verbal learning task, alongside better accuracy on a task-switch task". But no improvement was seen in delayed recall. Subjects in the blueberries group also exhibited higher total 24-hour urinary polyphenol levels compared to placebo after 12 weeks.

These findings demonstrate the cardio- and neuroprotective effects of blueberries. The daily intake of 178 g of fresh blueberries in this study lowered BP and improved blood vessel function, which also boosted cognitive function in older adults in the form of improved executive function and better short-term memory.

The beneficial effects of blueberries have been attributed to their anthocyanin content. Anthocyanins are red, blue or purple pigments found in fruits and vegetables and are potent antioxidants. Additionally, they have antidiabetic, anticancer, anti-inflammatory, antiangiogenesis, antimicrobial and antiobesity properties. They also play an important role in maintaining good vision.[2] Other sources of anthocyanins are purple vegetables, raspberries, strawberries and red grapes.

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Study Reveals Beneficial Effects of Changing the Existing Medication among Hypertensive Patients

According to recent research published in the *Journal of the American Medical Association* (JAMA), the effect of changing medications can be twice as powerful as increasing the patient's existing medication dose.

The study involved 280 patients. During the course of a year, each of these patients tested four different BP medications, one after the other. The researchers discovered that the treatment's efficacy varied greatly from person to person and that certain people attained reduced BP with one medicine rather than another. A change in medication can help BP-lowering therapy patients far more than raising the amount of their existing medication.

The study found that if a patient is given the proper BP medication, they can lower their BP and, in turn could provide better protection against potential cardiovascular illnesses sooner. The study's findings call into question the present treatment paradigm, which recommends four medication groups equally warmly for all individuals with high BP.

(Source: https://www.hindustantimes.com/lifestyle/health/changing-medication-more-effective-for-blood-pressure-treatment-study-101681279971951.html)

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