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YOUR HEALTH

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KNOW YOUR RISK, KNOW YOUR RESPONSE

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YOUR HEALTH

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Childhood Diabetes in India

Editorial

Dr. Kakali Sen
Hony. Editor, Your Health

India, home to the largest population of children, also bears the heaviest burden of childhood morbidity in the world. India is known as one of the global diabetes epicenters of the global diabetes epidemic. The vast number of adults living with diabetes in the country means that most attention is focused on them, and on type 2 diabetes. Children with type 1 diabetes continue to fight for their rightful place under the sun. Most epidemiologic studies and reviews of diabetes in India or South Asia focus on adults, while neglecting the significant burden of childhood diabetes. This review delves in to various facets of the epidemiology of paediatric diabetes in India.

Type 1 diabetes

The first attempt to assess the prevalence of insulin dependent diabetes in children was a population study carried out in 3 census zones of the northeastern part of Madras city (now named Chennai), in Tamil Nadu state. Cases were identified by data collection from hospitals, diabetes clinics, medical practitioners, chemists and druggists. Thirty children aged<15 years were identified, giving a prevalence of 0.261. The peak age at diagnosis was reported to be 12 years. This was followed by a diabetes registry in the same city. The incidence of insulin dependent diabetes was found to be 12.6±11 and 9.6±4.7 per 100,000 boys and girls per year, over a 4-year period (1991–1994). The overall incidence was 10.5/100,000/yr, and peaked at age 10–12 years.

The neighbouring state of Karnataka instituted a multicentric registry which collected data over 13 years. This reported an incidence of 3.7/100,000 boys and 4.0/100,000 girls. However, the low figures may have been due to incomplete reporting from many parts of the large state.

Karnal district in Haryana state was the site of a hospital-based prevalence study. This district is served by a single endocrine centre which caters to the entire population. This study revealed an overall prevalence of 10.20/100,000 population with wide rural: urban and male: female gradients. The prevalence in Karnal city was 31.9/100,000, urban areas was 26.6/100,000, and in rural areas was 4.27/100,000. Men had a prevalence of 11.56/100,000, and in women, it was 8.6/100,000. In the 5 to 14 years age group, the prevalence was 24.22/100,000, while in the 0 to 6 years age group, it was 3.82/100,000. The total prevalence in the 0- to 14-year cohort was 18.27/100,000. The gender ratio was similar in toddlers and adolescents, and became skewed only in the >15 years age group. The lower prevalence in rural areas suggests the lack of medical facilities, due to which many children with type 1 diabetes and undercurrent illness may not be diagnosed properly. The male: female discrepancy reflects gender discrimination, and the poor health care-seeking behavior exhibited by families for their daughters.

The government of India has conducted school surveys in Nainital (Uttarakhand state), Ratlam (Madhya Pradesh state), and Bhilwara (Rajasthan state) to assess the potential burden of childhood diabetes. According to the result, 1.467% of the 32,047 school children surveyed are suspected to have diabetes.

Comorbid endocrinopathy

Type 1 diabetes does not always occur in isolation. It may be associated with various complications and comorbidities. An a analysis of 617 children aged ≤20 years with type 1 diabetes, who had undergone a minimum of 3 years of follow-up, was reported from

Chennai. The authors detected retinopathy in 13.4% (background diabetic retinopathy 11.2%, proliferative diabetic retinopathy 1.9%, preproliferative 0.31%, maculopathy was seen in 13.3% of retinopathy cases), nephropathy in 7.1%, sensory neuropathy in 3.0%, ischaemic heart disease in 0.5% and peripheral vascular disease in 0.5% of participants. Duration of diabetes was positively associated with retinopathy, nephropathy and neuropathy. Glycosylated haemoglobin showed an association with retinopathy. Although the glycaemic control was suboptimal in this cohort, prevalence of vascular complications, especially macrovascular ones, seemed lower in Indian children as compared to what is reported from the west [7].

A large study conducted on 189 children with type 1 diabetes in Chandigarh revealed an 11.1% prevalence of celiac disease, which was diagnosed on the basis of serology and duodenal histology. In almost all cases, the diagnosis of diabetes preceded that of celiac disease by 5.18±4.75 years. Symptoms of celiac disease included short stature, anaemia, weight loss, diarrhea and abdominal pain.

Hypothyroidism is another auto immune endocrinopathy that commonly coexists with diabetes. In a single centre review of data at Karnal, 70 children aged <18 years (23 female, 47 male) with type 1 diabetes were screened for hypothyroidism. Four girls (17.4%) had a palpable goiter. Two girls were known cases of hypothyroidism, 5 girls were found to have overt hypothyroidism, and 2 boys were detected to have subclinical hypothyroidism. Thus the overall prevalence of hypothyroidism was 26.1% in girls and 4.2% in boys with type 1 diabetes.

Yet another endocrinopathy which is endemic to India is vitamin D deficiency. A study performed in Chandigarh assessed the plasma levels of 25-hydroxyvitamin D (25OHD), by high performance liquid chromatography, in 50 newly diagnosed children with diabetes. When compared with age matched healthy controls (6–12 years age), the mean levels of vitamin D were found to be significantly lower (20.02±10.63 ng/mL vs. 26.16±12.28 ng/mL, *P*=0.009). Vitamin D deficiency (25OHD<20 ng/mL) was detected in 58% children with diabetes as compared to 32% controls. When deficiency and insufficiency (25OHD<30 ng/mL) were collated, the prevalence rose to 86% in type 1 diabetes and 76% in healthy children.

Health economics

India is a pay-from pocket market, where health insurance coverage is sparse. A study in Chennai aimed to assess the economic burden of type 1 diabetes on the families of youth and adolescents with type 1 diabetes. A median annual expenditure on diabetes of Indian rupees 13,980 (USD 310) was reported. The median percentage of income spend on diabetes was 59% in low socioeconomic families, 32% in the middle socioeconomic stratum, and 12% in the high income group. The overall average was 22%. Indoor hospitalization was associated with higher economic burden (23% of family income) as compared to outdoor management (16% of income).

Type 2 diabetes

Not all childhood diabetes is type 1, and Indian researchers have been cognizant of this fact [13]. Perhaps the earliest report of type 2 diabetes in children was from Madras. A case series of 18 children with insidious onset of diabetes at age ≤15 years, response to oral glucose lowering drugs (preserved C peptide levels [≥0.6 pmol/mL]) and absence of decarboxylase 65 (glutamic acid decarboxylase 65) antibodies was reported.

Type 2 diabetes in children is gradually being reported across the country, through the prevalence is not as high as in Asian countries such as Japan. At referral centres such as Lucknow and Chennai, the proportion of children with type 2 diabetes is reported as 12% and 26.7% respectively. This, however, may be due to a referral bias. Various hospital and clinic based registries, reviewed by Chowdhury and Ghosh, suggest that the percentage of type 1 diabetes in children is showing a declining trend. This implies that the prevalence of type 2 diabetes in children is rising.

Glucose intolerance

A large project (n=1,519), which studied children aged 6–11 years in Chennai found an overall prevalence of 3%–7% of glucose intolerance (4.2% in girls, 3.2% in boys; *P*<0.001). The prevalence of dysglycaemia, as assessed by oral glucose tolerance test, was 12.7% in girls with abdominal obesity. Upon multivariate analysis, family history of diabetes was found to have significant association with glucose intolerance in girls (odds ratio [OR], 4.11; 95% confidence interval [CI], 1.28–13.22; *P*=0.018). Homeostasis model assessment-insulin resistance (HOMA-IR) was significantly associated with glucose intolerance in both boys (OR, 5.19; 95% CI, 1.54–17.44; *P*=0.008) and girls (OR, 11.22; 95% CI, 4.19–30.05; *P*<0.001). The high prevalence of glucose intolerance in this young age group is cause for worry

Monogenic diabetes mellitus

Monogenic diabetes mellitus is also documented and studied in India. A descriptive cohort study from Chennai (1999–2007: retrospective; 2008–2012: prospective design) included 40 infants with onset of diabetes at age ≤1 year. These constituted 8% of all children with onset of diabetes ≤12 years. Low birth weight was found in 63% of all infants with onset of diabetes ≤6 months of age, and 30% with onset at 6–12 months age. Monogenic forms of diabetes were found in 84.5% of infants with onset ≤6 months age, and 55.0% of those with onset at 6–12 months. The commonest form was Wolcott Rallison syndrome. Delayed diagnosis, recurrent hospitalization, developmental delay, and high childhood mortality (32.5% at 12.5-year follow-up) were noted by the authors.

A recent publication from the same city (Chennai) described the clinical presentation and molecular characterization of 33 Indian children with onset of diabetes below 12 months of age. Twelve mutations were identified. Novel mutations that were discovered included Asp 212Tyr mutation in ABCC8, Val67Met in Berardinelli Seip Syndrome and Leu1Arg in Fanconi Bickel syndrome. This study highlights the diversity of monogenic diabetes in India, and the need to screen for it carefully.

Indian contribution

Indian have a higher percentage of body fat and visceral fat, when compared with Caucasians of a similar body mass index. This has led to the characterization of a "thin fat" Indian diabetes phenotype. This phenotype is present from birth, and may be worsened by accelerated childhood growth. It is speculated that this pathophysiological state contributes to the earlier development of type 2 diabetes and metabolic syndrome in children in India [19]. Such understanding will facilitate further growth in diabetology.

This hypothesis is supported by findings that offspring of mothers with diabetes have thicker skinfolds, and higher glucose levels, insulin concentrations, HOMA-IR and systolic blood pressure, as compared to controls. Thus, gestational diabetes has now been identified as a target for prevention of diabetes in offspring.

Yet another hypothesis, which attempts to explain the increasing incidence of type 1 diabetes in India, is the A1/A2 milk hypothesis. Most cow milk protein is found in the form of casein and whey. One form of casein, beta casein, can be present as any of 12 genetic variants. The most common variant are the A1 and A2 variant. Proteolysis of the A1 variant in the gastro intestinal tract generates an immunogenic bioactive peptide called beta casomorphin 7 (BCM7), which is absorbed by the immature gut of infants.

In recent decades, Indian dairy production has shifted from using indigenous cow breeds (Zebu cows) to exotic breeds (taurine) and buffalos. While indigenous cow milk beta casein is A2/A2 in nature, buffalo milk contains A1/A2 beta casein, and exotic breeds have A1/A1 alleles. It is hypothesized that exposure to immunogenic A1/A1 milk may be linked with the rising incidence of type 1 diabetes in India. An interesting observation from the desert state of Rajasthan is the use of camel milk as adjuvant therapy in type 1 diabetes.

The classification of diabetes is a dynamic field of characterized by debate and discussion. There are significant differences, for example, between Japanese and American and international classifications of the condition. The Japan Diabetes Society classifies type 1 diabetes into fulminant, acute onset or slowly progressive, based upon clinical presentation and progression. Indian endocrinologists have begun recognizing these variants (personal communication: Prof Rakesh Sahay, Hyderabad), but continue to follow western classification systems.

Recently, Indian experts have proposed a clinico-etiological taxonomic rubric for type 1 diabetes. This is based upon three variables: etiology, mode of onset and clinical presentation. This system of classification includes both western and Japanese thought, is compatible with modern understanding of pathophysiology, clinically oriented, and lends support to therapeutic decision-making. The classification system can be used in settings where antibody estimation is not possible, as it includes a glucophenotypic basis of description as well.

Summary

Data from India reveals a significant prevalence of type 1 diabetes (over 10/100,000 population), with certain urban pockets reporting over 30/100,000 population). At the same time, the burden of glucose intolerance (associated with abdominal obesity) and type 2 diabetes is increasing in children. Novel explanations such as the A1/A2 milk hypothesis and "thin fat" Indian phenotype help explain the trend of increase in type 1 and type 2 diabetes in children. Newer clinical classification of diabetes provide a unified overview of the condition, through a clinico-etiopathologic prism.

From the Desk of Secretary

Dr. Samarendra Kumar Basu
Hony. Secretary, Your Health

World Diabetes Day (WDD) was created in 1991 by IDF and the World Health Organization in response to growing concerns about the escalating health threat posed by diabetes. World Diabetes Day became an official United Nations Day in 2006 with the passage of United Nation Resolution 61/225. It is marked every year on 14 November, the birthday of Sir Frederick Banting, who co-discovered insulin along with Charles Best in 1922.

The World Diabetes Day campaign aims to be the:

- Platform to promote IDF advocacy efforts throughout the year.
- Global driver to promote the importance of taking coordinated and concerted actions to confront diabetes as a critical global health issue.

The campaign is represented by a blue circle logo that was adopted in 2007 after the passage of the UN Resolution on diabetes. The blue circle is the global symbol for diabetes awareness. It signifies the unity of the global diabetes community in response to the diabetes epidemic.

The IDF Diabetes Atlas provides the latest figures, information and projections on the global impact of diabetes.

- 537 million adults (1 in 10) were living with diabetes in 2021. This number is expected rise to 643 million by 2030 and 783 million by 2045.
- Almost 1 in 2 adults (44%) with diabetes remain undiagnosed (240 million). The majority have type 2 diabetes.
- More than 3 in 4 people with diabetes live in low and middle-income countries.
- 541 million adults are at increased risk of developing type 2 diabetes.
- More than 1.2 million children and adolescents (0-19 years) live with type 1 diabetes
- Diabetes caused 6.7 million deaths in 2021.
- Diabetes was responsible for at least $966 billion in health expenditure in 2021 – 9% of the global total spent on healthcare.
- 1 in 6 live births (21 million) are affected by high blood glucose (hyperglycaemia) in pregnancy.

Every year, the World Diabetes Day campaign focuses on a dedicated theme that runs for one or more years. The theme for World Diabetes Day 2021-23 is Access to Diabetes Care.

In 2023, the campaign will focus on the importance of knowing your risk of type 2 diabetes to help delay or prevent the condition and highlighting

Type 2 diabetes accounts for over 90% of all diabetes. There are several steps that can be taken to reduce the risk of developing the condition.

Unhealthy eating habits and sedentary lifestyles associated with urbanisation are common factors contributing to the development of type 2 diabetes. There is overwhelming evidence from studies in the USA, Finland, China, India and Japan that lifestyle changes (achieving a healthy body weight and moderate physical activity) can help prevent the development of type 2 diabetes in people at risk.

Reducing the risk of type 2 diabetes involves a balanced diet and regular physical activity. Maintaining a healthy weight is crucial as overweight and obesity increases the risk. Even a small weight loss can make a big difference. Regular screenings and check-ups, especially for people with one or more of the risk factors, can detect early signs and help individuals make the necessary changes to delay or prevent the onset of type 2 diabetes.

Several risk factors have been associated with type 2 diabetes and include:

Family history of diabetes, Overweight, Unhealthy diet, Physical inactivity, Increasing age, High blood pressure, Ethnicity, Impaired glucose tolerance (IGT), History of gestational diabetes, Poor nutrition during pregnancy.

Diabetes currently affects one in ten people worldwide. Understanding the condition is the first step towards managing and preventing it. In conjunction with the World Diabetes Day 2022 focus on access to diabetes education.

I am thankful to the authors who contributed to this special issue. I am also thankful to GD Hospital & Diabetes Institute for their support.

Diabetes: Know your risk, know your response

CAMPAIGN TOOLKIT – World Diabetes Day 2023

Massage

Prof. Dr. Sukumar Mukhopadhyay
Chairman, GD Hospital & Diabetes Institute

On this world diabetes day, when we discuss about the different aspects of diabetes, we seen that India is now leading in the prevalence of diabetes. With the increase in population of India, the incidence of diabetes is also on the rising trend. Till now we have not been able to take adequate measures to prevent diabetes. Over the years of my practice, I have clearly understood the two most important factors governing the incidence and prevalence of diabetes are insulin resistance and insulin deficiency. Insulin resistance in India is an important factor and as years pass by, the amount of insulin secreted by the pancreatic beta cells also reduces, thus leading to aggravation of symptoms of diabetes. India has also a very high population of obese individuals and the incidence of obesity is on a rising trend. Indian phenotype obesity mainly characterizes by thin individuals with abdominal obesity and increased abdominal girth is closely associated with diabetes. We have not been able to follow a healthy lifestyle which would indirectly prevent obesity thus further aggravating incidence of diabetes. Hence lifestyle, obesity, the Indian trait and diabetes are all closely related. Lifestyle modification is sadly lacking in India. Previously treatment of diabetes used to mainly depend on insulin and few oral drugs, but now which scientific progress, newer molecules have been discovered which not only control diabetes but also has beneficial effects on a patient's weight along with several cardiovascular benefits. Despite discovery of newer antidiabetic molecules, insulin has always been the mainstay of diabetes treatment. Early initiation of insulin in diabetes has its own advantage. But in India initiation of insulin is delayed. There is resistance both from the patient's side as well as doctor. There is a taboo in patients that initiation of insulin is the last stage of diabetes and this thought further hampers adequate management of diabetes. With inadequate control of diabetes in the majority of population in India, complications of diabetes mainly cardiovascular & renal involvement have been on the rising trend, not only in populations above 50 years but also less than that. Some patients presenting with diabetes with associated complications are so severe that they had be admitted in the ICU set up. In the world of diabetes treatment, strict control of diabetes is not occurring in majority of the population. One of the primary markers of diabetes control namely HbA1c is not getting controlled to a desired level. We often see lots of patients with HbA1c of 8 or 9 whereas the control should be more strict.

Hence on this world diabetes day, let us take a pledge to improve control of diabetes by lifestyle modification, obesity reduction, early initiation of insulin, cost effective treatment to all category of patients and last but not the least proper counselling and encouragement to the patients. Like this we will be able to provide better care to the patients and they will be able to continue this long term treatment without getting exhausted economically or emotionally.

GD HOSPITAL & DIABETES INSTITUTE
CARE FOR LIFE

Informed Decision Making

Guest Editorial

Your Health is about propagating Health Awareness since 1952.

World Diabetes Day is also about observing the day to spread awareness about Diabetes.

An initiative of International Diabetes Federation since 1997. One of the rare day to be observed to create awareness about Diabetes by no other than United Nations since 2006.

Theme for this year being Know your risk, Know your response.

With this motto in mind GD Hospital is working to create access to care and create awareness. Encouraged by the dynamic vision & leadership of our CEO Musrefa Hossain we here organized "Haanto Bangla Haanto" our signature event till COVID struck us. We hope to initiate it in near future.

Key to awareness is engagement with patient. His or her access to care. The patient's, felt need and our ability to cater to those.

We should work with the person with diabetes. His concerns may be fall in sugar, getting overweight, loosing weight, kidney failure & so on.

Some medication may give good control of sugar but occasionally cause fall of sugar; we have to empower them with tools to self control diet, particularly timing it with medicines, dosage of Insulin, but not let go a very good control & consequent benefit.

Some medications particularly Insulin and Sulfoniylureas cause weight gain. We should jointly discuss to reach an optimumstate to achieve target HbA1C and manage weight increase. Same way some medicines like SGLT2 Inihibitors & GLP1 analogues are very good in controlling weight and sugar. But we are particularly worried about our physical appearance & social reaction to it. However the overwhelming good effects of such drugs on Heart and kidney needs to emphasized.

A particular drug may be very good but costly. Access to such therapy has to be discussed and shared decision making is needed.

Our own India's ICMR study INDIAB data are overwhelmingly concerning even for our state. Only way forward is to work with patient, make them co-partner in the long term management plan of Diabetes, which is unfortunately a lifelong life style disease in almost 90% of them.

Dr. Shaibal Chakraborty
Chief Medical Advisor,
GD Hospital & Diabetes Institute

We at GD Hospital has comprehensively checked nearly 600 patients in last 1 year.

Nearly 2000 HbA1C has been checked. Myself has seen more than 3000 patient in OPD. Nearly 900 patient's foot care study has been done. All this is to our humble effort to target this silent killer.

Let the soul of BANTING & BEST inspire us to achieve the goal.

WORLD DIABETES DAY

GD HOSPITAL & DIABETES INSTITUTE
CARE FOR LIFE

Debunking the Myths Surrounding Diabetes

Dr. Awadhesh Kumar Singh
MD, DM Senior Consultant Endocrinologist
G.D Hospital & Diabetes Institute, Kolkata

- **Taking medicines for diabetes for a long time damages your organs!**

Medicines used in the treatment of diabetes for a long time do not damage any organs and rather protect against any organ damage (nerves, kidneys, heart, and retina) owing to good glucose control. Indeed, some of the medicines used in the treatment of type 2 diabetes (T2D) directly protect the kidneys and the heart from any future damage, reduce death, and increase longevity. In other words, any medicines approved and used for diabetes that produce good glucose control shall protect against any future organ damage, and some of them may additionally protect the heart and kidneys beyond blood glucose control.

- **Once you start insulin in people with diabetes, you have to take it for your whole life!**

If you are having type 1 diabetes (T1D, common in children and adolescents but can happen at any age), insulin is the only medicine currently available to treat it. No oral tablets apparently work in T1D. Not taking insulin if you have T1D will lead to acute complications in a very short span of time that can lead to death. T1D happens due to an absolute lack of insulin production from the pancreas and therefore insulin administration from outside is the only solution.

If you have T2D and your doctor is suggesting you to take insulin - this can happen in three common circumstances. First, you could have diabetes for a very long time and take multiple tablets which have now failed to bring down your glucose under target. This is the most often encountered situation where insulin is initiated. If you fall under this category, there is a likelihood that you have to take insulin for your whole life since tablets are no longer working. However, in certain proportions of patients, a few months of insulin intake allows the same tablets to start working again and thus one can come out of insulin for at least some time. Second, we start insulin for the time being for certain complications or comorbidities. For example- if someone develops jaundice, heart attack, heart failure, acute infections, planning to undergo any operations, planning to contemplate pregnancy, or has conceived. However, we stop insulin and return to the previous medicine, once the problem is shorted. These conditions do not require lifelong insulin administration. Finally, we initiate insulin for a short period in people with T2D when they have very high blood sugar producing several symptoms. These people will be put on oral medicine once sugar is controlled after stopping insulin.

- **If I have diabetes, I cannot eat rice, potatoes, and sweets forever!**

This is not true! There is no diet that people with diabetes can not eat. Rice and potatoes can be eaten in moderation. Often, we discourage people with diabetes from consuming sugar, jaggery, honey, and products made from it because we believe one cannot have control over it. However, occasional intake in moderation by a motivated patient is fairly acceptable. Frankly, “diabetic diet” is a misnomer and no such terminology exists. “Balanced diet” is the key and there is no food that can not be eaten in moderation.

- **I religiously take medicine for diabetes but often miss medicines for high blood pressure (BP) and cholesterol!**

High BP and cholesterol are often seen in the majority of patients with T2D. Some develop diabetes first, and high BP and cholesterol later, while others develop high BP or cholesterol first and diabetes later. All these three diseases are products of the same soil (metabolic disarrangement in the body) that causes it. Control of BP and cholesterol is equally and perhaps more important than diabetes. BP checking is mandatory during every visit to the doctor and checking lipids is mandatory during the first visit or later if not done earlier. Please be mindful that even if your glucose is well controlled but your BP is not controlled, you are not protected from developing future strokes. Similarly, if your cholesterol is not under target, you are not protected from developing future heart attacks, despite good glucose control. Thus, we need to give equal importance to controlling diabetes, BP, and cholesterol.

- **Do I need to reduce or stop the medicine once my sugar, BP, and cholesterol are under control?**

Nope! Since you are taking all medicines, these conditions are under control. If you reduce or stop the medicines, optimal control will no longer remain and your chance of developing long-term complications from diabetes (such as damage to nerves, retina, kidneys, and hearts), high BP (such as stroke, heart attack, and heart failure), high cholesterol (such as heart attack and stroke) shall remain despite consuming suboptimal dose of all medicines. Please be mindful that these complications can only be prevented when your sugar, BP, and lipid levels remain under target not for once but consistently and nearly always.

Rheumatological Manifestations of Diabetes Mellitus

Dr. Somnath Bhar
MBBS (Cal), MRCP (UK), MRCPI
Consultant, GD Hospital & Diabetes Institute

Introduction:

Diabetes mellitus, emerging as a curse for human civilization in this new millennium, can virtually affect every organ system of our body. Among the complications, bone and joint disorders are less talked about; although they can pose significant morbidity and alter the quality of life. These musculoskeletal problems can hamper the daily activities of a diabetic patient rendering them unable to adhere to a strict lifestyle modification protocol. Different rheumatological disorders associated with Diabetes are discussed in the rest of this article.

Cheiroarthropathy:

Cheiroarthropathy or limited joint mobility is a long term complication of Diabetes and refers to joint contractures resulting in decreased passive mobility of the joints. Flexion contractures of the proximal interphalangeal (PIP) joints and metacarpophalangeal (MCP) joints of the hands are characteristic. The skin on the dorsum of the hands becomes tight and waxy and the patients often are unable to oppose the palmer surfaces at interphalangeal or MCP joints when the hands are placed in the prayer position (positive prayer sign). This condition is usually painless and features of synovitis are usually absent. Larger joints such as the wrists, elbows and ankles can also be affected. Limited joint mobility is strongly associated with the presence of microvascular complications like retinopathy and neuropathy in T1DM and macrovascular complications in T2DM. Better glycemic control, physiotherapy and local corticosteroid injection are the mainstay of therapy.

Frozen shoulder:

Adhesive capsulitis of shoulder joint is more common in diabetic (11-30%) than nondiabetic population (2-10%). This condition initially presents with pain in the shoulder joint followed by restriction of movement in all planes. The condition is usually self-limiting and takes about 30 months to get resolved. Analgesics and physiotherapy can be beneficial to control the symptoms. Some patients may experience persistent shoulder pain and restricted mobility necessitating intra-articular corticosteroids.

Dupuytren's contracture:

This is a fibroproliferative disorder of palmer fascia leading to the formation of a palmer aponeurosis cord and eventually there is flexion contractures of ring and little fingers. Diabetes is an important risk factor of Dupuytren's contracture. Surgical intervention should be considered as splinting and intralesional corticosteroids are frequently ineffective.

Trigger finger:

Trigger finger or stenosing tenosynovitis occurs due to thickening of synovial sheath over the flexor tendon hampering the smooth gliding movement of tendon through the sheath. This condition most commonly affects the ring finger, but other fingers can also be affected. Diabetic patients are at a higher risk of developing trigger finger compared to general population. A clicking sensation while moving the finger is often reported. Corticosteroid injection into the tendon sheath is an effective treatment.

Carpal tunnel syndrome:

Carpal tunnel syndrome or median nerve entrapment neuropathy is commonly associated with diabetes and it can be a part of diabetic polyneuropathy. Paresthesia of the thumb, index finger and middle finger particularly during the night is common

presentation. Late presentation includes thenar muscle wasting, weakness of thumb abduction and sensory loss over median nerve distribution. Phalen's test and Tinel's test may be positive but the diagnosis should be confirmed by nerve conduction testing (NCV). Splinting, oral or local corticosteroids and surgical release are mainstay of treatment.

Charcot joint:

Charcot joint is a destructive arthropathy seen is diabetic patients with severe peripheral neuropathy. It affects 0.1-0.4% of people with diabetes and can lead to foot deformity, ulceration and eventually amputation. Charcot foot presents as acute inflammation of foot with swelling and redness followed by bone resorption, fracture and dislocation. Classic rocker-bottom dislocation of the mid foot is due to the involvement of tarsometatarsal joints, midtarsal joints and neviculocuneiform joints. This aberrant inflammatory response is thought to be due to autonomic dysfunction as a part of diabetic neuropathy. Xray is useful in documenting osteolysis, bone fragments, sublaxation and fracture. MRI, done during early phase of the disease, can reveal bone marrow edema. Standard treatment includes immobilization by non-weight-bearing total contact cast. Clinical trials with bisphosphonates have shown varying results. Surgical management should be considered in later part of the disease for chronic foot ulcer and joint instability.

Diffuse idiopathic skeletal hyperostosis (DISH):

DISH is a disorder characterized by increased bone formation at the entheses (attachment of tendons and ligaments into bones). Ossification of anterior longitudinal ligament of the spine, particularly the thoracic spine can give rise to back pain and spinal fractures can occasionally be encountered. Diagnosis can be made radiologically by presence of ossification along the anterolateral aspects of at least four consecutive vertebrae, relative preservation of intervertebral disc height and absence of features of spondyloarthropathy. Obesity and diabetes are the recognized risk factor for DISH. Analgesics and physiotherapy can be offered to control the symptoms. Surgery may be indicated for compressive syndromes caused by florid hyperostosis.

Osteoporosis and skeletal fragility:

Association of osteoporosis and increased fracture risk with diabetes is well established. Treatment with thiazolidinediones (pioglitazone) increases the fracture risk further. Measurement of bone mineral density (BMD) is helpful in estimating fracture risk. Bisphosphonate treatment should be offered in appropriate subjects. Fracture healing is also delayed in diabetic patients. Risk of delayed union, non-union and malunion is increased in presence of diabetes.

Conclusion:

Bone and joint health is an important determinant of the quality of life of every diabetic patient. Early identification of joint problems, timely intervention with physiotherapy and medication are of paramount importance. Tight glycemic control is necessary to avoid or delay the onset of any joint or bone problem.

Dish for Diabetes

Dr. Rajdeep Basu
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Diabetes mellitus, which was first identified as a disease entity almost 3000 years ago, now has become a major health challenge in the modern era. Worldwide around 382 million adults are living with this problem and it is expected to cross more than 700 million by 2045 [1]. India, the second most populated country in the world, is burdened heavily with the excessively sweetened state of the body. It causes havoc in the health care budget and thus, lives are spent in misery. Effective management strategies in terms of diet, lifestyle modifications, and drugs are the only way to reduce this excess glucose from the blood.

When the diet plan is concerned, it can not be simply equated to 'less food to stay good' within much more complicated metabolic pathways to handle glucose. Thus, an organized Medical Nutrition Therapy (MNT) should be incorporated into daily life by qualified and trained healthcare providers and that would be accessible to the community, acceptable to the person, attractive in look, affordable by pocket, and appropriate to the need. The term, 'diabetic diet' is often used in general practice as a misnomer and should be discouraged, as the meal plan is for all, even for the non-diabetic population to stay healthier, not to isolate the person suffering from diabetes at the corner of a dining table.

The food items can be divided into macronutrients (carbohydrates, proteins, and fat) and micronutrients (minerals, vitamins, and water).

Curb to Carbohydrates: The total carbohydrate content of the food should be 50-60%, preferably high fiber (25-40 grams daily), complex carbohydrates, and foods with low glycemic index. Whole grains should be accepted while simple carbohydrates are discouraged [2]. Carbohydrate counts of the food may be necessary for more intense glycemic control.

Pros of Proteins: Protein intake should be encouraged to get 15-20% of total energy intake. A daily intake of 1mg/Kg of body weight is adequate for a person [2].

Fit Fats: 20-25% of total daily calories should come from fat. The intake of poly- and monounsaturated fatty acids is advisable. Restriction of saturated fats and trans fats is required [2]. Cooking by steaming or baking is preferred over frying.

Adequate amounts of minerals, vitamins, and water intake are to be ensured by dietary products. Artificial supplementation is not generally needed. Salt intake should be restricted to less than 6 grams per day.

Not only the components of eating but the ways of

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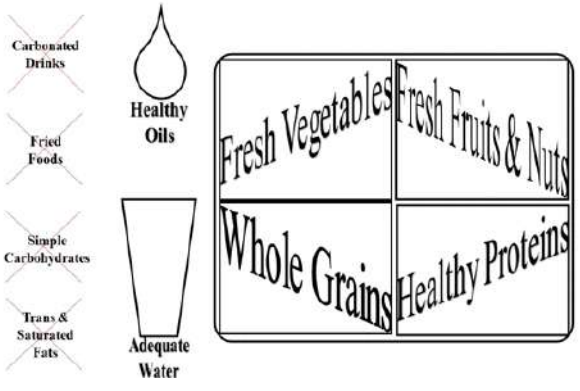
that are also important. Mindful and slow eating (to avoid watching television, reading a book or newspaper, talking to others while having meals), eating only in response to the sensation of hunger, and avoiding frequent snacking and skipping meals is recommended.

Though a moderate amount of alcohol intake does not deteriorate the blood glucose status, the glasses should be cheered after keeping other harmful effects in mind.

Artificial sweeteners like saccharin sodium, aspartame, acesulfame-K, sucralose, etc. which all are available in the market, have become the only hope for persons suffering from diabetes to start the day with a drinkable tea. However, various studies have shown that they are not devoid of risks of altered glucose metabolism and can impose the same risk as that of simple sugars in long-term use [3].

Regarding the various types of diets, like the Dietary Approach to Stop Hypertension (DASH), the Mediterranean diet (healthy fat-rich diet); the Vegetarian diet (Pescetarian, Lacto-ovo, Vegan); the Low-fat diet; and the Low-carbohydrate diet, etc. no diet plan was proven as *the best* when all the health parameters (body weight reduction, blood pressure management, glycemic control, lipid reduction, renal benefit, cardiovascular risk reduction, muscle mass protection) are concerned [4]. Thus, the pattern of diet should be individualized to one's lifestyle and other comorbid conditions after discussion with an Endocrinologist and a Nutritionist.

In the ancient era, the only management of diabetes was just a simple fast. This concept has been modified to *intermittent fasting*. This can be done as an alternate day fasting, 2 fast-5 feast cycle, or time-restricted meal. This plan also has benefits in controlling weight and lipids but studies have shown no benefit in glycemic control [5].



Thus, taken together, there is no hard and fixed meal plan for diabetes. All dietary components and patterns are to be person-specific. Diet is one of the various management options for diabetes, physical activity is one such close mate. And it is known to all that earning (of energy) is proportionate to expenditure (of calories). So, firstly meals should be granted as prescribed medicine, secondly, to be adjusted according to the needs of the individual, and lastly, and more importantly should be eternal rather than ephemeral.

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Diabetes Mellitus in Pregnancy – an Updated Review

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Abstract : Hyperglycemia in pregnancy, due to pregestational or gestational diabetes mellitus have multiple short-term and long-term consequences on the mother and offspring. Timely and appropriate diagnosis and management should be guided by evidence-based latest recommendations. The role of the treating physician starts from the pre-conceptional period and extends beyond the gestational period to postpartum follow-up of the mother and the baby, thus providing an opportunity to promote transgenerational metabolic health. The importance of early intermediate hyperglycemia and gestational diabesity are upcoming areas of research.

Keywords : Gestational Diabetes, metformin, pregestational diabetes, Early intermediate hyperglycemia, gestational weight gain

Introduction

Pregnancy is a state of gross metabolic and endocrine perturbations. The latter half of pregnancy is a state of insulin resistance and women with pre-existing insulin resistance, prediabetes, obesity, or reduced beta cell functioning have a high risk of developing hyperglycemia during this stage, known as gestational diabetes mellitus (GDM). Pre-existing diabetes mellitus (DM) and GDM have several short and long-standing consequences on the health of the mother and the fetus. Thus, pregnancy provides a window of opportunity to safeguard the health of two individuals at one time.

Classification :

DM during pregnancy could either be due to pre-existing DM diagnosed before pregnancy, also known as pre-gestational diabetes or could be hyperglycemia first detected in pregnancy. The latter could be overt diabetes mellitus in pregnancy or gestational diabetes mellitus, usually diagnosed during the latter half of pregnancy.

Pathophysiology of gestational DM :

Pregnancy is characterized by complex endocrine-metabolic rearrangement. In the initial weeks, there is a "maternal anabolic phase", or an increase in maternal energy reserves and enhanced insulin sensitivity, to meet the maternal-fetal needs of advanced gestation. Later , there is a "fetal anabolic phase" when there is reduction in maternal insulin sensitivity and an increase in maternal concentrations of glucose and FFAs. (1) In this phase, hormones like human placental lactogen (hPL) and placental growth

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hormone (pGH) produced by the placenta causes lipolysis and neoglucogenesis. The placenta also produces biomolecules like leptin, adiponectin and TNF-a that are important to maintain increased energy intake and adipose tissue storage in the mother to support fetal growth.

Therefore, in normal females, fasting plasma glucose may be lower than in the nonpregnant state due to insulin-independent glucose uptake by the fetus while there can be mild postprandial hyperglycemia due to the diabetogenic placental hormones, starting at around 16 weeks. In women with adequate pancreatic functioning, beta cells produce more of insulin to meet the challenge of this physiological insulin resistance this maintaining normoglycemia. However, females with diabetes – pregestational or gestational cannot cope up with this and end up with high glucose levels.

Complications :

GDM, if untreated, can lead to several complications to the mother and the fetus, some of which can have longstanding consequences on the metabolic health of the child and several generations afterwards.(2) A summary of potential complications is outlined in Table 1.

Table 1. Complications of gestational diabetes mellitus :

	Maternal	Neonatal
Short term	Preeclampsia Pregnancy induced hypertension. Poly/oligohydramnios Urinary tract infections Need for Caesarean section/instrumental delivery Perineal tear due to macrosomic infant Post-partum hemorrhage	Stillbirth Intrauterine fetal death Neonatal death Preterm delivery Congenital malformations Macrosomia Shoulder dystocia, brachial plexus injury Neonatal hypoglycemia Neonatal hyperbilirubinemia Neonatal hypocalcemia Neonatal respiratory distress syndrome
Long term	Recurrent GDM in future pregnancies Type 2 Diabetes Mellitus Hypertension Dyslipidemia Hypertension Atherosclerotic cardiovascular disease Chronic kidney disease	Childhood obesity Metabolic syndrome Hypertension Dyslipidemia Early onset atherosclerotic cardiovascular disease Future risk of PCOS, GDM for female babies

Screening and Diagnosis of GDM :

A number of criteria have been laid down by different bodies as summarized in Table 2. While each of the criteria have their own set of advantages and disadvantages, the choice of screening criteria may be an individualized opinion guided by the prevalence of DM, cultural influences, and patient preferences. (3-6) The one-step strategy with ADA cut-offs is one of the most used strategies in the country.

Table 2 : Screening and Diagnostic criteria for GDM

Methods	Cut-offs (in mg/dL)
One-step strategy / IADPSG / ADA / AACE / WHO Recommendations	
Time – 24-28 weeks of gestation Fasting required 75-g OGTT done	Diagnosis is made when any *one* of the following is met: Fasting: ≥ 92 1 hour: ≥ 180 2 hours: ≥ 153
Two-step strategy / NIH / ACOG recommendations	
1) Step 1 Time – 24-28 weeks of gestation Fasting not required 50-g glucose challenge test	If 1 hour: ≥ 140 – proceed to step 2.
2) Step 2 Time – 24-28 weeks of gestation Fasting required 100-g OGTT done	Diagnosis is made when any *at least two* of the following is met: *(Carpenter -Couston criteria)* Fasting: ≥ 95 1 hour: ≥ 180 2 hours: ≥ 155 3 hours: ≥ 140
DIPSI Criteria	
Fasting not required 75-g OGTT done	2 hours: ≥ 140

Management of GDM :

The main aim of GDM management is to achieve and maintain normoglycemia. The ACHOIS trial published in 2005 and the MFMU trial in 2009 demonstrated that dietary intervention, self-monitoring of blood glucose (SMBG) and pharmacotherapy in GDM reduced the perinatal complications like pre-eclampsia, shoulder dystocia, and death and incidence of macrosomia in the fetus. (7,8)

The management of GDM involves: 1) lifestyle and behavioral changes and 2) pharmacotherapy. Lifestyle and behavioral modifications include medical nutrition therapy (MNT) and exercise. It has been seen that around three-fourths of the GDM patients can be managed with these interventions without the use of pharmacotherapy. (9) MNT for a GDM patient should attempt to achieve the blood glucose level in the target range and at the same time it should provide calories sufficient to promote maternal health and weight gain and fetal well-being. Focus should not only be on the quantity of the food being taken but also on the quality of the food i.e., appropriate glycemic index and food enriched with nutrients. (10)

If behavioral modifications fall insufficient or there is substantially elevated blood glucose, then insulin is the preferred medication for management. (11) Both multiple daily injections and subcutaneous insulin pumps can be used in pregnancy. Regarding oral pharmacotherapy metformin and glyburide can be taken during pregnancy but they are not the first line agents as both cross the placenta and there are

concerns regarding its long-term safety. (10)

6.1 Role of metformin : Metformin has been shown to lower the risk of neonatal hypoglycemia and less maternal weight gain than insulin but it has been shown to readily crosses the placenta, resulting in high umbilical cord blood levels of metformin. (11) The MiG-TOFU and some recent meta-analyses showed metformin exposure could increase the risk for smaller neonates with accelerated postnatal growth, and high BMI or central obesity in childhood (12) Metformin has been seen to reduce the risk for pre-eclampsia, need for Caesarian section and NICU admission in some but not all studies (13Kala). However, metformin should preferably be avoided in pregnant women with hypertension, preeclampsia or at high-risk for intrauterine growth restriction (14).

Insulin in pregnancy : Current recommendations suggest insulin to be the medication of choice in mothers with GDM or pregestational DM. (15) Short acting insulin and premixed formulations , as a combination of NPH and rapid acting insulins, are commonly used. While majority of mothers can achieve glycemic control with these regimen, some need a basal bolus regimen with a long acting insulins and two or three shots of pre-prandial rapid acting insulin. Among the long and ultralong acting insulin, detemir and recently, degludec insulin has been recently been approved for use during pregnancy.(15) Use of oral anti-diabetic agents as an alternative only is indicated in mothers who might not be able to use insulin safely or effectively due to cost, comprehension barriers, or cultural influences, only after discussing the known risks.

Glycemic targets during pregnancy : The targets recommended by the American Diabetes Association (ADA) and the Fifth International Workshop-Conference on GDM are: (16,17). (Table 3)

Table 3. Glycemic targets of treatment during gestation

Time	Target glucose (mg/dL)
Fasting	< 95
1 hour postprandial	< 140
2 hours postprandial	< 120

It is important to review the medication list and stop all potentially teratogenic medications like ACEi inhibitors, Angiotensin receptor blockers or statins during pregnancy. Guidelines recommend starting low-dose aspirin 100–150 mg/day in pregnant women with pregestational DM, starting at 12 to 16 weeks of gestation in order to lower the risk of preeclampsia.

6.4 Role of Continuous glucose monitoring in pregnancy : Mothers with type 1 DM benefit from real-time Continuous Glucose Monitoring (CGM) in pregnancy with reduction in Hba1c, hypoglycemia, large-for-gestational-age births, length of stay, and neonatal hypoglycemia (16). The role of CGM in mothers with type 2 DM or GDM is less clear. The goal time-in-range (TIR) for a target blood glucose between 63–140 mg/dL should be >70% while the Time below range (< 140 mg/dL) should be <25%.

Early GDM – implications of diagnosis and management strategy :

While the standard screening recommendation for GDM starts around 24 – 28 weeks of gestation, up to 27% - 66% of GDM cases can be detected earlier in pregnancy. This entity is termed as early GDM, early abnormal glucose metabolism or early intermediate hyperglycemia. This early screening strategy can detect pre-existing DM, identifies mothers-at-risk for GDM and its consequences. The thresholds used for diagnosing early GDM are FPG values between 110 - 125 mg/dl and HBA1c% between 5.9 – 6.4%. (18)

The implications of early intervention versus the regular standard of care in women with early GDM are still unclear. Though some studies have shown decreased pre-eclampsia and LGA births with early intervention, others have shown increased risk of SGA and need for NICU admissions. (19). A recent study showed benefit of early intervention in preventing adverse neonatal outcomes but no differences in maternal outcomes.(20) Both metformin and lifestyle interventions have been tried in early GDM. Metformin use in early pregnancy was not found to prevent GDM in high risk women. (21)

Post-partum monitoring and follow-up :

The occurrence of GDM can increase the lifetime maternal risk for diabetes to around 50–60% (25). Mothers with GDM have 10-fold increased risk of developing type 2 diabetes compared with those without GDM (128), and the risk is particularly high for mothers with high pre-pregnancy BMI. Post-partum women with a recent history of GDM should be recalled and tested for hyperglycemia at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and using the nonpregnancy diagnostic criteria for prediabetes and diabetes. Mothers who to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent the

occurrence of diabetes. Breastfeeding should be encouraged as it can reduce the risk of maternal type 2 diabetes as well as provide metabolic benefit to the neonate. Women should also be tested every 1–3 years even if the 4–12 weeks postpartum 75-g OGTT is normal. (16)

Gestational "Diabesity" – how important is the entity?

Like GDM, maternal obesity also contributes to a wide range of complications during pregnancy including the occurrence of GDM or type 2 DM , hypertensive disorders of pregnancy (HDP) and adverse obstetric outcomes. Pre-gestational obesity and DM, gestational weight gain and GDM all have important cardiometabolic implications for the mother and the offspring and is termed as gestational diabesity. Excessive weight gain during pregnancy, also known as gestational weight gain (GWG) increases the risk for adverse pregnancy outcomes and future cardiometabolic conditions. (22) Excess GWG also increases the risk for LGA babies, macrosomia and caesarean delivery. (23) The Institute of Medicine (IOM) has laid down guidelines regarding the recommended weight gain at different pre-pregnancy BMI categories, which is usually 12.5 – 19 kgs , 11.5 to 16 kgs, 7 – 11.5 kgs and 5 – 9 kgs for mothers with pre-pregnancy BMI < 18.5, 18.5 – 24.9 , 25 – 29.9 and >= 30 kg/m^2 respectively.

Role of pre-conceptional visit – how early can we intervene ?

The earliest opportunity for intervention comes during the pre-conceptional period and given that organogenesis occurs primarily at 5–8 weeks of gestation, controlling pre-pregnancy hyperglycemia can reduce congenital anomalies in the fetus.. It is encouraging to note that many modern-day women are now coming for pre-conceptional visits to health care professionals.

Apart from the standard screenings and care recommended for any person planning pregnancy, prenatal vitamins with at least 400 mg of folic is recommended prior to conception in mothers with pregestational DM. Referral to a registered nutritionist for healthy eating habits to prevent excessive gestational weight gain is recommended for mothers with obesity. The risks of hyperglycemia to the mother and fetus and the ways to reduce risk must be explained to the mother including glycemic targets. Diabetes-specific testing in pre-conceptional period should include Hba1c% , creatinine, urinary albumin-to-creatinine ratio and retinopathy status check-up. (16) The medication list should be reviewed for potentially harmful drugs, like ACE inhibitors, angiotensin receptor blockers and statins, which should be stopped.

Conclusion : GDM is preventable while most of the adverse consequences of hyperglycemia in pregnancy can be avoided with appropriate and timely intervention. Diagnosing and managing GDM and pregestational DM can prevent adverse feto-maternal outcomes and ensure good cardiometabolic health of not only the mother and fetus but for several future generations as well.

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