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How Should India Tackle Diabetes - A Silent Syndrome Load?

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Abstract
Diabetes mellitus type 2 or (T2DM) or Non-Insulin Depended Diabetes Mellitus (NIDDM) is the most common endocrine disorder whose incidence has been continuously growing around the world with the number of individual's affected anticipated to double in the next decade as the world's population ages. As a result of this tendency, it is quickly becoming a syndrome in some parts of the world, with the number of individuals affected anticipated to double in the next decade as the world's population ages, adding to the already existing load on healthcare providers, particularly in poor underdeveloped and developing countries. World Health Organization (WHO) guidelines are still used for screening and diagnosis, which include both clinical and laboratory characteristics. There is currently no cure for the disease; however, therapy options include lifestyle changes, obesity management, oral hypoglycemic medications, and insulin sensitizers such as metformin, a biguanide that reduces insulin resistance which is used as first line medication especially for obese patients. Recent research into the biology of type 2 diabetes has led to the development of new medications such as glucagon-like peptide 1 analogues: dipeptidyl peptidase inhibitors, sodium glucose cotransporter 2 inhibitors, and 11- hydroxysteroid dehydrogenase 1 inhibitors, insulin releasing glucokinase activators. The novel drug delivery improves the treatment of diabetes by the inhaled insulin. Efforts should be made on a war footing to prevent diabetes and treat persons.
What is bringing the controversy in number? In terms of investigative measures, what are the disagreements? What conglomerates about managing hyperglycemia raised up in current studies? Why medical doctors are worried about the incidence of diabetes mellitus in India? What urgent stapes must be taken? What is the future in drug therapy?
Key Words: Diabetes, Syndrome, Complications, Factors, Diagnosis, Guidelines, Drug therapy

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I. Introduction

Diabetes has long captured the fancy of medical historians and landmarks in its history have been notable enough to result in multiple Noble prizes, The manifestation of the disease are so diverse and so complex that if is commonly referred to as a syndrome or a disorder rather than a disease. An elevated concentration of glucose in plasma under certain clearly defined conditions remains in the sine qua non of the diagnosis. It is essentially a silent chemical deviation from the norm and a fulminating clinical catastrophe. Severity of the glucose abnormalities trigger a vast group of complications, commonly classified as micro vascular (retina & glomerulus), macro vascular (accelerated atherosclerosis) and neuropathic. The metabolic abnormalities result in part from a deficiency of blood sugar lowering hormone insulin or from" insulin resistance" a defect in the body's capacity to respond to insulin far from being a mere pointer of affluence and physical inactivity until recent part, diabetes of late, has been growing steadily on prevalence scale among all sections of society as the world's largest endocrine disease. [1] Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the β- cells and glucagon is secreted by the α-cells both are located in the islets of Langerhans. Insulin decreases the blood glucose level by the glycogenesis and transport glucose into the muscle, liver and adipose tissue. Neutral tissue and erythrocytes do not required insulin for glucose utilization whereas α-cell plays important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis in addition to increased risk of obesity, metabolic and cardiovascular disorders, and malignancy in future life for fetus after delivery. Type 2 diabetes mellitus comprises 80% to 90% of all cases of diabetes mellitus. [2]

II. Development of Diabetes

Glucose is the exclusive fuel of the human nervous system and primary fuel for most of the body systems. The brain utilizes approximately 20% of all the glucose metabolized by the entire body at rest mainly via the two major alternative pathways of carbohydrate metabolism that is, glycolysis coupled to the tricarboxylic acid cycle and the pentose phosphate pathway. A healthy level of glucose in the blood is, therefore essential to maintain and sustain life and health. Hypoglycemia or reactive hypoglycemia is a state of low blood sugar that results from a reaction to rapid absorption of sugar. Sugar in and of itself is not a bad thing; it occurs naturally in many food stuffs. The body evolved over many generations to process the sugar consumed from natural sources. Sugar from natural sources is absorbed slowly and is metabolized as it is being released. Sugar from refined sources is concentrated, causing higher quantities to be consumed in a short time and without the associated fiber and other nutrients to slow down the absorption and release process. When excess sugar goes into the blood, the pancreas reacts instantly by releasing a large quantity of insulin into the blood. Since this is an "emergency" release, the insulin is generally in excess of what is required to maintain a steady state level and too much sugar is removed from the blood. When the blood sugar swings below the threshold level, a different panic response is triggered because a low level poses a serious crisis in the body. This response called hypoglycemia causes the adrenal glands to release glucocorticoid hormones which facilitate conversions of glycogen in the liver and muscle tissue into glucose. This results in the glucose level to rise again and, since this was a panic response, the glucose level will likely exceed its base level triggering yet another insulin release. The swing from high glucose levels to low glucose levels and back again may continue as a dampened oscillation for several hours. This is exactly what is observed in a glucose tolerance test (GTT). The patient fasts for 12 hours, has a blood sample taken to determine his base line, and then swallows defined amount of glucose. The blood sugar level is taken at half an hour to one hour intervals for the next several hours. In an individual demonstrating the reactive hypoglycemia response, the glucose level will rise sharply within half an hour. This rise is followed by a sharp drop and in the one to two hour interval; the blood sugar will be sharply lower. At this point, women become irrational and hysterical, men become aggressive and abusive and sweet old ladies curse like sailors. When the blood sugar level rises, the mood and behavior return to normal. The same response occurs when large amounts of refined sugar are consumed, although it is usually not as extreme. The amount of sugar consumed may not be as large as the 100 gram hit of glucose, and other food which releases glucose slower, is usually consumed with the sugar. When the insulin level is high, a lot of glucose is removed from the blood quickly, more quickly than it can be metabolized. This glucose is converted into fat in the cells. In addition, the individual craves for food, especially sweets, when the blood sugar is low, causing excess food consumption. This pattern of blood sugar swings contributes to the development of obesity and cumulative stress on the pancreas, adrenal glands and liver. The prolonged stress of compensating for the blood sugar swings contributes to the development of diabetes.[3]

III. The story so far

. A recent research paper published in Journal The Lancet, on the basis of world – wide study, It revealed more than 800 million adults having life with diabetes mellitus and remarkably greater than half are not getting treatment. As per the study, the sum total of adults living with either Insulin Dependent Diabetes Mellitus (IDDM) or Type – I diabetes and Non - Insulin Dependent Diabetes Mellitus(NIDDM) or Type- II diabetes world – wide are now over 4 times of as were in 1990. Among them, over one- fourth (212 million) are Indians [4] This estimation came as a bit of shock, because the last scientific countrywide estimate by Indian Council of Medical Research (ICMR – INDIAB) before last year study had picked the number at slightly over 100 million [5].

IV. Why is there a discrepancy in numbers?

Experts have noted that the key to it lies in the methods employed to test blood sugar test. Together with the World Health Organization (WHO), the NCD Risk Factor Collaboration (NCD-RisC) undertook a research published in The Lancet that incorporated data from more than 1,000 studies in various countries, encompassing over 140 million individuals aged 18 and older. For 200 nations and territories, they calculated changes in prevalence and treatment of diabetes mellitus from 1990 to 2022. They were, therefore, forced to make use of the data that was available in these countries, which included measuring fasting glucose, HbA1C, or a three-month glycated hemoglobin average. A two-hour postprandial value and a fasting measure were employed in the ICMR investigation, however, to determine the number of individuals with increased blood sugar levels.[6].This discrepancy has been caused by the use of different metrics to measure diabetes. While many nations have switched to measuring HbA1C, India continues to use the gold standard of fasting and two-

hour postprandial readings using an Oral Glucose Tolerance Test (OGTT), according to Viswanatham Mohan, Chairman of the Madras Diabetes Research Foundation in Chennai, who participated in the ICMR-INDIAB study. The figure would have been half of what was recorded, he claims, if they had just used the OGTT readings. When determining diabetes mellitus using HbAlC, they favored a single cut-off threshold of 6.5%. Depending on whether a person is a "normal glycator" or a "fast glycator," a tiny portion of their blood will transfer into the 6.5% HbA1c number, even if their plasma glucose levels are normal. [7] Age and anemia are two of the many factors that affect glycation. An elderly person with a high A1C test may also not have diabetes mellitus. He continues by explaining why the OGTT results are regarded as the gold standard: "In certain previous studies, we found a doubling of the figures when we used HbA1C." However, he notes that not all countries have OGTT, fasting and postprandial readings, and a worldwide research of the scope attempted in this exercise would need to employ the data presently available in countries. The chairperson of the Fortis CDOC Hospital for Diabetes and Allied Sciences, Anoop Mishra, adds that many data sources are used here, which causes apparent discrepancies in the overall figures. Additionally, he states that Type 2 diabetes mellitus is the condition that will cause issues in the future, with Type 1 diabetes mellitus accounting for a very tiny percentage of all diabetes mellitus occurrences in India. [8]

V. What are the areas of concern?

No matter 100 million or 200 million-the truth remains that many of them need diabetes care and are thus at risk for a multitude of potentially fatal consequences that affect the heart, kidneys, eyes, and peripheral nervous system. Putting aside disagreements over statistics, the Lancet research should be viewed as another warning that diabetes has increased and continues to increase in India's population, and that serious measures should be taken to prevent and treat the disease. Lack of access to therapy for diabetics was another issue that the study brought to light. Imperial College, London senior author Majid Ezzati states: "Our study highlights widening global inequalities in diabetes, with treatment rates stagnating in many low-and-middle-income countries where the number of adults with diabetes is drastically increasing." Those who have diabetes are more likely to be younger in low-income nations, and without proper care, they run the danger of developing lifelong problems including heart disease, kidney damage, eyesight loss, amputation, or even early death. [9] "When diabetes complications arise, no nation in the world can afford to treat patients," Dr. Mohan says. Even if we suppose that 20 percent of the 100 million people with diabetes develop renal failure, that means 20 million of them will require a kidney transplant. How are we going to assist everyone there? Dr. Mishra uses the metaphor of battle to emphasize the need to fight for problems that, like Hercules' labors, may appear unachievable yet simply call for almost superhuman effort. It will be difficult to prevent the numbers from increasing, he argues, unless drastic measures are taken, such as utilizing the media to spread awareness about physical activity and nutrition, and enacting new laws to limit carbohydrates and sugar-sweetened beverages. Peter Schwarz of the International Diabetes Federation, Passion for diabetes prevention and care discussed prevention as the main, most important component of this game in a statement made ahead of World Diabetes Day: "My heart is beating for prevention." Next comes prevention, followed by prevention once more. [10] "Countries like India have a responsibility to prioritize the lower middle class, semi- urban, rural, and vulnerable," Dr. Mishra continues. Women are more vulnerable to obesity after pregnancy and are at increased risk throughout menopause, therefore we must educate them. Despite all of these efforts, we must stop the growing trend of obesity since abdominal obesity has been found to be one of the main causes of diabetes in Indians. A ten-year or so long-term perspective is necessary," he says.

VI. Factors to consider

Professor Schwarz chimed in: "I'm a strong supporter of calming down to look at the science and the impact. We would move the patient from a lifelong treatment with insulin, which is becoming cheaper and cheaper, to a life-long treatment with an expensive drug. This has social and financial dimensions and there are side effects - all of which we have to consider." Dr. Mohan added that there is currently no long-term data on the side effects of the GLP-1 class of drugs, so it may not be advisable to use them as the first-line for everyone at this stage. Professor Schwarz added that the IDF is also developing a global diabetes index. "Once a year we will ask 100,000 physicians and 100,000 patients in every country in the world about their perception of the quality of diabetes care, and it will be translated into a score of up to 100. Then, immediately, we can compare the quality of diabetes care in Kerala with Wisconsin in the United States. Countries can learn best practices from each other. For instance, he said, the chain of institutions Dr. Mohan runs would be a role model on how to conduct diabetes care in different areas with varying income groups.

VII. What can individuals do?

Poor diets and obesity are major contributors to the growth in Type 2 diabetes mellitus prevalence, according to The Lancet report. In contrast to many high-income nations, particularly those in the Pacific and Western Europe, where obesity and diabetes rates generally did not rise or increased by a relatively small amount, other regions where obesity was or became prevalent between 1990 and 2022 had diabetes rates that were either already high or increased more. The evidence is clear: engaging in mindful eating and physical activity has been shown to help prevent diabetes and regulate blood sugar levels. However, the issue for governments is to enable people to make these healthy choices and to insist that their leaders do the same. According to Anjana Ranjit, a researcher on the ICMR-INDIAB study, "more ambitious policies that restrict unhealthy foods and make healthy foods affordable are needed." In addition to encouraging safe locations for walking and exercising, such as public parks and fitness centers, subsidies for nutritious foods, and free, nutritious school meals, it is imperative to guarantee opportunities for physical activity.

VIII. What new guidelines can be followed to treat Type 2 diabetes?

The International Diabetes Federation (IDF) is drawing up new guidelines for the treatment of Type 2 diabetes mellitus in consultation with a global expert panel. These guidelines are being evaluated. Professor Schwarz said: "Forming such a guideline is always a big undertaking, because we need to put all the evidence from science and clinical practice - together. What is unique about the International Diabetes Federation's guidelines is that it does not lose the science, but makes sure that the practice is applied on to the environment in specific countries. We are talking about putting not the drugs, but the patient in the middle of the care model." Antonio Ceriello, former head of the European Association for the Study of Diabetes (EASD) to give Indian diabetologist a sneak peek into the new set of guidelines, He added: "In many countries in the world, these guidelines are used by healthcare systems to justify some choices in terms of reimbursement or in terms of what can be allowed, how to access care. This is why we wanted to set the minimum, basic care that reflects the basic right of anyone with diabetes for treatment; less than this is not acceptable." While there are multiple guide lines for diabetes in the world, he said most focus on the best available chances because they are coming from the United States or Europe. "But our idea is to give instruments to be used at a local level in order to get the best options for the treatment of diabetes. “The current or existing guidelines from the American Diabetes Association (ADA) or EASD may not be suitable for all countries, because of accessibility and affordability issues, explained V. Mohan. The IDF, which is an organization comprising over 240 associations of diabetologists across the world, looks at it from a slightly different perspective from the national associations for diabetology. For instance, the ADA's recommendation that GLP-1 receptor agonists, including semaglutide, may be used as first-line treatment in certain cases "is questionable, for several reasons", Professor Ceriello said. "I can say that they are good drugs. But there are several problems. Firstly, the shortage of the drugs. In Australia, for example, people were forced to stop because the drug was not any more available. When these drugs which aid weight loss are stopped, the patients regain weight. So, as part of the guidelines we do not say GLP-1 first, then insulin. We keep insulin as our first choice, and if needed and suitable, you can add GLP-1."[11] Control of hyperglycemia is the main aim in the management of diabetes mellitus which is usually achieved by dietary modification exercise, oral hypo glycemia agent and insulin therapy [12]

IX. Future in drug therapy

Food and Drug Administration has approved the inhaled version of quickly acting insulin for the treatment of Type 2 diabetes mellitus. It is fast-acting insulin that has the benefit of being delivered straight into the lungs, has been found to be beneficial in studies [13]. The novel drug delivery improves the treatment of diabetes by the inhaled insulin.

Conflict of Interest Statement

The author declare that the review article was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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