Diabetes Mellitus: Prevalence, its Complication and Impact on the Quality of Life in India: A Review

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Abstract: *Diabetes is one of the largest global health emergency of this century. India is one of the epicentre of this diabetes mellitus pandemic. Rapid socio economic development and demographic changes along with increased susceptibility for Indian individuals have lead to the explosive increase in the prevalence of this disease over the past four decades. The data available regarding this disease reflects that the susceptibility of Asian Indian people to the complication of diabetes mellitus as compared to the western countries. The estimate of 2021 according to Ministry of Health and Family welfare that 74.2 million individuals has diabetes in India which is expected to increase 124.8 million in 2045. This increase is due to the fact that the management of this disease in India faces multiple challenges such as low level of awareness, paucity of trained medical and paramedical staff and unaffordability of medication and services. Moreover people with diabetes have a worse quality of life than people with non chronic illness, but a better quality of life than people with most other serious chronic disease. Complications of diabetes are the most important disease specific determinant of quality of life.*

Keywords: Diabetes mellitus, India, Asia, Socio economic.

1. Introduction

Diabetes mellitus is a chronic metabolic non communicable disease (NCD) has attained epidemic proportion worldwide. More than 95/ of all adults with diabetes mellitus have type 2 diabetes mellitus (T2DM). It is a metabolic disorder characterised by high blood sugar level (hyperglycemia) over a prolonged period of time [1]. This disease is characterised by frequent urination, increased thirst and increased appetite. If not treated on time it can cause many health complication, which includes diabetic ketoacidosis, hyperosmolar hyperglycemia state or death [2]. Serious long term complication includes cardiovascular disease stroke, chronic kidney disease, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment [3]. This disease is caused due to either the pancrease not producing enough insulin or the cells of the body not responding properly to the insulin produced [4]. This insulin hormone is responsible for helping glucose from food get into cell to be used for energy. As of 2019 an estimated 463 million people had diabetes worldwide (8.8/) of the adult population [5] and rates are similar in men and women. But trends suggest that rates will continue to rise [5] and diabetes at least doubles a person's risk of early death and in 2019 diabetes alone resulted in approximately 4.2 million deaths and is the 7th leading cause of death globally. India is one of the epicenter of the global diabetes mellitus epidemic and has the second highest number of people with the disease in the world (69 million individuals as of 2015) [6]. Other countries of the South Asian region, such as Bangladesh, Pakistan, Srilanka and Nepal also have large number of individuals with diabetes mellitus [6]. In addition countries such as UK, USA, Mauritius, Fiji, Malaysia, Singapore, South Africa, countries in the Middle East and Gulf region are home to large diaspora of Asian Indian individuals who have been found to have a much higher prevalence of diabetes mellitus than the native population of the respective countries [7].

The first multicentre study on diabetes mellitus in India was initiated by the Indian Council of Medical Research (ICMR) in 1971. The studies at that time estimated the prevalence of diabetes mellitus in six cities and surrounding villages in India (Ahmedabad, Kolkata, Cuttack, Delhi, Pune and Trivandrum). The prevalence of the disease were found to be 2.1/ in the urban areas and 1.5/ in the rural areas [8]. After two decades National Urban Diabetes study sampled individuals from six major metropolitan cities of India and reported the prevalence ranging from 9.3/ in Mumbai to 16.1/ in Hyderabad [9]. Around the same time, the diabetes prevalence was also reported from small towns and villages in India represented by about 5.9/ and 2.7/ respectively [10]. Until 2011 prevalence of diabetes mellitus in India from the International Diabetes Federation (IDF) were based on the result of these and other studies [11]. However none of these studies could be considered fully representative of India as a whole. For example the National Urban Diabetes study omitted the rural areas completely and large metropolitan cities.

The ICMR - India Diabetes (ICMR - INDIAB) study aims to address this knowledge gap by estimating the prevalence of diabetes mellitus in India using uniform sampling techniques and diagnostic criteria in a representative sample of individual from rural and urban areas of all states of India [12]. In India the burden of diabetes has been increasing steadily since 1990 and leaps and at a faster pace from the year 2000. The prevalence of diabetes in India has risen from 7.1/ in 2009 to 8.9/in 2019. Currently 25.2 million adults are estimated to have IGT which is expected to increase to 35.7 million in year 2045. It is also estimated that nearly 57/ of adults with diabetes are undiagnosed in India, which is approximately 43.9 million. The mean health care expenditure on diabetes per person is 92 US dollars, and total death attributes directly to diabetes account for one million [13]. The report on the state level disease burden in India from 1990 to 2016 was 64.3/, while age standardized prevalence was 29.3/ [14]. The Indian state level disease

burden Initiative Diabetes study collaborators reported that the prevalence and number of people with diabetes in India increased from 5.5 / and 26.0 million in 1990 to 7.7 and 65 million in the year 2016. According to this report Tamil Nadu has the highest prevalence in 2016 followed by Kerala, Delhi, Punjab, Goa and Karnatka.

Diabetes is becoming more prevalent in India based on the data obtained from cross sectional surveys conducted in various parts of the country. The First study was conducted in Mumbai in 1963 among 18, 243 individuals and prevalence of diabetes was found to be 1.5/ based on urine analysis [15]. The estimated number of diabetes patients in the 20 - 79 age groups is 74.2 millions in 2021 and is likely to increase to 124.8 million in 2045 said Mansukh Mandaviya, Union Minister of Health and Family welfare to the Lok Sabha on Dec.3 2021. He was quoting from diabetes Atlas 2021 of the International Diabetes Federation [16].

Types of Diabetes:

Type 1 diabetes:
This type of diabetes results from failure of the pancreas to produce enough insulin due to loss of beta cells. [2] This form was previously referred to as "insulin - dependent diabetes mellitus" or "juvenile diabetes". [2] The loss of beta cells is caused by an autoimmune response. [16] The cause of this autoimmune response is unknown. [2] Although Type 1 diabetes usually appears during childhood or adolescence, it can also develop in adults. [17]

Type 2 diabetes:
This begins with insulin resistance, a condition in which cells fail to respond to insulin properly. [2] As the disease progresses, a lack of insulin may also develop. [18] This form was previously referred to as "non insulin - dependent diabetes mellitus" or "adult - onset diabetes". [2] Type 2 diabetes is more common in older adults, but a significant increase in the prevalence of obesity among children has led to more cases of type 2 diabetes in younger people. [19] The most common cause is a combination of excessive body weight and insufficient exercise. [2]

Gestational diabetes:
This is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels. [2] In women with gestational diabetes, blood sugar usually returns to normal soon after delivery. However, women who had gestational diabetes during pregnancy have a higher risk of developing type 2 diabetes later in life. [20]

Type 1 diabetes must be managed with insulin injections. [2] Prevention and treatment of type 2 diabetes involves maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. [2]

Type 2 diabetes may be treated with oral antidiabetic medications, with or without insulin. [21] Control of blood pressure and maintaining proper foot and eye care are important for people with the disease. [2] Insulin and some oral medications can cause low blood sugar (hypoglycemia).

[22] Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes. [23]

Gestational diabetes usually resolves after the birth of the baby. [24] What are the most likely reasons for such a huge increase in the prevalence of diabetes mellitus in India? Have diagnostic criteria changed; is sampling and detection better; is the increase in population with improved longevity and demographic changes a factor; have risk factors for the disease increased; or are lifestyle changes leading to obesity, unhealthy diet and physical inactivity? In all likelihood, all of these factors probably contribute to the prevalence of the disease, and identifying the individual causes is difficult. More detailed studies need to be done to understand the impact of each of these factors on the rising diabetes mellitus in India.

Diabetes complication:
Complications of diabetes mellitus include problems that develop rapidly (acute) or over time (chronic) and may affect many organ systems. The complications of diabetes can dramatically impair quality of life and cause long - lasting disability. Overall, complications are far less common and less severe in people with well - controlled blood sugar levels [17]. Some non - modifiable risk factors such as age at diabetes onset, type of diabetes, gender and genetics may influence risk. Other health problems compound the chronic complications of diabetes such as smoking, obesity, high blood pressure, elevated cholesterol levels, and lack of regular exercise. Complications of diabetes are a strong risk factor for severe COVID - 19 illness [18]. If it is not controlled, diabetes can cause a host of complications that can affect nearly every organ in the body. Diabetes complications includes:

Heart Disease
Heart disease is one of the most common diabetes complications. During visit to doctor may perform various tests to check for heart disease and help you prevent any serious heart - related problems. At every visit, health care provider will check the blood pressure by placing a cuff around upper arm that tightens to read the flow of blood through arteries. They'll also take a small blood sample from the patient arm to check levels of LDL cholesterol and triglycerides. A baseline EKG should also be obtained as part of a complete medical record. The expert also knows regarding smoking, and work out a prevention plan that includes weight loss, regular exercise, and stress management, as well as keeping your blood pressure, cholesterol, and triglycerides at normal levels.

Stroke:
Signs and symptoms of stroke include sudden weakness on one side of the face or body; numbness in the face, arm, or leg; difficulty speaking; trouble seeing with both eyes; or dizziness. If such symptoms appear, consult a doctor immediately, Particularly to a neurologist or other stroke specialist.

Diabetic foot ulcers:
This is responsible for >30% of the hospitalisations related to diabetes mellitus113.25% of people with diabetes mellitus are estimated to develop a foot ulcer during their lifetime.

Diabetic foot ulceration is also an expensive complication of diabetes mellitus, owing to both medical care and on account of time lost from work and loss of income and financial independence [19]. The majority of foot ulcers in India arise in neuropathic feet, with only a third having vascular insufficiency, which importantly implies that most of these ulcers can be prevented with proper patient education on appropriate foot care.

Infections:
India is facing a double disease burden, with both the persistence of communicable diseases and the emergence of NCDs. Communicable diseases such as typhoid, cholera, malaria and dengue continue to be rampant in many parts of India, but tuberculosis deserves special mention. Diabetes mellitus and tuberculosis have a bidirectional relationship. Approximately 25% of patients with tuberculosis are estimated to have diabetes mellitus [21], and tuberculosis occurs in up to 8% of patients with diabetes mellitus. Tuberculosis in patients with diabetes mellitus might present with a typical features, such as predominant lower lobe involvement, and thereby delay the diagnosis. Also, cure rates of tuberculosis are lower in patients with diabetes mellitus than those with tuberculosis alone (treatment failure rates 4.2% versus 0.7%) [22]. Prompt diagnosis and initiation of antituberculosis chemotherapy, along with achievement of tight glycaemic control, are essential to ensure cure and prevention of reactivation of tuberculosis.

Diabetes Ketoacidosis:
Diabetes ketoacidosis (DKA) is an acute and dangerous complication that is always a medical emergency and requires prompt medical attention. Low insulin levels cause the liver to turn fatty acid to ketone for fuel (i. e., ketosis); ketone bodies are intermediate substrates in that metabolic sequence. This is normal when periodic, but can become a serious problem if sustained. Elevated levels of ketone bodies in the blood decrease the blood's pH, leading to DKA. On presentation at hospital, the patient in DKA is typically dehydrated and breathing rapidly and deeply. Abdominal pain is common and may be severe. The level of consciousness is typically normal until late in the process, when lethargy may progress to coma. Ketoacidosis can easily become severe enough to cause hypotension, shock, and death. Urine analysis will reveal significant levels of ketone bodies (which have exceeded their renal threshold blood levels to appear in the urine, often before other overt symptoms). Prompt, proper treatment usually results in full recovery, though death can result from inadequate or delayed treatment, or from complications (e. g., brain edema). Ketoacidosis is much more common in type 1 diabetes than type 2.

Hyperglycemia hyperosmolar State:
Nonkeyonic Hyperosmolar coma (NKC) is an acute complication sharing many symptoms with DKA, but an entirely different origin and different treatment. A person with very high (usually considered to be above 300 mg/dl (16 mmol/L)) blood glucose levels, water is osmotically drawn out of cells into the blood and the kidneys eventually begin to dump glucose into the urine. This results in loss of water and an increase in blood osmolarity. If fluid is not replaced (by mouth or intravenously), the osmotic effect of high glucose levels, combined with the loss of water, will eventually lead to dehydration. The body's cells become progressively dehydrated as water is taken from them and excreted. Electrolyte imbalances are also common and are always dangerous. As with DKA, urgent medical treatment is necessary, commonly beginning with fluid volume replacement. Lethargy may ultimately progress to a coma, though this is more common in type 2 diabetes than type 1 [23].

Hypoglycemia:
Hypoglycemia or abnormally low blood glucose is an acute complication of several diabetes treatments. It is rare otherwise, either in diabetic or non - diabetic patients. The patient may become agitated, sweaty, weak, and have many symptoms of sympathetic activation of the autonomic nervous system resulting in feelings akin to dread and immobilized panic. Consciousness can be altered or even lost in extreme cases, leading to coma, seizures, or even brain damage and death. In patients with diabetes, this may be caused by several factors, such as too much or incorrectly timed insulin, too much or incorrectly timed exercise (exercise decreases insulin requirements) or not enough food (specifically glucose containing carbohydrates). The variety of interactions makes cause identification difficult in many instances.

It is more accurate to note that atrogenic hypoglycemia is typically the result of the interplay of absolute (or relative) insulin excess and compromised glucose counter regulation in type 1 and advanced type 2 diabetes. Decrements in insulin, increments in glucagon, and, absent the latter, increments in epinephrine are the primary glucose counter regulatory factors that normally prevent or (more or less rapidly) correct hypoglycemia. In insulin - deficient diabetes (exogenous) insulin levels do not decrease as glucose levels fall, and the combination of deficient glucagon and epinephrine responses causes defective glucose counter regulation.

Furthermore, reduced sympathoadrenal responses can cause hypoglycemia unawareness. The concept of hypoglycemia - associated autonomic failure (HAAF) or Cryer syndrome in diabetes posits that recent incidents of hypoglycemia causes both defective glucose counter regulation and hypoglycemia unawareness. By shifting glycemic thresholds for the sympathoadrenal (including epinephrine) and the resulting neurogenic responses to lower plasma glucose concentrations, antecedent hypoglycemia leads to a vicious cycle of recurrent hypoglycemia and further impairment of glucose counter regulation. In many cases (but not all), short - term avoidance of hypoglycemia reverses hypoglycemia unawareness in affected patients, although this is easier in theory than in clinical experience.

In most cases, hypoglycemia is treated with sugary drinks or food. In severe cases, an injection of glucagon (a hormone with effects largely opposite to those of insulin) or an intravenous infusion of dextrose is used for treatment, but usually only if the person is unconscious. In any given incident, glucagon will only work once as it uses stored liver glycogen as a glucose source; in the absence of such stores,

glucagon is largely ineffective. In hospitals, intravenous dextrose is often used.

Erectile Dysfunction:
Estimates of the prevalence of erectile dysfunction in men with diabetes range from 20 to 85 percent when defined as consistent inability to have an erection firm enough for sexual intercourse. Among men with erectile dysfunction, those with diabetes are likely to have experienced the problem as much as 10 to 15 years earlier than men without diabetes. [24]

Female infertility:
This is more common in women with diabetes type 1, despite modern treatment, also delayed puberty and menarche, menstrual irregularities (especially oligomenorrhoea), mild hyperandrogenism, polycystic ovarian syndrome, fewer live born children and possibly earlier menopause. Animal models indicate that on the molecular level diabetes causes defective leptin, insulin and kisspeptin signalling. [25]

Immune compromise:
The immune response is impaired in individuals with diabetes mellitus. Cellular studies have shown that hyperglycemia both reduces the function of immune cells and increases inflammation. Respiratory infections such as pneumonia and influenza are more common among individuals with diabetes. Lung function is altered by vascular disease and inflammation, which leads to an increase in susceptibility to respiratory agents. Several studies also show diabetes associated with a worse disease course and slower recovery from respiratory infections. [26]

Increased risk of wound infections
Restrictive lung disease is known to be associated with diabetes. Lung restriction in diabetes could result from chronic low - grade tissue inflammation, microangiopathy, and/or accumulation of advanced glycation end products. In fact the presence restrictive lung defect in association with diabetes has been shown even in presence of obstructive lung diseases like asthma and COPD in diabetic patients. [27]

Lipohypertrophy may be caused by insulin therapy. Repeated insulin injections at the same site, or near to, causes an accumulation of extra subcutaneous fat and may present as a large lump under the skin. It may be unsightly, mildly painful, and may change the timing or completeness of insulin action.

Depression was associated with diabetes in a 2010 longitudinal study of 4, 263 individuals with type 2 diabetes, followed from 2005 to 2007. They were found to have a statistically significant association with depression and a high risk of micro and macro - vascular events [28].

Quality of Life and Diabetes
The World Health Organisation (WHO) has defined QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. QoL is considered an important health outcome, with good quality of life representing the ultimate therapeutic goal in chronic conditions. [5] The term was first used in medical literature in the 1960s and since then has gained considerable popularity in research and clinical practice. QoL includes four main components namely physical, psychological, social relationship, and environment.

India is currently second in the world in diabetes prevalence, with an estimated 77 million people affected in 2019, and this number is expected to reach 101 million by 2030. [1] The Indian Council of Medical Research (ICMR) -India DIABetes (ICMR-INDIAB) study has reported diabetes prevalence in 15 of the 31 states/union territories of India completed and published to date. The average prevalence was 7.3%; however, large differences in prevalence are observed between the states, indicating epidemiological transition. The earliest studies on diabetes QoL in India were conducted among T1D patients in 2007, and among T2D patients in 2009 [27] Since then, QoL assessment publications have increased however they are largely reported from tertiary care hospital settings and characterized by small sample sizes. Hence, the results of the studies cannot be generalized to the larger Indian population. In addition to the existing drawbacks as stated above, more QoL assessment tools are being developed, [17-19] increasing the complexity of generalizing from multiple QoL tools. A recent article reported a scarcity of QoL studies among diabetic patients in India as a major limitation of the current literature. [28] Hence, better recognition of the importance of the QoL construct in managing chronic conditions is important and a review of QoL studies, timely.

2. Conclusion

This review suggest that diabetes related complications are the most common problem in India. In addition prevalence estimates specify that prediction is much higher resulting in a substantial burden of diabetes in future Indian population. Therefore it is imperative to plan urgent strategies to reduce a further augment in diabetes in areas with high prevalence of pre diabetes.

With the increased prevalence of diabetes in India and around the world, it is becoming even more important to assess the QoL as an outcome measure in long-term illness and management. The current review showcased that poorer QoL was observed in people with diabetes as compared to those without diabetes. The knowledge we possess, if used appropriately with proper community empowerment, has the potential to slow the epidemic of diabetes mellitus. The dividend, in the form of improved health, productivity and economic development, is well worth the effort.

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