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Published Paper's Title : Present Scenerio Of Diabetes Mellitus and Its Treatment Possibilities

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Research Paper

Present Scenerio Of Diabetes Mellitus and Its Treatment Possibilities

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Declaration

The Declaration of the authors for publication of Research Paper in Asian Journal of Modern and Ayurvedic Medical Science (ISSN 2279-0772) We Amit Vaibhav,O. P. Singh and Anil Kr. Tripathi the authors of the research paper entitled Present Scenerio Of Diabetes Mellitus and Its Treatment Possibilities declare that , We take the responsibility of the content and material of our paper as We ourself have written it and also have read the manuscript of our paper carefully. Also, We hereby give our consent to publish our paper in ajmams , This research paper is our original work and no part of it or it's similar version is published or has been sent for publication anywhere else.We authorise the Editorial Board of the Journal to modify and edit the manuscript. We also give our consent to the publisher of ajmams to own the copyright of our research paper.

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Abstract : Diabetes mellitus is a medical disorder characterized by varying or persistent hyperglycemia (elevated blood sugar levels), especially after eating. It is one of the most common endocrine disorders affecting almost 6% of the world's population. It is a group of disease characterized by elevated blood glucose concentration because of diminished or exhausted insulin secretion from pancreatic β-cells and insulin resistance. Diabetes is a leading cause of blindness, renal failure, nerve damage which can lead to erectile dysfunction (impotence), foot and leg amputations in adults. Managed care and budgeted resources challenge clinicians to provide comprehensive health care to patients with diabetes. Diabetes mellitus is all the more dreaded because of its complications in almost every part or rather every cell of the body. In this present study an effort is made to give a concise view about diabetes in present global scenario along with its treatment possibilities.

***Keywords*:** Diabetic mellitus, hyperglycemia, blood glucose, pancreatic beta cell, global scenario.

Introduction :

Diabetes poses a major health problem globally and is one of the top five leading causes of death in most developed countries. A substantial body of evidence suggests that it could reach epidemic proportions particularly in developing and newly industrialized countries. It has been estimated that

the global burden of type 2 diabetes mellitus (T2DM) for 2010 would be 285million people (2010) which is projected to increase to 438 million in 2030; a 65 % increase. Similarly, for India this increase is estimated to be 58%, from 51 million people in 2010 to 87 million in 2030[1] Indeed, by the year 2025, three-quarters of the world's 300 million adults with diabetes will be in developing countries and almost a third in India and China alone.[2] The prevalence of diabetes in India is showing a sharp upswing as is evident from secular trends from different parts of the subcontinent and studies of migrant Indians.[3] The World Health Organization has estimated that in 1995, 19.4 million individuals were affected by diabetes in India and these numbers are expected to increase to 57.2 million by the year 2025 i.e. one- sixth of the world total.1 The revised figures are 80.9 million by the year 2030.[4]

The incidence of type 2 diabetes increases significantly with an increase in age, typically manifesting in middle age or the later part of life. The impacts of T2DM are considerable: as a lifelong disease, it increases morbidity and mortality and decreases the quality of life. At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society. A better understanding about the cause of a predisposition of Indians to get T2DM is necessary for future planning of healthcare, policy and delivery in order to ensure that the burdens of disease are addressed. With India having the highest number of diabetic patients in the world, the sugar disease is posing an enormous health problem in the country. Calling India the diabetes capital of the world,[5] The International Diabetes Federation estimates that the number of diabetic patients in India more than doubled from 19 million in 1995 to 40.9 million in 2007 [6]. It is projected to increase to 69.9 million by 2025. Currently, up to 11 per cent of India's urban population and 3 per cent of rural population above the age of 15 have diabetes. Diabetes affects all people in the society, not just those who live with it. The World Health Organization estimates that mortality from diabetes and heart disease cost India about $210 billion every year and is expected to increase to $335 billion in the next ten years [7]. These estimates are based on lost productivity, resulting primarily from premature death.

Various studies have shown that the high incidence of diabetes in India is mainly because of sedentary lifestyle, lack of physical activity, obesity, stress and consumption of diets rich in fat, sugar and calories.

The most prevalent is the Type 2 diabetes, which constitutes 95 per cent of the diabetic population in the country. In this, patients are non-insulin dependent and they can control the glucose in their blood by eating measured diet, taking regular exercise and oral medication. Worldwide, millions of people have Type 2 diabetes without even knowing it and if not diagnosed and treated, it can develop serious complications.

Diabetes: Complications:

All forms of diabetes increase the risk of long-term complications [8] These typically develop after many years (10–20), but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease. The main "macrovascular" diseases (related to atherosclerosis of larger arteries) are ischemic heart disease (angina and myocardial infarction), stroke and peripheral vascular disease.

Diabetes also causes "microvascular" complications—damage to the small blood vessels. Diabetic retinopathy, which affects blood vessel formation in the retina of the eye, can lead to visual symptoms, reduced vision, and potentially blindness. Diabetic nephropathy, the impact of diabetes on the kidneys, can lead to scarring changes in the kidney tissue, loss of small or progressively larger amounts of protein in the urine, and eventually chronic kidney disease requiring dialysis. Diabetic neuropathy is the impact of diabetes on the nervous system, most commonly causing numbness, tingling and pain in the feet and also increasing the risk of skin damage due to altered sensation[9]. Together with vascular disease in the legs, neuropathy contributes to the risk of diabetes-related foot problems (such as diabetic foot ulcers) that can be difficult to treat and occasionally require amputation. In addition, diabetes results in a reduced quality of life,[10] much higher rates of depression[11]. and mental illness,[12] and enormous societal and economic costs.[13].

There are numerous biochemical disturbances associated with diabetes.[14]. In particular, enhanced polyol metabolism, protein kinase C-b (PKC-b) activation, elevated levels of oxidative stress, and advanced glycation (glycosylation) end-product accumulation have emerged as prime candidates thought to promote many of the complications of diabetes.[15].

Interestingly, early clinical changes associated with the development of DR occur simultaneously with, or can be predictive of, other diabetic complications.[16-20]

Futhermore, tight control of blood glucose and blood pressure management has proven to be effective in reducing the development and rate of progression of all the major complications of diabetes.[21-23]

Glycaemic Control based on Recent Studies: The Diabetes Control and Complications Trial (DCCT) demonstrated that good metabolic control, resulting from intensive insulin therapy, reduced the risk of progression or development of retinopathy, nephropathy and neuropathy in type 1 diabetes [24]. The United Kingdom Prospective Diabetes Study (UKPDS) showed that intensive glycaemic control in type 2 diabetes significantly reduced the risk of development and deterioration of microvascular complications.[25]. The primary goal of the management of diabetes mellitus is the attainment of near normal glycaemia. The target for good glycaemic control recommended by the American Diabetes Association (ADA) [26].

is glycated hemoglobin A1c (HbA1c) < 7.0%.

Unmet needs with existing drugs :

Lifestyle modification is the most cost-effective intervention for prevention of diabetes in high-risk groups in India[27]. However, control of diabetes with diet, weight control and physical activity has been difficult and will not be sufficient for most of the patients. Moreover, the steady increase in the incidence of type 2 diabetes has significant socioeconomic implications [28].

Oral Antidiabetic Drugs (OADs) :

An oral antidiabetic drug (OAD) is the first line of drug treatment for type 2 diabetes. However, the progressive nature of type 2 diabetes usually requires a combination of two or more oral agents in the long term, often as a prelude to insulin therapy. Safety and tolerability (notably hypoglycaemia), and weight gain often limit the optimal use of OADs. Insulin treatment is the cornerstone of diabetes management. It is the only means of achieving good glycaemic

control in insulindeficient patients with type 1 diabetes. Insulin is also used as an intermittent or permanent therapy in some patients with type 2 diabetes. The UKPDS data showed that the current available treatment modalities were not satisfactory as evidenced by the high morbidity and mortality among subjects with type 2 diabetes[25].

Both OADs and insulin treatment increased the risk of hypoglycaemia. Weight gain was significantly higher in the intensive group with a sulphonylurea (SU) (chlorpropamide, glibenclamide or glipizide) or with insulin than in the conventional group with diet, and patients assigned insulin had a greater weight gain than those assigned chlorpropamide or glibenclamide. Studies in India indicate that more than 50% of people with diabetes have poor glycaemic control (HbA1c > 8%), uncontrolled hypertension and dyslipidaemia, and a large percentage have diabetic vascular complications [29-32].

Overall, diabetes care in India leaves much to be desired. Increased awareness amongst health professionals to improve the standard of diabetes care is urgently needed, along with the development of novel therapeutic agents that can effectively control diabetes and prevent the development and progression of its complications without compromising on safety. Type 2 diabetes is a complex, multifactorial disease. It is associated with progressive deterioration of β-cell function and insulin resistance [25].

The UKPDS and DCCT data showed that tight control of diabetes can significantly prevent the development of vascular complications [24-25].

. The UKPDS also suggested that 53% of type 2 patients would require insulin 6 years after diagnosis, and 75% of patients would require multiple treatments after 9 years[25].

Although insulin treatment is effective, its long-term use can lead to gains in fat mass, especially abdominal obesity, which may worsen insulin resistance. Moreover, repeated episodes of hypoglycaemia may cause major problems.

Future Treatment possibilities of Diabetes:

DM is defined by an absolute (type 1) or relative (type 2) deficiency of insulin. Type 2 DM is characterized by insulin resistance, abnormal hepatic glucose production, and progressive worsening of pancreatic β-cell function over time.21 Prevention and treatment of DM is a major public health challenges. Greater understanding of the pathophysiology of DM has contributed to the development of new pharmacological approaches. The currently available classes of anti-diabetic agents are glucagon-like peptide-1 (GLP-1) receptor agonists, dipeptidyl peptidase-IV (DPP-4) inhibitors, thiazolidinediones (TZDs; glitazones), insulin analogues, biguanides, sulphonylureas, meglitinides, α-glucosidase inhibitors, and synthetic amylin analogues (Table 1). In addition, endocannabinoid antagonists acting at the CB1 receptor show promise for affecting food intake and improving glucose homeostasis. Insulin treatment, particularly with new basal formulations, is used increasingly in type 2 diabetics.

New agents—primary treatment

GLP-1 receptor agonists
DPP-4 inhibitors
Thiazolidinediones
Insulin analogues, basal, and short-acting

Current proved agents—primary treatment
Biguanides
Sulphonylureas

New agents—**secondary treatment**
Meglitimides

α-Glucosidase inhibitors
Synthetic amylin analogues

DPP-4 inhibitors

include the oral drugs Januvia, Onglyza, and Tradjenta. These protect a natural compound in the body -- **GLP-1** -- from breaking down. GLP-1 helps lower blood glucose. **Incretin mimetics** or GLP analogs include the injected drugs Byetta and Victoza. They use the body's own signaling system to boost insulin after meals.
Other drugs includeSymilin, an injectable synthetic hormone. It helps lower blood sugar after meals in people with diabetes who use insulin.
Combination drugs have made a difference. They join different medications in one pill -- often metformin and a sulfonylurea, a meglitinide, a **DPP4 inhibitor**, a thiazolidinedione, or a thiazolidinedione in combination with a sulfonylurea. This cuts down the number of pills a person has to take. Combination drugs include Actoplus MET, Avandamet, Duetact, Glucovance, Metaglip, and PrandiMet. There can be drawbacks. They tend to cost more than generic drugs. They can also make it harder to fine-tune the treatment. New types of insulin allow some people to take just one injection of a long-acting insulin each day. That can be much easier than multiple injections of standard insulin Future medications. Other classes of medication are in development. One type doesn't affect insulin, unlike most diabetes drugs. It blocks the body from reabsorbing glucose from urine, Current drugs available for the treatment of diabetes mellitus.

As part of the quest for newer agents, research has focused on insulin-independent mechanisms. The investigators concluded that addition of dapagliflozin to metformin provided a new therapeutic option Sodium glucose co-transporter inhibitor One of the newest agents is dapagliflozin,[33] an SGLT2 inhibitor. Sodium-glucose co-transporter 2 (SGLT2) is located mainly in the proximal tubule of the nephron. It reabsorbs most of the glucose filtered by the glomerulus. Binding of dapagliflozin inhibits renal glucose reabsorption and promotes urinary glucose excretion. One study of more than 500 patients, who had inadequate diabetic control with metformin alone, found that the addition of dapagliflozin reduced HbA1c and FPG, with no increased risk in hypoglycaemia but with an increased incidence of genital infections.—insufficient data at present .While the FDA has not approved any drug from this class, it could in the future.

Conclusion:

Diabetes poses a major health problem globally and is one of the top five leading causes of death in most developed countries. A substantial body of evidence suggests that it could reach epidemic proportions particularly in developing and newly industrialized countries. Diabetes is a complex condition with a multitude of metabolic imbalances involving the regulation and utilization of insulin and glucose (sugar) in the body.

Diabetes is currently considered an epidemic disease that is largely preventable and treatable through diet, exercise and lifestyle changes. Considering the enormous burden due to diabetes in India, it is important to realize the cost-effective measures of diabetes care like early screening, tight metabolic control, monitoring of risk factors and assessing of organ damage.Published data from several epidemiological, experimental human and animal studies as well as the data from several mega trials like DCCT and UKPDS [34]have convincingly proved the importance of tight metabolic control in arresting and preventing the progression of target organ damage. In the last two decades there is better

understanding of pathophysiology of type 2 diabetes and availability of newer oral drugs for diabetes, newer insulin and improved delivery systems should translate to improve diabetes control in a newer dimensions.

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