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Diabetes mellitus (DM) is a common metabolic disorder resulting from defects in insulin secretion or action or both, is characterized by hyperglycemia often accompanied by glycosuria, polydipsia, and polyuria. Some form of diabetes mellitus are characterized in terms of their specific etiology or pathogenesis, but the underlying etiology of the most common form remains unclear. Regardless of the etiology, DM progresses through several clinical stages during its natural history. Persons developing the disease can be categorized according to clinical stages and other characteristics even in the absence of knowledge of the etiology. The chronic hyperglycemia of DM is associated with long term damage, dysfunction, and failure of different organs, especially the eyes, nerves, kidneys, heart and blood vessels.

Diabetes mellitus (DM) is the most common endocrine disease and is attracting global importance because it is racking the world as a noninfectious epidemic or pandemic. The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1995 to 177 million in 2000. Based on current trends, >360 million individuals will have DM by the year 2030. The prevalence of Type 2 Diabetes Mellitus (t2dm) is rising much more rapidly due to several reasons. WHO projected that global prevalence of t2dm will be from 13
million in 1995 to 300 million by 2025\textsuperscript{5}. It is projected that the disease prevalence will be 5.4\% by the year 2025\textsuperscript{6}. Type 2 diabetes mellitus (T2DM) is one of the most common noncommunicable diseases in all regions of the world\textsuperscript{7}. This is true with reference to the Indian subcontinent which has been declared by WHO as the diabetes capital of the world. It is estimated that by the year 2025, the number of diabetes in India will be around 57 million, a staggering figure. India will thus be probably housing the largest population of diabetes in the whole world\textsuperscript{8}. India has the largest number of people with diabetes approximately 51 million in 2010 and its likely to rise to 81 million by 2030\textsuperscript{9}. It is noted that DM is diagnosed incidentally in more than half of the cases. All studies have shown that the glycemic outcome was poor in nearly 50\% of the patients even in urban areas. These conclusions are from the reports on the profile of diabetes care in India available from the tertiary diabetes care centre\textsuperscript{10}, a community study\textsuperscript{11}, and also from a population based study\textsuperscript{12}. India has more than 30 million diabetics. Prevalence of diabetes among adults in India has found to 2.4\% in rural and 4-11.06\% in urban dweller and impaired glucose tolerance from 3.3.6-9.1\%. It indicates the potentiality of raising diabetes mellitus in coming years\textsuperscript{45}. It is expected to affect around 57 million by the year 2025.
DM has different forms:

a) General—genetic and other factors are not precisely defined.

   It is of two type

   1) Type 1 (formerly called insulin dependent diabetes mellitus or IDDM).

      Type 1 again is of two type’s type1A (autoimmune & common) & type1B (non-autoimmune) type.

   2) Type2 (formerly called noninsulin dependent diabetes mellitus or NIDDM).

      Type 2 may be insulin dependent (Type2 IDDM-transient) and non-insulin dependent (Type2 NIDDM) and maturity onset diabetes mellitus of the young (MODY)\(^{24}\).

b) Specific—gene mutation has been defined

c) Secondary to pancreatic disease, other endocrinopathies, immune suppression and associated with genetic syndrome and drug therapy.\(^{24}\)

   Both type1 and type2 are increasing. Type 2 DM is the predominant form of diabetes worldwide; accounting for 90% of the cases globally\(^{31}\). Type 2 DM has become one of the world’s most important public health problems\(^{31}\). Epidemiologic determinant and risk factor for t2dm are many like genetic factor (family history, thrifty gene), demographic characters
(sex, age, ethnicity) behavioral and life style related factor (obesity including of distribution of obesity and duration, physical inactivity, diet, stress, westernization, modernization, urbanization) and other metabolic determinant and intermediate risk categories (impaired glucose tolerance, insulin resistance, parity, gestational diabetes, intrauterine malnutrition and over nutrition)\(^{31}\). So the simply genetic basis cannot explain the rapid rise of incidence of type 2 DM in such a short time. Thus other contributing factors like increasing age, obesity, sedentary life style, low birth weight must account for this dramatic increase. Although prevalence data exist for type 2 DM it should be noted that there is an equal number of undiagnosed cases\(^{24}\).

Due to asymptomatic nature of the disease for many years diagnosis of DM is delayed and most of the patients fail to receive appropriate care; management is far from satisfactory. Where as hyperglycemia is the most important single cause of chronic complication in diabetes which has been proved by the Diabetes Control and complications trial (DCCT). But now it is well known from different DCCT and UKPDS studies that good metabolic control can definitely help to delay the onset of complications as well as slow down their progression to a large extent\(^{23}\). United kingdom Prospective Diabetes Study (UKPDS) among type 2 DM patients for a period of 10 years capable of reducing the risk of long term microvascular complication by controlling blood glucose adequately. In DCCT study among patient with insulin dependent DM whose intensive insulin therapy
resulted in HbA1c values of 2% lower than those receiving conventional insulin therapy, had a 76% lower incidence of retinopathy, a 54% lower incidence of nephropathy, and a 60% reduction in neuropathy\textsuperscript{23}. DM is a group of syndrome characterized by hyperglycemia; altered metabolism of lipids, carbohydrate and proteins; and increased risk of complication from vascular diseases\textsuperscript{24} leading to long term effect involving eyes, kidneys, nerves and blood vessels.

Now it is virtually true that the t2DM cases are increasing rapidly. Prospective randomized clinical trials have documented improved rates of microvascular complications in patients with T2DM treated to lower glycemic targets\textsuperscript{31}. Multiple epidemiologic studies have suggested that there is an association between cardiovascular risk and HbA1c, FBG, and the 2-hour level in the OGTT\textsuperscript{31}. There is an emerging consensus that the common form of t2dm are polygenic in nature and are due to a combination of insulin resistance and abnormal insulin secretion\textsuperscript{31}. From a pathophysiologic standpoint, it is the inability of the pancreatic beta cell to adapt to the reductions in insulin sensitivity that occur over the lifetime of human subjects that precipitates the onset of T2DM.

Hyperglycemia in t2dm resulted from impaired insulin action and reduced insulin secretion. Therefore treatment of t2dm are

a) optimum nutrition intake by medical nutrition therapy
b) increased physical activity including aerobic exercise and perform resistance exercise targeting all muscle group three times a week

c) Pharmacotherapy with

1) Insulin sensitizer—with predominant action on liver like metformin and with predominant action on peripheral insulin-sensitive tissue like pioglitazone

2) Insulin secretagogues sulfonylurea like glibenclamide, meglitinides like repaglinide

3) Physiologic incretin mimetic like exenatide

4) DPP4 inhibitors like sitagliptin

5) Carbohydrate digestion and absorption reducing agents — alfaglucosidase inhibitor like acarbose

6) Insulin itself as last remedial agent.

In t2dm beta cell mass is already reduced (<50%) and reduction is also gradually progressing. Insulin resistance is one of the most important factor of T2DM. To overcome this insulin resistance β-cell secrete more to increase plasma insulin level. Hyperglycemia in T2DM is itself a strong stimulus for insulin secretion. Still secretagogues are used to raise the insulin level in plasma. But hyperinsuliemia may adversely affect the different physiological system of the body. On the other hand chronic over
secretion of insulin also cause over secretion of co-package amyloid polypeptide (amylin) which may be b-cell cytotoxic and may resolved in the progressive deterioration of β-cell function in genetically susceptible individual. So the drugs act by improving insulin resistance is the better alternative as they improve the action of insulin in peripheral tissue.

Basically secretagogues have limited role in the long term treatment of T2DM and even might cause increased arrhythmic cardiovascular events in larger dose. Insulin sensitizer improve insulin action, diminished insulin resistance, reduce insulin requirement. So concomitant use of insulin sensitizers is not only remarkably effective but also safe and tolerable. Which insulin sensitizer will be more effective? In this study search has been made to find out the effective, tolerable, scientific, economic insulin sensitizer.