International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

The Review of Study on Diabetes Mellitus

Shubham Dadaji Pawar[1], Assistant Prof. Rutuja S. Abhonkar[2]

[1,2] Swami Vivekananda Sanstha's Institute of Pharmacy, Mungase, Malegaon.

ABSTRACT:

"Diabetes mellitus", is one of the most common non-communicable diseases worldwide. India faces several challenges in diabetes management, including a rising prevalence in urban and rural areas, lack of disease awareness among the public, limited health care facilities, high cost of treatment, suboptimal glycaemic control, and rising prevalence of diabetic complications. Insulin therapy for diabetes is most commonly delivered via subcutaneous injections, up to four times a day. Long-term insulin therapy, compounded by the invasive nature of its administration, has caused problems with patient compliance, ultimately influencing patient outcomes. Type 2 diabetes mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world. As a result of this trend, it is fast becoming an epidemic in some countries of the world with the number of people affected expected to double in the next decade due to an increase in aging population, thereby adding to the already existing burden for healthcare providers, especially in poorly developed countries. This review is based on a search of Medline, the Cochrane Database of Systemic Reviews, and citation lists of relevant publications.

Keywords: Type 2 diabetes mellitus; Diagnosis; Management; Newer drugs.

Introduction:

Diabetes mellitus (DM) is probably one of the oldest diseases known to man. It was first reported in an Egyptian manuscript about 3000 years ago. In 1936, the distinction between type 1 and type 2 DM was clearly made. Type 2 DM was first described as a component of metabolic syndrome in 1988. Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. Type 2 DM results from the interaction between genetic, environmental, and behavioral risk factors. People living with type 2 DM are more vulnerable to various forms of both short- and long-term complications, which often lead to premature death. This tendency of increased morbidity and mortality is seen in patients with type 2 DM because of the commonness of this type of DM, its insidious onset, and late recognition, especially in resource-poor developing countries like Africa. Diabetes mellitus is a chronic disorder of carbohydrates, fats, and protein metabolism. A defective or deficient insulin secretory response, which translates into impaired carbohydrate (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemia. [1]

Diabetes mellitus (DM) is commonly referred to as a "sugar" and it is the most common endocrine disorder and usually occurs when there is a deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance). The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025. Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan's. Insulin decreases the blood glucose level by glycogenesis and transports glucose into the muscles, liver, and adipose tissue. Neural tissue and erythrocytes do not require insulin for glucose utilization whereas alpha (α) cells play an important role in controlling blood glucose by producing glucagon and it increases the blood glucose level by accelerating glycogenolysis. In addition to increased risk of obesity, metabolic and cardiovascular disorders, and malignancy in the future life of the fetus after delivery. Type II diabetes mellitus comprises 80% to 90% of all cases of diabetes mellitus. Geographical variation can contribute to the magnitude of the problems and to overall morbidity and mortality. Moreover, people with diabetes who undertake moderate amounts of physical activity are at an inappreciably lower risk of death than inactive persons. It is now well established that a specific genetic constitution is required for such an event to cause. The growing burden of diabetes and other non-communicable diseases is one of the major health challenges to economic developments bedeviling WHO African Region states. In diabetes, there is an aberration either in the synthesis or secretion of insulin as seen in Type 1 diabetes mellitus (T1DM) and stenosis in the pancreatic duct, or the development of resistance to insulin or its subnormal production as in the case of Type 2 diabetes (T2DM) and certain secondary diabetes. Classification of Diabetes Mellitus.[2]

The first mostly accepted classification of diabetes mellitus was published by WHO in the year 1980 and, it is modified in the year 1985. The most common and important form of Primary or idiopathic diabetes mellitus is the focus of our discussion. It must be different from secondary diabetes mellitus which includes forms of hyperglycemia associated with identifiable causes in which destruction of pancreatic islets is induced by inflammatory Pancreatic diseases, surgery, tumors, certain drugs, iron overloaded (Hemochromatosis) and certain acquired or genetic endocrinopathies. The classification encompasses both clinical stages and aetiological types of diabetes mellitus and other categories of hyperglycemia. Assigning a type of diabetes to an

individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single class. Primary diabetes mellitus probably represents a heterogeneous group of disorders that have hyperglycemia as a common feature.[3]

Pathophysiology:

Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure. This leads to a decrease in glucose transport into the liver, muscle cells, and fat cells. There is an increase in the breakdown of fat with hyperglycemia. The involvement of impaired alpha-cell function has recently been recognized in the pathophysiology of type 2 DM.30 As a result of this dysfunction, glucagon and hepatic glucose levels that rise during fasting are not suppressed with a meal. Two therapeutic approaches to this problem have been developed:

GLP-1 analogs with increased half-lives, and DPP IV inhibitors, which prevent the breakdown of endogenous GLP 1 as well as GIP. Both classes of agents have shown promise, with the potential not only to normalize fasting and postprandial glucose levels but also to improve beta-cell functioning and mass. Studies are ongoing on the role of mitochondrial dysfunction in the development of insulin resistance and etiology of type 2 DM.31 Also very important is adipose tissue, as endocrine organ hypothesis (secretion of various adipocytokines, i.e., leptin, TNF alpha, resistin, and adiponectin implicated in insulin resistance and possibly beta-cell dysfunction)[4,5]

Insulin Dependent Diabetes Mellitus:

(Type1 IDDM) This type of diabetes mellitus is also called autoimmune diabetes and was previously known as juvenile-onset or ketosis-prone diabetes. The individual may also seek other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease. Type I diabetes mellitus is also known as insulin-dependent diabetes mellitus (IDDM), this occurs mainly in children and young adults; the onset is usually sudden and can be life-threatening. Type 1 is usually characterized by the presence of anti-glutamic acid decarboxylase, islet cell, or insulin antibodies which identify the autoimmune processes which lead to beta-cell destruction. Type 1 diabetes (due to the destruction of B-cells which is usually leading to absolute insulin deficiency) (American Diabetes Association, 2014). The rate of destruction of beta cells is quite variable; it can occur rapidly in some individuals and slowly in others. There is a severe deficiency or absence of insulin secretion due to the destruction of ß-islets cells of the pancreas. Treatment with injections of insulin is required. Markers of immune destruction, including islet cell auto-antibodies, and/or autoantibodies to insulin, and autoantibodies to glutamic acid decarboxylase (GAD) are present in 85-90 % of individuals with Type 1 diabetes mellitus when fasting diabetic hyperglycemia is initially detected. The exact cause of diabetes mellitus is remain unknown, although, in most people, there is evidence of an autoimmune mechanism involving auto-antibodies that destroy the beta islet cells.[6,7,8]

Non-Insulin Dependent Diabetes Mellitus:

(Type2 NIDDM) Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance (American Diabetes Association, 2014). People with this type of diabetes frequently are resistant to the action of insulin. Long-term complications in blood vessels, kidneys, eyes, and nerves occur in both types and are the major causes of morbidity and death from diabetes. The causes are multifunctional and predisposing factors including Obesity, Sedentary lifestyle, increasing age (affecting middle-aged and older people), and Genetic factors (Ross and Wilson 2010), such patients are at increased risk of developing macrovascular and microvascular complications.[9,10]

Gestational Diabetes Mellitus:

The glucose intolerance occurring for the first time or diagnosed during pregnancy is referred to as gestational diabetes mellitus (GDM). Women who develop Type1 diabetes mellitus during pregnancy and women with undiagnosed asymptomatic Type 2 diabetes mellitus that is discovered during pregnancy are classified with Gestational Diabetes Mellitus (GDM). Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly over diabetes). Gestational diabetes mellitus may develop during pregnancy and may disappear after delivery; In the longer term, children born to mothers with GDM are at greater risk of obesity and type 2 diabetes in later life, a phenomenon attributed to the effects of intrauterine exposure to hyperglycemia.[11]

Some Common Sign and Symptoms:

In diabetes mellitus, cells fail to metabolize glucose in a normal manner, and effectively become starved. The long-term effect of diabetes mellitus which includes progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, neuropathy with risk of foot ulcer, Charcot joint and features of autonomic dysfunctions, and sexual dysfunction. People with diabetes are at an increased risk of diseases. Other, various symptoms are observed due to:

(i). Gluconeogenesis from amino acids and body protein causes muscle wasting, and tissue breakdown and further increases the blood glucose level.

(ii). Catabolism of body fat, releasing some of its energy and excess production of ketone bodies.[12,13]

Etiology of Diabetes Mellitus:

The word etiology is derived from the Greek word "aetiologia". Hence, etiology is defined as the science of finding causes and origins in which a disease arises, It includes –

1. It is currently believed that the juvenile-onset (insulin dependent) form has an autoimmune etiology.
2. Viruses may also play a role in the etiology of diabetes like coxsackie.
3. Mumps and rubella viruses all have been shown to produce morphologic changes in the islet-cell structure.
4. The genetic role in the etiology of diabetes is controversial. Possibly a genetic trait makes an = individual's pancreas more susceptible to one of the above viruses. [14,15,16]

Causes of Diabetes Mellitus;

Disturbances or abnormalities in glucose-receptor of ß cells so that they respond to higher glucose concentration or relative ß cell deficiency. Either way, insulin secretion is impaired; may progress to ß cell failure. The theory of principal in microvascular disease leading to neural hypoxia, and the direct effects of hyperglycemia on neuronal metabolism.[17]

1. Reduced sensitivity of peripheral tissues to insulin: reduction in the number of insulin receptors, 'down-regulation of insulin receptors. Many are hypersensitive and hyperinsulinaemic, but normal glycaemic; and have associated dyslipidemia, hyperuricemia, and abdominal obesity. Thus there is relative insulin resistance, particularly at the level of liver, muscle, and fat. Hyper insulin anemia has been implicated in causing angiopathy.[18]
2. Excess of hyperglycaemia hormone (glucagon) etc. /obesity; causes relative insulin deficiency –the ß cells lag behind. Two theories have demonstrated abnormalities in nitric oxide metabolism, resulting in altered perineural blood flow and nerve damage.[19]
3. Other rare forms of diabetes mellitus are those due to specific genetic defects (type 3) like "maturity onset diabetes of young" (MODY) other endocrine disorders, pancreatectomy and gestational diabetes mellitus (GDM).[20]

Diagnosis of Diabetes Mellitus:

The diagnosis of diabetes in an asymptomatic subject should never be made on the basis of a single abnormal blood glucose value. If a diagnosis of diabetes is made, the clinician must feel confident that the diagnosis is fully established since the consequences for the individual are considerable and lifelong. The diagnosis of diabetes Mellitus includes urine sugar, blood sugar, glucose tolerance test, the renal threshold of glucose, diminished glucose tolerance, increased glucose tolerance, renal glycosuria, extended glucose tolerance curve, cortisone stressed glucose tolerance test, intravenous glucose tolerance test, oral glucose tolerance test.[21]

Treatment of Diabetes Mellitus:

The treatment is to overcome the precipitating cause and to give high doses of regular insulin. The insulin requirement comes back to normal once the condition has been controlled the aims of management of diabetes mellitus can be achieved by: 1. To restore the disturbed metabolism of the diabetic as nearly to normal as is consistent with comfort and safety. 2. To prevent or delay the progression of the short and long term hazards of the disease. 3. To provide the patient with knowledge, motivation, and means to undertake this own enlightened care. [22]

Types of Therapy Involved In Diabetes Mellitus:

1. Stem cell therapy

Researchers have shown that monocytes/ macrophages may be the main players which contribute to these chronic inflammations and insulin resistance in T2DM patients. Stem cell educator therapy, a novel technology, is designed to control or reverse immune dysfunctions. The procedure includes the collection of patients' blood circulating through a closed-loop system, purification of lymphocytes from the whole blood, co-culture of them with adherent cord blood-derived multi-potent stem cells (CB-SCs) in vitro, and administration of the educated lymphocytes (but not the CB-SCs) to the patient's circulation.[23]

2. Antioxidant therapy

A variety of antioxidants, such as vitamins, supplements, plant-derived active substances, and drugs with antioxidant effects, have been used for oxidative stress treatment in T2DM patients. Vitamin C, vitamin E, and β carotene are ideal supplements against oxidative stress and its complications. Antioxidants play an important role in lowering the risk of developing diabetes and its complications.[24]

3. Anti-inflammatory treatment

The changes indicate that inflammation plays a pivotal role in the pathogenesis of T2DM and its complications. In T2DM, especially in adipose tissue, pancreatic islets, the liver, the vasculature and circulating leukocytes, which include altered levels of specific cytokines and chemokines, the number and activation state of different leukocyte populations, increased apoptosis and tissue fibrosis. Immuno-modulatory drugs are provided.[25,26]

Dietary Management:

Adequate caloric value Dietary management should be taken properly by both diabetic and non-diabetic patients such as:

1. Balanced in regard to protein, carbohydrates, and fats, in all cases, it is necessary to restrict carbohydrate intake.
2. Should conform as closely as possible to normal
3. Food intake should be divided into regularly spaced meals of similar size
4. Reduce total calorie intake by decreasing both fat and carbohydrate
5. Patient must be advised to be constant in his dietary habits from day to day.[27,28,29]

Conclusion:

Diabetes mellitus is a serious complication in today's life. Lifestyle and day-to-day circumstances play a major role in occurring this type of serious complication. In this review, we get some ideas regarding diabetes mellitus. Novel drugs are being developed, yet no cure is available in sight for the disease, despite new insight into the pathophysiology of the disease. Management should be tailored to improve the quality of life of individuals.[30]

References:

1. Wassmuth R, Lernmark A. The genetics of susceptibility to diabetes, ClinImmunol, Immunopathol. 1989; 53:358- 399,
2. Atkinson MA, Eisenbarth GS. Type 1 diabetes new perspectives on disease pathogenesis and treatment, Lancet. 2001; 358:221-229.
3. Hoet JJ, Tripathy BB, Rao RH, Yajnik CS. Malnutrition and diabetes in the tropics, Diabetes Care. 1996; 19:1014- 17,
4. Tripathy BB, Samal KC. Overview and consensus statement on diabetes in tropical areas, Diabetes Metab Rev. 1997; 13:63-76.
5. Betterle C, Zanette F, Pedini B, Presotto F, Rapp LB, Monsciotti CM et al., Clinical and subclinical organ– specific autoimmune manifestations in type 1 (insulin– dependent) diabetic patients and their first-degreerelatives, Diabetologia. 1983; 26:431-36.
6. Bearse MA Jr, Han Y, Schneck ME, Barez S, Jacobsen C. Localmultifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy, Invest Ophthalmol Vis Sci. 2004; 45:3259-3265.
7. Zimmet PZ, Tuomi T, Mackay R, Rowley MJ, Knowles W, Cohen M et al. Latent autoimmune diabetes mellitus in adults (LADA): the role of antibodies to glutamic acid decarboxylase in diagnosis and prediction of insulin dependency, Diabetic Med. 1994; 11:299-303.
8. Verge CF, Gianani R, Kawasaki E, Yu L, Pietropaolo M, Jackson RA et al., Predicting type I diabetes in first– degree relatives using a combination of insulin, GAD, and ICA512bdc/IA-2autoantibodiesDiabetes. 1996;45:926-33. 12. American Diabetes Association, Diagnosis and classification of diabetes mellitus, Diabetes Care, 2014, 1.
9. DeFronzo RA, Bonadonna RC, Ferrannini E, Zimmet P. Pathogenesis of NIDDM, International Textbook of Diabetes Mellitus. 1997, 635-712.
10. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E et al., Insulin resistance and insulin secretory dysfunction as precursors of non–insulin–dependent diabetes, N Engl J Med. 1993;329:1988-92.
11. Mooy JM, Grootenhuis PA, de Vries H, Valkenburg HA, Bouter LM, Kostense PJ et al., Prevalence and determinants of glucose intolerance in a Dutch population, Diabetes Care. 1995; 18:1270-73.
12. Harris MI. Undiagnosed NIDDM, clinical and public health issues, Diabetes Care. 1993; 16:642-52,
13. Jun SK, Yoon YW. A new look at viruses in Type 1 diabetes, Diabetes/Metabolism Research and Reviews. 2002; 19:8-31.
14. Gupta OP, Joshi MH, Daves SK. Prevalence of Diabetes in India, Adv Metab Disord. 1978; 9:147-65.
15. Alemu S, Dessie A, Seid E. Insulin-requiring diabetes in rural Ethiopia: should we reopen the case for malnutrition related diabetes, Diabetologia. 2009; 52:1842-1845.
16. Wild S, Roglic G, Green A, Sicree R, King. Global prevalence of diabetes: Estimates for the year 2000and projections for 2030, Diabetes Care. 2004; 27:1047-53.
17. Mohan V, Pradeepa R. Epidemiology of diabetes in different regions of India. 2009; 22:1-18.

18. Kadiki OA, Reddy MR, Marzouk AA. Incidence of insulin-dependent diabetes(IDDM) and non-insulin dependent diabetes (NIDDM) (0-34 years at onset) in Benghazi, Libya, Diabetes Res Clin Pract. 1996; 32:165- 173.
19. The World Health Report. Shaping the future, 2003.
20. Shaw J, Zimmet P, de Courten M, Dowse G, Chitson P, Gareeboo Het al., Impaired fasting glucose or impaired glucose tolerance, Diabetes Care. 1999; 22:399-402
21. Ramachandran A, Snehalatha C, Latha E, Vijay V, Viswanathan M. Rising prevalence of NIDDM in an urban population in India Diabetologia1997; 40:232-237.
22. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance, Diabetes Atlas International Diabetes Federation, 2006, 15-103.
23. Sridhar GR, Rao PV, Ahuja MMS. Epidemiology of diabetes and its complications In: RSSDI t18. Barlow SE and the Expert committee. Expert committee recommendations regarding the prevention, assessment, and treatment of childhood and adolescent overweight and obesity: Summary report. Pediatrics 2007;120:S164-S192.
24. Lang IA, Galloway TS, Scarlett A, Henley WE, Depledge M, Wallace RB, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. JAMA 2008 Sep;300(11):1303-1310.
25. Rother KI. Diabetes treatment–bridging the divide. N Engl J Med 2007 Apr;356(15):1499-1501.
26. McCarthy MI. Genomics, type 2 diabetes, and obesity. N Engl J Med 2010 Dec;363(24):2339-2350.
27. Walley AJ, Blakemore AI, Froguel P. Genetics of obesity and the prediction of risk for health. Hum Mol Genet 2006 Oct;15(Spec No 2): R124-R130.
28. Camastra S, Bonora E, Del Prato S, Rett K, Weck M, Ferrannini E; EGIR (European Group for the Study of Insulin Resistance). Effect of obesity and insulin resistance on resting and glucose-induced thermogenesis in man. Int J Obes Relat Metab Disord 1999 Dec;23(12):1307-1313.
29. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome–a new worldwide definition. Lancet 2005 Sep;366(9491):1059-1062.
30. Powers AC. Diabetes mellitus. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J (eds). Harrison's Principles of Internal Medicine.17th ed, New York, McGraw-Hill; 2008: 2275-2304.