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Diabetes Mellitus: A Review

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Abstract

Diabetes Mellitus (DM) has become an international health issue as it is one of the most common non-communicable metabolic disorder and ranked 7th leading cause of death in the world. According to a report based on data collected from 130 countries, 382 million cases of diabetes have been reported in 2013 and the number is expected to approach 592 million by 2035. With respect to India, about one million deaths due to diabetes have already been recorded during the year 2013. Estimation by International Diabetes Federation has raised alarms for India, as about 50.8 million diabetic cases, ageing 20-79 years during the year 2010 will approach 87.0 million by 2030. These projections, thus, suggest that India may emerge as a diabetic capital of the world within a few years.

Keywords: Diabetes Mellitus, classification, causes, diagnosis

Introduction to Diabetes Mellitus

The situation is getting grimmer in countries with rapidly developing economies and urbanization where resources for dealing with the associated clinical problems are most scarce (Holt et al., 2011; Shaw et al., 2010) Besides, millions of cases are yet to be diagnosed or going through pre diabetic stages worldwide, thus diabetes is turning out to be a big challenge and its prevention, is the need of the hour in the 21st century.

Clinically DM is diagnosed with the typical symptoms of hyperglycemia (high glucose levels in blood plasma). Damage of beta cells, insulin deficiency or insulin resistance are some of the main reasons responsible for the development of disease. Besides this, lack of physical exercise, sedentary life style, high calorie diet and smoking are the other risk factors that promote metabolic diseases including diabetes (Leng et al., 2016). Normally insulin maintains the blood glucose homeostasis and keeps the glucose levels within a specific range. But in diabetic patients, the homeostasis get disturbed and blood glucose levels tend to be persistently high. Thus based on etiology of disease, DM can be classified into two main categories i.e. Type I and Type II which are also known as IDDM (Insulin Dependent Diabetes Mellitus) and NIDDM (Non-Insulin Dependent Diabetes Mellitus), respectively. The etiology of DM is intricate and multifactorial, hence manifestations of diabetic symptoms (increased risk of atherosclerotic, cardiovascular, peripheral arterial and cerebrovascular complications) may vary from patient to patient, depending upon the duration of disease and associated complications. Besides this, diabetic patients often experience hypertension and abnormalities of lipoprotein metabolism (TA, 2014). In this regards, hyperglycemia has been considered as the central axis of diabetic complications including tissue level changes (Mapanga and Essop, 2016). The microscopic modifications at tissue level are of great concern and considered as serious issue in the diabetic pathology. These microangiopathic changes may leads to organ dysfunction or failure. Some of the critical microangiopathic modifications include basement membrane thickening, inflammation, malformed mitochondria, fragmentation or swelling of organelles and nephrosclerosis etc. which predisposes to conditions like, cardiovascular complications, neuropathy, nephropathy and ulcerations etc.

Since, more than 50% of the diabetic patients suffer from the cardiovascular diseases (Goldberg, 2000), it is considered to be primary cause of death not only through the intensification of the associated predisposing factors but also through the direct deleterious effect of diabetes on the myocardial tissue. A condition widely recognized as diabetic cardiomyopathy. Several mechanisms involving mitochondrial dysfunction, fatty acid oxidation, impaired calcium metabolism, transforming growth factor 1 (TGF-1 over

expression) and advanced glycosylated end products (AGE), production have been suggested to be linked with systolic dysfunction, heart failure and diabetes (Yilmaz et al., 2015).

Diabetic nephropathy and chronic kidney disease (CKD) are another most common underlying cause of chronic dialysis, among the diabetic patients. The classical, five- stage natural history of diabetic nephropathy after an initial phase of hyperfiltration, is characterized by a progressive increase of albuminuria from normoalbuminuria to proteinuria, followed by a decline of glomerular filtration rate (GFR) (Pugliese, 2014). However CKD aggavate in diabetic condition and lead to end stage renal disoders (Yale et al., 2013).

Further, DM has also been reported to cause a variety of chronic and acute neuropathies in diabetic patients (Gupta and Gupta, 2014; Pandhare et al., 2012). It usually results in behavioral and sensory abnormalities like unpleasant abnormal sensation (dysesthesia), an increased response to painful stimuli (hyperalgesia) and pain in response to a stimulus that does not normally provoke pain (allodynia) (Yadav, 2014). Several pathological changes such as vascular alterations, disturbed synaptic plasticity, damaged mitochondria followed by increased production of reactive oxygen species (ROS) and impaired antioxidant associated immunity etc. have also been reported in diabetic neuropathy (Pandey et al., 2015).

As liver is considered as one of the main sites of metabolic activities, and tends to be an important target of diabetic complications. Diabetes and liver disorders have been documented to have mutual relationship i.e. diabetic patients usually suffer from liver disorders and, vice versa (García et al., 2016). Liver disorders related to diabetes include a wide spectrum of conditions, from a simple steatosis to cirrhosis, hepatocellular carcinoma and acute liver failure etc. (Bruha et al., 2013). It appears that diabetes is the most common cause of chronic liver disorders in developed countries.

Mechanistically, the altered biochemical pathways and dysfunctional neuroendocrine interactions appear to be the root cause of severe diabetic complications. The metabolic dysfunctions associated with hyperglycemia include augmented flux through the polyol pathways, an increased formation of AGE, oxidative stress along with the activation of protein kinase C, impaired trace element and lipid metabolism as well as pancreatic enzyme abnormalities (Abou-Seif and Youssef, 2004). Persistent hyperglycemia leads to increased production of ROS that occurs due to glucose auto- oxidation, glycosylation of proteins and their consequent oxidative degradation (Kakkar et al., 1998). Alterations in the ROS levels interrupt the functional role of oxidants in cellular protection and host defense leading to cell death simultaneously. An increase in ROS levels comprises a stress signal activating specific redox sensitive signaling pathways (Sedeek et al., 2012). Moreover, decline of antioxidant defense mechanism and high levels of free radicals lead to disturbances of enzymatic activity along with increased lipid peroxidation (LPO) as well as development of insulin resistance. These developments injure the vessel wall directs an irregular modeling of vasculature. These features are further supported by distorted cell and matrix turnover and an abnormal vascular permeability along with an impaired coagulation pattern (Di Mario and Pugliese, 2003). Thus metabolic hypothesis suggests that uncontrolled hyperglycemia leads to the development of diabetic complications (Matough et al. 2012). These observations thus beacon for immediate attention as for developing novel treatment paradigms.

Classification

1. **Type 1 Diabetes:** Caused by a Complete insulin insufficiency due to autoimmune death of β-cells that produce insulin [3].

Related Conditions:

Adults with latent autoimmune diabetes (LADA): a kind of adult kind 1 diabetes that advances more slowly [4].

2. **Type 2 Diabetes:** Caused by a combination of insulin insufficiency (inadequate production of insulin) and insulin resistance (cells that do not react to insulin). [5]

Related Conditions:
Metabolic syndrome (high blood pressure, obesity, etc.) [6]

3. Additional Particular Types:

Exocrine Pancreatic Diseases: Disorders that impact the synthesis of insulin, such as hemochromatosis, cystic fibrosis, and pancreatitis. [7]

Endocrine Disorders: Diabetes can result from diseases such as pheochromocytoma, acromegaly, and Cushing's syndrome. [8]

Genetic Defects: Disorders such as MODY (Maturity-Onset Diabetes of the Young) impact the generation or function of insulin. [9]

Drug-Induced: Drugs such as interferons, glucocorticoids, and neuroleptics can induce diabetes. [10]

Infections: Diabetes can result from pancreatic damage caused by some viral infections [11].

4. Diabetes during pregnancy:

Reason: occurs during pregnancy as a result of insulin resistance; it usually goes away after delivery, but it raises the chance of developing Type 2 diabetes in later life [12].

Diagnosis

1. Glucose in Venous Plasma [1,13]:

Occasional Plasma Glucose: Regardless of the time of day or the time since the previous meal, a random or casual plasma glucose measurement of ≥ 200 mg/dl (or ≥ 11.1 mmol/l) is regarded as a diagnosis for diabetes.

Fasting plasma glucose (FPG): After 8–12 hours of fasting, a fasting plasma glucose level of > 126 mg/dl (or ≥ 7.0 mmol/l) is indicative of diabetes.

Oral Glucose Tolerance Test (OGTT): Diabetes is diagnosed if, following a 75g oral glucose load, the plasma glucose value is > 200 mg/dl (or ≥ 11.1 mmol/l) after two hours. When prediabetes or poor glucose tolerance are suspected, this test is very helpful.

2. Glycated haemoglobin, or HbA1c [1]:

Diabetes is diagnosed when the HbA1c measurement is > 6.5%, or ≥ 48 mmol/mol Hb. HbA1c is a useful tool for both diagnosis and long-term monitoring since it shows the average blood glucose levels over the previous two to three months.

Avoidance

Physical Activity: Consistent exercise lowers the incidence of type 2 diabetes and enhances insulin sensitivity [14].

Diet and Lifestyle Changes: Reducing body weight, eating well, and exercising are essential for enhancing metabolic health and avoiding diabetes [15].

Insulin therapy for management [1]:

Basal Insulin: Long-acting insulin that helps to manage blood glucose levels overnight and in between meals by supplying a constant, background dose of insulin throughout the day.

Bolus Insulin: In order to prevent postprandial glucose spikes, which occur when blood sugar levels rise after eating, this short-acting insulin is administered prior to meals.

In order to give background insulin and meal coverage in a single injection, premixed insulin combines basal and bolus insulin in a predetermined ratio.

Medications used orally [16,17,18,19]:

Typical therapies for type 2 diabetes include:

Sulfonylureas: Promote the release of insulin.

Biguanides: such as metformin, increase insulin sensitivity.

Alpha-glucosidase inhibitors: Slow absorption of carbohydrates.

Thiazolidinediones: Increase sensitivity to insulin.

DPP-4 Inhibitors: Reduce glucagon levels and increase insulin release.

GLP-1 receptor agonists: Glucagon secretion is suppressed and glucose-dependent insulin secretion is enhanced by GLP-1 receptor agonists.

SGLT2 Inhibitors: Increase glucose excretion by decreasing glucose reabsorption in the kidneys.

Observation and Monitoring:

Blood Glucose Monitoring: Monitoring blood glucose levels on a regular basis to help guide therapy modifications and guarantee that glucose management is within goal ranges.

HbA1c Testing: This quarterly test measures the average blood glucose levels over the previous two to three months in order to assess long-term blood glucose management.

Regular Health Check-ups: Continual visits to medical professionals to check for diabetes-related consequences (including heart disease, kidney damage, and neuropathy) and to modify therapy as needed.

Critical Search regarding Diabetes Mellitus

The current treatments include use of synthetic antidiabetic drugs and some herbal and natural products. Most of the synthetic drugs or compounds are associated with side effects during chronic use. For example, metformin use is associated with gastrointestinal irritation, and lactic acidosis in patients with related co-morbid conditions (Bolen et al., 2007). Likewise, Sulfonylureas like glimepride may result in obesity, hypererinsulinemia, hypoglycemia etc (Sreenivasan et al., 2015). Therefore several drugs have been restricted in the anti-diabetic therapy due to expensive, not user friendly like insulin injections and/or associated with the issues like drug resistance, therapeutic ineffectiveness and associated side effects. Therefore, the development of drugs which are cost effective, efficacious and safe for long term therapy is a challenge for researchers. The management of diabetes needs a multi targeted approach to combat this disease. The natural products and herbal remedies are good source of antioxidants and antidiabetic compounds. Plants are considered as a rich as yet unexplored source of potentially antidiabetic drugs. However, detailed scientific reports investigating plants are scarce. World Health Organization (WHO) has also recommended the use of medicinal plants in oral therapy since they are less toxic and do not pose side effects. Therefore, the present research is inclined towards the herbal and natural products.

Several medicinal plants with proven antidiabetic and related beneficial effects are available. Among several herbs like Catharanthus roseus L., Gymnema sylvestre R.Br., Ocimum sanctum L, Azadirachta indica A. Juss (A. indica) etc. tested for hypoglycemic effect, the A. indica has been documented to have highest blood glucose lowering effect (Atawodi et al., 2009; Chattopadhyay, 1999). A. indica a tropical plant belonging to family Meliaceae, is widely known for its anti-microbial, anti-fungal and anti-pyretic activities (Perumal et al., 2010). Each part of A. indica is being used as folk medicine, viz. for respiratory disorders, constipation, leprosy, intestinal helminthiasis, and also acts as a general health promoter (Sreenivasan et al., 2015). There are several reports suggesting the anti-diabetic potential of A. indica, has been carried out on the intestinal glucosidase activity, glucose-6-phosphate dehydrogenase activity and hepatic, skeletal muscle glycogen content or in combination with Abroma augusta L. (Halim, 2003). The alcoholic extract of root bark (70%) of neem has also resulted in glucose lowering activity at a dose of 800 mg/ Kg BW. in diabetic animals (Patil et al., 2013). Besides this, Gupta et al., (2004) have reported the antidiabetic potential of neem seeds and Oluwole et al., (2011) have reported the role of ethanolic leaf extract of A. indica in diabetic nephropathy. Further, besides having hypoglycemic activity, also has been found to affect the activity of the anti-oxidant enzyme, superoxide dismutase and serum albumin content. Moreover, it also significantly reduces the plasma lipid peroxide levels in diabetic rats (Mahdi et al., 2003). Along the lines it has also been documented to have considerably high hepatoprotective effect in diabetic rats (Ebong et al., 2008).

In view of these observations and extensive literature analysis still few notable gaps have been found viz. none of the study has been reported an efficacious dose, or dose dependent effect of A. indica which is the foremost requirement for illustrating the effect of a drug. Secondly

oxidative stress has been correlated with blood glucose levels but same time pathological changes (microscopic) have not been correlated under diabetic conditions. Moreover, there is little information on their role in alleviating diabetes induced microangiopathic changes, cardiac dysfunction, nephropathy and diabetic liver disease. There is also paucity of reports regarding the potential ameliorative role of A. indica in diabetic neuroinflammation and behavioral changes. Owing to such observations, the current study has been aimed at evaluating the combined beneficial effects of A. indica leaf extract (ALE) in streptozotocin induced diabetic rats. Further, ALE has been tested for anti-oxidants potential, blood glucose lowering and its role in diabetes induced microangiopathic related complications in liver, kidney, heart and brain tissues.

Conclusion

The phrase "diabetes mellitus" refers to a group of metabolic diseases that, if untreated, all cause the blood to have excessively high levels of the sugar glucose. When the pancreas stops generating a sizable amount of the hormone insulin, it is known as diabetes mellitus type 1. This is often caused by the autoimmune death of the pancreatic beta cells that create insulin. In contrast, diabetes mellitus type 2 is currently believed to be caused by insulin resistance and/or pancreatic autoimmune assaults. A person with type 2 diabetes may have normal or even abnormally high insulin production from their pancreas. Restoring a normal state of glucose metabolism is the primary objective of diabetic therapy.

In order to do this, those who have a complete insulin deficit need insulin replacement treatment, which is administered as pills or injections. Exercise and nutritional changes, on the other hand, can help reverse insulin resistance. Other aims of diabetes management are to avoid or treat the myriad problems that might emerge from the illness itself and from its treatment. Diabetes may be managed so that the patient can live a happy life by controlling their blood sugar levels.

A major health problem that is impacting more and more individuals globally is diabetes mellitus. Daily routines and lifestyle choices are major contributors to the onset of this illness. This review emphasises the intricacy of diabetes and the necessity of an all-encompassing strategy for its management.

References

1. Sreenivasan, V., Kandasamy, C.S., Kumar, M.G., Prabhu, K.G., Arulraj, P., Johnson, J.S., Chander, U. and Venkatanarayanan, R. (2015). Review on different natural herbals associated with the anti-diabetic activity. WJPPS. 4(8): 585-595.
2. Srinivasan, S. and Pari, L. (2012). Ameliorative effect of diosmin, a citrus flavonoid against streptozotocin-nicotinamide generated oxidative stress induced diabetic rats. Chem Biol Inter. 195(1): 43-51.
3. Stancel, N., Chen, C.C., Ke, L.Y., Chu, C.S., Lu, J., Sawamura, T. and Chen, C.H. (2015). Interplay between CRP, atherogenic LDL, and LOX-1 and Its potential role in the pathogenesis of atherosclerosis. Clin Chem. 2(2): 127- 135.
4. Tiwari, V., Kuhad, A. and Chopra, K. (2011). Emblica officinalis corrects functional, biochem and mol deficits in experimental diabetic neuropathy by targeting the oxido-nitrosative stress mediated inflammatory cascade. Phytother Res. 25(10): 1527-1536.
5. Tolman, K.G., Fonseca, V., Tan, M.H. and Dalpiaz, A. (2004). Narrative review: hepatobiliary disease in type 2 diabetes mellitus. Ann Intern Med. 141(12): 946-956.
6. Törnblom, H. (2015). Treatment of gastrointestinal autonomic neuropathy. Diabetologia. 59(3): 409-413.
7. Oluwole Busayo, A., Laura, Z., Olufunke Olubusola, D., Oluwafunmike Sharon, A., Luciana, D. and Ezekiel Ademola, C.M. (2011). Ameliorative effects of ethanolic leaf extract of Azadirachta indica on renal histologic alterations in streptozotocin-induced diabetic rats. Am J Chinese Med. 39(05): 903-916.

8. Osellame, L.D., Blacker, T.S. and Duchen, M.R. (2012). Cellular and molecular mechanisms of mitochondrial function. Best Practice & Res Clin Endocrinol & Metab. 26(6): 711-723.
9. Östlund, I. and Hanson, U. (2003). Occurrence of gestational diabetes mellitus and the value of different screening indicators for the oral glucose tolerance test. Acta Obstet Gyn Scan. 82(2): 103-108.
10. Oury, T.D., Day, B.J. and Crapo, J.D. (1996). Extracellular superoxide dismutase: a regulator of nitric oxide bioavailability. Laboratory investigation; Am J Tech Method Pathol. 75(5): 617-636.
11. Mahmoud, M.F., Hassan, N.A., El Bassossy, H.M. and Fahmy, A. (2013). Quercetin protects against diabetes-induced exaggerated vasoconstriction in rats: effect on low grade inflammation. PloS one. 8(5): 1-11.
12. Maletkovic, J. and Drexler, A. (2013). Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin N Am. 42(4): 677- 695.
13. Malik, Z.A., Singh, M. and Sharma, P.L. (2011). Neuroprotective effect of Momordica charantia in global cerebral ischemia and reperfusion induced neuronal damage in diabetic mice. J Ethnopharmacol. 133(2): 729-734.
14. Malone, J.I., Schocken, D.D., Morrison, A.D. and Gilbert-Barness, E. (1999). Diabetic cardiomyopathy and carnitine deficiency. J Diabetes Compl. 13(2): 86-90.
15. Kovacic, P., Pozos, R.S., Somanathan, R., Shangari, N. and O'Brien, P.J. (2005). Mechanism of mitochondrial uncouplers, inhibitors, and toxins: focus on electron transfer, free radicals, and structure-activity relationships. Curr Med Chem. 12(22): 2601-2623.
16. Kuhad, A. and Chopra, K. (2009). Tocotrienol attenuates oxidative–nitrosative stress and inflammatory cascade in experimental model of diabetic neuropathy. Neuropharmacol. 57(4): 456-462.
17. Kumar, A., Negi, G. and Sharma, S.S. (2012). Suppression of NF-κB and NF- κB regulated oxidative stress and neuroinflammation by BAY 11-7082 (IκB phosphorylation inhibitor) in experimental diabetic neuropathy. Biochimie. 94(5): 1158-1165.
18. Kumar, S.M., Swaminathan, K., Clemens, D.L. and Dey, A. (2015). GSH protects against oxidative stress and toxicity in VL-17A cells exposed to high glucose. European J Nutr. 54(2): 223-234.
19. Balazs, M. and Halmos, T. (1985). Electron microscopic study of liver fibrosis associated with diabetes mellitus. Exp Patholo. 27(3): 153-162.
20. Bandeira, S.D.M., Guedes, G.D.S., Fonseca, L.J.S.D., Pires, A.S., Gelain, D.P., Moreira, J.C.F., Rabelo, L.A., Vasconcelos, S.M.L. and Goulart, M.O.F. (2012). Characterization of blood oxidative stress in type 2 diabetes mellitus patients: increase in lipid peroxidation and SOD activity. Oxidative Med and Cellular Longevity. 2012: 1-13.
21. Baud, V. and Karin, M. (2001). Signal transduction by tumor necrosis factor and its relatives. Trends Cell Biol. 11(9): 372-377.
22. Bazinet, R.P. and Layé, S. (2014). Polyunsaturated fatty acids and their metabolites in brain function and disease. Nature Rev Neurosci. 15(12): 771- 785.
23. Ata, A. and Udenigwe, C.C. (2008). The discovery and application of inhibitors of glutathione S-transferase as therapeutic agents-a review. Curr Bioact Compounds. 4(1): 41-50.
24. Atkinson, M.A., Eisenbarth, G.S. and Michels, A.W. (2014). Type 1 diabetes. The Lancet. 383(9911): 69-82.
25. Atli, T., Keven, K., Avci, A., Kutlay, S., Turkcapar, N., Varli, M., Aras, S., Ertug, E. and Canbolat, O. (2004). Oxidative stress and antioxidant status in elderly diabetes mellitus and glucose intolerance patients. Arch Gerontol Geriat. 39(3): 269-275.