REVIEW ARTICLE

Basic Concepts of Diabetes Mellitus

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ABSTRACT:
Pakistan is at the seventh position on diabetes prevalence rates. Many risk factors are linked to the development of type 2 diabetes like increased body mass index (BMI), altered body lipids, increased blood pressure, smoking, less physical activity ,bad dietary habits, family history, and also some genes. Environmental factors together with a genetic tendency for diabetes set off an autoimmune response that causes damage of the pancreatic β-cells over prolong duration leading to type 1diabetes. Failure of β cell compensation for insulin resistance causes impaired glucose tolerance that can exhibit as type 2diabetes.Diabetes Mellitus either type 1 or type 2 can lead to various acute and chronic complications. Diagnosis can be made on levels of blood glucose concentration, urine ketone test, glycosylated hemoglobin (HbA1c), glycated serum protein and glycated serum albumin. Type 1 diabetic patients are directly given insulin. Patients with type 2 diabetes may be managed with diet and exercise. However when diet and exercise fail to control raised blood sugar level, an oral antidiabetic agent is started. This may be added with more drug(s) from the same family and or insulin depending upon the glycemic index of the patient.Type 2 diabetes is a progressive disease in which ultimately the function of β cells decreases, and eventually exogenous insulin may be required to maintain blood sugar level. This review thoroughly describes the prevalence, classification, etiology, pathophysiology, complications, diagnostic criteria and treatment of Diabetes Mellitus.
Keywords: Diabetes Mellitus, Classification, Etiology, Pathophysiology, Complications, Diagnostic criteria, Treatment

INTRODUCTION:

Diabetes Mellitus (DM) is a chronic disorder of metabolism due to inadequate production of insulin from the pancreas or the resistance of body to its action.[1] It is approximated that the prevalence of diabetes worldwide in 2010 among adults of ages between 20-79 years was 6.4%, affecting 285 million adults.[2] The Global number of people with diabetes is estimated to rise up to 396 million in 2030.[3] Pakistan is at the seventh position on diabetes prevalence rates. About 6.9 million people are suffering from diabetes in Pakistan. According to estimates by International Diabetes Federation (IDF), this number will increase to 11.5 million by 2025 unless attempts are made to control this disorder.[4]

METHODOLOGY:

This review is specifically designed to present the basic concepts of Diabetes Mellitus through an extensive literature review using multiple electronic databases like PubMed/MEDLINE/EMBASE, Science direct and Google Scholar during the year 2000-2015 using various key words like: diabetes mellitus, classification, etiology,

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pathophysiology and treatment. A total of 155 articles were found and after filtration, 46 articles were selected and are included in this review.

LITERATURE REVIEW:

Classification: Diabetes is categorized into two major types on the basis of requirement of insulin: insulin dependent diabetes mellitus or Type-1 and non-insulin dependent diabetes mellitus or Type-2. It also includes gestational diabetes and diabetes due to other specific reasons such as

- Genetic defects in insulin action e.g. leprechaunism
- Disease of exocrine pancreas, e.g. pancreatitis
- Endocrinopathies, e.g. acromegaly
- Drug- or chemical-induced, e.g. glucocorticoids
- Infections, e.g. congenital rubella
- Rare type of immune-mediated diabetes e.g. 'Stiff Man' syndrome
- Other genetic syndromes associated with diabetes e.g. Down's syndrome.[5]

Type-1 diabetes also known as insulin dependent diabetes mellitus (IDDM) accounts for 5 to 10 % of cases, is characterized by pancreatic β cell destruction (either autoimmune or idiopathic), causing inability to produce insulin.[6]It is usually diagnosed in childhood or adolescence and causes absolute insulin deficiency. Environmental factors together with a genetic tendency for diabetes set off an autoimmune response that causes damage of the pancreatic β-cells over prolong duration.[7] Symptoms of type 1 diabetes develop rapidly. Weight loss, frequent urination, increased desire to take food, increased thirst, blurred vision and fatigue are the main symptoms. This type of diabetes usually comes into view before the age of 40.[8]"Latent Autoimmune Diabetes in Adults" (LADA) is a latent form of type -1 diabetes present in approximately 6 to 10% of adults over the age of 25 years. Although LADA can initially be misdiagnosed as type- 2 diabetes due to occurrence in young age group but patients are typically younger as compared to type- 2 disease.[9]

Type -2 diabetes or NIDDM is characterized by insulin resistance (i.e. decreased tissue response to the actions

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of endogenous insulin) and abnormal insulin secretion from the pancreas (i.e. â cell failure), either of which may predominate in a given individual This type of diabetes usually occurs after age 30 and depending on the population studied, the mean age at diagnosis is often well into the sixth decade.[10]Most type-2 diabetics are older adults and overweight, and diabetes runs in family. Symptoms are same as of type-1 diabetes. Patients are endangered for developing heart disease, kidney problems, disorders of vision, nerve damage, and other difficulties on long standing diabetes.[11]

Gestational diabetes (Diabetes diagnosed in pregnancy) consists of pre-existing diabetes and diabetes developed during pregnancy. The symptoms and treatment is similar to that of the type-2 diabetes. It generally vanishes after delivery.[12]

Etiology of type 2 diabetes: Many risk factors are linked to the development of type 2 diabetes like increased Body mass index (BMI), altered body lipids, increased blood pressure, smoking, less physical activity ,bad dietary habits, family history, and also some genes.[13]

Body mass index: Research has shown that increased BMI is a strong risk factor for type 2 diabetes.[14]Adipose tissues in fatty individuals secrets increased quantities of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors responsible for causing insulin resistance. This accompanied by dysfunction of the â- cells eventually leads to the development of type 2 diabetes .[15]

Blood lipids: Unfavorable blood lipids level is another important risk factor for type 2 diabetes. There is an inverse relationship between high density lipoprotein (HDL) cholesterol level and risk of type 2 diabetes.[16]

Blood pressure: Increased blood pressure is also an independent risk factor for type 2 diabetes.[17]Endothelial dysfunction could be one of the common pathophysiological pathways for both diabetes and hypertension.[18]

Smoking: Several studies have documented smoking as a risk factor for developing type 2 diabetes.[19,20] Smoking causes insulin resistance and compensatory increased insulin secretion.[21]

Physical activity: Many clinical trials adopting physical activity as a vital life style modification proved that onset of type 2 diabetes can be prevented or delayed by increased physical activity.[22] Physical activity performs its role directly by improving insulin sensitivity and reducing insulin resistance, and indirectly by positive changes in body mass and composition.[23]

Dietary habits: Positive associations have been reported between the risk of type 2 diabetes and different habits of food intake.[24] Increased glycemic intake in diet increases the risk of type 2 diabetes.[25]Increased ingestion of polyunsaturated fat and long-chain fatty acid is favorable for health as compared to saturated fat and trans fat which badly influences glucose metabolism and insulin resistance. Increased intake of fruits and vegetables also reduces the risk of type 2 diabetes.[26]

Genetics: The role of some genes in causing diabetes is supported by various studies.[27,28]Studies in high risk diabetic patients including both first degree relatives

and non-diabetic monozygotic co-twins of type 2 diabetic patients have shown that abnormalities in both insulin secretion and action were present many times before appearance of type 2 diabetes ,especially in low birth weight babies.[29] Variants in 11 genes (TCF7L2, PPARG, FTO,KCNJ11, NOTCH2, WFS1,CDKAL1, IGF2BP2, SLC30A8, JAZF1, and HHEX) are found to be markedly associated with the risk of type 2 diabetes and variants in 8 of these genes were linked to impaired â-cell function. Among these genes, the transcription factor7-like 2 (TCF7L2), is highly associated to type 2 diabetes.[30]

Pathophysiology of diabetes: Normally body maintains blood glucose levels within a narrow range (70 to 130mg/dl).Blood glucose is balanced between endogenous production from liver (through glycogeno-lysis and gluconeogenesis) and kidney, exogenous appearance from intestine (following a meal) and utilization of glucose by all tissues. Body regulates all these processes of glucose production and storage by secreting hormone insulin from β cells of pancreas.[31] Type-2 diabetes is usually preceded by a long period of asymptomatic hyperinsulinemia which in turn leads to insulin resistance .The failure of β cell compensation for insulin resistance causes impaired glucose tolerance which overts as type- 2 diabetes[32] as evident in Figure 1

Figure:1
Adapted from Weyer C et al, ,1999[33]
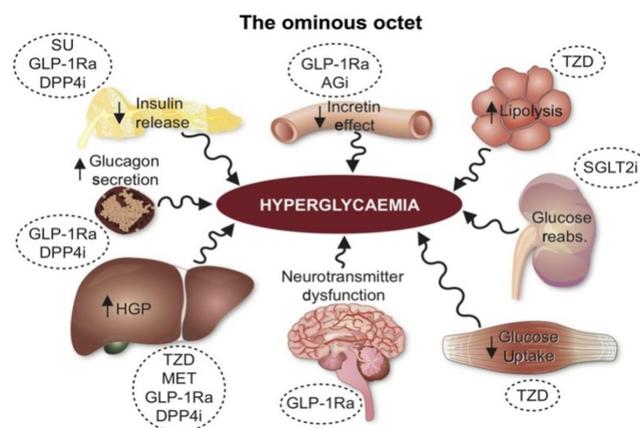
Complications of diabetes mellitus: Around 3.2 million deaths every year are assigned to complications of diabetes at the rate of six deaths every minute.[33]The world estimated cost of treating diabetes and its complications was minimum 376 billion US Dollar (USD) in 2010.This number is anticipated to surpass 490 billion USD up to 2030.The associated cardiovas-cular disease (CVD) along with diabetes leads largely to these expenses.[34]

Complications are classified as acute or chronic. Acute complications include hypoglycemia, hyperglycemia, diabetic ketoacidosis (DKA), non ketotic hyperosmolar coma, and diabetic coma. Macro vascular and micro vascular complications are the most common chronic complications of diabetes.[35]Microvascular complications lead to retinopathy, neuropathy and nephropathy, while

macro vascular complications include Coronary artery disease, leading to myocardial infarction or angina, stroke, peripheral vascular disease, as well as diabetic foot.[36]

Hyperglycemia induces tissue damages by various mechanisms like increased polyol pathway, activation of protein kinase C isoforms, hexosamine pathway, increased superoxide release from mitochondria and advanced glycation end products formation. All these processes form reactive oxygen species which alter intracellular redox state and provoke oxidative stress.[37]

Diagnostic criteria and treatment:

(1) Blood glucose concentration: The blood glucose levels of a healthy man are 80 mg/dL on fasting and up to 160 mg/dL after meal. DM is demonstrated by recurrent or persistent hyperglycemia, and is diagnosed by exhibiting one of the following:
Fasting plasma glucose level at or above 126 mg/dL or 7.0 mmol/l,plasma glucose at or above 200 mg/dL or 11.1 mmol/L two hours after a 75 g oral glucose load in glucose tolerance test, Random plasma glucose at or above 200 mg/dL or 11.1 mmol/l.Two fasting glucose measurements above 126 mg/dL or 7.0 mmol/l or random blood sugar level > 200mg/dL or 11.1 mmo/l on two occasions is taken diagnostic for diabetes mellitus. Patients with fasting sugars between 6.1 and 7.0 mmol/L (110 and 125 mg/dL) are considered to have impaired fasting glucose and patients with plasma glucose at or above 140 mg/dL or 7.8 mmol/L two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance.[38]

(2) Urine ketone test: Blood glucose levels of >300 mg/dl or 16.7mmol/l, and acute illness can raise the urinary ketones due to decreased insulin level.[39]

(3) Glycosylated hemoglobin (HbA1c): The normal HBA1c level ranges between 4-6% of the total hemoglobin. The HB1Ac more than 6.5% indicates type -2 diabetes.[40]

(4) Glycated serum protein and glycated serum albumin: Fructosamine assay is the method for determining the levels of glycated serum proteins.[41]

Treatment: The treatment of diabetes is determined by its cause .Type -1 diabetic patients are given insulin, while patients with latent diabetes have residual pancreatic β cells at the time of diagnosis, so they are not given insulin right away, however ultimately they also need insulin. Patients with type 2 diabetes may be managed with diet and exercise. However when diet and exercise fail to control raised blood sugar level, an oral hypoglycemic agent is started. Type 2 diabetes is a progressive disease in which ultimately the function of β cells decreases, and eventually exogenous insulin is given to patients to maintain blood sugar level.[42]

Modification in dietary patterns have important role in treating type-2 diabetes. Dietary guidelines are available for diabetic patient. The diabetic patient has to consume balanced meal. A balanced diet that is consisted of extensive variety of fruits and vegetables and minimal processed food not only normalize the appetite, control the weight but also decreases the risk of many chronic degenerative diseases. A diabetic meal chart is made according to the caloric intake, physical activity and insulin level of the diabetic patient. The diabetic patient has to take 50 to 60% of the calories from carbohydrates, 15% from proteins, and the remaining from fats or oils. If insulin medication is taken, a constant daily routine should be followed. The aim is to balance the carbohydrate and insulin peeks. The WHO recommends a minimum consumption of 5 - 10 portions of fruits and vegetables per day.[43]

Exercise also plays an important therapeutic role in the management of type-2 diabetes and is often prescribed along with diet and pharmacologic therapy.[44] Exercise reduces blood glucose level, improves insulin sensitivity and cardiovascular risk factors by improving blood lipid levels and decreasing body weight.[45]

Moreover previous concept that type-2 diabetes is encountered in adults only is also changing as children and teenagers are also been diagnosed in various parts of world to have type-2 diabetes.[46]

CONCLUSION:

Diabetes is being predicted as the world's main disabler and murderer disease in the next 25 years. Its prevalence is increasing day by day because of its multifactorial etiology and can lead to diverse types of acute or chronic complications. Treatment depends on type of diabetes. Type- 1 diabetic patients are directly given insulin.Whereas type- 2 diabetic patients may be managed with diet and exercise. However when diet and exercise fail to control raised blood sugar level, an oral hypoglycemic agent is started and eventually exogenous insulin is given to patients to maintain blood sugar level.

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