International Journal in Physical and Applied Sciences
Volume 06 Issue 05, May 2019 ISSN: 2394-5710 Impact Factor: 4.657
Journal Homepage: http://ijmr.net.in, Email: irjmss@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal

A Study of Current Trends in Type 2 Diabetes Mellitus

Authors- Dr. Ashok Kumar Mehra[1#], Dr. Ghanshyam Ahirwar[2]

1. BHMS, MSW,MSC Biochemistry,[#] PhD persuiting
2. Asstt. Professor, Community Medicine, Govt. Medical College, Datia M.P.

Abstract

Diabetes mellitus (DM) is a long-term metabolic condition marked by persistent hyperglycaemia. It could be caused to a lack of insulin secretion, resistance to insulin's peripheral activities, or both. In patients with diabetes mellitus, chronic hyperglycemia, in combination with other metabolic abnormalities, can damage various organ systems, leading to the development of disabling and life-threatening health complications, the most prominent of \1 A which are microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications, which lead to a 2- to 4-fold increased risk of heart attack and stroke. Type 2 Diabetes is due to insulin resistance and it causes various metabolic derangements and oxidative stress, which when not controlled could lead to fatal complications. In this article we are going to assess such parameters that might prevent complications when screened at the earliest.

Keywords: Diabetes mellitus (DM); hyperglycemia; microvascular; insulin

Introduction

Diabetes Mellitus (DM) is probably one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago (Diabetes mellitus history from ancient times). In1936, the distinction between type 1 and type 2 DM was clearly made (Patlak, 2002). Type2 DM was first described as a component of metabolic syndrome in 1988 (Maitra, 2005).Type2DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency (Wild, 2002) .Type2 DM results from interaction between genetic, environmental and behavioral risk factors (WHO,1999.diabetes data group,1979)

Type 2 Diabetes Mellitus is the most common form of diabetes and it accounts for 90- 95% of all diabetic cases.(Report of WHO ,1999) Type 2 diabetes Is rapidly growing into a potential epidemic in India. India ranked first in 2000, among countries having the largest population with type 2 Diabetes Mellitus. The prevalence of Diabetes Mellitus would be doubled from 171million (2000)

to 366 million (2030), with India topping the list, as predicted (Wild, 2004).

The International Expert Committee on the Diagnosis and Classification of Diabetes sponsored by ADA revised the previous classification in 1995(Burtis, 2012)

1. Type 1 DM
2. Type 2 DM
3. Other specific types
4. GDM

Type 1 Diabetes Mellitus (T1DM)

Constitutes only 5- 10% of all cases of diabetes. The disease begins before the age of 18 in approximately 75% cases (Michael, 2013). Type 1 Diabetes is usually autoimmune in origin with the destruction of Islets of Langerhans of pancreas.Autoantibodies are directed against several particles of Islet cells encompassing antibodies to Insulin, Glutamicacid decarboxylase, tyrosine phosphatase IA-2and IA- 2B (Edelstein, 1997). Clinical features include polydipsia, polyphagia, polyuria, rapid weight loss, hyperventilation, abrupt onset, insulin dependence and ketotic tendency (Edelstein, 1997).

Type 2 Diabetes Mellitus (T2DM)

T2DM (type 2 diabetes mellitus) accounts for almost 90% of all diabetes cases. Insulin resistance is described as a reduced response to insulin in people with T2DM. Insulin is inefficient in this state, thus an increase in insulin production is used to maintain glucose homeostasis. However, insulin production diminishes over time, culminating in T2DM. T2DM is most typically found in those over the age of 45. Despite this, because to increased levels of obesity, physical inactivity, and energy-dense meals, it is becoming more common in children, adolescents, and younger people.

GESTATIONAL DIABETES MELLITUS (GDM)

Any level of glucose intolerance recognized for the first time during or after 24 weeks of pregnancy; must be considered as a risk factor for Type 2DM. Etiology is related to metabolic changes of late pregnancy and its insulin requirements. Diabetes identified at the initial visit itself during pregnancy is diagnosed as ―over diabetes. With rising prevalence of obesity the rates of diagnosing GDM or overt diabetes is soaring.

PATHOPHYSIOLOGY

Two main pathological defects have been identified (KahnCR, 1994.Sacks.Flier, 1992)

1. **Insulin resistance**–insulin's ability to act on peripheral tissues is reduced

2**. β-cell dysfunction**-pancreas cannot sufficiently produce insulin to match insulin resistance.

It's now clearly established that type 2 DM is a heterogeneous syndrome and there is no single cause for the incidence and progression of diabetes.

INSULIN RESISTANCE: Defined as—a decreased biological response to normal concentrations of circulating Insulin (NCEP 2001). It is due to defective Insulin action. Insulin resistance can assume two spectra: Euglycemia (with high endogenous Insulin) and Hyperglycemic (despite large doses of exogenous Insulin)(Carr,2008) Insulin Resistance Syndrome (Metabolic syndrome/ syndrome X).

It' s established if a person meets three or more of the following criteria. (Carr, 2008)

- Abdominal obesity (waist circumference> 35 inches in females or > 40 inches in males)
- TGL > 150 mg/dL
- HDL < 50mg/dL (females) or < 40mg/dL (males)
- Blood pressure ≥ 130/ 85mmHg
- Fasting plasma glucose ≥ 110mg/dL

LOSS OF β-CELL FUNCTION: Hyperglycemia over a period of time renders the β-cells unresponsive to its increase. This is termed glucotoxicity (zimmetPZ, 1988, stern 1991.kulkarni, 1999). The degree of unresponsiveness correlates with glucose concentration and duration of hyperglycemia. But reverting to euglycemia rapidly restores the defect. Increased serum fatty acid has also been found to be involved in the β-cell failure (Kulkarni,1999) .Recent evidences suggest that insulin resistance could lead to alterations in the β-cell production of insulin ,type2 diabetes (knowler, 2002).

RENAL COMPLICATION OF DIABETES MELLITUS

Diabetic nephropathy is the major cause for end-stage renal disease (ESRD) and chronic kidney disease (CKD). As in other micro vascular complications, the pathogenesis of diabetic nephropathy is also due to chronic hyperglycemia. Chronic hyperglycemia elicits its effect through soluble factors (growth factors, angiotensinII, and endothelin, advanced Glycation end products [AGEs]), alterations in the renal microcirculation (glomerular hyper filtration or hyper perfusion, increased glomerular capillary pressure), and structural changes in the glomerular (increased extracellular matrix, basement membrane thickening, mesangial expansion, fibrosis).Smoking has tens the above processes.

The terms used to refer to increased urinary protein are

- —micro albuminuria -30–299 mg/dina24-h collection or 30–299μg/mg creatinine in a spot

collection

- Macroalbuminuria as defined as>300 mg/24 h.

The American Diabetes Association now recommends that the above terms be replaced by the phrases " **persistent albuminuria- (30– 299 mg/24h**)" (148) the nephropathy that develops in type 2 DM exhibits the following characteristics (1) Microalbuminuria or macroalbuminuria may be already present at the time of diagnosing type2DM, indicating its long asymptomatic period; (2) Micro albuminuria or macroalbuminuria is more commonly accompanied by hypertension in type2 DM; (3) Microalbuminuria may be less predictive of likelihood of progression to macroalbuminuria in type 2 DM, mostly due to increased cardio vascular mortality in this population. It should also be noted that albuminuria in type 2 DM may be secondary to causes unrelated to DM, like hypertension, congestive heart failure (CHF), infection or prostate disease.

DIABETIC NEUROPATHY

As with other microvascular complications of T2DM, neuropathy also is correlated well with the duration of diabetes and glycemic control over the period. It may be polyneuropathy, Mononeuropathy and/or autonomic neuropathy. Distal symmetrical poly neuropathy is the most common manifestation. Mononeuropathy is very rare and its pathogenesis is not clearly understood yet.

Gastro paresis and abnormalities in bladder-emptying are the common manifestations of autonomic neuropathy. Autonomic neuropathy causes defective or nil release of counter-regulatory hormones during a hypoglycemic episode. This leads to hypoglycemic unawareness, a fatal complication. Upper extremities exhibit hyper hydrosis while lower extremities exhibit hyper hydrosis due to dysfunction of sympathetic nervous system.

LIPID ABNORMALITIES IN DIABETES MELLITUS

In type2 diabetes Plasma lipoprotein profiles are often abnormal reflecting an elevation in the level of the apoprotein B(Apo B)-containing components; namely very low density lipoprotein (VLDL) and low density lipoprotein (LDL) (Moran,1997) .High levels of circulating advanced Glycation end products (AGEs) also occur in diabetes. AGE-modified LDLs circulation.

The blood of diabetics and all these damage β-cells. The defect so produced is reversible till it reaches a stage where pancreatic β-cells become exhausted due to lipotoxicity and glucotoxicity (Gleason, 2000, Carlsson, 1999) The mechanism of beta-cell damage by glucotoxicity and lipotoxicity is through generation of free radicals (Patane,2000).Palmitate exposure generates reactive oxygen species in the islets and treatment with met form in (which has antioxidant

properties) protects it from the deleterious effect of the fatty acid (Toru,2010) . Insulin resistance of type2 Diabetes in the liver shows failure of hyper insulinemia to suppress gluconeogenesis. This causes fasting hyperglycemia and depleted glycogen storage by the Hepatocyte in the postprandial state.

Insulin resistance in adipose tissue results in lipolysis and an increase in free fatty acid mobilized from adipocytes, leading to high levels of lipid (very low) density lipoprotein [VLDL] and triglyceride) synthesis in liver. This leads to non-alcoholic fatty liver disease and dyslipidemia found in type 2DM (elevated triglycerides, reduced high-density lipoprotein [HDL], and increased small dense low-density lipoprotein[LDL]particles (Brownlee,2005).

Evaluation

CASES INCLUSION CRITERIA

+ Patients diagnosed with type2 DM irrespective of the duration of treatment
+ age group of 40-60years
+ both genders

EXCLUSION CRITERIA

1. Type1DiabetesMellitus
2. Patients with micro and macro vascular complications
3. Pregnancy
4. Lactation
5. Individuals with history of alcoholism/ smoking
6. Patients with malignancy
7. Patients with Arthritis, Cardiac and Renal diseases
8. Patients with history of smoking and alcohol

SAMPLECOLLECTION

3mL venous blood sample was collected in a red tube and 2mL venous sample collected from the same puncture site with a heparinised tube. Samples were collected between 7-9 am after a 10-hour fasting and immediately centrifuged. The plasma of the samples were separated and storedat-20and the heparinized plasma were stored at -60.

METHODOLOGY

ESTIMATED PARAMETERS

1. Fasting blood glucose -by Glucose oxidase-peroxidase method

2. HbA1c -particle enhanced immune turbidimetry
3. LIPIDPROFILE
    - Serum Total Cholesterol-Cholesterol Oxidase-Peroxidase
    - Serum Triglycerides -Glycerol3-phosphate Oxidase
    - Serum HDL-c -Direct Enzymatic method

ESTIMATION OF FASTING BLOOD SUGAR METHODOLOGY

Glucose on oxidation gives Gluconic acid by the enzyme Glucose Oxidase releasing Hydrogen Peroxide, which on further reaction by Peroxidase releases nascent oxygen and water by the enzyme peroxidase.4- Aminoantipyrine takes up the oxygen, simultaneously with phenol, forms pink colored Chromogen which is measured at 505 nm.

Glycated Hemoglobin (Hb) A1C

Total hemoglobin and HbA1C are combining in hemolysed blood with equal affinity for particles in R1. The concentration of both the substances in blood is proportional to the level of binding. Mouse anti-humanHbA1C monoclonal antibody (R1) binds with particleboundHbA1C.Then Goat antimouse IgG polyclonal antibody (R3) interacts with R2and agglutination takes place. The calculated absorbance is proportional to theHbA1Cboundparticles. This is used to calculate the % of HbA1C

Take 20µL of sample and 750µL of reagent (R1), mixed well and incubated for2 minutes. Then 250µL of reagent (R2) was added and mixed, incubated for 3minutes and then 125µL of reagent (R3) was added and mixed. After 2 minutes of incubation absorbance was measured at 660nm. Temperature:31°Coptic.

It has been found from various studies that the major burden in type 2DM is the cardiovascular risk due to hyperglycemia and dyslipidemia associated with it. This mechanism of complications from hyperglycemia and dyslipidemia is through the generation free radicals and reactive oxygen species.

In our study we compared the levels of oxidative stress and antioxidant capacity in the blood of people with Type 2 Diabetes Mellitus and that of people without diabetes. The main objective of the study was to understand how far the decrease in TAC and the increase in Oxidative Stress is and to assess the associated cardiovascular risk in type 2 DM patients. The diabetic sand the controls were matched for age, gender and BMI. The biochemical parameters were also analysed

between them. Among the parameters, Fasting Blood Sugar, HbA1C High, Density Lipoprotein, Triglycerides, Total Cholesterol and Total Antioxidant Capacity were statistically significant between the cases and controls.

CONCLUSION

It is found that insulin resistance is the culprit of hyperglycemia and dyslipidemia in type2 DM which in turn is responsible for the increased oxidative stress. This links type2 diabetics directly in to life-threatening complications of atherosclerosis.

REFERENCE

- Aalkjaer C, Heagerty AM, Petersen KK, et al. Evidence for increased media thickness, increased neural amine uptake,and depressed excitation-contraction coupling in isolated resistance vessels from essential hypertensives.CircRes. 1987;61:181– 186.
- Abdella N, al AwadiF, SalmanA,Arm strongD.Thio barbituric acid test a same asure of lipid peroxidation in Arab patients with NIDDM. Diabetes Res. 1990; 15:173– 7.
- Barrett-ConnorE, GrundySM, HoldbrookMJ, Plasma lipids and diabetes mellitus in an adult community.AmJEpidemiol1982:115;657-63. 13.
- Basha B, Samuel SM, Triggle CR, and Ding H. Endothelial Dysfunction in Diabetes Mellitus: Possible Involvement of Endoplasmic Reticulum Stress? Exp Diabetes Res.2012;2012:481840.
- BaynesJW, ThorpeSR .Role of oxidative stress in diabetic complications: A new perspective on an old paradigm.Diabetes.1999; 48:1– 9.
- BeckmanJA, LibbyP, CreagerMA: Diabetes and Atherosclerosis: Epidemiology, pathophysiology and management.JAMA2002; 287(19):2570-82.
- Bell GI, Polonsky KS. Diabetes Mellitus and generally programmed defects in beta-cell function. Nature 2001; 414:788-91.
- Berneis KK, Krauss RM: Metabolic origins and clinical significance of LDL heterogeneity. J Lipid Res43:1363– 1379,2002.
- DeFronzo RA: Banting Lecture: from the triumvirate to the ominousoctet: a new paradigm for the treatment of type 2 diabetes mellitus.Diabetes58:773– 795, 2009.
- DeFronzo RA: Banting Lecture: from the triumvirate to the ominousoctet: a new paradigm for the treatment of type 2 diabetes mellitus.Diabetes58:773– 795, 2009.

- DeFronzo RA: Lilly Lecture: the triumvirate: beta cell, muscle, liver: acollusion responsible for NIDDM.Diabetes37:667– 687, 1988.
- DeFronzoRA, Bandanna RC,FerranniniE.Pathogenesis of NIDDM :a balance over view. Diabetes care 1992; 15:318-68.
- deGraafJ,HakLemmersHLM,HectorsMPC,Demacker PNM, Hendriks JCM, StalenhoefAFH: Enhanced susceptibility to in vitro
- DelRioD, StewartAJ,PellegriniN(2005)Are view of recent studies on Malondialdehyde as toxic molecule and biological marker of oxidative stress. Nutr Metab Cardiovasc Dis15:316-328.