An Analysis upon the Level of Lipid Profile among Patient with Diabetes Mellitus: A Review

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Abstract – Mellitus has been known to be associated with lipid disorders and cardiovascular complications. The age of the patient and duration of ailment has been variously believed to influence the lipid Pattern. The lipid parameters studied were Triglycerides, Total cholesterol, Low Density lipoprotein and High Density lipoprotein. There were anomalies in lipid profile whose pattern did not skew to any age group nor duration of illness (p>0.05). In Diabetes mellitus age and duration of illness are not reliable indices for lipid profile prediction.

India continues to be the "diabetes capital" of the world, and by 2030, nearly 9 percent of the country's population is likely to be affected from the disease. Overall diabetes mellitus is closely associated with Dyslipidaemia but age group and DM duration may not be strong indices for lipid profile prediction especially with respect to subjects under management.

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INTRODUCTION

Studies gathered over the years have demonstrated that diabetes mellitus (DM) is an independent risk factor for CVD and it further increases the effects of other common risk factors, such as hypertension, smoking and hypercholesterolemia. 1, 2 In addition, mortality related to cardiovascular events in diabetic patients is significantly higher than in non-diabetic individuals.

Indian population is developing rapidly and becoming more urbanized and adopting a more western lifestyle which is probably resulting in an increase in the prevalence of DM in India from about 1±2% in the 1960s to 10% in the 1990s.

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by increase blood glucose level resulting from defects in insulin secretion, insulin action, or both. The prevalence of diabetes is on the rise, more alarmingly in the developing nations. The number of diabetic patients in the world has been estimated more than 175 million. Diabetes mellitus is ranked 7th among leading causes of death & has been rated 3rd when all its fatal complications are taken in to account. Patients with type-2 diabetes have increased risk of cardiovascular disease associated with atherogenic dyslipidemia. Coronary artery disease, especially myocardial infarction is the leading cause of morbidity and mortality worldwide. Hyperglycemia and atherosclerosis are related in type-

2 diabetes. Besides multiplying the risks of coronary artery diseases, diabetes enhances incidences of cerebrovascular strokes. Moreover, it is the leading cause of acquired blindness & accounts for more than 25% cases with end stage renal diseases as well as 50 % non-traumatic lower limb amputations. Being a pan metabolic disorder, diabetes is characterized by alteration in lipid profile, both quantitative & qualitative. Persistent hyperglycemia causes glycosylation of all proteins, especially collagen cross linking and matrix proteins of arterial wall. This eventually causes endothelial cell dysfunction, contributing further to atherosclerosis. The prevalence of dyslipidemia in diabetes mellitus is 95%. The dyslipidemia is a major risk factor for Coronary Heart Disease (CHD). The cardiovascular disease is a cause of morbidity and mortality in patients with diabetes mellitus because of disturbance in lipoproteins i.e. serum triglycerides (TC) 69%, serum cholesterol 56.6%, Low-Density Lipoprotein cholesterol (LDL) 77% and High Density Lipoprotein cholesterol (HDL) 71%.6,7

In uncontrolled diabetes, serum triglycerides, Very Low Density Lipoproteins (VLDL), cholesterol are raised both at fasting & following fixed meal. In post mixed meal Chylomicrons remnants & Low Density Lipoproteins (LDL) remain high for longer period than normal. Total cholesterol & LDL are mild to moderate high in 1/3 patients. On other end HDL remain significantly low particularly in type-2 diabetes patients with central obesity. Among changes in

composition of Lipoproteins high proportion of small, dense triglyceride rich LDL & glycoxidation products of LDL are considered to be most atherogenic. Age adjusted incidence of coronary artery diseases is 3 to 5 times higher in both male & female diabetics compare to general population. Individuals with diabetes may have several forms of dyslipidemia leading to additive cardiovascular risk of hyperglycemia. So lipid abnormalities should be aggressively detected & treated as a part of comprehensive diabetic care. The rationale of this study was to detect the lipid abnormality in diabetic patients.

DM classified either the absence o f insulin that is Insulin-Dependent Diabetes Mellitus IDDM or type1 or which is insensitive to the insulin that is N on-Insulin Dependent Diabetes Mellitus NIDDM or type2 the m ost common form is effecting ever younger age groups striking young adults and even adolescents (Wild *et al.,* 2004).

Most o f the studies agreed that diabetes mellitus is an epidemic diseases in most countries it has become almost universal killer, it was announced that sugar has become the fourth largest diseases leading to death in the world, World Health Organization (WHO) estimated that the number o f people w ith diabetes worldwide in year 2000 was 177 million, this increase to at least 336 million by the year 2030, with prevalence around 5.4% to major concern are that much o f this increase will be in the developing countries (approximately 75% o f all persons) (WHO., 1999; DM Guideline 2008).

DM is chronic illness that requires continuous medical care and educating patients on self management to achieve normal or near normal blood glucose levels in patients with diabetes and this will prevent acute complications and reduce the risk o f long term complications (Guideline o f DM 2008).

DM include damage and dysfunctions for many organs and system s lipid abnormalities one o f the diabetes dysfunctions, it commonly occurs in type2, so that analysis o f serum lipid has become an important health management, (American Diabetes Association) reported that lipid profile test to determine levels o f serum total cholesterol, triglycerides, HDL cholesterol (HDL-C), and LDL cholesterol(LDLC).

Nevertheless, lipid testing rates among individuals with diabetes have been far less than ideal (A.D.A), and can be broadly categorized into two groups: those that are common to the general population, for example elevated total and LDL cholesterol and additional diabetes related abnormalities for example elevated triglycerides and reduced HDL cholesterol.

Diabetic patients are at high risk for dyslipidemia, cardiovascular disease (CVD) and mortality. Dietary modification and lipid lowering medication can reduces serum lipid levels and lower the occurrence o f (CDV) events. In diabetic patients lipid profile is characterized by an elevation in both postprandial and fasting plasm a triglyceride (TG) and low level o f HDL cholesterol. Therefore in fact diabetes mellitus is characterized not only by alteration in glucose insulin axis but marked features described as the diabetic dyslipidemia. The increased lipid level and total cholesterol synthesis during hyperglycem ia may contribute to the acceleration of atherosis in diabetes mellitus.

Lipid profile, which is altered in diabetes state, is one o f the significant factors in development o f cardiovascular diseases studies have shown that increased plasma triglyceride and cholesterol levels may be a risk factor for vascular disease (Kamata *et al.,* 2001; Shahar *et al.,* 2003). Also oxidative modification of LDL is an important step in the development of atherosclerosis (Felmeden *et al.,* 2003). The prevalence of type2 DM is increasing at dramatic rate, and the economic costs o f caring for patients with diabetic complications are high, this increase in is closely associated with the epidemic of obesity in industrialized countries. Reduced physical activity is a contributing factor as sedentary lifestyles become m ore common. Increased body fat, particularly in the visceral compartment, is a strong risk factor for the development of type2. Elucidation of such risk factors will lead to interventions that can delay the onset or protect against the development o f type2 DM.

Dyslipidemia is one of the major cardiovascular disease (CVD) risk factors and plays an important role in the progress of atherosclerosis, the underlying pathology of CVD. The prevalence of dyslipidemia in type 2 diabetes is double with respect to the general population. These are more complex abnormalities that are caused by the interrelation among obesity, insulin resistance and hyperinsulinism, when the overweight subjects were compared with their respective thinner counterparts, they presented 2.4 to 7.1 times higher probability to have an elevated total cholesterol, LDL cholesterol, triglycerides and blood pressure as well as 12.6 times higher probability to have hyperinsulinemia. It is worth to emphasize that the fatty tissue is exclusively related to risk factors, such as the altered insulin and lipid profile, which can contribute to the development of the insulin resistance syndrome, which comprises several risk factors for the emergence of cardiovascular complications. In patients with type 2 diabetes, which is equivalent to CHD *(Juutilainen et al, 2005),* it is most commonly characterized by elevated TG and reduced HDL-C *(Goldberg 2001).* These abnormalities can be present alone or in combination with other metabolic disorders. The prevalence of dyslipidaemia varies depending on the population studied, geographic

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location, socioeconomic development and the definition used. Very few cross-sectional studies have evaluated the relationship between lipid and blood glucose concentrations in type 2 diabetics. The present study was planned to identify the prevalence of abnormalities in lipid profile among type 2 diabetic.

CLASSIFICATION OF DIABETES MEILITUS

The World Health Organization has described diabetes under the clinical classes of DM and impaired glucose tolerance (IGT). The major classes of DM include:

• Insulin Dependent Diabetes Mellitus (IDDM), known as typel DM.

• Non-Insulin Dependent Diabetes Mellitus (NIDDM), known as type2 DM.

Persons with IDDM require insulin treatment for survival, due to pancreatic islet (3-cell destruction and are prone to ketoacidosis.

Non-Insulin Dependent Diabetes Mellitus can progress to the state o f requiring insulin treatment, but this progression is not necessarily related to p-cell destruction but rather to deficiency in insulin production or a condition o f insulin resistance (a decreased biological response to insulin).

• Gestational Diabetes Mellitus (GDM).

• Other types o f diabetes mellitus associated with specific conditions.

Insulin Dependent Diabetes Mellitus (IDDM): The onset of IDDM or typel diabetes is most common in children or young adults and accounts for around 10% or less of the total number of people with diabetes (WHO., 1999). Typel indicates the processes of (β - cells destruction that may ultimately lead to diabetes mellitus in which insulin is required for survival to prevent the development of ketoacidosis (acidosis due to an excess of ketone bodies, which accumulate due to the incomplete metabolism of fatty acids), com a and death. An individual with a typel process may be metabolically normal before the disease is clinically manifest, but the process o f (β -cells destruction can be detected. Typel is usually characterized

by the presence of anti-glutamic acid decarboxylase (anti-GAD) antibodies, islet cell or insulin antibodies which identify the autoimmune processes that lead to (β-cells destruction. In some subjects with this clinical form of diabetes, particularly non Caucasians, no evidence of an autoimmune disorder is demonstrable and these are classified idiopathic typel. Etiological classification may be possible in some circumstances and not in others. Thus, the category of typel diabetes

can be identified if appropriate antibody determinations are performed (WHO., 2003).

Non -Insulin Dependent Diabetes Mellitus (NIDDM): The second type of diabetes mellitus is (NIDDM) or type2 is m ore complex in etiology and characterized by a relative insulin deficiency reduce insulin action and insulin resistance of glucose transport in skeletal muscle and adipose tissue.

It develops gradually without obvious symptoms and the progression to full diabetes ensues when pancreatic p-cells hypersecretion o f insulin fails to compensate for insulin resistance. Type2 DM usually diagnosed by tests that indicate glucose intolerance, it is linked with behavior (life style), environment and social factor such as over weigh and unhealthy dietary habits and obesity. Patients with type2 DM have two fourfold increase in cardiovascular disease (CVD) and dramatically higher risk of accelerated cerebral and peripheral vascular disease. The metabolic alternation observed in N IDDM are milder than those described for the insulin-dependent diabetes mellitus form of the disease, and are thought to be due to a combination of two factors dysfunctional P-cells and insulin resistance. The incidence and prevalence o f type2 diabetes mellitus are rapidly increasing worldwide in both developing and developed nations.

Gestational Diabetes Mellitus: Gestational diabetes is a state of carbohydrate intolerance resulting in hyperglycem ia of variable severity, with onset or first recognition during pregnancy. It does not exclude the possibility that the glucose intolerance may antedate pregnancy but has previously gone unrecognized. The definition applies irrespective o f w hether or not insulin is used for treatment or whether the condition persists after pregnancy.

Women who are known to have diabetes mellitus and who subsequently become pregnant do not have gestational diabetes but have (diabetes m ellitus and pregnancy) and should be treated accordingly before, during and after the pregnancy (WHO., 1999). In the early part o f pregnancy fasting and postprandial glucose concentrations are normally lower than in normal, non-pregnant women. Elevated fasting or postprandial plasma glucose levels may well reflect the presence o f diabetes that antedates pregnancy, but criteria for designating abnorm ally high glucose concentration at this time in pregnancy have not yet been established. The occurrence of higher than usual plasma glucose levels at this time in pregnancy mandates careful management and m ay be an indication for carrying out an OGTT. Nevertheless, normal glucose tolerance in the early part o f pregnancy does not itself establish that gestational diabetes will not develop later. Individuals at high risk

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for gestational diabetes include older women, obese, women those with previous history o f glucose intolerance, any pregnant woman who has elevated fasting or casual blood glucose levels those with a history of gestational diabetes mellitus those with a history of large for gestational age babies, women from certain high risk ethnic groups and strong family history of diabetes mellitus. It may be appropriate to screen pregnant women belonging to high risk population groups during the first trim ester o f pregnancy in order to detect previously undiagnosed diabetes mellitus. Women at high risk who screen negatively and average risk women should be tested between 24 and 28 weeks of gestation.

IMPACT OF DURATION OF DIABETES AND AGE

Diabetes mellitus has emerged as a major non-communicable disease globally as well as regionally. India accounts for the largest number of people 50.8 million suffering from diabetes in the world, followed by China (43.2 million) and the United States (26.8 million) reveal new figures released by the International Diabetes Federation (IDF). India continues to be the "diabetes capital" of the world, and by 2030, nearly 9 per cent of the country's population is likely to be affected from the disease.1 The As per Indian Council of Medical Research study, the pooled Estimates of prevalence rate in India were 62.47 per thousand. It was also estimated that diabetes is directly responsible for 9% of Acute Myocardial Infarction cases, 4% of stroke cases, 2% of neuropathy, and 32% of cataract cases.2 Diabetes mellitus is a worldwide health problem predisposing to markedly increased cardiovascular mortality and morbidity.

Lipid abnormalities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetic's .There is a growing body of evidence showing that hyperglycemia and Dyslipidaemia are linked to increased cardiovascular risk. Nowadays, the term "Dyslipidaemia" is increasingly being used to describe abnormal changes in lipid profile, replacing the old term "hyperlipidaemia". Dyslipidaemia encompasses changes in HDL-cholesterol (HDL-C), the size and density of LDL-cholesterol (LDL-C) and the total cholesterol/HDL-C ratio (TC/HDL-C). The term diabetic Dyslipidaemia comprises a triad of raised triglycerides, reduced HDL-C and excess of small, dense LDL particles. The lipid abnormalities are prevalent in diabetes mellitus because insulin resistance or deficiency affects key enzymes and pathways in lipid metabolism. In particular, the following processes are affected: apoprotein production, regulation of lipoprotein lipase, action of cholesterol ester, transfer proteins and hepatic and peripheral actions of insulin .Even more, it has been proposed that the composition of lipid particles in diabetic dyslipidaemia is more atherogenic than other types of dyslipidaemia. This means that even normal lipid concentrations might be more atherogenic in diabetic than in nondiabetic people.7 Atherosclerosis accounts for up to 80% of deaths in diabetic patients due to coronary heart disease (CHD) and cerbrovascular or peripheral vascular disease This study was conducted to know the impact of duration of illness and age on the lipid profile and glycaemic control in type 2diabetic patients.

CHARACTERIZATION OF LIPID PARAMETERS

Diabetes is associated with the development of many cardiovascular diseases (CVD). Diabetes impairs the utilization of lipids and lipoproteins which cause diabetes induced atherogenic dyslipidemia that, is one of the most important risk factor for the development of atherosclerosis in diabetic individuals. Atherosclerosis is one of the major causes in the development of CVD. Certain modifiable and non-modifiable risk factors contribute in the progression of atherosclerosis. Non-modifiable risk factors include age, gender and genetics, whereas modifiable risk factors include obesity, smoking, hypertension, diabetes and dysli-pidemia. Diabetic dyslipidemia is characterized by increased serum low-density lipoprotein (LDL), triglycerides (TG) and decreased high-density lipoprotein (HDL). Diabetic individuals are more prone to dyslipidemia as compared to normal individuals, therefore, the chance of mortality and morbidity is high in diabetic individuals.

Geographic location, social and economic status of population affects the prevalence of dyslipidemia. Prevalence of dyslipidemia with respect to different risk factors is well studied. Age is an important risk factor in atherosclerosis. Cholesterol and lipoproteins levels increase with age in both genders, but the more pronounced increase has been reported in females than in males. The purpose of the study was to assess the effect of age and gender on dyslipidemia in diabetic versus non-diabetic atherosclerotic patients.

METHODOLOGY

The study was carried out at randomly selected hospitals of Patna. Total two hundred patients of diabetes Mellitus were selected from diabetic clinic, outdoor patient department, in door admissions for this study, amongst which, one hundred patients were of type-1 DM with age group of 13-56 years and another one hundred patients were of type-2 DM with age group of 35 -74 years. 50 normal healthy volunteers between age group of 13-75 years were selected for control study. The detail history was taken; relevant clinical examination and all routine investigations were performed. An informed consent was taken from every patient after full explanation of

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procedure. Every patient was advise for at least 12-14 hours overnight fasting and the 5ml venous blood sample were collected in a disposable syringe on next morning (before breakfast) for the serum lipid profile and fasting blood sugar (for the assessment of blood glucose level). The lipid profiles were evaluated. The known cases of type 2 diabetes mellitus will also be evaluated for their blood sugar (control or un-control) by advising the HbA1C level. The data was collected by predesign, pretested proforma and analyzed using SPSS 17.0 (Trial version).

RESULTS

Maximum number of patients (37% and 44%) were from age group of 20-29 years in type-1 DM & 50-59 years in type-2 DM respectively. Mean age in type 1 DM group was 32.6 years & in type 2 DM group was 53.2 years. Majority of cases (40%) of type 2 DM showed positive family history, in contrast only 13% type 1 DM cases showed of positive family history. Majority of the type 2 DM patients (16%) were diagnosed within 5 years and majority of the type 1 DM patients (43%) were diagnosed more than 10 years. 68% of the patients of type 2 DM were obese, in contrast only 11% of the patients of type-1 DM were obese. 53% cases of type-1 DM and 70 % cases of type-2 DM had less than 140 mg/dl level of Fasting Blood Sugar (FBS. 49 % patients of type-1 DM and 30% of type-2 showed more than 200 mg/dl level of Post Prandial Blood Sugar (PPBS).

Majority of type 2 DM patients (72%) showed high serum cholesterol level, while only 12% of the type1 DM patients showed high serum cholesterol level. In control group all persons had normal serum cholesterol level . 95% of type 1 DM patients showed normal (10-190 mg/dl) serum triglyceride level, while only 26% of type 2 DM subjects showed normal level. Serum LDL level was high (>160 mg/dl) in 78% of type 2 DM patients, while only 19% of type 1 DM patients showed higher value. In type 1 DM patients 95% of them showed normal (<40 mg/dl) serum HDL value and 5% showed higher value. All patients of type 2 had normal serum HDL level . In type 1 DM patients, all the mean values of lipid profile were in normal limit in both sexes. Female have shown slight higher mean level of S. cholesterol, S. triglyceride, S. LDL and S. HDL level as compared to male.

CONCLUSION

It is equally important to note that the diabetic subjects were on medications (oral hypoglycemic). Such treatment reduces the blood glucose level and most probably alters the overall pathophysiology, including the lipidemia of the condition. Overall diabetes mellitus is closely associated with Dyslipidemia but age group and DM duration may not be strong indices for lipid

profile prediction especially with respect to subjects under management.

Hyperlipidemia is the commonest complication of diabetes mellitus and it predisposes them to premature atherosclerosis and macro vascular complications. Common lipid abnormalities in diabetes are raised triglycerides, raised serum LDL, raised serum cholesterol and low serum HDL. The important impact of dyslipidemia on cardio vascular complications requires undivided attention throughout the course of disease.

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