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Prevalence of the dyslipidemia in Bihar patients diagnosed with the diabetes

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Abstract
Dyslipidemia one of the major cardiovascular modifiable risk factor, is characterized by high levels of plasma triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) particles, and low levels of high-density lipoprotein cholesterol (HDL-C) and insulin resistance. It increases the risk of macrovascular and microvascular complications in type 2 diabetes. Hence the present study was planned for evaluation of Prevalence of the Dyslipidemia in Bihar Patients Diagnosed with the Diabetes.
The present study was planned in department of General Medicine, Patna Medical College and Hospital, Patna, Bihar, India. The 60 patients were enrolled in the present study. The patients were divided in two study groups as diagnosed with diabetes and another are non-diabetic patients. The biochemical parameters like Fasting glucose level, Glycated haemoglobin (HbA1c), Total cholesterol, Triglycerides, High Density Lipid, and Low Density Lipid were estimated. The diabetic patients had elevated serum total cholesterol, elevated triglyceride (triacylglycerol) and slightly elevated low density lipoprotein and reduced levels of high density lipoprotein indicating that diabetic patients were more prone to cardiovascular diseases.
The data generated from the present study concludes that lack of knowledge among people in developing countries on dyslipidemia which can be effectively managed in type 2 diabetes patients by life-habit modifications in combination with strict adherence to pharmacological interventions. There remains the need to impart awareness on the dosage, potential side effects and benefits of continuing uninterrupted medication of the prescribed medications in order to optimise the management of dyslipidemia.

Keywords: dyslipidaemia, Bihar patients, diabetes, etc

Introduction
Dyslipidemia is an abnormal amount of lipids (e.g. triglycerides, cholesterol and/or fat phospholipids) in the blood. In developed countries, most dyslipidemias are hyperlipidemias; that is, an elevation of lipids in the blood. This is often due to diet and lifestyle. Prolonged elevation of insulin levels can also lead to dyslipidemia. Likewise, increased levels of O-GlcNAc transferase (OGT) may cause dyslipidemia.
Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time. Symptoms often include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, and damage to the eyes.
Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise [1].
The classic symptoms of untreated diabetes are unintended weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. Other symptoms of diabetes include weight loss and tiredness [2].
Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurred vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Long-term vision loss can also be caused by diabetic retinopathy. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes [3].
People (usually with type 1 diabetes) may also experience episodes of diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. A rare but equally severe possibility is hyperosmolar hyperglycemic state (HHS), which is more common in type 2 diabetes and is mainly the result of dehydration [4].
Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such

as confusion, changes in behaviour such as aggressiveness, seizures, unconsciousness, and (rarely) permanent brain damage or death in severe cases. Rapid breathing, sweating, and cold, pale skin are characteristic of low blood sugar but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in sugar. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon [5].

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time. The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in people with diabetes are due to coronary artery disease [6]. Other macrovascular diseases include stroke, and peripheral artery disease.

The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. It is recommended that people with diabetes visit an eye doctor once a year. Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes [7]. The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness.

There is a link between cognitive deficit and diabetes. Compared to those without diabetes, those with the disease have a 1.2 to 1.5-fold greater rate of decline in cognitive function. Having diabetes, especially when on insulin, increases the risk of falls in older people.

Type 2 diabetes is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type of diabetes mellitus. Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver's glucose production [8].

Type 2 diabetes is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio [9].

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk. The type of fats in the diet is also important, with saturated fat and trans fats increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice also may increase the risk of diabetes, whereas substitution of brown rice or other whole grains for white rice may lower the risk of diabetes. A lack of physical activity is believed to cause 7% of cases [10].

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1. Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus [11].

The body obtains glucose from three main sources: the intestinal absorption of food; the breakdown of glycogen (glycogenolysis), the storage form of glucose found in the liver; and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. Insulin plays a critical role in regulating glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen [12].

Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin [13].

If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency [14].

When glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia). In addition, intracellular glucose deficiency stimulates appetite leading to excessive food intake (polyphagia) [15].

There is no known preventive measure for type 1 diabetes. Type 2 diabetes—which accounts for 85–90% of all cases worldwide—can often be prevented or delayed by maintaining a normal body weight, engaging in physical activity, and eating a healthy diet. Higher levels of physical activity (more than 90 minutes per day) reduce the risk of

diabetes by 28%. Dietary changes known to be effective in helping to prevent diabetes include maintaining a diet rich in whole grains and fibre, and choosing good fats, such as the polyunsaturated fats found in nuts, vegetable oils, and fish. Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help prevent diabetes. Tobacco smoking is also associated with an increased risk of diabetes and its complications, so smoking cessation can be an important preventive measure as well [16].

The relationship between type 2 diabetes and the main modifiable risk factors (excess weight, unhealthy diet, physical inactivity and tobacco use) is similar in all regions of the world. There is growing evidence that the underlying determinants of diabetes are a reflection of the major forces driving social, economic and cultural change: globalization, urbanization, population aging, and the general health policy environment [17].

Diabetes management concentrates on keeping blood sugar levels as close to normal, without causing low blood sugar. This can usually be accomplished with dietary changes, exercise, weight loss, and use of appropriate medications (insulin, oral medications) [18].

Learning about the disease and actively participating in the treatment is important, since complications are far less common and less severe in people who have well-managed blood sugar levels. As Per the American College of Physicians, the goal of treatment is an HbA1C level of 7-8%. Attention is also paid to other health problems that may accelerate the negative effects of diabetes. These include smoking, high blood pressure, metabolic syndrome obesity, and lack of regular exercise. Specialized footwear is widely used to reduce the risk of ulcers in at-risk diabetic feet although evidence for the efficacy of this remains equivocal. People with diabetes can benefit from education about the disease and treatment, dietary changes, and exercise, with the goal of keeping both short-term and long-term blood glucose levels within acceptable bounds. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure.

Weight loss can prevent progression from prediabetes to diabetes type 2, decrease the risk of cardiovascular disease, or result in a partial remission in people with diabetes. No single dietary pattern is best for all people with diabetes. Healthy dietary patterns, such as the Mediterranean diet, low-carbohydrate diet, or DASH diet are often recommended, although evidence does not support one over the others. According to the ADA, "reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia", and for individuals with type 2 diabetes who cannot meet the glycemic targets or where reducing anti-glycemic medications is a priority, low or very-low carbohydrate diets are a viable approach. For overweight people with type 2 diabetes, any diet that achieves weight loss is effective [19].

Lifestyle changes, including increased physical activity and dietary modifications remains the cornerstone of management of atherogenic dyslipidemia in type 2 diabetes. Dyslipidemia, one of the major cardiovascular modifiable risk factors, is characterized by high levels of plasma triglycerides (TG) and small dense low-density lipoprotein cholesterol (LDL-C) particles, and low levels of high-density lipoprotein cholesterol (HDL-C) and insulin resistance. It increases the risk of macrovascular and microvascular complications in type 2 diabetes. Hence the present study was planned for evaluation of Prevalence of the Dyslipidemia in Bihar Patients Diagnosed with the Diabetes.

Methodology

The present study was planned in Department of General Medicine, Patna Medical College and Hospital, Patna, Bihar, India. The 60 patients were enrolled in the present study. The patients were divided in two study groups as diagnosed with diabetes and another are non-diabetic patients. The biochemical parameters like Fasting glucose level, Glycated haemoglobin (HbA1c), Total cholesterol, Triglycerides, High Density Lipid, and Low Density Lipid were estimated.

The blood samples were drawn in the fasting state. The venepuncture was done in the cubital fossa. Tourniquet was used but was released just before sampling to avoid artificial increase in the concentration of serum lipids. About 10 ml of blood was drawn using perfectly dry and sterile syringes and the blood was transferred to dried glass vials. Serum was separated within 2 hours of collection to prevent artificial changes in concentration of HDL. The blood was centrifuged at 5000 rpm for 10 minutes. The supernatant clean serum was then pipetted out using dry piston pipettes with disposable tips and stored in dry thin walled vials at 4cc. The samples were analyzed the same day. Care was taken to exclude the hemolysed serum

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: For cases Type 2 diabetes patients in the age group of 30- 75 years and who are on either: a) Oral hypoglycemic agents b) Insulin c) Both. For controls Patients without type 2 diabetes mellitus age and sex matched.

Exclusion criteria Known type 2 diabetics in the age group 30-75 years who are on oral hypolipidemic drugs. Known type 2 diabetics in the age group 30-75 years who are suffering from a) Chronic liver disease b) Hypothyroidism Known type 2 diabetics who are on drugs which cause hyperglycemia a) Thiazides b) Corticosteroids c) Oral contraceptives.

Results & Discussion

DM is a group of metabolic disease characterized by hyperglycemia, glucosuria, hyperlipidemia, negative nitrogen balance and sometimes ketonemia. Dyslipidemia is defined as elevated total cholesterol, low-density lipoprotein (LDL) cholesterol, or triglycerides (TG); low high-density lipoprotein (HDL) cholesterol; or a combination of these abnormalities. Diabetic dyslipidemia is manifested as raised LDL, decreased HDL, and elevated TG. Elevated TG level is a significant risk factor for coronary heart diseases.

DM if left untreated can leads to several life threatened macrovascular and microvascular complications. The microvascular complications are retinopathy, nephropathy, and neuropathy, while the macrovascular complications of diabetes include angina, myocardial infarction, transient ischemic attack, and stroke.

Dyslipidemia was defined by presence of one or more than

one abnormal serum lipid concentration [20]. In patients with diabetes, many studies have clearly established that complications are mainly due to chronic hyperglycemia that exerts its injurious to health effects through several mechanisms: dyslipidemia, platelet activation, and altered endothelial metabolism [21 22]. Both lipid profile and diabetes have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension and cardiovascular diseases [23]. Lipids play a vital role in the pathogenesis of diabetes mellitus. Dyslipidemia as a metabolic abnormality is frequently associated with diabetes mellitus. Abnormalities in lipid metabolism have been reported in patients with diabetes mellitus accompanied by the risk of cardiovascular arteriosclerosis [24].

Diabetic patients have many complications which include elevated levels of LDL-C and triacylglycerols, low levels of HDL-C and a preponderance of abnormalities in the composition of the smaller, dense particles [25]. Similar findings found in study done by Idogun, *et al*. [26] and Albrki, *et al*. [27] and observed that lipoprotein profiles of the diabetics were found higher than normal reference values.

Different mechanisms are responsible for the development of dyslipidemia in individuals with diabetes. Defects in insulin action and hyperglycemia could lead to dyslipidemia in patients with diabetes. In the case of T2DM, the obesity/insulin-resistant state can in itself lead to lipid abnormalities independently of hyperglycemia In T2DM, this situation is not usually fully corrected with glycemic control. Therefore conclusively insulin resistance and not hyperglycemia is the culprit. Some of the incriminating mechanisms are Insulin-controlled apoprotein production in the liver, regulation of lipoprotein lipase (LPL), actions of cholesteryl ester transfer protein (CETP) and peripheral actions of insulin on adipose tissue and muscles [28]. Hyperglycemia not only causes apoptosis of β-cells in the islets of Langerhans (Glucotoxicity) but also determines the degree of accumulation of oxidized LDLs. Moreover dyslipoproteinemia itself has a toxic effect on β-cells, but only in the presence of increased blood glucose levels, thus exponentially enhancing risk of cardiovascular disease. In fact diabetes and the lipid metabolism disorder are so tightly intertwined that 'Diabetes Lipidus' would be an appropriate term [29].

Moreover Diabetic dyslipidemia is associated with insulin resistance, visceral obesity and liver fat content. Insulin resistance causes excessive generation of substrates like free fatty acids for synthesis of very low density lipoproteins (VLDL) in the liver. It also upregulates the production of VLDLs by other means. Also elevated apoprotein B, prolonged postprandial lipemia also worsen the condition. In addition, LDL particles are converted to smaller, perhaps more atherogenic, lipoproteins termed 'small-dense LDLs. Chronic hyperglycemia exerts a deleterious effect on the vascular wall and, by glycation of apolipoproteins, interferes with the normal pathways of lipoprotein metabolism [30].

Table 1: Comparison of General Parameter

Group	Group I	Group II
Type of Patients	Diabetic patients	Non Diabetic patients
No. of Patients	30	30
Age Group	38 – 52 years	34 – 55 year
Males	23	20
Females	7	10

Table 2: Comparison of Bio Chemical Parameter

Group	Group I	Group II
Type of Patients	Diabetic patients	Non Diabetic patients
Bio Chemical Parameter	Observation	
Lipid Profile		
Triglycerides (mg %)	199.2 ± 22.4	183.4 ± 24.7
Total cholesterol (mg %)	185.4 ± 13.4	163.4 ± 11.5
High Density Lipid (mg %)	42.4 ± 6.1	52.4 ± 6.9
Low Density Lipid (mg %)	121.3 ± 14.8	95.4 ± 21.4
Other Parameters		
Fasting glucose level (mg %)	159.8 ± 7.5	99.5 ± 6.9
Glycated haemoglobin (HbA1c) (%)	8.9 ± 0.9	6.4 ± 1.1

In 2006, Shepherd *et al*. [31] reported high-dose statin monotherapy as safe with no treatment-related adverse events and no elevated levels of liver enzymes. Although, statins have represented the evidence-based treatment of choice for reducing LDL-C levels and decreasing cardiovascular events but it is unfortunate that statins are frequently not available, specifically to poor and people with low-income for several reasons including high cost, and also statins cause intolerance, side effects such as myopathy, myalgia, elevation in several hepatic and renal enzyme. Thus, they do not have patient preference, and if prescribed, high chances of nonadherence even with the literate group of patients. In developing and poor economic countries including India, there continues to be low medical education and awareness on effective usage of medications prescribed by doctors.

The illiterate and poor patients tend to abruptly quit medication or do not stick to the prescribed dosage regimen of the medication leading to suboptimal use and clinical outcome. Hence, these patients remain undertreated for diseases that can be effectively treated. The interpretation of a recent study in patients with rheumatoid arthritis suggested that patients who were not taking their biological drug on the day agreed with their healthcare professional had poorer clinical outcomes than those who did take their drug, emphasising the need for strict adherence to biological therapy in patients with this condition [32].

Strict adherence to treatment is essential to avail maximum benefits of therapy. In one study, we observed that due to suboptimal compliance of the patient to the treatment, his LDL-C levels rose from 75 to 85 mg/dL and the beneficial effects of treatment were abolished. Similar results in terms of higher risk of death, nonfatal MI and loss of beneficial effects of statins with abrupt discontinuation were reported in patients with acute coronary syndrome [33].

The management of dyslipidemia diabetes needs a comprehensive strategy to regulate the levels of lipid and to discuss over associated metabolic complicated disorders and modifiable risk factors like hypertension, diabetes, obesity, and cigarette smoking. There are mainly 2 principal approaches for dyslipidemia, lifestyle intervention and lipid modifying drug therapy.

Conclusion

The diabetic patients had elevated serum total cholesterol, elevated triglyceride (triacylglycerol) and slightly elevated low density lipoprotein and reduced levels of high density lipoprotein in comparision to non-diabetic indicating that diabetic patients were more prone to cardiovascular diseases.

The data generated from the present study concludes that lack of knowledge among people in developing countries on dyslipidemia which can be effectively managed in type 2 diabetes patients by life-habit modifications in combination with strict adherence to pharmacological interventions. There remains the need to impart awareness on the dosage, potential side effects and benefits of continuing uninterrupted medication of the prescribed medications in order to optimise the management of dyslipidemia.

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