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Studying the Effect of Fed Status on Serum Lipid Profile Values in Type 2 Diabetes Mellitus

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Abstract

***Introduction and objectives:** Diabetes mellitus is a disease that leads to abnormalities of metabolism. Accurate lipid profile is vital for a diabetic individual. Most guidelines recommend a fasting serum lipid test. This is based on achieving consistency between patients and over multiple tests by ensuring a standardised metabolic state. A fasting sample does not reflect the true biological state in which people spend most of their time. Here we test the hypothesis that lipid levels change only minimally in response to normal food intake in individuals with diabetes mellitus. The objective was to study the effect of fed status on serum lipid profile values in type 2 diabetes patients.*

***Material and methods:** A cross-sectional observational study of 110 known cases of type 2 diabetes mellitus fulfilling inclusion and was carried out. Qualifying patients underwent detailed history, clinical examination, biochemical tests including lipid profile. Study compared fasting, one hour and 2 hours after normal diet intake lipid profile values including total cholesterol, triglycerides, HDL, VLDL, and LDL in study subjects.*

***Results:** Statistical analysis was performed by student's t-test (paired). P - values < 0.05 were considered statistically significant. In our study serum total cholesterol decreased 1.06% ($p > 0.05$) after 1 hour and decreased 1.65% ($p > 0.05$) after 2 hour of diet. Serum triglycerides increased 1.76% ($p < 0.01$) after 1 hour and 3.81% ($p < 0.001$) after 2 hour of diet. Serum HDL increased 0.06% ($p > 0.05$) after 1 hour and 1.86% ($p > 0.05$) after 2 hour of diet. Serum VLDL increased 1.73% ($p < 0.01$) after 1 hour and 3.80%($p < 0.001$) after 2 hour of diet and serum LDL decreased 2.43% ($p < 0.05$) after 1 hour and 4.72% ($p < 0.01$) after 2 hours of diet.*

***Conclusion:** The post-prandial state did not affect total cholesterol and HDL levels but there was significant rise in serum triglyceride level. LDL levels showed paradoxical decrease in post-prandial state.*

***Key words:** Fed status, lipid profile, fasting, type 2 diabetes mellitus.*

Introduction

Diabetes mellitus is a disease in which relative or absolute insulin deficiency leads to abnormalities in carbohydrate, fat and protein metabolism. Diabetics are at increased risk of complications involving the heart, blood vessels, eyes, kidneys and nerves.

Diabetes is classified into primary and secondary, with primary cases divided into autoimmune: mainly type 1 diabetes and non-autoimmune: predominately type 2 diabetes. Approximately 85 to 90% of diabetic patients have type 2 diabetes, which is associated with defects in insulin secretion and usually, resistance to the action of insulin[1].

The prevalence of diabetes is increasing rapidly worldwide in developing and developed countries. India currently contributes to 49 per cent of the world's diabetes burden, with an estimated 72 million cases in 2017, a figure expected to almost double to 134 million by 2025. Diabetes prevalence has increased by 64 per cent across India over the quarter-century, according to a November 2017 report by the Indian Council for Medical Research, Institute for Health Metrics and Evaluation, both research institutes, and the Public Health Foundation of India, an advocacy.

Metabolic syndrome is the major morbidity in diabetes mellitus and cardiovascular disease is the primary cause of death in patients with diabetes mellitus. Measurement of lipid profile is essential for diagnosing metabolic syndrome and also necessary for predicting risk of cardiovascular disease[2]. Therefore, accurate lipid profile data are vital to provide best practice care for diabetic individuals and has now become a routine test.

Human consumption of food is usually evenly distributed throughout the day. The fasting state occurs, by definition, after an 8 hour fast. Thus, most humans find themselves in a non-fasting state for the majority of a 24-hour period, perhaps with the exception of early morning hours. People

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with diabetes exhibit magnified and extended post-prandial responses in glucose and lipid handling which may be due to loss of first phase and extended second phase insulin secretion.

At present, most guidelines recommend a fasting serum lipid test. This recommendation is based on achieving consistency between patients and over multiple tests by ensuring a relatively standardised metabolic state[3]. It is also because most of the research has been performed using fasting lipids, therefore it was assumed that making comparisons and analysing risk would be less precise if non-fasting tests were used.

Most previous studies have focused on change in lipid profile after a fat tolerance test, rather than normal food. A reason is the increase in triglyceride levels post-prandially seen during a fat tolerance test, in which patients typically consume 1 g fat per 1 kg body weight.

In the recent past, efforts have been made to simplify blood sampling by replacing fasting lipid profile with non-fasting lipid profile. Fasting requirements; however, are difficult for some patients and can reduce adherence with testing requests, delay results and place strain on testing facilities as a large influx of patients present for testing each morning. In addition, a fasting state is more difficult for diabetic patients to maintain in rural areas because of long distances that must be travelled to obtain medical care and the ever presence threat of hypoglycaemia because of diabetic therapy. And, a fasting sample does not reflect the true biological state in which people spend most of their time.

Recently it has been proposed that post-prandial lipoprotein may be a better indicator of deranged lipoprotein metabolism and hence of cardiovascular disease. Post-prandial hypertriglyceridaemia and delayed triglyceride rich lipoprotein clearance have been found to impair endothelial function significantly either directly or by increasing superoxide anions. It has also been reported that the magnitude and duration of post-prandial lipidaemia is directly related to pathogenesis and progression of cardiovascular diseases[4].

Therefore, our study tested the hypothesis that levels of serum total cholesterol, triglycerides, low density lipoprotein and high density lipoprotein change only minimally in response to normal food intake rather than oral fat tolerance test in individuals with diabetes mellitus.

The aims and objectives of the study were to study serum lipid profile values in patients with type 2 diabetes mellitus in fasting status, 1 hour and 2 hour after a major meal and thus, to study the effect of fed status on serum lipid profile values in type 2 diabetes mellitus patients.

Material and methods

The study was a cross-sectional observational study conducted with 110 patients of type 2 diabetes mellitus selected from Medicine Wards and OPD of JLN Medical College and associated Hospitals, Ajmer. 55 male and 55 female patients were taken for study. Known cases of type-2 diabetes mellitus (according to ADA criteria) were included in the study. Type-1 diabetes mellitus, hypothyroidism and hyperthyroidism, known cases of familial dyslipidaemia syndromes, chronic kidney disease, chronic liver disease, pregnant and lactating women, malignancies, with history of consumption of alcohol within last 48 hours and patients on hypolipidaemic drugs, beta blockers, thiazides, diuretics, corticosteroids were excluded from the study.

Information was collected in a predesigned format from each patient. Consenting patients underwent detailed history, through clinical examination and relevant biochemical examinations including lipid profile. Serum lipid profile was estimated using 3 ml of venous blood in plain dry vial at three times, first after 8 hours of fasting, second after 1 hour of major meal and last after 2 hours of major meal. Blood was allowed to clot and immediately centrifuged at 2,000 rpm for 10 minutes and serum was used for lipid profile test.

Lipid profile (total cholesterol, triglycerides, HDL-cholesterol) were measured by enzymatic methods. For detection of LDL and VLDL, Friedwald formula was used:-

VLDL = TG/5

LDL = total cholesterol-{(TG/5) + HDL}.

Results

Statistical analysis was performed by student's t-test (paired). P values < 0.05 were considered statistically significant. In our study, mean fasting cholesterol level was 169.58 ± 57.51 mg/dl and after one hour of meal was 167.77 ± 54.81 mg/dl which was statistically insignificant (p = 0.093) and after two hours of meal was 166.77 ± 53.76 mg/dl which was also statistically insignificant (p = 0.117). Mean fasting triglyceride level was 178.63 ± 126.54 mg/dl and after one hour of meal was 181.78 ± 122.39 mg/dl which was statistically significant (p = 0.005) and after two hours of meal was 185.45 ± 123.56 mg/dl which was statistically significant (p < 0.001).

Mean fasting HDL cholesterol level was 32.74 ± 12.6 mg/dl and after one hour of meal was 32.76 ± 11.96 mg/dl which was statistically insignificant (p = 0.963) and after two hours of meal was 33.35 ± 11.97 mg/dl which was also statistically insignificant (p = 0.175). Mean fasting VLDL-cholesterol was 35.73 ± 25.3 mg/dl and after one hour of meal was 36.35 ±

24.47 mg/dl which was statistically significant (p = 0.005) and after two hours of meal was 37.09 ± 24.71 mg/dl which was statistically significant (p < 0.001). Mean fasting LDL-cholesterol level was 101.11 ± 43.35 mg/dl and after one hour of meal was 98.65 ± 42.52 mg/dl which was statistically significant (p = 0.035) and after two hours of meal was 96.33 ± 42.16 mg/dl which was statistically significant (p = 0.009), (Fig. 1).

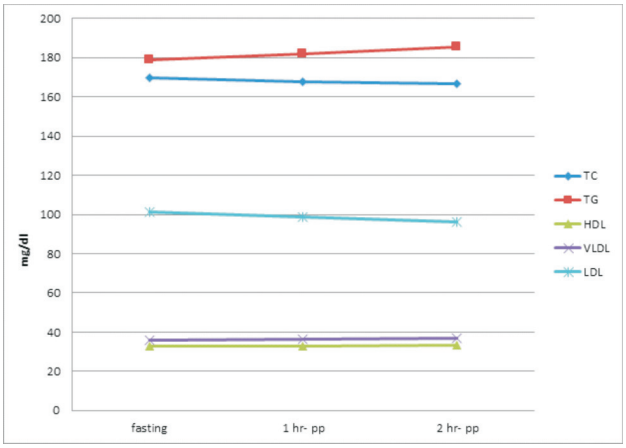

Fig. 1: *Line diagram showing various lipid parameters in fasting, one and, two hour post-prandial serum in type 2 diabetes mellitus.*

Serum total cholesterol decreased 1.06% (p > 0.05, not significant) after one hour of diet and decreased 1.65% (p < 0.05, not significant) after two hours of diet. Serum triglycerides increased 1.76% (p > 0.01, significant) after one hour and 3.81% (p < 0.001, significant) after two hours of diet. Serum HDL cholesterol increased 0.06% (p > 0.05, significant) after one hour and 1.86% (p > 0.05, not significant) after two hours of diet. Serum VLDL cholesterol increased 1.73% (p < 0.01, significant) after one hour and 3.80% (p < 0.001, significant) after two hours of diet and last serum LDL cholesterol decreased 2.43% (p < 0.05, significant) after one hour and decreased 4.72% (p < 0.01, significant) after two hours of diet (Fig. 2).

Discussion

Lipid profile and diabetes are important predictors of metabolic disturbances such as dyslipidaemia, metabolic syndrome, hypertension, and cardiovascular diseases. Dyslipidaemia as a metabolic abnormality is commonly associated with diabetes. Abnormalities in lipid metabolism have been reported in patients with diabetes mellitus accompanied by the risk of cardiovascular arteriosclerosis[5]. Most studies were conducted on fasting lipid levels in type 2 diabetes mellitus, but there are very few studies on post-prandial lipid levels in type 2 diabetes mellitus. There are studies that have reported that post-prandial dyslipidaemia is more important in the pathogenesis of the vascular

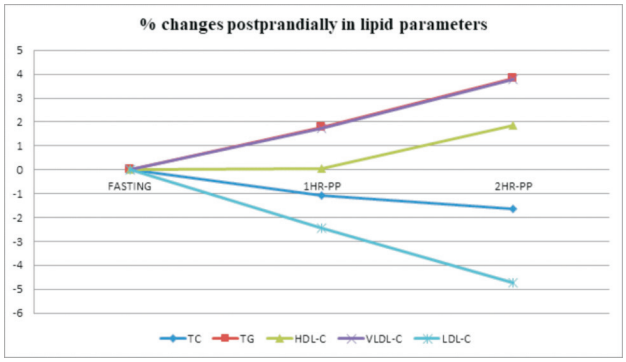

Fig. 2: *Line diagram showing changes in various lipid parameters with diet in type-2 diabetes mellitus.*

changes and atherosclerosis and it increases the risk of cardiovascular events[7].

We found no significant change in total and HDL cholesterol but significant increase in triglycerides and significant decrease in LDL cholesterol post-prandially (up to 2 hours) and this result is consistent with most of previous studies.

According to studies conducted in the past, no substantial evidence demonstrates that fasting lipid levels are superior to non-fasting levels for cardiovascular risk prediction. It is therefore reasonable to review the arguments often used in favour of fasting versus non-fasting lipid measurements[8,9].

The fasting requirement possibly makes blood sampling unnecessarily difficult for millions of patients worldwide, especially for diabetics. One argument often presented in favour of measuring lipids, lipoproteins, and apolipoproteins in the fasting state is the increase in triglyceride levels seen during fat tolerance tests (Schaefer EJ *et al*; 2001). However, our findings show that levels of lipids, and lipoproteins, after normal food intake differ only minimally from levels in the fasting state, probably because most people consume much less fat at ordinary meals than during a fat tolerance test. Another argument often presented is that calculating LDL cholesterol with the Friedewald equation requires fasting triglyceride measurement but the main reasons for measuring lipid levels in the fasting rather than the non-fasting state are simply that it has become the norm worldwide and that the fasting requirement has been applied in almost all randomised lipid-lowering trials[10,11].

Total and LDL cholesterol levels were reduced for up to 3 to 4 hours after normal food intake; this reduction was explained by haemodilution resulting from fluid intake in relation to the meal. A similar fall in LDL cholesterol, but not in total cholesterol, from fasting levels was observed among 115 subjects 3 to 5 hours after a normal breakfast[12]. The modest increase in triglyceride levels during normal food intake, together with the recent demonstration of high predictive ability of non-fasting triglycerides for risk of

cardiovascular events and risk of myocardial infarction, ischaemic heart disease, and death, suggests the possibility that non-fasting rather than fasting triglyceride levels could be used for cardiovascular risk prediction[13,14].

Most previous studies have focused on the change in levels of lipids, lipoproteins, and apolipoproteins after a fat tolerance test rather than after normal food intake. These studies usually have the participants consume a meal containing a so-called "oral fat load" of 1 g of fat per 1 kg body weight and detect increases in triglycerides of 1 to 2 mmol/l. However, most studies find that 30 g fat in a meal has no or very little effect on post-prandial lipidaemia, which is in accordance with the present demonstration of minimal changes in levels of lipids, lipoproteins, in response to normal food intake in individuals in the general population[18,19].

Many studies have found that atherogenesis may be a post-prandial phenomenon so future research should focus on studies reducing the levels of non-fasting triglycerides and thus remnant lipoprotein cholesterol to reduce the risk of cardiovascular disease and death[20].

However, our study had limited number of patients and only one ethnic group was included. Future research in this direction is required with large number of diabetics and with different ethnic groups because if non-fasting, rather than fasting, lipid profiles is used, it would simplify clinical care for patients worldwide specially for diabetics and for remote and rural populations in which maintaining fasting state is a difficult task.

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