STUDY OF DYSLIPIDAEMIA AMONG PRE-DIABETIC PATIENTS
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ABSTRACT

BACKGROUND
Diabetes mellitus is a very common health problem in India. Pre-diabetes is defined by American Diabetes Association (ADA) as impaired fasting glucose (FBS 100-125 mg/dl), impaired glucose tolerance (plasma glucose 140-199 mg/dl after 75 gm 2 hrs. oral glucose tolerance test) or both. Lipid disorders are not atypical in diabetes. They contribute to the considerable increase in the risk of atherosclerosis and consequent mortality in diabetes and pre-diabetes. Hence, the present study aims at evaluating dyslipidaemia in pre-diabetic subjects. We wanted to study the prevalence of dyslipidaemia among prediabetic patients attending OPD in a tertiary care centre.

METHODS
An institution-based case control study was conducted over a period of 18 months in inpatient as well as the outpatient prediabetic patients at ESIC Hospital, Rajaji Nagar, Bangalore. Patients were screened for their glycaemic status by performing fasting sugar and post prandial glucose level or two hours oral glucose tolerance test. Qualifying patients underwent detailed history taking, clinical examination, fasting lipid profile and routine investigations.

RESULTS
After a thorough screening of a total of 100 patients with either Impaired Fasting Glucose (IFG) or Impaired Glucose Tolerance (IGT) or both, they were included in the case group and 100 patients with normal glucose levels were included as controls in the study after consideration of the inclusion and exclusion criteria. Dyslipidaemia was observed in 37 prediabetic patients and 16 patients in the control group. Out of the 100 patients with prediabetes (cases), the mean total cholesterol was 177.06 ± 27.16 mg/dl and the mean triglycerides were 145.25 ± 19.72 mg/dl, mean HDL-cholesterol was 46.88 ± 8.36 mg/dl, and mean LDL-cholesterol was 120.14 ± 15.85 mg/dl respectively.

CONCLUSIONS
Lipid disorders can be seen among prediabetes. Indians, being one of the groups with high prevalence of diabetes, diagnosis is often delayed through lifestyle interventions. Early identification and treatment of persons with prediabetic conditions has the potential to reduce both the incidence of diabetes as well as its complications.

KEYWORDS
Lipid Profile, Pre-Diabetes, Diabetes Mellitus, Serum Cholesterol

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BACKGROUND
Diabetes is a condition affecting over 150 million persons worldwide. Diabetes mellitus has become an important public health problem with major complications, not only for its adverse health impact on individuals, but also for its economic burden on the health care system and society. The International Diabetes Federation in 2005 confirmed that diabetes is one of the most common non-communicable disease globally. The Indian population have been identified as the ethnic group with one highest prevalence of diabetes and diagnosis is often delayed until complications occur. Diabetes can be prevented or delayed through lifestyle interventions. The pathogenesis of diabetes demonstrates that the disease has a prolonged pre-diabetic phase.

Pre-diabetes is defined by American Diabetes Association (ADA) with impaired fasting glucose (FBS 100-125 mg/dl), impaired glucose tolerance (plasma glucose 140-199 mg/dl after 75 gm 2 hrs. oral glucose tolerance test) or both. These glucose levels are above normal but below the level that is diagnostic for diabetes. They have a significant risk of developing type 2 diabetes mellitus and they have an increased risk of cardiovascular diseases and
thus are an important target group for primary prevention. The average annual risk of developing diabetes for someone with normoglycemia is approximately 0.7% per year. In contrast, the risk is about 5-10% per year in individuals with IFG and IGT.\(^6\)

Those with diabetes are at risk of complications. These complications involve both cardiovascular diseases and micro vascular diseases. Epidemiologic evidence suggests that these complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes.\(^7\) Early identification and treatment of persons with pre-diabetic condition has potential to reduce both the incidence of diabetes and related complications.

Lipid disorders are not atypical in diabetes. They contribute to the considerable increase in the risk of atherosclerosis and consequent mortality in diabetes and pre-diabetes. These patients have distinctive forms of dyslipidaemia characterized by low high-density lipoproteins (HDL) cholesterol levels and modestly elevated levels of triglyceride rich lipoproteins.\(^8\) There may or may not be elevation of low-density lipoproteins (LDL) cholesterol levels, although commonly there is a dysmetabolism of triglyceride rich lipoproteins leading to an overabundance of smaller, denser LDL particles.

In a study done by 1800 subjects showed that risk for cardiovascular events in patients with pre-diabetes increases in patients with concomitant dyslipidaemia.\(^9\) Early detection and treatment of dyslipidaemia decreases the cardiovascular mortality and morbidity.

Hence, the present study aims at evaluating dyslipidaemia in pre-diabetic subjects attending the OPD.

**METHODS**

This is an institution-based case control study was conducted for over a period of 18 months in outpatient prediabetic patients at ESIC hospital Rajaji Nagar Bangalore. Ethical clearance of the study was obtained from the institution’s ethics committee so as to permit data collection. Patients were included in the study if they were willing to consent, fasting blood glucose levels between 100-125 mg/dl (according to the ADA criteria), two hours post load oral glucose of 75 g with blood glucose levels between 140-190 mg/dl. The study excluded diabetic, renal failure and critically ill patients.

Patients were screened for their glucose regulation by performing fasting sugar and post prandial glucose level or two hours oral glucose tolerance test. Qualifying patients underwent detailed history, clinical history, clinical examination, fasting lipid profile and routine investigations. Fasting lipid profile testing included total cholesterol, triglycerides, high density lipoprotein - C (HDL - C), low density lipoprotein - C (LDL - C) and very low-density lipoprotein cholesterol (VLDLC).

**Statistical Analysis**

Data was analysed using the software, SPSS Version 20.0. Descriptive and inferential statistical analysis was carried out in the present study. Student t test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups on metric parameters. Levene’s test for homogeneity of variance was performed to assess the homogeneity of variance. Chi-square and Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. Significance was assessed at 5% level of significance.

**RESULTS**

After thorough screening a total of 100 patients with either Impaired Fasting Glucose (IFG) or Impaired Glucose Tolerance (IGT) or both were included in the case group and 100 patients with normal glucose levels were included as controls in the study after consideration of the inclusion and exclusion criteria.

The subjects were age matched with mean SD 58.74 ± 13.38 and SD 16 ± 83 amongst the total number of cases and controls. (Table 1) There were 55% males and 45% females in both the groups studied. (Table 2) Off the 100 patients with prediabetes, family history of Type 2 Diabetes Mellitus was present in 63 of them which was significantly associated (p = 0.002*) with the occurrence of IFG and / or IGT. (Table 3) Dyslipidaemia was observed in 37 prediabetic patients and 16 patients in the control group. (Table 4) Out of the 100 patients with prediabetes (cases), the mean total cholesterol was 177.06 ± 27.16 mg/dl and the mean triglycerides were 145.25 ± 19.72 mg/dl, mean HDL - cholesterol was 46.88 ± 8.36 mg/dl, and mean LDL - cholesterol was 120.14 ± 15.85 mg/dl respectively. Among the 100 control subjects, the mean total cholesterol (161.99 ± 22.58 mg/dl), mean triglycerides (137.09 ± 11.35 mg/dl), mean HDL - cholesterol (48.58 ± 7.14 mg/dl), and mean LDL - cholesterol (116.28 ± 10.55 mg/dl) were also observed. (Table 5) The observed HDL cholesterol in the subjects were statistically significant. Total cholesterol, triglycerides and LDL cholesterol values were significant with the p value < 0.05.

Lipid profile which includes total cholesterol, total triglycerides, and HDL - cholesterol and LDL - cholesterol of each subject included in the study were assessed. The total cholesterol levels in 11 patients were high (>200 mg/dl) and 89 patients were normal or border line high (<200 mg/dl) amongst the prediabetic patients. In the control subjects, 6 patients had high total cholesterol levels and the remaining 94 patients had levels <200 mg/dl with p value of <0.001. Triglyceride levels in 24 prediabetic patients was high (>150 mg/dl), whereas only 7 control subjects had the levels high with significant p value of <0.001. Similarly, patients with prediabetes had low HDL cholesterol (<40 mg/dl) in 19 subjects as compared to 9 subjects in the control group with p value of 0.042 LDL cholesterol of >150 mg/dl was seen in 7 patients of prediabetes as compared to one patient in control group with significant p value (0.030). (Table 6). Samples are age matched with p= 0.827.
Out of 100 patients with prediabetes, family history of type 2 diabetes mellitus was present in 63 of them and it was significantly associated (p = 0.0002*) with occurrence of IFG and/or IGT (prediabetes). Out of 100 subjects without prediabetes a positive family history of type 2 DM was present in 52 patients. The comparative p value was p = 0.116 and was significant. In our study dyslipidaemia was observed in 37 patients of prediabetes and 16 patients in control group. Out of 100 patients with patients, mean total cholesterol 177.06 ± 27.16 and mean triglyceride was 145.25 ± 19.72, mean HDL - cholesterol was 46.88 ± 8.36, and mean LDL - cholesterol was 120.14 ± 15.85 mg/dl. Out of 100 controls subjects, mean total cholesterol was 161.99 ± 22.58 and mean triglyceride was 137.09 ± 11.35, mean HDL - cholesterol was 48.58 ± 7.14, and mean LDL - cholesterol was 116.28 ± 10.55. Total cholesterol, triglycerides and LDL cholesterol value significant with p value <0.05 and HDL cholesterol were statistically insignificant. In the 100 patients with prediabetes, the total cholesterol was >200 in 11 patients and 89 patients had total cholesterol of <200. In the control subject's total cholesterol was >200 in only 6 patients and <200 in 94 patients with p value of <0.001. Triglyceride level in 24 prediabetic patients was >150, whereas only 7 normal subjects had triglyceride level >150 with significant p value of <0.0.1. Similarly, patients with prediabetes had HDL <40 in 19 subjects as compared to 9 subjects in control group, with p value of <0.042. LDL cholesterol of >150 was seen in 7 patients with prediabetes as compared to 1 patient in control group with significant p value <0.030.

**DISCUSSION**

The progression from prediabetes to type 2 diabetes mellitus occurs over many years before the development of overt hyperglycaemia as seen in the condition. There is accumulating evidence which suggests prediabetes is also associated with dyslipidaemia. The present case - control study evaluated the prevalence of dyslipidaemia in prediabetic subjects.

Several studies have been conducted around the world to determine the prevalence of prediabetes among individuals above the age of 20. The AusDiab study found the prevalence of prediabetes amongst the Australian population to 16.4% and newly detected diabetes to be 3.7% respectively. Studies conducted throughout India in the ICMR - INDIAB study in the states of Tamil Nadu, Maharashtra, Jharkhand and Chandigarh, the prevalence of prediabetes was found to be 8.3%, 12.8%, 8.1% and 14.6%. In the present study, off the 100 the patients who were prediabetic, 55 were males and 45 were females. The prevalence also increased with age and peaked at 27.37% among those above the age group of 70 years. A cross sectional survey conducted by Mustafa N et al in the urban rural populations of Malaysia showed an overall prevalence of prediabetes of 22.1% in which 30.2% and 69.8% were men and women. Prevalence also increased with age and peaked at 27.37% among those above the age group of 70 years. A cross sectional survey conducted by Mustafa N et al. The American Diabetes Association enlists family history of diabetes as an established risk factor for the occurrence of diabetes. Amongst the 100 subjects with prediabetes, family history of type 2 diabetes mellitus was present in 63 of them which was statistically significant (p = 0.0002*). Like the findings of the present study, Moran MR et al, found that the presence of family history of diabetes in a first...
Dyslipidaemia is considered as one of the conditions most closely associated with diabetes mellitus. A study conducted by Suhrko Soebardi detected dyslipidaemia in 54.32% of newly detected diabetic patients. In the present study, the prevalence of dyslipidaemia was noted in the control as well as the case subjects. Dyslipidaemia was present in 37% of prediabetic and 16% of the control subjects. Three different studies conducted by the Diabetes Prevention Research Group, Lalitha P et al and M Das et al found the prevalence of dyslipidaemia among prediabetics to be 20.43%, 28.6% and 40.82% respectively.

Several studies which have evaluated the presence of dyslipidaemia in impaired fasting glucose and impaired glucose tolerance have found dyslipidaemia in 25-30% of prediabetic patients. The more careful characterization of long term glycaemia and documentation of dyslipidaemia in the pre-diabetic state supports the notion that dyslipidaemia may occur over a wider continuum of glycaemia that is encompassed by current diagnostic criteria. These findings are suggestive that early detection and prudent lifestyle changes should be considered in patients with dyslipidaemia.

CONCLUSIONS
Dyslipidaemia was found in pre-diabetic patients. Dyslipidaemia contributes to the development of both micro and macro-vascular complications among patients of diabetes. Hence, screening of dyslipidaemia among pre-diabetics can help in preventing vascular complications. Epidemiologic evidence suggests that these complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes. Indians, being one of the groups with high prevalence of diabetes, diagnosis is often delayed through lifestyle interventions. Early identification and treatment of dyslipidaemia in persons with prediabetic conditions has the potential to reduce both the incidence of diabetes as well as its vascular complications.

REFERENCES