Comparative Study on Lipoprotein Abnormalities and Evaluation in Diabetic and Non-Diabetic Hyperlipidemic Patients

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Abstract: It is a known fact that lipoprotein abnormalities contribute significantly to the risk of development of cardio vascular disease and diabetes. Furthermore abnormal glycemic state, lipid and lipoprotein abnormalities, such as hyperlipidemia have been shown to be important contributors to early atherosclerosis. Present study evaluates and compares the status of apolipoproteins A and B in hyperlipidemic patients both in diabetes and non-diabetic conditions. One hundred and thirty one patients of both gender, sub-grouped as 88 non-diabetic hyperlipidemic (NDHL) and 43 diabetic hyperlipidemic (DHL) patients were included in the study.Total cholesterol and Apo B was noted to be significantly higher in DHL than NDHL patients. Moreover, levels of Apo B was higher than Apo A in both DHL and NDHL groups when compared with healthy control group. Elevated levels of both triglyceride and total cholesterol in both DHL and NDHL groups depicts a strong hyperlipidemic state. It is concluded that diabetes and hyperlipidemia are important risk factors for subsequent occurrence and manifestation of cardiac abnormalities. Additionally higher levels of Apo B and A and that of higher Apo B than Apo A are indicative of dyslipidemic state and thus significant parameters for assessing the prevailing conditions and extent of risk for developing coronary heart disease (CHD) and atherosclerosis.

Key Words: Apolipoprotein A, B, Hypertriglyceridemia, Hyperlipoproteinaemia.

INTRODUCTION

One of the known metabolic abnormality is hyperlipoproteinaemia and is mainly controlled by apolipoproteins [1,2]. Additionally, best indicator of such abnormality is the concentration of apolipoproteins such as Apo B and Apo A as compared to cholesterol and total lipoprotein concentrations [3-5]. The main components of apolipoproteins in the plasma lipoproteins are Apo A, which is the major protein of the high density lipoprotein or HDL, and Apo B which is the major protein in the low density lipoprotein or LDL. Furthermore, Apo B is also a major protein component of other lipoprotein classes as well such as intermediate density lipoprotein (IDL) and very low density lipoprotein (VLDL) fractions [6]. It is documented that hyperlipoproteinaemia may arise from an abnormality of plasma lipoprotein metabolism, relating to some factors such as diabetes mellitus or defective function of plasma apolipoprotein [6,7]. It is also noted that as far as diabetes mellitus is concerned and its relation to lipoprotein abnormalities, the major physiological manifestations arises are that of metabolic origin [8]. In this regard, correlation exist between increased levels of glucose, cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and decreased high density lipoprotein cholesterol (HDL-C) and diabetes mellitus [9-12]. Thus clinicians and physicians, who are involved and interested in solving the anomalies relating to diabetic patients and desired to have a comparative data with non-diabetics for proper evaluation, has gained great importance for detection of early changes related to carbohydrate and lipid metabolism (lipoprotein abnormalities) and possible measures to evaluate some of the complications such as cardio-vascular disease (CVD).

It is known and generally acknowledge that lipoprotein abnormalities contribute significantly to the risk of development of CVD [16] and diabetes and lipid and lipoprotein abnormalities have been shown to be important contributors to early atherosclerosis [1,13-17]. Therefore the present study was undertaken to compare and evaluate the status of apolipoproteins concentration and abnormalities in hyperlipidemic, diabetic and non-diabetic patients.

MATERIALS AND METHODS

Present study includes 131 patients of both gender, sub-grouped as 88 non-diabetic hyperlipidemic (NDHL) and 43 diabetic hyperlipidemic (DHL) patients. Twenty healthy control subjects with no known family history of diabetes mellitus were included as control. Both control and diabetic related subjects were in an age group of 28-50 years, from lower and middle socio-economic group. The patients were enrolled at Laboratory services and referred from Endocrinology, General Medicine and Diabetic OPDs, both from within the hospital and outside referrals. The study carried prospectively for the period of November 2008 to

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December 2009. Among control group there were 12 males and 8 females while in the NDHL group, 49 males, 39 females, and DHL group, 24 males and 19 females. Fasting blood samples of both control and NDHL/DHL persons were drawn. Measurements of plasma glucose, cholesterol (TC), triglycerides (TG), HDL cholesterol, low density lipoprotein (LDL), Apo A, Apo B, uric acid were performed on a Hitachi 912 autoanalyzer (Roche Diagnostics, Basel). Lp(a) was determined using a double-monoclonal antibody-based ELISA [18].

Protocols of Akanji (2002) [16] was followed for all research design of anthropometric and chemical analysis. The average of two weight measurements (electronic scale) and two height measurements (stadiometer) were used to calculate body mass index (BMI; kilograms per square meter). Percentiles for BMI were determined to be specific to sex and month of age using the algorithms of the Centers for Disease Control and Prevention (based on the 2000 Centers for Disease Control and Prevention growth charts) and used to classify study participants. Statistical significance of the results was evaluated by SPSS version 13.

RESULTS

Results are summarized in Table **1** and Figs. **1-3**. There were a total of 131 patients and 20 healthy controls. Out of 131 patients, 88 were grouped in NDHL (males 49, female 39) and 43 in DHL group (males 24 and females 19). Average ages were 45.8 y, 49.1 year and 35 years, respectively in NDHL, DHL and healthy groups. BMI was more or less similar in NDHL and DHL groups where as 24.5 kg/m2 in healthy group. Waist hip ratio was also found to be similar in all three groups. Lipid components such as TC, TG LDL, Apo A and B and Lp (a) in healthy controls was noted to be in normal range according to specified reference value. However, in both DHL and NDHL groups all mentioned parameters showed significantly higher concentrations when compared with healthy control group exhibiting level of significance ranging from $P < 0.01$ to $P < 0.001$. In addition, glucose was significantly higher ($p < 0.01$) in DHL group only, when compared with NDHL and healthy groups. Simultaneous comparison of specific parameters in all groups depicts that LDL in NDHL group was significantly higher ($P< 0.001$) than healthy group but

Table 1A. Anthropometric Indices in Non-Diabetic (n = 88) and Diabetic (n = 43) Hyper-Lipidemic Patients

Parameters	H (n = 20)	NDHL (n = 88)	DHL (n = 43)
Age, years	35.0±4.1	45.8±12.6	49.1±5.2
BMI, kg/m2	24.5±3.8	31.3±3.3	30.5±4.4
WHR	0.82±0.05	0.94±0.09	0.97±0.04

Results are expressed as Mean ± SD; BMI = Body mass index; WHR = waist/hip ratio; NDHL = non-diabetic, hyperlipidaemic; DHL = diabetic hyperlipidaemic; H = healthy non-diabetic non-hyperlipidaemic.

Table 1B. Biochemical Parameters in Non-Diabetic (n = 88) and Diabetic (n = 43) Hyper-Lipidemic Patients

Parameters	H (n = 20)	NDHL (n = 88)	DHL (n = 43)
TC, mg/dl	151±11.4	244±41.2[d]	274±31.2[a, d]
TG, mg/dl	105±9.6	262±39.3[d]	289±32.4[d]
HDL, mg/dl	56.0±4.67	47±6.31	45±5.43
LDL, mg/dl	112±9.78	166 ±15.1[C]	170±11.23 [d]
Apo A, mg/dl	111± 10.11	140±12.12[d]	146±21.12 [d]
Apo B, mg/dl	89± 5.48	169±18.47[d]	182±16.11[a]
Glucose, mg/dl	76±5.2[b]	90±3.7	155±13.23
Uric acid, mg/dl	3.2± 0.31	4.2 ±0.82	4.7±0.51
Lp(a), mg/dl	29.2± 4.67	51.0± 5.1[d]	46.3 ±3.67[d]

Results are expressed mean ± SD.
[a] Significantly differ from NDHL group ($P< 0.05$) and HL ($P < 0.001$).
[b] Significantly different from DHL group ($p < 0.01$).
[C] Significantly different from Healthy group ($p < 0.01$).
[d] Significantly different from other members of group ($p < 0.01$).
NDHL = non-diabetic, hyperlipidaemic; DHL = diabetic hyperlipidaemic; H = healthy non-diabetic non-hyperlipidaemic; TC = total cholesterol; TG = triglycerides; LDL = low-density lipoproteins; HDL = high-density lipoproteins.

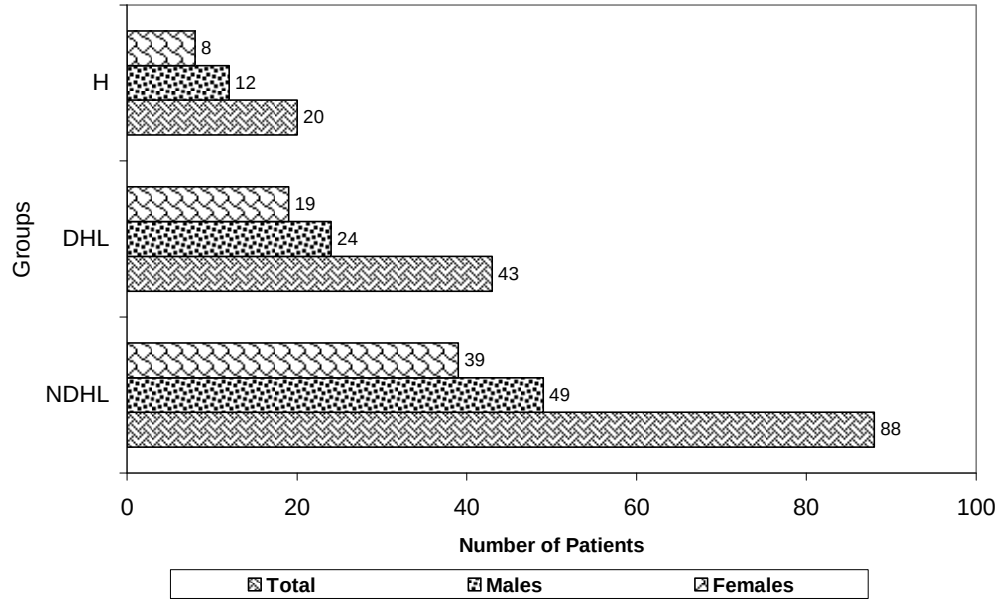

Fig. (1). Total and gender-wise distributin of patients and control in non-diabetic hyperlipedimic and healthy control groups.

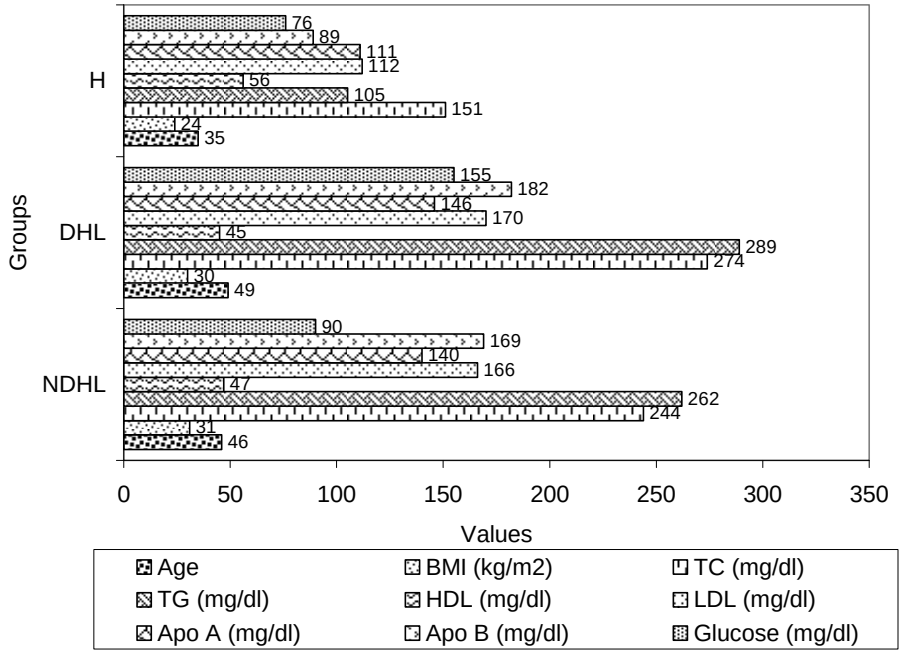

Fig. (2). Anthropometric indices and biochemical parameters in non-diabetic and diabetics hyperlipidemic patients.

comparatively within the similar range of DHL group. Moreover, TC and Apo B concentrations in DHL was noted to be moderately high when compared with NDHL group ($P< 0.05$) but significantly higher when compared with healthy group ($P< 0.001$). The assessment also reveals that Apo B component showed a much higher concentration in both NDHL and DHL groups than Apo A. In present study, the elevated concentration of TC and TG in NDHL and DHL groups depicts a hyperlipidemic state.

DISCUSSION

It is reported that the existing lipoprotein abnormalities in type 2 diabetes are related to increased serum triglycerides, decreased HDL concentrations, presence of increased amounts of LDL in the circulation and increased postprandial lipaemia [12,16,19]. Moreover, Hyperlipoproteinemia, when occurred due to lipoprotein abnormalities or dysfunction, is regarded as one of the most important risk factors for the

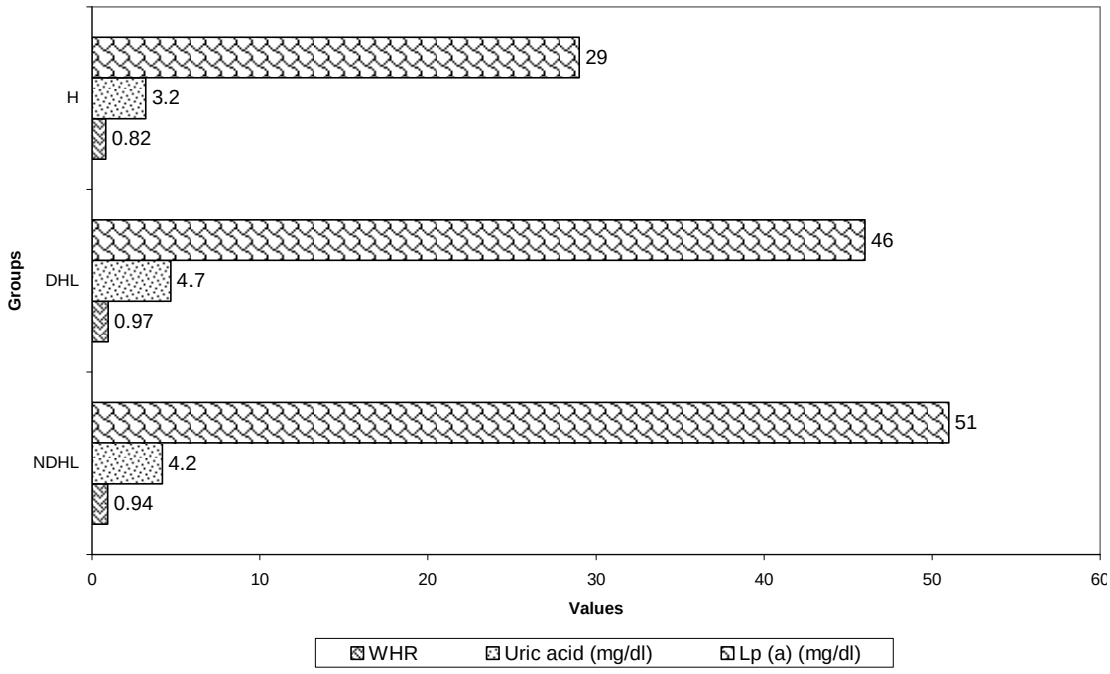

Fig. (3). Anthropometric indices and biochemical parameters in non-diabetic and diabetics hyperlipidemic patients.

development of atherosclerosis diseases. Several studies indicated that in addition to the routine determinations of triglycerides and cholesterol, quantitative determination of the corresponding apolipoproteins is also important for proper diagnosis and management. One of such specific component would be Apo B, which is a carrier protein for low density lipoprotein (LDL b-lipoprotein). Apo B determination noted to be useful in the differential diagnosis of hyperlipoproteinemia as a replacement for the complicated determination of LDL (b) cholesterol by ultracentrifugation. When evaluated in a normal population, the Apo B determination usually detects only b-lipoprotein or LDL. However, in hyperlipemic subjects (especially type IV), the results is also affected by the Apo B content of the pre-b-lipoproteins or VLDL [16]. Another component Lp(a) and its role in diabetes is a matter of debate and still needed to be explored thoroughly [20]. Few and conflicting data are available in the literature on the association between Lp(a) levels and the severity of coronary artery disease (CAD) in diabetic patients. The reported data suggest that Lp(a) levels and apo(a) polymorphism may be reliable predictors of CAD severity in type 2 diabetic patients [21].

It has been stated that these lipid abnormalities are often present before the clinical onset of diabetes and are known to become worse with the development of diabetic long-term complications such as nephropathy [16]. A study carried out in Kuwaiti population, agrees with our study as well as documented that the commonest lipid abnormalities seen in diabetic patients are, hypertriglyceridaemia with low HDL levels and variable LDL levels. Interestingly non diabetic but hyperlipidemic group (NDHL) also demonstrated similar pattern, but in a lower range as compared to DHL. It is also been noted that there were important differences in the statistical relationships between LDL and HDL and their respective apolipoproteins, apo B and apo A-1, in diabetic, non-diabetic and healthy subjects [22]. Similar pattern was reported in selected diabetic and non-diabetic Kuwaiti population [16,22]. Moreover, Lp(a) levels were somewhat similar in our study in both NDHL and DHL group but significantly higher than the healthy group.

Several studies had established that Apolipoprotein A (Apo A) and more specifically its sub-form A-1, is the main protein component of HDL and accounts for approximately 65% of the total protein content of HDL. It is widely known that low-density lipoprotein cholesterol (LDL-C) is an established risk factor for atherosclerosis [23]. However, recent research reported that serum levels of apolipoprotein B (Apo B) and Apo B to apolipoprotein A-1 (Apo A-1) ratio were better predictors of atherosclerotic vascular disease compared with LDL-C [23].

Recently it was reported that in youth with type 1 diabetes, elevated apoB and dense LDL were not highly prevalent, whereas elevated apoB and dense LDL were common lipoprotein abnormalities in youth with type 2 diabetes. The prevalence of these risk factors substantially increased with poor glycemic control in both groups, stressing the importance of achieving and maintaining an optimal glucose control [24]. A previous study carried out in diabetic and non-diabetic patients showed the ratio of apoB/LDL cholesterol ratio was significantly higher ($P<0.002$) among diabetic compared to nondiabetic subjects. Furthermore, it was also observed that the diabetic subjects with ischaemic heart disease (IHD) had significantly higher ($P<0.003$) apoB/non-HDL cholesterol ratio compared to

those without IHD. These findings suggest that the ratios of apoB/LDL cholesterol and apoB/non-HDL cholesterol may have a role in the risk stratification of diabetic patients with dyslipidaemia [25]. In two groups of hemodylasis patients, diabetic and non-diabetic, higher triglyceride and IDL cholesterol (P <.001), and lower high-density lipoprotein (HDL) cholesterol (P <.01) and apo A-I (P <.001) levels were noted as compared to the control group, even after adjustment for age and body mass index (BMI). However, no differences were found in lipid, lipoprotein, and apoprotein concentrations between diabetic and nondiabetic hemodialysis (HD) patients, except for high LDL triglyceride content of diabetic HD patients (P <.01) [26].

A study carried out earlier showed outcomes which are in agreement with our study, where a group of hypertriglyceridemic subjects had shown increased non-high density lipoprotein cholesterol (non-HDLc) components, and several (n = 24) showing increased apoB, as compared to normal triglyceridemic group, where as considerable number (n = 44) shown increased non-HDLc, and a much higher number (n = 68) had increased apoB [27]. Furthermore, as seen in our study, decreased Apo A appears to be a main component of the dyslipidaemic serum profile observed in diabetic patients as well as those with atherosclerotic occlusive disease of the lower extremities [28]. Perceptively, it was reported that increased Lp(a) levels is an independent risk factor and decreased HDL-cholesterol is also involved in the dyslipidaemic profile [28]. Similarity with our outcome have been reported earlier where dyslipidemic profile was characterized by increased triglyceride level, decreased apolipoprotein A1 level and small dense LDL associated with both NIDDM and non-diabetic subjects [29].

It is concluded that diabetes and hyperlipidemia are important risk factors. Additionally higher levels of Apo B and A and that of higher Apo B than Apo A are indicative of dyslipidemic state and thus significant parameters for assessing the prevailing conditions and extent of risk for developing coronary heart disease (CHD) and atherosclerosis.

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