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Serum Lipid and Lipoprotein Profile in Nigerian Patients with Haematological Malignancies

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Abstract

Purpose: To evaluate the changes in lipid and lipoprotein patterns in adult patients with haematological cancers with any possible risk of cardiovascular event.
Patients and Methods: The clinico-pathological types of haematological cancers, body mass index and ages of the of all 74 haematological cancer patients attending University of Benin Teaching Hospital, Benin City, Nigeria between January 2005 and September 2008 were evaluated. The serum lipid and liporprotein levels of the blood samples collected from the patients were assayed. The data were analysed and compared statistically with those of 45 health control subjects.
Results: The mean serum total cholesterol and low density lipoprotein in the patients (2.5±1.0mmol/l and 1.5±1.0mmol/l) were significantly lower than those of controls (4.1±1.1mmol/l and 2.4±1.1mmol/l), respectively (p=0.0004). However, the mean serum triglyceride of the patients was significantly higher than the controls (p=0.007).
Conclusion: Patients presenting with haematological malignancies have reduced levels of total serum cholesterol and LDL-cholesterol but elevated level of serum triglyceride.

Keywords: Haematological cancers, lipids and lipoprotein, cardiovascular risk.

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Introduction

Abnormal blood lipid profile have been found to be associated with cancer [1]. This abnormality is a common feature of both haematological malignancies and solid tumors.[1] The success of cancer chemotherapy is dependent on the ability to utilize biological differences between malignant and normal cells to selectively destroy the tumor cells [2]. One such difference that has been reported is that of the receptor-mediated cellular uptake of low density lipoprotein (LDL) [2]. Many studies have reported a return to normal values of lipid profile after effective chemotherapy [1]. Previous studies have found that certain malignant cell types have elevated LDL receptor activity and that the possibility of LDL consumption by tumor cells causes hypocholesterolaemia [3]. An inverse relation between plasma cholesterol and the occurrence of cancer has also been indicated [3]. Lipid parameters are therefore considered as reliable markers of complete remission and may be useful in the follow up of cancer patients [1]. However, there is paucity of information on the role and the profile of lipids and lipoprotein levels in haematological malignancies seen in Africans.

In this study, the profile of serum lipids in haematological cancer patients was examined with the aim of elucidating the type of lipoprotein disorders associated with the cancers. This is aimed at evaluating the changes in lipid pattern and the possible risk of cardiovascular event in adult patients with haematological cancers.

Patients and Methods

All patients with haematological malignancies attending the Oncology clinics and those admitted to in the Medical wards of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria were prospectively studied (July 2007-December 2008). The clinico-pathological types of haematological cancers, the ages of the patients, anthropometric indices (body mass index, BMI), and lipid and lipoprotein levels (LPA) of the patients were analysed. The various haematological malignancies were diagnosed based on typical clinical features, standard cytomorphological and histological findings including type-specific diagnostic criteria. The BMI at baseline and at each respective age was calculated using the formula: weight (in kilograms) at the given age divided by baseline height squared (in meters). BMI ≤19 was considered underweight, 20-25 normal weight, 26-29 overweight and ≥30 obesity [4]. The blood lipid and lipoproteins assayed include serum total cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C). The LPA levels of 74 apparently healthy age-and-sex matched subjects without any history of clinical disorders and having no diseases that could affect the blood lipid profile served as controls.

Clinico-pathological and LP levels were analyzed after adjusting for age, cigarette smoking, alcohol ingestion, hypertension and diabetes mellitus. The Ethical committee of the hospital granted approval for the study and informed consent was obtained from all patients. Patients received appropriate cytotoxic therapy for their type of haematological malignancies.

Laboratory and Lipid assay

The subjects were fasted overnight (12-14 hours) and 10 ml of venous blood was obtained from the antecubital veins after routine aseptic procedure. The LPA was assayed using already standardized and well established methodologies.[5-8] All assays were performed using kits manufactured by Human Diagnostic Laboratory (Wiesbaden, Germany). Total cholesterol (TC) was done using the modified Liebermann-Burchards method of Abell et al [5], and high density lipoprotein-cholesterol (HDL-C) by precipitation method [6]. Triglyceride (TG) was assayed using enzymatic colorimetric

method after hydrolysis of the TG [7]. Low density lipoprotein-cholesterol (LDL-C) was calculated by indirect method using Friedewald et al's [8] equation summarized as

$$[LDL-C]=[TC]-[HDL-C]-\frac{[TG]}{2.2}$$

The current Adult Treatment Panel (ATP) III [8] in comparing the values was adopted and all concentrations were given in millimoles per litre.

Data analysis

Statistical multivariate analysis of data obtained was performed using Instat Graph Pad software version 2.05a. Means and SD were determined for quantitative data and frequency determined for categorical values. At 95% confidence interval, any 2-tailed p value <0.05 was considered statistically significant.

Results

A total of 74 consecutive patients with hematological cancers were seen during the study. This comprised 46 males (62.2%) and 28 females (37.8%) with a male-to-female ratio of 1.6:1. These were compared with 45 non-cancer apparently healthy controls (25 males and 20 females) who were pre-screened and found without any history of clinical disorder. The mean age of the patients' was 49.2±15.9 yr with a median age of 55 yr (range, 18-80 yr).

The haematological malignancies consisted of 32 (43.2%) chronic leukaemias (18 chronic myeloid leukaemia (CML), 12 chronic lymphocytic leukaemia (CLL) and 2 hairy cell leukaemia, HCL); 18 (24.3%) lymphomas (12 non Hodgkin's lymphoma, NHL and 6 Hodgkin's lymphoma, HL); 12 (16.2%) multiple myeloma; 10 (13.5%) acute leukaemia (6 acute lymphoblastic leukaemia, ALL and 4 acute myeloblastic leukaemia, AML); and 2 (2.7%) had aplastic anemia. Lymphoma and chronic leukaemias were the most common haematological cancers seen.

The results of total serum lipid and lipoprotein levels of the cancer patients combined compared with controls are shown in Table 1. Mean basal levels of TC and LDL-C of the patients was significantly lower than the mean basal level observed in the controls ($p<0.001$). TG of the cancer patients was significantly higher than that observed in controls ($p=0.007$). The ratio of TC to HDL-C in cancer patients was 2.5 compared to the control value of 3.5. The TG to HDL-C ratio, which is a predictor of coronary events, was 3.3. There was no significant difference in mean BMI between the controls and the patients ($p>0.05$) and majority of the patients (56.8%) were within the normal weight category while 6.76% were obese.

The overall mean serum lipid and lipoprotein levels in the different haematological cancers including chronic leukaemia, lymphomas and multiple myeloma compared with controls is shown in Table 2. TC and LDL-C of chronic leukaemia patients was significantly lower

Table 1: The mean serum lipid and lipoprotein findings of combined haematological cancers at presentation over the study period

Parameter	Patient value (n=74)	Control value (n=45)	P value
Total cholesterol (mmol/l)	2.7±41.1	4.1±1.1	<0.0001
Triglyceride (mmol/l)	1.6±0.8	1.2±0.4	0.007
LDL-C (mmol/l)	1.5±1.0	2.4±1.1	0.0004
HDL-C (mmol/l)	1.1±0.7	1.2±0.3	ns
BMI (kg/m^2)	23.0±3.4	23.9±4.2	ns

Table 2: The mean serum lipid and lipoprotein findings in controls, chronic leukaemia, lymphomas and multiple myeloma

Parameters	Haematological cancers	Controls (n=45)	P values
Chronic leukaemia (n=32)			
Total cholesterol (mmol/l)	2.5±1.0	4.1±1.1	<0.0001
Triglyceride (mmol/l)	1.6±0.8	1.2±0.4	0.0036
LDL-C (mmol/l)	1.6±0.8	2.4±1.0	0.0007
HDL-C (mmol/l)	1.2±0.8	1.2±1.3	ns
Lymphomas (n=18)			
Total cholesterol (mmol/l)	3.7±1.1	4.1±1.1	ns
Triglyceride (mmol/l)	2.0±0.8	1.2±0.4	0.0003
LDL-C (mmol/l)	1.8±1.4	2.4±1.0	ns
HDL-C (mmol/l)	1.2±0.8	1.2±0.3	ns
Multiple myeloma (n=12)			
Total cholesterol (mmol/l)	1.9±0.8	4.1±1.1	<0.0001
Triglyceride (mmol/l)	1.3 ±0.6	1.2±0.4	ns
LDL-C (mmol/l)	0.9±0.7	2.4±1.0	0.0003
HDL-C (mmol/l)	1.1±0.6	1.2±0.3	ns

than in controls while TG was higher than the values seen in controls (p=0.0036). The lymphoma patients only showed a significant increase in TG when compared with the controls (p=0.0003). In multiple myeloma patients, TC and LDL-C values were significantly lower compared with controls (p<0.001).

Discussion

The risk associations between lipid/ lipoprotein levels and different types of tumor/cancer remain controversial and largely unexplored [9]. The association between high cholesterol levels and increased risk of cancer has been an interesting area of investigation because the pathway for cholesterol synthesis may produce various tumorigenic compounds and because cholesterol serves as a precursor for the synthesis of many sex hormones linked to increased risk of various cancers.[10] The findings in this study could therefore serve to determine the pattern of lipid profile in order to evaluate whether there is a possible risk factor.

It was hypothesized that there could be hypercholesterolaemia and hyperlipoprotein-aemia in haematological cancer patients seen in Nigeria as hypercholesterolaemia is a risk factor for coronary events in older men and women.[L5] However, in considering TC and LDL-C as lipid risk factors, hypocholesterolaemia and hypolipoprotein-aemia were found, suggesting that there is no risk of cardiovascular disorders in these patients compared with normal individual. This is similar to Ishibashi findings of hypolipid in haematologic disorders [11]. The hypocholesterolaemia in cancer patients may be caused by the possibility of elevated LDL-C receptor activities in the malignant cells [3]. During a chemotherapy regimen in a CML patient a reciprocal relation between LDL-C levels and the degree of leucocytosis and splenomegaly was found [12]. It was reported that tumor load, presence of an enlarged spleen and changes in lipid metabolism of circulating cells contributed to

the reduction in LDL-C levels leading to the hypolipoproteinaemia.

The association between haematological cancer/solid tumors and blood lipid/ lipoprotein profile has been reported to be altered [13,14]. Abnormal lipoproteins as shown by agarose gel electrophoresis has been reported as far back as 70 yr ago in multiple myeloma where presence of extra lipoprotein fractions was shown [15]. The haematological cancer patients studied with the exception of patients with lymphoma, showed significantly lower TC, LDL-C and HDL-C than age-and-sex matched non-cancer subjects along with high levels of serum TG. These are similar to the findings of Fiorenza et al [13] that the lowest values of TC, LDL-C and HDL-C are found in haematological cancer patients. They reported that the abnormality which is a common feature of both haematological and solid tumors is not entirely explained by poor nutrition. This is corroborated by the non significant BMI levels found in our patients. Cerhan et al in a study also found no evidence that height, weight, body mass or physical activity play important roles in NHL in particular.[16] However, in other studies several anthropometric measures, including body mass[17] and height [18] have been suggested as NHL risk factors.

The high lipid levels and their ratios may pose a threat by predisposing the cancer patients to coronary events which may contribute to mortality. The TC: HDL-C ratio of 2.5 suggests that these patients are not exposed to higher risk than normal people; but the TG: HDL-C ratio which is a strong predictor of future coronary events was 3.3, showing the potential high risk to the patients. This could have arisen from the combined grouping of the cancer patients at the different disease stage. According to Foder et al[19] in their study on target lipid values and risk level, they suggested that patients' values should be kept below 4 in very high-risk patients.

The decrease HDL-C found in this study is similar to the observation of another study which demonstrated that decrease in HDL-C is dependent on disease stage [20]. However, updated National Cholesterol Education Program Adult Treatment Panel III guidelines emphasize that a low level of HDL alone or in association with hypertriglyceridemia increases the risk of cardiovascular disease [21], but our patients had low, non significant level of HDL-C. This supports current understanding that HDL-C exerts antiatherogenic effect by transporting cholesterol from peripheral tissues back to the liver for excretion. Hypertriglyceridaemia found in our cancer patients has been implicated as an increased risk factor in coronary artery disease (CAD) development; but the increased triglyceride is said to be a risk factor that is modifiable with health education and dietary controls. The total lipaemia and lipoprotein fraction alterations observed in a study make the diagnostic value of atherosclerotic threat in patients with CLL doubtful with the use of this parameters [20].

Lipid lowering agents for LDL-C has been repeatedly shown in large clinical trials to improve survival dramatically and reduce cardiac events in both primary and secondary prevention.[22]The patients though few in number were not prone to cardiovascular events since we did not find elevated level of TC and LDL-C. The V-shaped associated between LDL-C and cancer risk suggests multiple mechanisms being involved [10].

Conclusion

Patients presenting with haematological malignancies have reduced levels of total serum cholesterol and LDL-cholesterol but elevated level of serum triglyceride. We however advocate the assessment of lipid profile regularly in patients with haematological malignancies.

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