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Dyslipidaemia and Albumin Levels in Male Subjects with Prostate Disorders

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Abstract

Prostate cancer accounts for 11% of all male cancers in Nigeria and its increasing prevalence among men in their early 50's has become a public health concern. This present study determined dyslipidaemia and albumin levels in Prostate disorders. A total of 139 human subjects were randomly recruited for the study from the Urology Unit of the University of Benin Teaching Hospital. Subjects were grouped into benign prostatic hyperplasia, prostate cancer subjects (on drug and without drug therapy). Blood samples obtained from subjects were used to assess lipid profiles (LP), Albumin and prostate specific antigen (PSA) using ELISA and spectrophotometry method. Results revealed higher mean level of LP [total cholesterol (203.44±37.54), triglyceride (115.24±37.45), high density lipoprotein cholesterol (43.96±9.45), low density lipoprotein cholesterol (135.68±39.70) and very low-density lipoprotein cholesterol (23.04±7.50)] in prostate cancer subjects when compared with control subjects. Significantly lower mean level of Albumin (27.47±3.60) and higher mean level of PSA (32.26±26.44) were observed in prostate cancer subjects when compared with controls. Dyslipidaemia is associated with prostate cancer and could be a consequence of its progression, the lower level of albumin could be used as a prognostic factor in monitoring metabolic stability in these subjects.

Keywords: Dyslipidaemia, Albumin, Prostate Disorders

Introduction

Worldwide, prostate cancer is the most common male genital cancer (Haas and Sakr, 1997). Several factors, including genetics have been implicated in the development of prostate cancer (Baade *et al.*, 2009). Prostate cancer has accounted for about 11% of all male cancers in Nigeria (Ogunbiyi and Shittu, 1999). Studies from Kano, Zaria, Benin, and Maiduguri (Mohammed *et al.*, 2003; Dawam *et al.*, 2000) showed prevalence of prostate cancer between 6.15% and 16.5%.

A complete understanding of the causes of prostate cancer remains elusive (Hsing and Chokkalingam, 2006). Although the specific etiological factors of cancer are not yet known, considerable evidence indicate that both genes and the environment play a role in the evolution of prostate cancer. Diet may not initiate prostate cancer but rather may promote its progression. Fat consumption on the other hand has long been suspected to be a risk factor for prostate cancer, high levels of dietary fat can stimulate proliferation of prostate cancer cells both in-vitro and in-vivo; while association between linoleic acid and prostate cancer has been reported (Gann *et al.*, 1994; Giovanucci *et al.*, 1993).

Early prostate cancer may present symptoms that are similar to benign prostatic hyperplasia such as frequent urination, nocturia (increased urination at night), difficulty starting and maintaining a steady stream of urine, haematuria (blood in the urine), and dysuria (painful urination). About a third of patients diagnosed

with prostate cancer have one or more such symptoms, while two thirds have no symptoms (Miller *et al.*, 2003). Serum albumin level has also been implicated as a prognostic factor in various cancers but has not been studied in early stage prostate cancer (Richter *et al.*, 2000).

This study is therefore aimed at assessing dyslipidaemia and albumin levels in male subjects with prostate disorders.

Materials and Methods

A total of 50 prostate cancer (PCa) subjects and 37 benign prostatic hyperplasia (BPH) subjects were recruited for this study. The PCa subjects were classified based on drug administration into those on treatments (n=22) and those without drug treatments (n=28). A total of 52 human subjects without evidence of prostatic disorders, urological dysfunction and history of drug therapy for prostate disorders were used as controls. They were grouped as follows: Group A: Controls; Group B: Benign prostatic hyperplasia (BPH) subjects; Group C: Prostate cancer (PCa) subjects; Group D: PCa subjects on drug therapy (PCADT) and Group E: PCa subjects without drug therapy (PCAWDT)

Blood collection

About 4 ml of blood sample was collected by venipuncture and dispensed into plain tubes for analyses of Prostate Specific Antigen assay (PSA), serum albumin and lipid profile.

Inclusion/exclusion criteria

Participants with clinical evidence of BPH and PCa with no other underlying disease or other forms of cancer were included in this study. Also, individuals with no history of PCa, urological dysfunction or other forms of cancer were recruited to serve as control subjects. Patients found to have urinary tract infection or Prostatitis were excluded from the study.

Drug administration

All prostate cancer subjects on treatment were on Goserelin-implant (3.6 mg SC q 28days) monthly and 150 mg of Flutamide daily (50 mg pills 8 hourly). These were administered for 12 weeks prior to radiotherapy.

Serum Albumin Analysis

Test tubes were labeled according to the number of tests. Additional batch of tests were carried out. Into the reagent blank tube, 0.01 ml of distilled water was added. 0.01 ml of the standard was added to the standard test tube, while 0.01 ml of the participants' serum was added to the remaining test tubes according to their numbers. Bromocresol reagent (1.0 ml) was added to all the tubes and mixed properly. The tubes were then bench incubated for 2 minutes and read at 630 nm (Doumas *et al.*, 1971).

Prostate Specific Antigen assay

Exactly 0.025 ml of the calibrators, samples and controls were pipetted into assigned micro titer wells; 0.1 ml of the immobilized goat antibody reagents were then added to each well and swirled gently for 20 seconds to mix. Left for 60 minutes and washed to remove any unbound antigen. 0.1 ml of the monoclonal anti-PSA-HRP conjugate was then added to each well and allowed to react with the immobilized antigen for 60 minutes at room temperature resulting in the PSA molecules being sandwiched between the solid phase and enzyme-linked antibodies. The wells were later washed with water and 0.1 ml of TMB reagent added for 20 minutes and left to stand at room temperature. The resulting blue colour development was stopped by the addition of 0.05ml stop solution changing the color to yellow and read at 450 nm (Wild, 1994).

Total Cholesterol Assay by Enzymatic Method

To 1000 μ L of reagent present in test tubes labeled blank, sample tubes, control tube and standard tube 10 μ L of water, sample, control serum and standard was added respectively, mixed thoroughly and incubated for 10 minutes at 37 °C. The absorbance of test, standard and control were read against reagent blank using a spectrophotometer at 500 nm (Allain *et al.*, 1974).

Calculation:

Concentration of cholesterol in sample = ΔA_{sample}
X Concentration of Standard $\Delta A_{\text{standard}}$

Triglyceride Assay by Enzymatic Method

To 1000 μ L of reagent present in test tubes

labeled blank, sample tubes, control tube and standard tube 10 µL of water, sample, control serum and standard was added respectively, mixed thoroughly and incubated for 10 minutes at 37 °C. The absorbance of test, standard and control were read against reagent blank using a spectrophotometer at 500 nm (Buccolo and David, 1973).

Calculation:

$$\text{Concentration of Triglyceride} = \frac{\Delta A_{\text{sample}}}{\Delta A_{\text{standard}}} \times \text{Concentration of Standard (mg/dl)}$$

HDL-Cholesterol Assay by Precipitation

Stage 1: Precipitation

Test tubes were labeled sample and control and 200 µL of sample and 200 µL of control serum were added to the tubes respectively. 500 µL of precipitant was added to all the tubes and were mixed thoroughly. The tubes were left to stand for 10 minutes at room temperature and spun at 4000 rpm for 10 minutes (Benzie, 1979).

Stage 2: Enzymatic Assay

A 50 µL each of water, supernatant of test, supernatant of control sera and standard solution were added to the appropriate test tube labeled reagent blank, sample, control and standard tube respectively. 1000 µL of reagent were added to

all the tubes, mixed thoroughly and incubated for 10 minutes at 37 °C and read at 500 nm (Benzie, 1979).

Calculation:

- HDL Cholesterol:
 Concentration HDL Cholesterol in supernatant = $\frac{\Delta A_{\text{sample}}}{\Delta A_{\text{standard}}} \times \text{Concentration of Standard (mg/dl)}$

LDL Cholesterol (Friedewald *et al.*, 1972)
 LDL Cholesterol = Total Cholesterol – (Triglycerides/5 – HDL Cholesterol)

Statistical Analysis

The data obtained from the different groups employed was subjected to analysis of variance (ANOVA) and post hoc using LSD at 0.05 level of significance (SPSS 16.0, 2007).

Results

The lipid profile of groups A, B, C, D and E is illustrated in Table 1. The difference in mean serum concentrations of total cholesterol, serum concentrations of triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol and very low-density lipoprotein cholesterol of groups A, B, C, D and E were all significant (p<0.001).

Table 1: Lipid profile of Groups A, B, C, D and E.

Subjects	Total cholesterol(mg/dl)	Triglycerides (mg/dl)	High- density lipoprotein cholesterol (mg/dl)	Low- density lipoprotein cholesterol (mg/dl)	Very low-density lipoprotein cholesterol (mg/dl)
GROUP A (N=52)	-----	97.31 ± 19.17	53.35 ± 7.71	82.10 ± 33.57	19.90 ± 3.95
GROUP B (N=37)	223.22 ± 22.27	173.97 ± 29.97	56.03 ± 7.94	132.49 ± 25.10	35.16 ± 6.02
GROUP C (N=50)	203.44 ± 37.54	115.24 ± 37.45	43.96 ± 9.45	135.68 ± 39.70	23.04 ± 7.50
GROUP D (N=22)	188.27 ± 20.83	112.18 ± 38.38	46.91 ± 10.48	119.45 ± 25.78	22.44 ± 7.68
GROUP E (N=28)	215.36 ± 43.42	117.64 ± 37.22	41.64 ± 8.01	148.43 ± 44.27	23.51 ± 7.46
p-value	0	0	0	0	0
f-value	59.74	75.67	25.88	38.06	75.11
POST HOC					
GROUP A VS GROUP B	0	0	0.142	0	0
GROUP A VS GROUP C	0	0.003	0	0	0.009
GROUP A VS GROUP D	0	0.069	0.004	0	0.123
GROUP A VS GROUP E	0	0.007	0	0	0.018
GROUP B VS GROUP C	0.004	0	0	0.667	0
GROUP D VS GROUP E	0.003	0.55	0.034	0.004	0.557

*Data is expressed as Mean ± SD
 Statistical Significance=p<0.05

Table 2 illustrates albumin concentrations and PSA levels of groups A, B, C, D, and E. The mean serum concentrations of albumin and concentrations of groups A, B, C, D, and E were significantly different ($p < 0.001$). Post hoc

analysis on the other hand showed that Group B, C, D and E had significantly higher levels of mean serum concentrations of Prostate specific antigen than Group A at ($p < 0.001$).

Table 2: Albumin concentrations and PSA levels of Groups A, B, C, D and E.

Subjects	Albumin Concentration (g/l)	PSA (ng/ml)
GROUP A (N=52)	38.77 ± 3.10	1.72 ± 1.34
GROUP B (N=37)	35.61 ± 2.86	32.26 ± 26.44
GROUP C (N=50)	27.47 ± 3.60	15.85 ± 7.23
GROUP D (N=22)	27.06 ± 3.98	15.84 ± 11.60
GROUP E (N=28)	27.79 ± 3.31	45.17 ± 27.77
p-value	0.000	0.000
f-value	110.241	33.486
POST HOC		
GROUP A VS GROUP B	0.000	0.000
GROUP A VS GROUP C	0.000	0.000
GROUP A VS GROUP D	0.000	0.002
GROUP A VS GROUP E	0.000	0.000
GROUP B VS GROUP C	0.000	0.000
GROUP D VS GROUP E	0.444	0.000

*Data is expressed as Mean ± SD

Statistical Significance= $p < 0.05$

Discussion

This study was performed to determine the neutrophil phagocytic function, lymphocyte transformation and biochemical changes in benign prostatic hyperplasia and prostate cancer subjects.

High mean values of lipid levels (TC, Triglycerides and LDH) in BPH and PCa might indicate an association of high lipids in these conditions. This agrees with the findings of Nandeesh *et al.* (2006) and Gokce *et al.* (2010) that reported higher cholesterol values in BPH and PCa subjects than in the control. Nandeesh *et al.* (2006) suggested that cholesterol-lowering medication may reduce the risk in BPH patients. Santos and Schulze (2012) further elaborated on the increased level of lipids and reported that the increased cholesterol as well as mobilization of free fatty acids from triacylglycerol may lead to an increase in the level of lipids with a signaling function that can contribute to tumorigenesis.

This holds true because of the possible lipogenic nature of prostate cancer cells which tend to alter their metabolic priorities towards the synthesis of macromolecules.

The low levels of HDL and VLDL cholesterol observed in subjects with BPH could have been as a result of higher cholesterol and triglyceride levels due to increased utilization to mop up esterified lipids. Lloyd *et al.* (2010) in their investigation on the role of dietary fat in prostate cancer observed that a diet high in fat does not increase prostate tumor growth. They observed that dietary fat could be affected by formulation, body mass index and body metabolism which vary from person to person. This present study does not agree with their opinion due to the fact that from our investigations, lipid levels of BPH subjects were lower amongst those on therapy over time. Also, we observed that as the total cholesterol and triglyceride levels decreased, the high-density lipoprotein increased, indicating

that the initial lower levels were affected by higher serum cholesterol and triglyceride.

Significantly lower levels of total cholesterol (TC) and LDL in PCa subjects on drug treatments when compared with PCa subjects without drug treatment could have been as a result of the effects of the Goserelin-implants (Androgen Deprivation therapy) on the cancer cells inhibiting lipogenesis. However, the TG, HDL and VLDL levels of both PCa subjects irrespective of treatment status showed no significant difference. Contrasting reports by Saylor and Smith (2009) on the metabolic complications of Androgen deprivation therapy for prostate cancer showed higher TC and HDL levels in prostate cancer patients. Also, Smith *et al.* (2008) showed normal TC and lower HDL levels in men receiving Androgen deprivation therapy.

The significantly low Albumin levels and high PSA levels of BPH and PCa subjects is consistent with data obtained by Gokce and Colleagues (2010) from urological investigations in prostate cancer subjects. They found PSA levels to be significantly higher in BPH cases as against their controls. PSA levels are normally very low and disruption of the normalcy of the prostate by disease or trauma allows greater amount of PSA to enter the general circulation. Elevated serum PSA level is thus an important marker of many prostatic disease including BPH and PCa (Ramos *et al.*, 1999; Alexander *et al.*, 1996). Rosette *et al.* (2006) also reported high PSA values and proposed that the higher the PSA values, the greater is the probability of having prostate cancer as the level of PSA might predict the natural history of BPH meaning the chances of having PCa is strongly related with the serum value of PSA. Significantly lower levels of Albumin obtained correlate with the work of Zew (2013), who in his work on prediction of biochemical recurrence in PCa population, observed lower pre-operative serum Albumin which among other factors predicted lower survival outcome. This could be due to trans-capillary escape rate and increased catabolic rate of albumin due to inflammatory response with the release of interleukin-6, cytokines and other factors. The non-significant difference observed

in Albumin levels between prostate cancer subjects on drug treatment and those without drug treatment correlate with the study of Richter *et al.* (2000). He observed that albumin appears to be of clinical utility to augment assessment of pretreatment pathological stage and that serum albumin levels has been implicated as a prognostic factor in various cancers. Also, significantly lower PSA levels in prostate cancer subjects on drug treatment when compared with those without drug treatment could be as a result of the effect of Androgen Deprivation Therapy on the prostate cells.

Conclusively, high TC levels observed in BPH and PCa patients indicates that both conditions are associated with hyperlipidaemia while the low albumin level in BPH and PCa subjects can be an important prognostic factor in monitoring metabolic stability in these conditions.

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