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Prostate disorders in an apparently normal Nigerian population 2: *Relationship with some biochemical parameters*

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Abstract

Globally, prostate disorders constitute a lot of health concern for men. Early identification of risk factors and groups at risk minimizes the adverse effects of these disorders. The possible relationship between prostate disorders and parameters like age, blood group, Rhesus factor, haemoglobin genotype, serum total cholesterol level and fasting blood glucose concentration, in Nsukka was studied. A total of 101 apparently normal subjects who were not on prescription drugs and who did not have sex or prostatic massage at least two days before sampling were recruited for assays. Standard procedures were used for all the assays. There was no significant mean difference in the Prostatic acid phosphatase (PAP) means of the different groups, per parameter, ($p>0.05$), except for age where a significant mean difference ($p<0.05$) was noticed between those aged 40-49 and 70+. PAP levels correlated positively with PSA ($r = 0.670$, $p<0.01$), age ($r = 0.271$, $p<0.01$). It also correlated positively with serum total cholesterol ($r = 0.528$, $p<0.05$) in subjects older than 69 years only. No correlation was noticed between PAP and the other parameters measured ($p>0.05$ in each case). Age and serum total cholesterol (in those older than 69 years only) but not the other parameters, may predispose to prostate disorders.

Keywords: prostate disorder, age, serum total cholesterol, risk factor

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INTRODUCTION

Pathologies of the prostate reduce the quality of life of men and constitute a lot of men's health burden world-wide. Alterations in the endocrine system, heredity, diet, micro-organisms, environmental factors, etc, have been linked to prostate disorders[1,2]. Prostatic acid phosphatase (PAP) and prostate specific antigen (PSA) are enzyme markers used in the diagnosis of, and screening for, prostate disorders. Elevated levels of these prostatic secretions are an indication of a disorder of the prostate[3]. Due to the fact that early detection of prostate disorder is central to effective management of the patient, the identification of risk factors and groups more at risk would certainly reduce the state of morbidity and mortality from the disorders, thereby increasing, generally, the quality of life of men. This study set out to find out if there is a relationship, or not, between increased PAP and PSA levels in the serum and factors like age, blood group, Rhesus factor, haemoglobin genotype, serum total cholesterol level and fasting blood glucose concentration. This would help elucidate the involvement of these parameters as risk factors (or not) for prostate disorders.

MATERIALS AND METHODS

Subjects

A hundred and one (101) subjects were recruited from a pool of adult males aged forty (40) years or older, who had no apparent symptoms of ill-health and who were not on prescription drugs. Only those who did not have sex or prostatic massage at least two days prior to the day of sampling were recruited for the assays. The purpose of the study was explained to the participants and their consents gotten without coercion. No honoraria were paid to participants; however, results of the tests were communicated to individual participants personally.

Methods

Blood groups, Rhesus factors and haemoglobin genotypes were determined using the methods of Murakami[4], Donskov *et al.*[5] and Evans[6] respectively. Fasting blood glucose concentration was determined using the Roche Diagnostics[7] method. The method of Stein[8] was employed in estimating the level of serum total cholesterol. Serum prostatic acid phosphatase (PAP) level was determined by the method of Fishman and Lerner[9] while serum prostate specific antigen (PSA) level was determined by the method of Kuriyama *et al.* [10]. The data generated from the assays were analysed statistically using the version 11 of the SPSS for windows package.

RESULTS

Table 1 shows a progressive increase in the mean PAP values from the age range 40-49 to 70+. While the mean PAP value for those aged 40-49 years is at 1.62±0.10, that for those 70 years and older is at 2.89±1.77. A significant difference in the means of the PAP values of the age groups was seen between only the groups 40-49 and 70+ ($p<0.05$).

Table 1: Means ± standard deviations of the PAP values of the different age groups

Age Range (Yr)	N	Mean ± SD of PAP Concentration (U/L)
40-49	23	1.62±0.10
50-59	29	2.23±1.63
60-69	27	2.51±1.73
70+	22	2.89±1.77

Table 2 shows the mean PAP values of the different blood groups within the different age ranges. No significant difference was seen ($p>0.05$) in the means of the different blood groups with both the one-way analysis of variance and post hoc tests.

Table 2: Means ± standard deviations of the PAP values of subjects with different blood groups

	Prostatic Acid Phosphatase Values (U/L)									
	40-49		50-59		60-69		70+		All Together	
B.Grp	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N
A	1.35±0.82	6	2.53±2.00	12	2.19±1.49	6	1.85±1.00	6	2.09±1.55	30
AB	2.02±1.24	5	1.49±1.04	5	2.53±1.30	4	1.77±0.97	4	1.93±1.11	18
B	1.68±0.58	3	2.02±1.75	3	1.52±0.71	2	4.44±2.33	5	2.80±2.07	13
O	1.57±1.14	9	2.28±1.44	9	2.77±2.02	15	3.32±1.40	7	2.48±1.68	40

Table 3: Means ± standard deviations of the PAP values of subjects with different Rhesus factors

	Prostatic Acid Phosphatase Values (U/L)									
	40-49		50-59		60-69		70+		All Together	
RhF	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N
+ve	1.61±1.02	22	2.23±1.66	28	2.57±1.73	26	2.73±1.77	20	2.28±1.61	96
-ve	2.02±0.00	1	2.02±0.00	1	1.01±0.00	1	4.55±0.71	2	2.83±1.66	5

Table 4: Means ± standard deviations of the PAP values of subjects with different haemoglobin genotypes

	Prostatic Acid Phosphatase Values (U/L)									
	40-49		50-59		60-69		70+		All Together	
Genotype	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD	N
AA	1.60±1.13	17	2.14±1.75	22	2.50±1.92	17	2.75±1.86	18	2.25±1.72	74
AS	1.68±0.52	6	2.45±1.29	7	2.53±1.45	10	3.54±1.30	4	2.47±1.29	27

Table 5: Means ± standard deviations of fasting blood glucose concentrations and PAP values of subjects

		Fasting Blood Glucose (FBG) Concentration (mmol/l)	
Age	Factor	Normal	High
40-49	FBG	5.31±0.60	12.47±4.82
	PAP	1.57±0.90	2.02±1.75
	N	20	3
50-59	FBG	5.11±0.62	9.90±3.18
	PAP	2.16±1.69	2.69±1.17
	N	26	3
60-69	FBG	4.99±0.71	10.66±3.70
	PAP	2.35±1.79	3.23±1.32
	N	22	5
70+	FBG	4.80±0.60	-
	PAP	2.89±1.77	-
	N	22	-
All Together	FBG	5.05±0.65	10.95±3.64
	PAP	2.25±1.64	2.75±1.36
	N	90	11

Table 3 shows the values obtained for the PAP of the different Rhesus factors of the subjects, according to their respective age ranges. No significant difference ($p>0.05$) was observed between the PAP means of Rhesus positive and negative individuals, using the one-way analysis of variance test.

Table 4 shows the mean PAP values of the different age ranges within the haemoglobin genotypes found in the subjects. A one-way analysis of variance test revealed no significant mean difference ($p>0.05$) between the two groups of genotypes.

Table 5 shows the mean PAP values of subjects with normal and high blood glucose concentrations, reflecting their age ranges. A one-way analysis of variance showed no significant mean difference ($p>0.05$) in the PAP values of normal and high blood glucose groups.

Table 6 shows the mean PAP values of the three total cholesterol groups of the subjects with respect to their age ranges.

Table 6: Means ± standard deviations of serum cholesterol concentrations and PAP values of subjects.

		Serum Total Cholesterol Concentration (mmol/l)		
Age	Factor	Normal	Border line high	High
40-49	Cholesterol	4.15±0.67	5.66±0.22	8.50±2.02
	PAP	1.75±1.04	1.52±0.71	1.35±1.04
	N	15	2	6
50-59	Cholesterol	4.26±0.90	5.80±0.00	7.51±1.86
	PAP	2.34±1.84	2.02±0.00	1.95±1.18
	N	20	1	8
60-69	Cholesterol	4.38±1.01	5.79±0.28	6.93±0.68
	PAP	3.33±2.87	2.11±1.05	2.36±1.13
	N	7	11	9
70+	Cholesterol	4.90±0.00	5.72±0.33	7.06±0.74
	PAP	4.04±0.00	2.33±0.96	3.66±2.53
	N	1	13	8
All together	Cholesterol	4.25±0.82	5.74±0.29	7.42±1.44
	PAP	2.33±1.85	2.17±0.96	2.40±1.74
	N	43	27	31

Table 7: Means ± standard deviations of the PAP values of PSA positive and negative subjects.

	Prostatic Acid Phosphatase Concentration (U/L)			
	PSA Positive		PSA Negative	
Age Range	Mean ± Standard deviation	N	Mean ± Standard deviation	N
40-49	-	-	1.62±0.10	23
50-59	8.08±0.00	1	2.01±1.21	28
60-69	9.19±0.00	1	2.25±1.12	26
70+	8.08±0.00	1	2.65±1.37	21
All Together	8.45±0.64	3	2.12±1.21	98

Table 8: Correlations between the parameters studied

	Age	**Blood Glucose**	**Total Cholesterol**	**PAP**	**PSA**
Age	1	-.174	.190	**.271***	.086
Blood Glucose	-.174	1	-.103	.101	-.085
Total Cholesterol	.190	-.103	1	**.528*****	**.573*****
PAP	**.271***	.101	**.528*****	1	**.670***
PSA	.086	-.085	**.573*****	**.670***	1

**correlation is significant at 99% confidence interval for all age ranges*
***correlation is significant at 95% confidence interval for all age ranges*
****correlation is significant at 95% confidence interval only for those older than 69 years*

No significant difference was found ($p>0.05$) between the mean PAP values of the three groups when both one-way analysis of variance and post hoc tests were carried out.

Table 7 shows the mean PAP values of PSA positive and negative subjects within their respective age ranges. A one-way analysis of variance showed a significant mean difference ($p<0.05$) between the PAP values of negative and positive subjects

Table 8 shows that PAP correlated positively with PSA ($p<0.05$, $r=0.67$) and age ($p<0.05$, $r=0.21$) in all the subjects. PAP also correlated positively with serum total cholesterol in only subjects older than 69 years ($p<0.05$, $r=0.528$). Blood groups, Rhesus factors and haemoglobin genotypes do not involve figures and are therefore not represented here.

DISCUSSION

PAP, in recent times, is useful in the care of patients whose tumours do not secrete PSA. It offers no additional benefit or information to PSA in monitoring therapy, and in diagnosis, screening, and staging of prostate cancer (and other prostate disorders). However, owing to the absence of the necessary equipment for a quantitative assay of PSA in the subjects, a semi-quantitative PSA test cassette was used and PAP was quantitatively assayed to corroborate the PSA results.

The results generated showed that all the positive PSA values were of the range 4-10ng/ml (test band weaker than reference band), and none of the PAP values exceeded 10U/L. There was a significant mean difference between the PAP values of PSA positive and negative subjects (Table 7) ($p<0.05$). A positive correlation was also found between PSA and PAP ($r = 0.670$) at 99% confidence interval (Table 8).

Only the mean PAP values of the age-ranges 40-49 and 70+ were statistically different at 95% confidence interval. A positive correlation was found between age and PAP. The progressive increase in PAP values with advancing age points to age as a major predisposing factor to prostate disorders. This is in tandem with an array of published scientific data[2,11,12,13].

The blood groups, Rhesus factors and haemoglobin genotypes of the subjects are markers that genetically classify the individuals

to some extent. Some reports have associated these factors with a variety of diseases[14,15].

At 95% confidence interval, no significant difference was found in the means of the PAP values of the four blood groups. This shows that blood group may not be a predisposing factor to the development of prostate disorders.

On checking the variation between the mean PAP values of both Rhesus positive and negative groups, no significant difference was seen between the groups at 95% confidence interval. The import of this is that the Rhesus factor of an individual may not play a key role in predisposing an individual to prostate disorders.

All the subjects studied were either HbAA or HbAS. None was HbSS, HbAC, HbSC or HbCC. Using the one-way analysis of variance test, no significant difference was detected in the mean PAP values of the HbAA and HbAS groups at 95% confidence interval. Thus the haemoglobin genotypes of the studied population did not affect their corresponding PAP values positively or negatively. Haemoglobin genotype may therefore not predispose an individual to prostate disorders.

Taking the upper limit for fasting blood glucose concentration[16] to be 6.66mmol/l, the subjects were divided into two groups – normal and high fasting blood glucose concentration groups. From The apparent increase in the mean PAP values of those with high blood glucose concentration when viewed against those with normal blood glucose concentration was not significant statistically ($p>0.05$). No significant correlation was also seen between fasting blood glucose concentration and PAP. The absence of statistically significant difference in the mean PAP values, and correlation between PAP and fasting blood glucose may be due to the large deviations from the means of each group. This suggests a lot of overlap in the exact values obtained from the biochemical assays.

Insulin release is, known to be, related to the rapidity of increase of the blood sugar after ingestion of carbohydrates. Non-fibre containing carbohydrates, otherwise known as insulin stimulating carbohydrates (ISCs) increase the level of insulin in the system. Hammarsten and Hogstedt[17] support the hypothesis of a causal relationship between high insulin levels and the development of BPH. Their results suggest that BPH is a component of the metabolic syndrome and that BPH patients may share the same metabolic abnormality of a defective insulin-mediated glucose uptake and secondary hyperinsulinaemia as patients with the metabolic syndrome. The result of this study, however, does not implicate fasting blood glucose concentration since there was no statistically established relationship between fasting blood glucose concentration and PAP or PSA.

Using the interpretation for total cholesterol levels found in the Randox Total Cholesterol kit, the subjects were divided into three groups – desirable/normal, borderline high and high total cholesterol concentration groups. The mean PAP values of those aged 40-49 decreased as their total cholesterol concentration increased. The same is true for those aged 50-59 as seen in Table 6. For the age ranges 60-69 and 70+, the mean PAP values increased with increasing total cholesterol concentration, but dropped with those with high total cholesterol concentration. There was no statistically significant difference in the mean PAP values of the three cholesterol groups at 95% confidence interval. There was also no significant correlation between total cholesterol and the other parameters assayed. However, when the age ranges were analysed separately and correlation checked, correlation was seen to exist between total cholesterol and PAP at 95% confidence interval for the age range 70+ ($r = 0.528$). This was not observed for the younger age ranges.

This may suggest that increasing serum total cholesterol may cause increases in PAP values and may predispose to prostate disorders, among the older people in the population but not the younger ones. Cholesterol is the backbone of steroid hormone synthesis. Dietary fat intake and endogenous synthesis of cholesterol are the major means through which serum cholesterol is known to increase. Bosland [18] suggests that dietary fat intake may affect the risk of prostate cancer (disorders) through an alteration of

androgen levels, production of free radicals and pro-inflammatory fatty acid metabolites and alteration of insulin-like growth factor levels in serum. Dagnelie *et al.*[19] support this view. Haas and Sakr[12] also reported an association of dietary intake of animal fat and increased risk of prostate cancer. The results of this study agree with these researchers only to the extent that the population of interest is 70 years and older. It appears that the younger ones have some capacity to forestall excessive conversion of cholesterol to steroid hormones (that, in excess, have been implicated with causing prostate abnormalities). The association may still be tenuous since carcinogenesis is a chronic process that takes decades to develop.

From the results we conclude that age and to some extent, serum total cholesterol may predispose to prostate disorders, going by the results obtained. Blood group, Rhesus factor, haemoglobin genotype and fasting blood glucose concentration may not have any significant effect on the development of prostate disorders. Probably a steady increase in serum total cholesterol by 70+ years irreversibly enhance the progression to malignant cells (clinical cancer) as against histologic cancer cells said to be found in all age groups. There is, however, some need to carry out a similar but expanded work in collaboration with hospitals that have urology and histopathology units where confirmatory tests can be done.

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