The Association between Metabolic Syndrome, Its Components and the risk of Prostate Cancer among Healthy Men in Northern Nigeria; A Community Survey.

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ABSTRACT

Background: Previous studies demonstrated that individual components of metabolic syndrome affect prostate-specific antigen levels negatively or otherwise in men. However the influence of metabolic syndrome on serum PSA is inconclusive and unknown in this community setting. The aim of the study was therefore to investigate the relationships between metabolic syndrome and its components with serum PSA levels. **Methods:** The survey was a cross sectional conducted in a semi urban community in Jigawa state, Northern Nigeria. The subjects comprises 352 healthy men. Simple convenient sampling technique was used to recruit consenting adults. The study protocols was approved by the local health authority. All persons with symptoms of prostitis or urinary obstruction were excluded. The data obtained included personal and anthropometric, while lipids, glucose, TSH and serum PSA were measured using ELISA technique. The IDF criteria of metabolic syndrome were used. Serum PSA levels of >5.0 ng/ml is considered as risk of prostate cancer. The data was analysed using SPSS 23 version. **Results:** A total of 352 adults were screened with mean age 37.8(9.4) years and mean serum total PSA of 2.73(4.10)ng/ml. The proportion found with total serum PSA >5.0ng/ml was 10.8% (38/350). Metabolic syndrome was found in 6.8% (24/350) of the study subjects and had serum total PSA of 1.8(1.1) as against 2.9(4.2) in those without metabolic syndrome p<0.05. The Weight, WC, BMI and TG levels were higher in those with raised serum PSA than in those with normal serum PSA values; 64.4(12.5)/61.9(9.7)kg, 83.6(12.9)/78.8(9.8)cm, 22.8(3.5)/22.0(3.8) and 1.08(0.67)/0.89(0.52)mmol/L respectively >0.05. Logistic regression showed positive linear relationship between central adiposity with total serum PSA. p<0.05. **Conclusion:** It is concluded that the risk of prostate cancer is inversely related to the metabolic syndrome and positively associated with central adiposity.

Keywords: Metabolic syndrome, Prostate cancer, PSA, Nigeria

INTRODUCTION

Metabolic syndrome (MetS) is a cluster of metabolic and hormonal factors including obesity, altered glucose metabolism, dyslipidaemia and or high blood pressure on a background insulin resistance state, having a central role in the initiation and recurrence of many chronic and dangerous diseases including hormonal-related cancers, [1,2] Metabolic syndrome is sought to play a potential role in the aetiology, progression and tumour outcome of cancers, prostate inclusive, but the mechanism is not yet fully elucidated.

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Prostate-specific antigen (PSA) is a serine protease that is secreted by prostate cells and it is useful as a tumour marker for prostate cancer. PSA is the most useful biomarker for the detection and monitoring of prostate cancer, although not very sensitive. Elevated serum PSA concentrations are known to be connected with the three most common prostatic diseases, i.e prostate cancer (PCa), benign prostatic hyperplasia and prostitis,[3]

Although metabolic syndrome has not been linked directly as a cause of prostate cancer, many evidences have shown that the individual metabolic components exhibited heterogeneous association with carcinogenesis, tumour progression and severity,[4-6] Metabolic syndrome and prostate cancer are prevalent conditions worldwide. A recent meta analysis on the role of MetS on prostate cancer, by Gacci M. et al, [7] showed that MetS is significantly associated with pathologic (Gleason Score⩾8) PCa, worse oncologic outcomes in men with PCa, in particular with more aggressive tumour features, and

biochemical recurrence. This emerging evidence suggested that MetS could play a role in the development and progression of PCa.

The interplay between hormones and cytokines such as adipokines may play a pivotal role in the pathogenesis of PCa, however, the exact mechanisms behind the relationship between metabolic syndrome and prostate cancer remain largely unknown. A review by Rhee H. et al, [8] revealed in a large proportion of men with MetS, alteration in levels of hormones such as testosterone, leptin and adiponectin has been shown to contribute towards the aggression of prostate cancer. Also an earlier review on PCa pathogenesis by Baillargeon J,[9] documented that Adipokines, defined as biologically active polypeptides produced by adipose tissue, have been linked with a number of carcinogenic mechanisms, including angiogenesis, cell proliferation, metastasis, and alterations in sex-steroid hormone levels.

The relationship between individual metabolic syndrome components and PCa, the third most common cancer in men worldwide, is heterogeneous, inconclusive and varies substantially according to geographic region and race/ethnicity. The association between obesity and prostate cancer incidence is complex and has yielded inconsistent results. Some reviews that have linked obesity with prostate cancer have indicated that obesity may not necessarily increase the risk of prostate cancer, but may promote it once established.[9]

A similar finding was documented in a study among healthy Koreans that showed higher waist circumference and fasting plasma glucose level were significantly associated with lower PSA (low risk for PCa) but not with MetS, [10] while in another meta analysis by Esposito et al, [11] found higher waist circumference to be significantly associated with increased levels of PSA.

Previous studies demonstrated that men with type 2 diabetes mellitus consistently had significantly lower serum prostate-specific antigen levels than healthy men. In a nationwide screening programme among the Swedish population that showed a reduced risk of being diagnosed with prostate cancer among men with T2DM, especially for low risk tumours and there was a trend of decreasing risk with increasing levels of glycated haemoglobin A1c. [12]

Among all the individual metabolic components, hypertension is the most consistently associated with increased PSA levels hence higher risk of PCa. Several meta analyses,[10, 11, 13] have revealed that hypertension singularly or in collaboration with other components, is associated with an increased risk of prostate cancer. In another study, [4] it was observed that there was an inverse relationship between the body mass index, HDL, and FBG with the serum PSA level. This further buttress the fact that the relationship between MetS and its

components and that of the risk of prostate cancer is complex.

Therefore the aim of the study was to investigate the relationships between MetS, its components and serum PSA levels and hence the risk of prostate cancer.

MATERIALS AND METHODS

The survey was a cross sectional conducted in a semi urban community population in Dutse, North western Nigeria comprising 352 healthy men in a screening exercise. The subjects included peasant farmers, traders, artisans and middle cadre civil servants. Simple convenient sampling technique was used to recruit consenting adults who fulfilled the inclusion criteria of absence of symptoms of prostitis or evidence of urinary obstruction.

The study protocols were approved by the local health authority and the hospital ethical committee of the Jigawa state specialist hospital, Dutse.

The data obtained included personal, anthropometric, lipids, glucose, thyroid stimulating hormone (TSH) and serum prostate specific antigen measurements.

Serum total PSA and TSH were determined using AccuBind ELISA Microwells while enzymatic and glucose oxidase methods were used for fasting cholesterol, triglyceride and glucose estimations.

The IDF criteria for the diagnosis of metabolic syndrome ethnic specific recommended for black Africans were used.

i. Central obesity define by waist circumference in centimetres, greater than >94cm in males or >80cm in female plus any two of the following confirms diagnosis of metabolic syndrome.

ii. TG ≥150mg/dl (1.7mmol/L)

iii. HDL ≤40mg/dl (1.03mmol/L) in males ≤50mg/dl (1.29mmol/L) in females

iv. Hypertension ≥130/85mmHg

v. FBG ≥100mg/dl (5.6mmol/L)

Serum PSA levels of >5.0 ng/ml is considered high or risk of prostate cancer.

Statistical analysis

The data were analysed statistically using SPSS package version 23.0 and presented as mean ± standard deviation, correlation coefficient (r-value) using Pearson's correlation and regression analysis with $p < 0.05$ level as significant.

RESULTS

A total of 352 adults were screened with mean age 39.6(9.4) years and mean serum total PSA of 2.73(4.10) ng/ml. The proportion found with total serum PSA >5.0ng/ml was 10.8% (38/350) figure 1.0

In figure 2.0, Metabolic syndrome was found in 6.8% (24/350) of the study subjects and serum total PSA of 1.8(1.1) as against 2.9(4.2) in those without metabolic syndrome p<0.05.

In table 1.0, the Weight, WC, BMI and TG levels were higher in those with raised serum PSA than in those with normal serum PSA values; 64.4(12.5)/61.9(9.7)kg, 83.6(12.9)/78.8(9.8)cm, 22.8(3.5)/22.0(3.8) and 1.08(0.67)/0.89(0.52)mmol/L respectively, while TSH levels were higher in those with MetS group than in those without MetS ; 5.9(5.1) /4.9(3.6) p>0.05

The blood glucose, HDL-C and blood pressure measurements were found to have no difference between the two groups. Logistic regression showed significant positive linear relationship between central adiposity with total serum PSA level. p<0.05
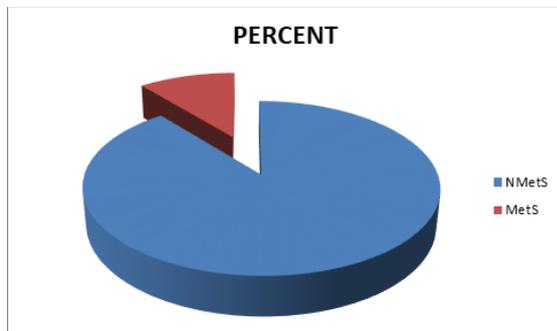

Figure 1: Showing the percentage distribution of Metabolic syndrome among the study population.

Metabolic syndrome (MetS) = 6.8%
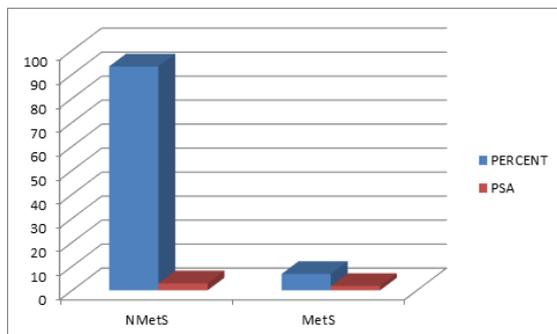No metabolic syndrome (NMetS) = 93.2%

Figure 2: Showing the proportions of PSA among the two groups

NMetS= no metabolic syndrome, MetS= metabolic syndrome

Table 1: Depicting the comparism of means of the two groups.

Variable	PSA>5.0ng/dl ± SD N=38	PSA<5.0 ±SD N = 312	P value
AGE	41.9 ±8.7	38.8 ± 9.1	0.134
BMI	22.7 ± 3.5	22.0 ±3.8	0.410
WC	83.6 ± 12.9	78.8 ± 9.8	0.056
SBP	115.5 ± 12.9	115.0 ±	0.922
DBP	77.7 ± 12.1	15.6	0.910
FBG	4.5 ± 0.96	77.6 ± 10.6	0.958
TC	3.47 ± 0.93	4.5 ± 1.3	0.967
HDL	1.25 ± 0.35	3.49 ± 1.06	0.815
TG	1.08 ± 0.67	1.27 ± 0.40	0.162

LDL	1.73 ± 0.80	0.87 ± 0.52	0.805
TSH	4.96 ± 3.6	1.79 ± 0.85 5.95 ± 5.16	0.419

BMI=body mass index, WC=waist circumference, HC=hip circumference, WHR=waist hip ratio, SBP=systolic blood pressure, DBP=diastolic blood pressure, FBG=fasting blood glucose, TC=total cholesterol, HDL=high density cholesterol, TG=triglyceride, LDL=low density cholesterol, TSH=Thyroid stimulating hormone.

DISCUSSION & CONCLUSION

The prevalence of raised serum total PSA and that of metabolic syndrome were found to be 10.8% and 6.8% respectively. The mean serum total PSA levels were found to be lower in the metabolic syndrome group than in those without. A significant positive association was documented between central adiposity, as measured by waist circumference, and the serum PSA.

Considering the fact that the mean age of the study subject is on the low side, one would have expected similar lower prevalence rate of the raised PSA level but a higher one was found in this study. This is in concordance with previous studies in southern Nigeria, [14] Caucasians [15] and Chinese[16] who have documented a near similar prevalence rate of 10% and positive linear relationship between age and serum PSA levels which means the older the subject is the higher the serum PSA level.

In this study population a prevalence rate of metabolic syndrome was found to be 6.8% and metabolic syndrome was negatively associated with the risk of prostate cancer or lower serum PSA. This was in keeping with previous studies where an inverse relationship between metabolic syndrome and serum PSA was reported. [7,8,17]

The metabolic syndrome group in this study exhibited significant lower serum PSA or reduced risk of prostate cancer than the other group without metabolic syndrome. This showed that in this study metabolic syndrome is associated with an inverse relationship with serum PSA and by extension the risk of prostate cancer. Most of the reviews and meta analysis are as varied as always on the complicity of metabolic syndrome in prostate cancer pathogenesis.

A meta analysis by Esposito K. et al, [11] showed that metabolic syndrome is weakly and non significantly associated with prostate cancer and this varies with geography, race and/or ethnicity while Gacci M. et al, [7] and Rhee H. et al,[8] in a more recent meta analysis revealed that metabolic syndrome may not be involved directly in the pathogenesis of prostate cancer rather it is associated with severity of the tumour including its aggressiveness, worse outcome and biochemical recurrence on the background hormones dysregulation.

Although the relationship between metabolic syndrome and prostate cancer is inconclusive and more often than not confusing, the individual components of metabolic syndrome maintain a

rather definitive heterogeneous relationship with serum total PSA.

We documented in this study positive association between waist circumference (central adiposity) and serum PSA level whereas no association was observed with the BMI. However, a similar community based surveys among the Koreans by Park JH. et al,[18] and Park SG et al[19] found an inverse relationship between BMI and serum PSA while positively associated with waist circumference, visceral and subcutaneous adipose tissue.. Another study of the same nature among the North Americans by Grubb RL. et al, [20] reported a similar pattern with BMI.

A higher serum TGD was documented in the metabolic syndrome group although it has not attained significance while other components of metabolic syndrome including HDL and systemic blood pressure showed no preferential difference. However similar studies showed that hypertension and dyslipidaemia favoured positive relationship with raised serum total PSA, [13] This dissimilarity between our findings and the results of other previous studies might have arisen from perhaps the small sample size of our survey or other intrinsic demographic factors of the study population.

It is concluded that the risk of prostate cancer among this population is on the high side and it is inversely associated with metabolic syndrome. The risk of prostate cancer among those with metabolic syndrome is predicted by increasing central adiposity.

The study was on the assumption that, serum PSA as potent tumour marker,[3] was used alone as surrogate to detect or predict risk of prostate cancer. This and other draw backs including relatively small sample size and young age of the study population may limit the strength of this study.

The outcome of our study implies that caution is needed when screening for the risk of prostate cancer, using PSA levels, among subjects with metabolic syndrome in the studied population. The low levels of PSA recorded in these subjects may mask the presence of prostate cancer as such this may warrants to establish a new critical PSA value for diagnosis or deployment of other complimentary diagnostic procedures.

Future studies on this topic especially involving the individual components of metabolic syndrome, with larger sample size and relatively elderly subjects need to be explored before any meaningful interpretation of the findings.

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