Metabolic Alteration in Prostatic Neoplasm-An Eastern Indian Study

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Abstract: Prostate cancer, a disease of aging men, is a growing problem in Asian countries in last two decades. To find out any metabolic alterations in prostatic neoplasm. One hundred non diabetic men aged 50 to 80 yrs were selected, among them 50 cases were of benign hyperplasia of prostate and 50 cases of cancer prostate. Age and sex matched healthy subjects were taken as control. All subjects were assessed for body mass index, fasting plasma glucose, serum prostate specific antigen, fasting insulin, lipid profile & homeostasis model assessment indices of insulin sensitivity. Results were analyzed by statistical software. The study revealed an increase in serum prostate specific antigen, fasting insulin, altered lipid profile and insulin sensitivity indices in study cases compared to control group. Metabolic alterations are associated with prostatic neoplasm. However longitudinal studies are required to establish any cause effect relationship.
Keywords: altered biochemical parameters, prostatic neoplasia.

INTRODUCTION

Prostate cancer is the second most frequent cause of cancer in males. Worldwide 1.1 million prostate cancer cases were detected in 2012; of it nearly 70% occurred in more developed countries. It is also a growing problem in Asian countries over the last two decades. Five years survival rate was nearly 64% in 2012 and now a days it is nearly 100% for localized and 29% in metastatic prostate cancer [1].

So besides cancer treatment, one should also take into Consideration of other aspects like metabolic alteration and treat it accordingly, that will help for better rehabilitation and improve the quality of life in carcinoma prostate cases.

Tumors are associated with various metabolic derangements. It is evident that Insulin has predominant action on the metabolism of the body. It is a potent mitogen and has role in cell growth and differentiation. It acts through phosphorylation cascade and any alteration may lead to altered cell growth resulting in tumor formation. The increased production and circulating levels of hormones are associated with a decreased sensitivity which leads to insulin resistance resulting in hyperlipidaemia and altered metabolism [2].

In the light of the above facts the present study was designed to find out whether metabolic alterations exist in the tumors of prostatic origin, like benign hyperplasia of prostate(BHP) and prostatic carcinoma(Ca).

MATERIALS AND METHODS
Study population

Study was done at Department of Biochemistry and Urology, of a tertiary care hospital of Eastern India. Clinically diagnosed and histopathologically confirmed non diabetic (as per guideline of American diabetes association) male patients of BHP and prostate carcinoma in age group of 50-80years were recruited as cases in the present study. For control age sex matched apparently healthy individuals were selected.

Sampling technique

Clotted and fluoride blood samples were taken from the patients selected for the Trans rectal ultrasound guided biopsy of prostate. Serum was separated and stored at -20degree centigrade. Biopsy reports were collected and only confirmed prostate

cancer and BHP patients were selected for the study. All groups were assessed for body mass index (BMI), fasting plasma glucose (FPG), serum prostate specific antigen (PSA), fasting insulin, lipid profile, quantitative insulin sensitivity check index (QUICKI) and homeostasis model assessment (HOMA) indices of insulin sensitivity(HOMA-%S) and insulin resistance(HOMA-IR).All HOMA values were calculated by downloading HOMA-2 calculator of Oxford University. Ethical clearance was duly obtained from the Institutional Ethics Committee. Informed consent was taken from each patient.

RESULTS

The data analysis of this study was done by the statistical software Minitab Version-18. The p value <0.05 was considered as statistically significant. The results were depicted in table 1, figures 1 and 2.

DISCUSSION

Altered metabolism of tumor cells increases energy expenditure, which results in negative energy balance and progressive weight loss. Contrary to the above fact, obesity has long been associated with increased risk of prostate cancer [3]. In most of the studies BMI was used as a marker of obesity [4].In the present study it was found that BMI (kg/m²) was increased in prostate carcinoma (mean ± SD) (23.824±0.912) and BHP cases (21.118±1.360) in comparison to control group (20.792±1.098).

PSA a glycoprotein is a marker of prostate cancer. It is established that PSA may be raised in different conditions like Ca prostate, BHP & prostatitis. With increasing age serum PSA value is also increased. It may be due to age related increase of prostate gland as well as increased PSA synthesized from prostate tissue. The present study noticed that PSA value (ng/ml) was increased in Ca prostate (18.54 ±4.164, p<0.05) and BHP cases (4.76±1.839, p<0.05) in comparison to control group (1.28±0.959) along with a significant positive Pearson correlation of serum PSA with BMI($r=0.624$, p<0.05) in prostate carcinoma cases.

Coming to metabolic derangement, it was noticed that fasting glucose level was increased in non-diabetic prostate carcinoma cases [5]. Glucose is required for the growth of cancer cells. With increasing FPG the prostate cancer as well as its recurrence risk is also increased [6]. It is also evident that increased FPG may be associated with BHP [7]. In the present study the FPG (mg/dl) of Ca prostate cases was (116.19±3.63) high in comparison to BHP (111.09±6.86) and control group(81.0±6.47).The study also found a significant positive correlation between FPG and serum PSA level ($r=0.777$, p<0.05) in Ca prostate cases.

In this study it was found that insulin level (µIU/ml) was significantly increased (14.12±1.705, p<0.05) in prostate carcinoma and BHP cases (7.436 ±0.976, p<0.05) compared to control group (5.18 ±0.4) and there was a significant positive correlation with serum PSA and fasting insulin in case of prostate carcinoma ($r=0.696$, p<0.05) as well as BHP cases ($r=0.554$, p<0.05) similar to other studies [5]. It was obvious that with increasing FPG there was compensatory increase in insulin secretion also. It is related to decrease in insulin sensitivity. Hyperinsulinemia (Fasting insulin> 25µIU/ ml) is associated with insulin resistance and cancer development [2]. Insulin is a growth stimulatory hormone .It stimulates mitosis by protein kinase B mediated signal transduction and deoxyribonucleic acid synthesis. High level of circulating insulin decreases the production of insulin like growth factor 1(IGF-1) binding proteins and increases free IGF-1 which promotes carcinogenesis by blocking induction of apoptosis through *transforming growth factor-* β (TGF-β)[8]. The expression of insulin receptor increases in prostate carcinoma. Higher circulating level may play a role on progression of cancer by increasing insulin-insulin receptor binding in prostate Ca cell membrane, resulting tumor cell proliferation [9].

The present study noticed that HOMA-%S was lower in prostate Ca cases (52.678 ±6.536), than BHP cases (100.10±13.51) and control group (153.23±10.08). It was also noticed that the QUICKI value in prostate carcinoma cases was lower (0.3124±0.007), than BHP cases (0.344±0.009), and control group (0.382±0.004). HOMA-%S and QUICKI of the study resulted in a negative correlation with serum PSA in both Ca prostate and BHP cases similar to other studies [10]. HOMA-IR of the present study was (1.928±0.2313) in Ca prostate cases, (1.016±0.1346) in BHP cases and (0.64±0.05) in control group. The present study possessed a significant positive correlation of HOMA-IR with PSA in Ca prostate and BHP cases.

This is known that besides hyperlipidemia lipid has tremendous role in development of various diseases including cancer [11].As per American Heart Association the optimal cut off of total cholesterol is <200mg/dl, high density lipoprotein (HDL) cholesterol >40mg/dl, low density lipoprotein (LDL) cholesterol <100mg/dl, and triglyceride <150mg/dl. In present study it was found that higher total cholesterol value ((mg/dl) in Ca prostate (200.62± 25.81), BHP cases (196.43± 24.75) compared to control group (171.26± 29.01) including a significant positive correlation between serum PSA & total cholesterol level in Ca prostate cases. In certain studies it was found that elevated cholesterol may be associated with aggressiveness of the disease [12]. Cholesterol may play role in prostate cancer progression by its action on cell proliferation, membrane organization, inflammation and steroidogenesis [13].

This study resulted in higher LDL cholesterol value in Ca prostate (162.62±18.91), BHP cases(148.67±25.73) compared to control group(121.55±23.06) and a significant positive correlation between serum PSA and LDL cholesterol level in Ca prostate cases(r=0.555,p<0.05). Some studies reported that elevated LDL cholesterol is associated with increased aggressiveness of the Ca prostate cases [14].

Low HDL cholesterol is a risk factor for development of BHP [15] and associated with increased aggressiveness of Ca prostate [16]. The present study resulted in lower HDL cholesterol value (mg/dl) in Ca (33.576±1.997) and BHP cases (38.010±2.99) compared to control group (41.85±3.508) and a significant negative correlation between serum PSA and HDL cholesterol level in Ca prostate(r= **-**0.983, p<0.05), as well as in BHP cases(r= **-**0.538, p<0.05) similar to other studies[17].There is a mixed finding regarding association of serum triglyceride(TG) and prostate Ca recurrence[18]. Higher TG value in Ca (167.39±14.28) and BHP cases (163.22±19.99) compared to control group (155.40±27.80) was found in the present study. High value of serum TG may be explained by reduced lipoprotein lipase activity, which is responsible for the clearance of TG from the plasma. The exact role of different lipid parameters on prostate tumors needs further evaluation.

CONCLUSION

The present study revealed altered insulin sensitivity, insulin resistance and lipid profile in 50-80yrs non diabetic prostate carcinoma as well as in BHP cases compared to age and sex matched healthy control group. In addition, it was also found that there was an association between the metabolic alteration and tumors of prostatic origin. However longitudinal studies are required to establish any cause-effect relationship.

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