Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 7
Open Access

Relationships between insulin levels, androgens, lipid and cytokine profile, and metabolic parameters in prostate and precancer malignant

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Cite this paper as: Dr.Dudekula Moulali, Dr. A.Padma Vijaya sree, M.D Shamshad Hussain, Dhamendra Talwar, Dr. P.Jyoshna, (2024) Relationships between insulin levels, androgens, lipid and cytokine profile, and metabolic parameters in prostate and precancer malignant. *Frontiers in Health Informatics, 13* (7), 782-788

Abstract

Introduction

Prostatic diseases are highly prevalent in men worldwide among which Prostate cancer (PCa) is a significant cause of morbidity and mortality especially in many western countries and second leading cause of death in India. Relationship between Prostate cancer, Precancer and obesity has been observed in previous studies, however it is unlikely in Indian scenario, but the possibility of its association with cytokines, lipids and androgens level derangement can't be ignored. So, the study is planned to observe the association of metabolic outline, lipid and cytokines profiling, androgens, insulin in Precancer and in Prostate cancer risk and aggressiveness.

Methods

This is a prospective and observational study was conducted in the Department to Biochemistry at

Viswabharathi Medical College & General Hospital. Total 80 males of age 40–80 years with nested cases of PCa were included in this study. All participants were divided in two groups. For the analysis of serum concentrations of Biochemical Paraments, fasting venous blood samples were collected.

Conclusions

This study indicated increased levels of serum Vaspin, Chemerin, Omentin, Interleukins IL-1β, interleukin-8 (IL8), Colony-stimulating factor (GM-CSF) and CC chemokine ligand 18 (CCL18) in patients with Prostate cancer. These findings suggest that the cytokines, and adipokines, whose levels were elevated in the chemotherapy-treated patients may be involved in the pathophysiology of prostate cancer. Vaspin, Chemerin and Omentin might play an important role in Prostate cancer progression through their association with Adipokines and proinflammatory cytokines. More studies are needed to investigate the possible role of Vaspin, Chemerin and Omentin as potential markers in the development of Prostate cancer.

Key words

Precancer, Prostate cancer, Androgens, Insulin, Lipid Level.

Introduction

Prostate cancer is one of the most common cancers in men and its incidence continues to rise in many countries[1]. Screening for and management of early prostate cancer is one of the most challenging and controversial issues in all of medicine. [2] Recent articles are focusing on role of obesity and lipid abnormalities operating at the root of PCa. Currently, there is insufficient evidence to directly indicate specific exercise guidelines to ameliorate Pre-cancer and risk factors in prostate cancer patients in Indian population. The incidence of prostate malignancy is also rising in India. Major contribution in the occurrence and progression of prostate cancer include genetic polymorphisms, obesity, diet, altered hormonal status , socioeconomic status and others.[3]

The factors contributing to the aggressiveness of prostate cancer lesions are not fully explored due to which the early detection is also not possible. So, it is very essential to discuss first about the precancer with respect to prostate. [4] It is well established that prostate is hormonally influenced and there is evidence signifying that androgenic influences over a period time encourage the process of prostate carcinogenesis, lipid metabolism anti hormonal abnormalities are fundamental aspect of prostate cancer cell biology.[5] Therefore, they may be a potential target for the prevention of the prostate cancer. A welldefined association with cancer and nonneoplastic condition that is 90% chances to be has developed cancer. [6]

Precancer in respect to Prostate is designated as Prostatic intraepithelial neoplasia – PIN (Earliest stages of cancer development). Previously it was graded as PIN-1, PIN-2 and PIN-3. Now cases are grouped into-Low grade PIN and High-grade PIN. 10 PIN is currently preferred term for the process involving prostatic ducts and acini, which has also been described as intra-ductal and ductal- acinar dysplasia. [7]

The relationship between obesity and prostate cancer is currently a passionately debatable topic. There is clustering evidence that high dietary fat intake might be associated with the risk of prostate cancer. Obesity is a rising risk factor for the development of several malignancies. Therefore, obesity associated with high leptin levels should be considered a risk factor in patients with prostate cancer. [8]

Adipocytokine secreted by fat tissue play a role in the genetic predisposition to type-2 diabetes, obesity and insulin resistance. Adiponectin and leptin adipocyte secrete insulin sensitizer, appear to play an important role not only in glucose and lipid metabolism but also in the development and progression of several obesity-related malignancies. [9] Studies in western countries have shown that PCa is associated with obesity. Relationship between Prostate cancer, Precancer and obesity has been observed in previous studies, however it is unlikely in

Indian scenario, but the possibility of its association with cytokines, lipids and androgens level derangement can't be ignored. [10] So, the study is planned to observe the association of metabolic profile, lipid profile, levels of cytokines, androgens, and insulin in Precancer with prostate cancer risk and aggressiveness including genetic biomarkers have several advantages over clinicopathologic indicators in future.

Material and methods

This is a prospective and observational study was conducted in the Department to Biochemistry at Viswabharathi Medical College & General Hospital. Inclusion criteria: Total 80 males under the age of 40–80 years were included in this study. These participants were nested case of PCa. All participants were screened by Medical Examination, estimating their PSA levels and by Histological investigations. Exclusion Criteria: Men with Chronic liver diseases, Kidney diseases, Heart disease, Diabetes mellitus, and 5-alpha reductase inhibitors and those taking lipid-lowering drugs were excluded.

Selected participants were randomised in two groups of 40 each by Histopathological examinations. These two groups are known as Prostate cancer and Pre Cancer Group. Both groups were compared for anthropometric measurements of height (cm), weight (kg), and waist circumference (cm) and body mass index (BMI) was calculated. Metabolic syndrome (MS) was diagnosed when central obesity defined as waist circumference ≥94 cm plus any two of four other factors were present.

Central obesity was always assumed if BMI was greater than 30 kg/m2 . Total 04 ml of Fasting venous blood samples were collected from all participants. The serum was obtained by centrifugation at 3000× g for 10 min and Biochemical analysis were performed. In all men, the metabolic profile was assessed (fasting glucose concentrations and lipid profile: total cholesterol CHOL, high-density lipoprotein cholesterol HDL-C, triacylglycerol TG) using a standard enzymatic method. Serum leptin, testosterone, Adiponectin and insulin concentrations were assessed by ELISA methods using commercial assays. The presence of metabolic syndrome (MS) was assessed according to the International Diabetes Federation definition (IFD), 2006. We used the following IFD cut-off limits: 1. Fasting glucose ≥100 mg/dL; 2. TG >150 mg/dL; 3. HDL-C 130/85 mmHg

Statistical Analysis: SPSS version 29.0 was used for the statistical analysis. The findings were displayed as Mean±SD. The differences between prostate cancer and pre-cancer patients were compared using the unpaired t-test for normally distributed data. A p-value of 0.05 or lower was regarded as significant

Results:

Table 01 indicates about Distribution of anthropometry between Prostate cancer and Pre-cancer. Basic demographic information was sought and participants were asses for parameters like Age, Height, Weight, BMI and WHR. Study results indicated that Age and other parameters are approximately similar between two groups.

Table 1: Distribution of anthropometry between Prostate cancer and Pre-cancer

Parameters	Prostate cancer Mean±SD	Pre-cancer Mean±SD	**p value**
Age (Years)	65.24±7.20	60.01 ± 7.80	0.533
Height (cms)	172.47±11.43	172.41±11.78	0.628
Weight	80.59±8.23	83.51±8.53	0.413
BMI	23.38±3.50	24.52±3.62	0.844
WHR	0.81±0.13	0.85±0.13	0.791

Table 2: Distribution of Androgenic parameters and Insulin levels between Prostate cancer and Pre-

cancer

Parameters	Prostate cancer Mean±SD	Pre-cancer Mean±SD	**p value**
Testosterone (ng/ml)	5.34±0.43	7.60±0.84	<0.05
Estradiol (pg/ml)	6.92±0.59	8.0±0.72	<0.05
Insulin (µIu/ml)	17.40±6.39	10.39±5.79	<0.05

Table Number 02 highlighted that when Biochemical parameters such as Testosterone were compared between Prostate and Pre-cancer group. Testosterone level of Prostate cancer group was 5.34±0.43ng/ml and Pre-cancer group was 7.60±0.84ng/ml. This indicates the statistically significant difference between two groups. Levels of Estradiols and Insulin were comaped by Inter group comparison. It is indicated that both Biochemical parameter has significant difference

Table 3: Distribution of Leptin and Adiponectin Levels between Prostate cancer and Pre- cancer

Parameters	Prostate cancer Mean±SD	Pre-cancer Mean±SD	**p value**
Leptin (ng/mL)	13.28±0.82	7.50±0.72	<0.01
Adiponectin (µg/mL)	16.23 ±2.71	11.70±2.32	<0.01

When level of Leptin and Adiponectin were compared between Prostate cancer and Pre-Cancer conditions, it is observed that Adiponectin is significantly higher in patients with Prostate cancer than Pre-cancer, while leptin may potentiate the growth of cancer cells, adiponectin appears to have an opposite effect in table 3.

Table 4: Distribution of Lipid profile between Prostate cancer and Pre-cancer

Parameters	Prostate cancer Mean±SD	Pre-cancer Mean±SD	**p value**
Cholesterol(mg/dl)	198.35±31.49	169.30±17.34	<0.0001
Triglyceride(mg/dl)	148.24±13.51	122.25±11.32	<0.0001
HDL(mg/dl)	40.45±4.72	30.14±3.50	<0.0001
LDL(mg/dl)	125.02±23.05	112.51± 12.55	<0.0001
VLDL	28.83±2.68	24.23± 2.1	<0.0001

In table 4, Lipid indices are also shows the positive significant relation with Prostate cancer in comparison to Pre-cancer. Serum Cholesterol (mg/dl) level of Prostate cancer group 198.35±31.49mg/dl and Pre-cancer group 169.30±17.34mg/dl. Triglycerides Levels of Prostate cancer group 148.24±13.51mg/dl and Pre-cancer group mg/dl. 122.25±11.32

Discussion

Weight, BMI, waist circumference, triceps skinfold thickness, and calculated total body water all exhibited negative trends with PSA levels. When stratified by race/ ethnicity, all of these trends were seen among white men; a trend for BMIwas found in Mexican American men; and a trend for triceps skinfold thickness was found in black men. Our overall negative association between BMIand PSA is consistent with those found in several recent studies. [11]

Baillargeon et al. found similar geometric mean PSA values using the WHO obesity classifications in a population-based San Antonio sample containing a much higher proportion (37%) of Hispanic men than our weighted NHANES sample (5%). Our findings are very similar to the statistically significant moderate decline in PSA values with increasing BMIreported by Kristal et al. [12] The nationally representative data reported here expand the validity of these previous results to a national scale. We were able to verify the categorical effect modification reported by previous authors. [13]

The PSA test is a commonly used test in older men and any factors that influence its accuracy may have important consequences for the diagnosis of prostate cancer. Some authors have suggested that lower PSA

values in obese men may decrease the test sensitivity, leading to a later diagnosis with a less favorable prognosis in this population. [14] Supporting this assertion are studies showing that obese men with prostate cancer present with later stages, have a poorer prognosis, and have a higher biochemical failure rate than healthy-weight men. [15]

When comparing men at extremes of the BMIscale, our model predicts only a 16.1% lower PSA level for a man with a BMIof 40 kg/m2 relative to a man with a BMIof 25 kg/m2 (predicted margin geometric means, 0.98 and 0.83 ng/mL, respectively). The predicted magnitude of the BMIeffect is well within the range of the normal analytic and biological day-to-day variation of the PSA test. [16] Therefore, we do not believe that this difference is likely to cause delayed detection. We believe that other factors are at least partially responsible for the poorer outcomes observed for obese men. The diagnosis and treatment of prostate cancer in the PSA era is complicated by a number of factors, including access to screening, the presence of comorbidities, prostate size, and surgery success rate. Obese men may be slightly more likely to be screened with PSA and this may be due to a higher prevalence of benign prostatic hyperplasia and prostatic symptoms. [17]

However, obese men often present with comorbidities, and such men are less likely to be screened in accordance with many PSA screening guidelines. Prostate volume is another potentially important confounder of disease detection. Obese men have larger prostates than nonobese men, which may decrease the sensitivity of prostate biopsy, perhaps leading to delayed detection of disease. [18] An additional factor to consider is the increased difficulty of surgical intervention in obese men. Obese men undergoing radical prostatectomy are more likely to experience incomplete removal of the prostate because of capsular incision, and this may be adversely associated with posttreatment survival. [19] It seems plausible that a combination of these factors explains the association between obesity and poor prostate cancer outcomes, but currently the relative importance of each factor is unclear.

CONCLUSIONS

Our results highlight the role of serum cytokines and adipokines as potential prognostic biomarkers in prostate cancer patients, which could contribute to tumour growth and progression. These results suggest that cytokines and adipokines might represent candidate PC biomarkers. It is concluded that the administration of palliative chemotherapy to patients with prostate cancer not only yields clinical advantages but also exerts a positive influence on the production and release of cytokines and adipokines in these individuals. The findings of this investigation revealed that the cytokines, chemokines, and adipokines that exhibited increased levels in patients undergoing chemotherapy may play a role in the pathophysiology of prostate carcinoma.

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