

## Research Article

# Study of insulin resistance and antioxidant vitamin status in prostate cancer patients

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**Received:** 1 March 2014

**Accepted:** 14 March 2014

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### ABSTRACT

The incidence of prostate cancer is 5 per 100000 in southern and eastern Asia. Both genetic and environmental factors have been implicated in its etiology. The mitogenic and growth stimulatory effects of Insulin growth factor may be involved in prostate carcinogenesis. To evaluate serum insulin and insulin resistance was passed by HOMA- IR. Prostatic specific antigen passed by immune-enzymatic assay. Vitamins were estimated by high performance liquid chromatography. In our study 30 prostate cancer patients aged 60-80years were taken as cases. 30 normal age matched disease free person were taken as controls in both groups, Insulin resistance and antioxidant vitamin status was studied. In the present study, the value of HOMA-IR was ( $P < 0.05$ ) is significantly higher compare to controls. Serum vitamin E and vitamin C values for cases was reduced ( $P < 0.05$ ) significantly lower than controls. The development of prostate cancer is a multistep process. Hyperinsulinemia associated with insulin resistance may play a role in pathogenesis of prostate cancer. Prostate cancer cells generate high levels a ROS.

**Keywords:** Prostate cancer, Insulin resistance, Antioxidant vitamin, Hyperinsulinemia

### INTRODUCTION

Prostate cancer is the most common malignancy among men in developed countries and its incidence is 5 per 100000 in southern & eastern Asia. An increased risk of disease has been reported among subjects with high weight or body mass<sup>1,2</sup> there is an increased risk among individuals with elevated serum levels of insulin like growth factor,. Some studies have shown that the metabolic syndrome characterized by central obesity insulin resistance, high serum glucose levels and dyslipidemia my play a role in the dvpt of cap. Insulin has potent mitogenic and growth stimulatory effects on the prostate and other tissues and alterations in these effects could potentially contribute to dvpt of malirnamcy<sup>3</sup> protecture factors include isoflavinoind genistein (which inhibits 5  $\alpha$  reductase) crucifeeneus

negetables that contains isothiocyanate sulfuraphase, retinoids such as lycopene and inhibitors of cholesterol biosynthesis. The antioxidant  $\alpha$  tocopherol (vitamin E) and selenium may also reduce the risk<sup>4</sup> both genetic and environmental factors have been implicated in the etiology of prostate cancer. Several molecular etiological pathways have been suggested for prostate cancer – androgen transactivation pathways, vitamin D metabolism, insulin like growth factor signaling pathways and chemical carcinogenic pathways.<sup>5</sup> Insulin resistance is associated with a higher risk of prostate cancer among men and that insulin sensitivity is associated with a reduced risk of prostate cancer among men.<sup>6</sup> Association between prostate cancer risk and oxidative stress has been well recognized. There is considerable evidence suggesting oxidative stress

contributes to etiology and pathogenesis of prostate cancer.<sup>7</sup>

PSA had been found to correlate with pathological states of tumour extension and metastasis. Advanced pathological stages are associated with higher PSA levels in the serum.<sup>8</sup> Elevated fasting plasma insulin and other components of the metabolic syndrome were associated with greater prostate cancer mortality with clinical stage T2-3 prostate cancer.<sup>9</sup> Previous studies have hypothesized that catecholamines might have a tropic effect on the growth of prostate cells by slowing down the apoptotic process suggesting a link between hyperimmunity and the development of prostate cancer.<sup>10</sup> Diabetes mellitus duration is inversely correlated with the risk of prostate cancer.<sup>11</sup> DM might induce local microvascular dysfunction and prostate ischemia which present initiation and development of carcinoma prostate.<sup>12</sup> Vitamin C has role in regeneration of tocopherol from phenoxy free radical derivative<sup>13</sup> vitamin E and Vitamin C levels are reduced in prostate cancer patients.<sup>14</sup>

Insulin can mediate its mitogenic effect on prostate cells through signal transduction mechanism. Recent physiological and genetic studies have levels that the insulin signaling pathway plays a pivotal role in the regulation of variety of interrelated fundamental processes such as metabolism, growth, reproduction, and aging the mammalian target of rapamycin a downstream molecule of the P13K / PTEN - AKT-mTOR pathway of insulin and IGF -1 receptor this signaling network lays a crucial role in the translational level by modifying phosphorylation of pivotal targets such as the translation initiation factor eIF-4E-binding proteins and S6Ks. The mTOR pathway seems also to be involved in prostate cancer. Specifically it mediates cell growth and proliferation as well as increase and angiogenesis induced by platelet derived growth factor - D (PDGF-D) in PDGF-D over expressing prostate cancer cells.<sup>15</sup> In the early stages of prostate cancer, every cancer cells are mainly androgen dependent and highly sensitive to anti androgens. Recent work has shown that vitamin E suppresses the expression of androgen receptor in prostate cancer cells and helps to establish new therapeutic concepts for the prevention & treatment of prostate cancer.<sup>16</sup>

## METHODS

Patients of prostate cancer were recruited from the dept. of urology, Narayana medical college, Nellore 60-80 year old males with biopsy proven adenocarcinoma of prostate irrespective of the staging were taken as cases. 60-80 year old age matched disease free individuals, without any complications were taken as controls the study was conducted over a period of one year. Thirty prostate cancer cases and 30 controls age matched without any complications were tested. Sample collected 5 ml of fasting blood sample was collected by venipuncture and allowed to clot for serum separation serum was kept

immediately in freezing temperatures, to preserve insulin and ascorbic acid as their half-lives are 4 to 6 minutes and 2 min respectively. Serum insulin was estimated by immunoenzymatic assay using insulin calibrators and insulin enzyme reagent, in this procedure, immobilization takes place during the assay at the surface of a microplate well through the interaction for streptavidin coated on the calculated as fasting glucose (mg/dl) x fasting insulin (mU/mL)/405.

## RESULTS

The results of the present study are consistent with the findings showing an association between increased insulin resistance, lowered antioxidant vitamin status and the pathogenesis of prostate cancer.

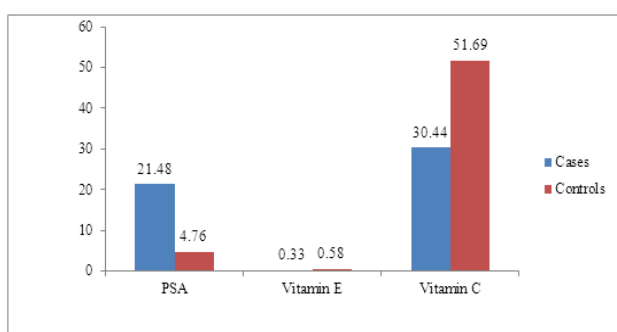
PSA levels for cases were found to be  $21.489 \pm 7.1592$  which is significantly higher when compared to controls levels of  $4.76 \pm 0.695106$ . The two tailed P value less than 0.0001 by conventional criteria; this difference is considered to be extremely statistically significant. The mean PSA of cases minus mean PSA of controls equals 1672900000 95% confidence interval of this difference from 14.10028167 to 19.35771833. The 30 prostate cancer patients aged 60-80 were taken as cases. So normal age matched, disease free without any complications were taken as controls. In both group insulin resistance and antioxidant vitamin status was studied. The fasting insulin values for cases are  $19.266667 \pm 3.52266879$ , which is significantly higher when compared to controls value of  $15.133333 \pm 3.3909955$ . The two tailed P value is less than 0.0001 by conventional criteria this difference is considered to be extremely statistically significant the mean fasting insulin of cases minus mean fasting insulin of controls equals 4.13333367000. 95% confidence interval of difference from 2.34637650118 to 5.92029083882. HOMA-IR for cases is  $3.073333333 \pm 0.753361814$ , which is significantly higher compared to the mean value of controls  $2.357333333 \pm 0.587583792$ . The two tailed P value equals 0.001 this difference is statistically extremely significant. The mean HOMA-IR of cases minus mean HOMA-IR of controls equals 0.7160000000. Serum vitamin E values in the present study for cases found to be  $0.339333333 \pm 0.124732357$ , which is significantly lower compared to controls value  $0.585666667 \pm 0.117845116$ . The two tailed P value is less than 0.0001 which is statistically significant. The mean serum vitamin E of cases minus mean serum vitamin E of controls equals 0.24633333402. 95% confidence interval of this difference from -0.30904560726. A decreased prostate cancer risk was observed with increasing intakes of vitamin C risk vegetable (16) in this study serum calcium values for cases was  $9.95666666 \pm 0.360730421$  which is significantly higher compared to controls value  $9.45 \pm 0.604437613$  the two tailed P value 0.002 which is statistically significant.

The mean serum calcium of cases minus mean serum calcium of controls equals 0.506666700. 95%

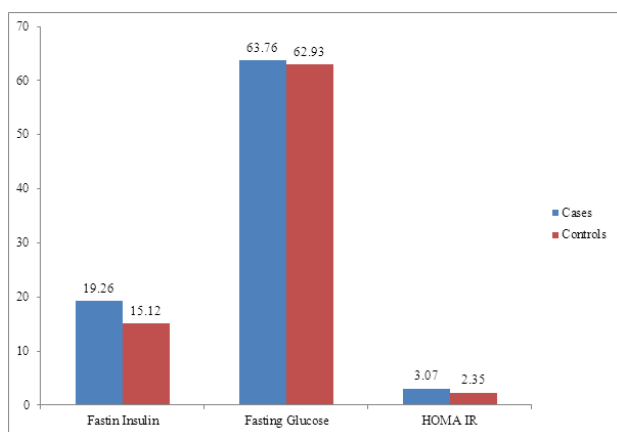
confidence interval of this difference from 0.24941906325 to 0.7691427075.

**Table 1: Shows biochemical parameters in prostate cancer.**

Parameter	Patients	Controls	P value	T value
	Mean ± SD	Mean ± SD		
PSA	21.48 ± 7.15	4.76 ± 0.69		
Fasting insulin	19.26 ± 3.52	15.13 ± 3.39	<0.0001	4.6301
Fasting glucose	63.76 ± 3.90	62.93 ± 2.44	0.3258	0.991
HOMA-IR	3.07 ± 0.75	2.35 ± 0.58	0.0001	4.1047
Vitamin E	0.33 ± 0.12	0.58 ± 0.11	<0.0001	7.8627
Vitamin C	30.441 ± 0.72	51.69 ± 14.49	<0.0001	6.4524



**Figure 1: Low level of antioxidant vitamin status and PSA pathogenesis of prostate cancer.**



**Figure 2: Shows increased levels insulin resistance in prostate cancer.**

**DISCUSSION**

Development of prostate cancer is a multistep process hypermethylation of glutathione transference Pi (GSTPi) gene promoter leading to a loss of function of a gene those detoxifies carcinogens is one early change. Several molecular etiological pathways have been suggested for prostate cancer. Androgen transactivation pathways clearly have received the greatest attention. Among the

most prominent of these additional pathways is vitamin D metabolism, insulin like growth factor signaling pathways and chemical carcinogen pathways. Hyperinsulemia associated with insulin resistance may play a role in the pathogenesis of prostate cancer through its sympathoexcitatory effect by altering exhormine metabolism activating the IGF pathway through signal transduction mechanisms and via dyslipidemia dn inflammation. The results of the present study are consistent with these finding showing an association between increased insulin resistance lowered antioxidant vitamin status and the pathogenesis of prostate cancer. The development of prostate cancer is a multistep process. Hyperinsulinemia associated with insulin resistance may play a role in the pathogenesis of prostate cancer through its sympathoexcitatory effect, by altering sex hormone metabolism, activating the IGF pathway, through signal transduction mechanisms and via dyslipidemia and inflammation.

Whether increased insulin resistance, either through lifestyle changes or genetic susceptibility, increases the risk of prostate cancer warrants further investigation, especially in prospective studies. Elevated fasting plasma insulin and other components of the metabolic syndrome were associated with greater prostate cancer mortality. Prostate cancer cells generate high levels a ROS and the generation of ROS increases with aggressiveness of the cells. Recent work has shown that vitamin E suppresses the expression of androgen receptor in prostate cancer cells and helps to establish new therapeutic concepts for the prevention and treatment of prostate cancer. Vitamin C has role in regeneration of tocopherol from phenoxy free radical derivative. A decreased prostate cancer risk was observed with increasing intakes of vitamin C-rich vegetables.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

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DOI: 10.5455/2320-6012.ijrms20140551

**Cite this article as:** Vardhan SP, Krishnamma M, Naidu JN, Naidu MP. Study of insulin resistance and antioxidant vitamin status in prostate cancer patients. *Int J Res Med Sci* 2014;2:643-6.