Relationship between Prostate Sspecific Antigen and Testosterone, Insulin, Adeponectin on Prostate Cancer Patients with Metabolic Syndrome

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Abstract

Prostate cancer (PCa) is a very common visceral malignancy in men it counts about one-third of all male cancers and it is the second cause of cancer death in males in United States of America. The conduction of this trail is to know the relationship between prostate specific antigen PSA, testosterone T , insulin and adiponectin in prostate cancer patients suffering From metabolic syndrome (MetS). There is significant difference ($p < 0.05$) in PSA level (39.04 ± 5.05, 2.93 ± 0.26) ng/ml respectively in prostate cancer group compared with control group.Significant Difference ($p<0.05$) in prostate cancer testosterone level   (2.44 ± 0.15, 3.10 ± 0.14) ng/ml respectively compared with control group.Significant difference ($p<0.05$) in prostate cancer adiponectin level (3.82 ± 0.12, 4.50 ± 0.39) µiu/ml respectively compared with control group.Significant difference ($p<0.05$) in prostate cancer insulin level (6.13 ± 0.86, 3.77 ± 0.27) µu/ml respectively compared with control group. There is weak negative correlation between PSA and T (-0.29).weak negative correlation between PSA and insulin (-0.11). Correlation between PSA and adiponectin is undetectable.

Key words:-prostate cancer, metabolic syndrome, testosterone, adiponectin, mechanism

الخلاصة

بعد سرطان البروستات من الاورام الحشويه الخبيثه الشائعه في الرجال ويشكل نسبه 3/1 سرطانات الرجال والمسبب الثاني للموت بالسرطان للرجال في الولايات المتحده الامريكيه. صممت التجربه لمعرفة العلاقه بين المستضد الخاص بالبروستات وهرمون التيستيستيرون وهرمون الانسولين وهرمون الادييونكتين في مرضى سرطان البروستات اللذين يعانون من المتلازمه الايضيه. تبين من الدراسه وجود فرق معنوي بمستوى ($p \leq 0.05$) في مستوى مستضد الخاص بالبروستات لمرضى سرطان البروستات مقارنه مع مجموعة السيطره($0.26 \pm 5.02,2.93\pm39.04$) ng/ml على التوالي. وجود فرق معنوي بمستوى ($p \leq 0.05$) في مستوى هرمون الشحمون الخصوي لمرضى سرطان البروستات مقارنه مع مجموعة السيطره($0.14 \pm 0.15,3.10\pm2.44$) ng/ml على التوالي مقارنه مع مجموعة السيطره. وجود فرق معنوي بمستوى ($p \leq 0.05$) في مستوى هرمون الادييونكتينن لمرضى سرطان البروستات مقارنه مع مجموعة السيطره (0.19 ± 9.80, 8.79 ± 0.14) µiu/ml على التوالي. وجود فرق معنوي بمستوى ($p \leq 0.05$) في مستوى هرمون الانسولين في مرضى سرطان البروستات بالمقارنه مع مجموعة السيطره(0.27 ± 3.77, 6.13 ± 0.68) µu/ml على التوالي. وجود علاقه عكسيه ضعيفه بين مستوى مستضد الخاص بالبروستات وهرمون الشحمون الخصوي ($-o.29$) وهرمون الانسولين (-0.11).علاقه ايجابيه ضعيفه بين مستوى مستضد الخاص بالبروستات وهرمون الادييونكتين (0.21).

الكلمات المفتاحية: سرطان البروستات، المتلازمة الايضية، هرمون الذكورة، الادييونكتين، تقنية.

Introduction

Prostate cancer (PCa) is the very common visceral malignancy in men. It countS about one-third of all male cancers and it is the second cause of cancer death in males in United States of America (Jemal *et al*.,2005). PCa is now known as a major public health case affecting western countries. It remains the prevalent malignancy and cause of cancer deaths between men in the USA; with an about 233000 new cases represent 27% of tumors and 29480 represent 10% of deaths during 2014 in the United States of America (American cancer society, 2014). The greatest threat from PCa its ability to

metastasize (Bubendorf *et al*., 2000). Prostate specific antigen PSA screening, digital rectal examination DRE were mainly used for PCa diagnosis , definitive diagnosis of PCa is made by transrectal ultrasound (TRUS)–guided needle biopsy (Matlaga *et al*., 2003). the presence of the insulin receptors InR directly on prostate tumor tissue has only recently been reported and showN that increased InR expression correlates with increasing Gleason grade and Castration-resistant prostate cancer (CRPC) (Cox *et al*.,2009)) providing further evidence that insulin and insulin receptor signaling may have a critical role driving progression of advanced Pca (Belfiore *et al*.,2009). Adiponectin encoded by adipose most abundant gene transcript 1(APM1) which has been mapped to chromosome 3 q27, synthesized and secreted by the adipose tissue. Adeponectin is associated with cancer risk and key mediator in development and progression of several types of cancers (Paz-Filho *et al*., 2011) and circulating adiponectin levels are decreased in patients with diabetes and obesity-associated cancers (Kelesidis *et al*.,2006). Upregulation of adiponectin is a partial cause of the insulin-sensitizing and antidiabetic actions. Therefore, adiponectin and adiponectin receptors represent potential therapeutic targets to combat obesity-linked diseases characterized by insulin resistance (IR) (Kadowaki *et al*., 2006). Testosterone (T) is essential for the normal development of the prostate both during fetal life and during puberty (Macleod *et al*., 2010). The testosterone is also necessary for normal function of the prostate during adulthood. Testosterone has a major influence on many tissues and is synthesized from cholesterol in a series of enzymatic steps involving several of the cytochrome p450 enzymes (Waterman *et al*., 1992). The metabolites of testosterone can bound to the other receptors causing different effects. Testosterone converted to dihydrotestosteron DHT by the enzyme 5α –reductase, the intraprostatic DHT/T Ratio is 6/1 (Marks *et al*., 2008). The critical role of androgens in the development and growth of prostatic tissue, including its influence on benign prostatic hyperplasia, has been well characterized.

Material and methods

Blood was collected from (50) patients and (40) healthy subjects (ages between 50-≥ 70 years) by 5 ml syringe and vacuolated in jell and clot activator test tube (Jordan)

Centrifugation after 45 minutes of the blood 3000 rpm for 5 minutes to obtain the serum.

Total PSA   kits (biomerieux,france) for detection of prostate specific antigen level by minVIDAS(USA).

Testosterone hormone kits (biomerieux ,france) for detection of testosterone assay by minVIDAS(USA).

Insulin hormone kit (cobas/Roche) for detection of insulin assay by (C.411,Germany)

Adeponectin hormone kits (sigma/Aldrich) for detection of adeponectin by (ASYS,Austeria).

Data Analysis

The analyses were performed using the statistical package for social (spss) version 16(ANOVA), ($P<0.05$) between prostate cancer patients group and control group and within patients group (Elston and Johonson, 2008).
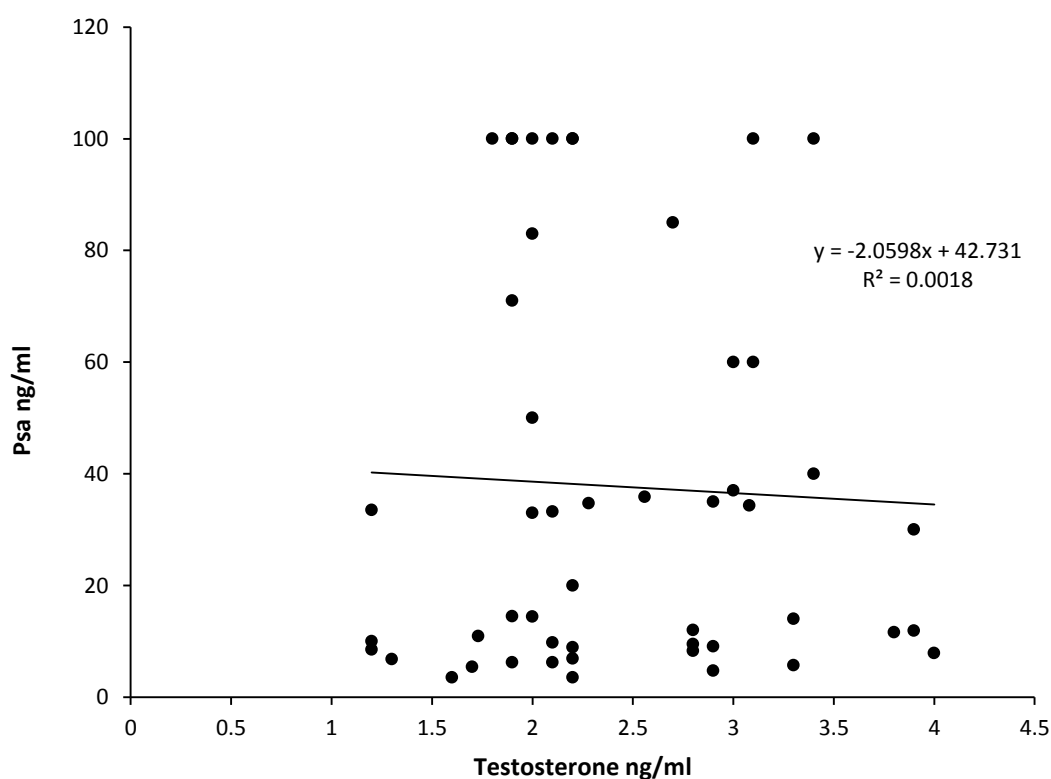
Result

Data refer there is significant difference (p≤0.05) in PAS levels in prostate cancer patients group compared with control group(39.04±5.02, 2.93±0.26)ng/ml receptively .There is significant difference (p≤0.05) in decreased testosterone level in prostate cancer patients group compared with control group (2.44±0.15 , 3.10± 0.14) ng/ml receptively .There is significant difference (p≤0.05) in decreased adiponectin level in prostate cancer patients group compared with control group(8.79±0.14, 9.80± 0.19) µiu/ml receptively .insulin level increased significantly (p≤0.05) in prostate cancer patients group compared with control group(6.13±0.86, 3.77±0.27)µu/ml receptively .(table- 1)

Table- 1: Levels of prostate specific antigen, testosterone, adiponectin and insulin in prostate cancer patients group and control group mean ± SE
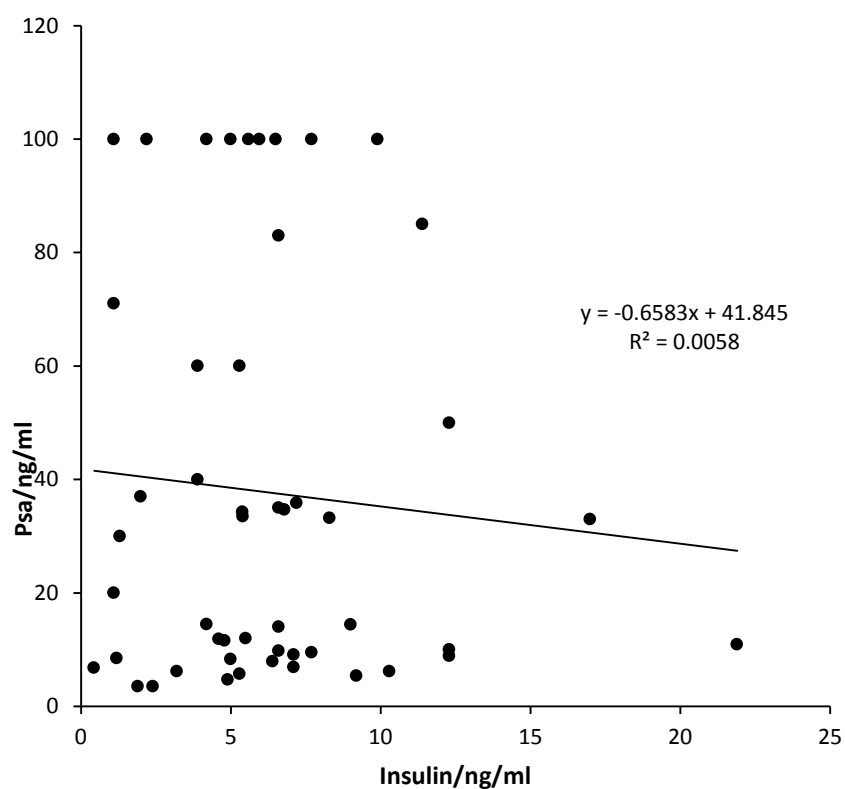
group test	PSA/ng/ml	Testosterone ng/ml	Adiponectin µiu/ml	Insulin /µu/ml
Prostate cancer patients	39.04 ±5.02 b	2.44±0.15 b	8.79±0.14 b	6.13±0.86 b
control	2.93 ± 0.26 a	3.10± 0.14 a	9.80± 0.19 a	3.77± 0.27 a

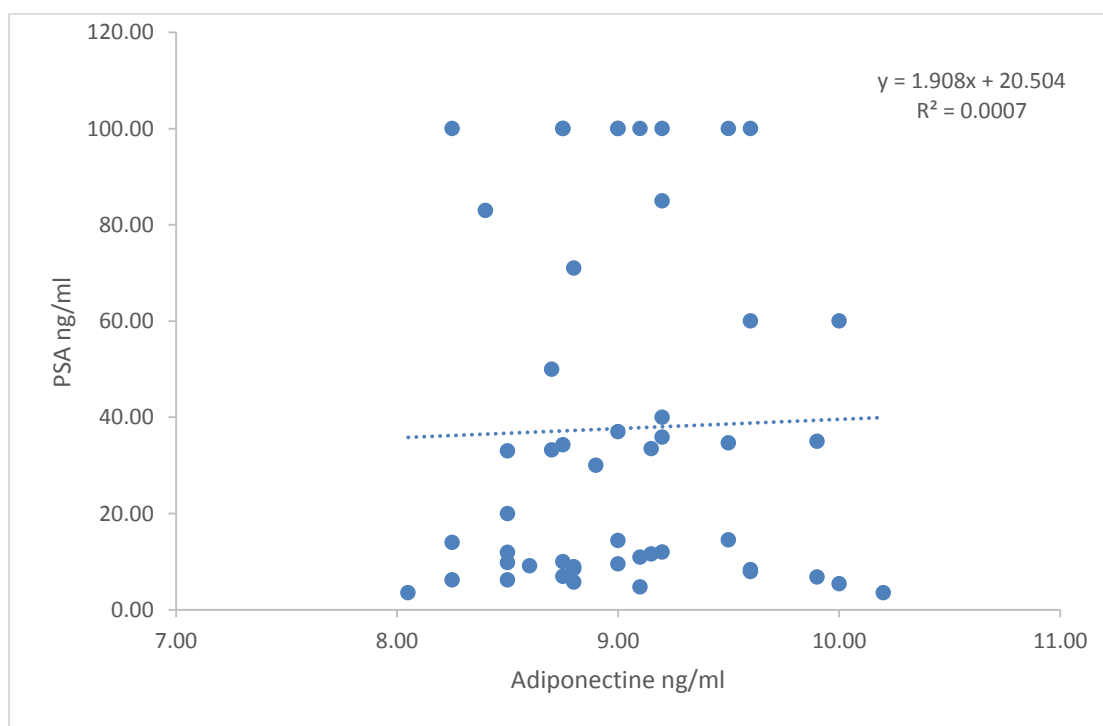Different litters indicate significant difference (p≤0.05)

There is weak negative correlation between PSA and testosterone (-0.29), weak negative correlation between PSA and insulin (-0.11).correlation between PSA and adiponectin negligible.

y = -2.0598x + 42.731
R² = 0.0018

Figure (1) weak negative correlation between prostate specific antigen and testosterone in prostate Cancer patients.

Figure (2) weak negative correlation between prostate specific antigen and insulin in prostate cancer patients.

Figure (3) correlation between prostate specific antigen and adiponectin negligible

Discussion

prostate cancer diagnosis performed by PSA test and digital rectal examination (DRE) and confirmed by Trans rectal biopsies Table (1) showed increased in PSA level of the patients .This result may be due to The luminal active PSA which did not undergoes proteolysis to yield inactive PSA, which enter the circulation in the free in addition to the tissue architecture is lost which results in relative increase in binding PSA and proPSA in serum in PCa (Lilja *et al*.,2008). The real cause of decline in testosterone levels because most PCa patients are diabetic and Plasma levels of total Testosterones are lower in men with type 2 Diabetes (Pitteloud *et al*., 2005). Diabetes might impair testosterone secretion from the Leydig cell, may be directly via insulin receptors on the Leydig cell (Pitteloud *et al*., 2005). Adeponectin is correlated with cancer risk and key mediator in development and progression of several types of cancers (Paz-Filho *et al*., 2011). Adiponectin levels are decreased in patients with diabetes and obesity-associated cancers (Kelesidis *et al*., 2006). Adiponectin negatively impacts growth of most obesity-concerning cancer types, such as prostate (Bub *et al*., 2006) Reduced adiponectin expression developed mammary tumors by downregulating Phosphatase and Tensin homolog (PTEN) and upregulating Phosphoinositide-3 kinase PI3K/Akt signaling (Lam *et al*., 2009).and reduced the activity of ceramidase in converting ceramide to sphingosine -1-phosphate potent inducer of proliferation and inhibitor of apoptosis (Takabe *et al*., 2008). Insulin can activate lipogenesis, steroidogenesis, and protein synthesis and antiapoptotic survival pathways in many cell types (Belfiore *et al*., 2009). Insulin signals take place through two insulin receptors A and B (InSR-A and InSR-B) (Belfiore *et al*., 2009), that belong to a family of tyrosine kinases receptors which includes the insulin-like growth factor 1 receptor (IGF-1R). Many tumors types have upregulated expression of IGF-1R, InSR, and potentially hybrid InSR/IGF-1Rs which facilitate increased activation of mitogenic, prosurvival and protein synthesis pathways with the increased levels of ligands insulin, IGF-1 or IGF-2 (Zhang *et al*., 2010). The inverse correlations between testosterone and PSA as result of the expression of PSA are more prominent in the reduced Testosterone level (Weigel, 2007).

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