Overlap of Vitamin D and Cholesterol, Triglyceride and High Density Lipoprotein in Prostate Cancer Patients (with Metabolic Syndrome)

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Abstract
Prostate cancer PCa represents a heterogeneous disease with different degrees of aggressiveness, patterns of metastasis and response to therapy (Vesovic, 2005) It occur from a complex etiology that include both exogenous (diet, environment, etc.) and endogenous (hormonal imbalance, family history) factors. Our attempt designed to know the overlap of vitamin D and lipid profile in prostate cancer patients and its relationship in incidence and progression of PCa .Data showed high prostate specific antigen PSA in Pca patients compared with control subject (33.01±6.01 2.93±0.62) mg/ml respectively .Decline in vitamin D level in Pca patients compared with control subject (17.34 ±1.5; 26.42 ±1.05) mg/dl respectively. Significant difference (p<0.05) in triglyceride level compared with control subject (129.63± 8.99, 101.26± 3.50) mg/dl respectively, no Significant difference (p>0.05) in HDL and cholesterol levels in Pca patients compared with control group .Weak Negative correlation between Vitamin D with cholesterol (-0.24) .Correlation between vitamin D and high density lipoprotein, triglyceride undetectable.

Key words:-prostate cancer, vitamin D, lipids, mechanism

Introduction
The data of National Health and Nutrition Examination Survey (NHANES) showed that Vitamin D insufficiency is a general public health problem, especially for elderly and minority populations (Zadshir et al., 2005). In both low and high1, 25-dihydroxyvitamin D levels were concurrent with an increased risk of prostate cancer (PCa) (Tuohimaa et al., 2004). Low levels of 1, 25-dihydroxyvitamin D related with an increased fear for earlier exposure to prostate cancer with high aggressive development of PCa, particularly before the andropause (Li et al., 2007). The PCa risk was highest between younger men (<52 years) with low serum 1, 25-dihydroxyvitamin D (Ahonen et al., 2000). High vitamin D level might lead to vitamin D resistance by increased inactivation thought enhanced expression of 24-
hydroxylase (Tuohimaa et al., 2004) vitamin D reduces the incidence of many forms of cancer by inhibiting tumor angiogenesis, (Iseki et al., 1999; Mantell et al., 2000) stimulating adherence of cells (Palmer et al., 2001) and promote intercellular communication over gap junctions (Fujioka et al., 2000) that ways strengthening the inhibition of proliferation that occurs from tight physical contact with close cells within a tissue (contact inhibition). 1,25(OH)2D enhances pulsatile release of ionized calcium from intracellular, including the endoplasmic reticulum, induces terminal differentiation and apoptosis (Campbell et al., 1997; Garland et al., 2006). Cholesterol is an important role player in tumorigenesis as a neutral lipid within the lipid bilipid of all cells and plays an important role in signaling from the cell surface to various subcellular compartments. It is collected in detergent-resistant membrane domains called lipid rafts. Lipid rafts in turn serve as membrane platforms for signal transduction mechanisms that promote tumor cell growth inhibits apoptotic signals and actively stimulates other malignant cellular behaviors (Freeman and Solomon, 2004). Survival mechanism of PCa cells is entirely processed through specialized membrane microdomains that are dependent on cholesterol for signal transduction. Studies refer that majority of patients suffering from PCa have high levels of total serum cholesterol (Maqura et al., 2008; Mittal et al., 2011). Survival mechanism of PCa cells is entirely processed through specialized membrane microdomains that are dependent on cholesterol for signal transduction. Studies (Lim et al., 2007; Kotani et al., 2013; Chen et al., 2009) refer that majority of patients suffering from PCa have high levels of total serum cholesterol (Maqura et al., 2008; Mittal et al., 2011). Hypercholesterolemia in prostate tumor cell membranes results in the gathering of raft domains. This process inhibits positive regulators of oncogenic signaling within rafts, while maintaining negative regulators in the liquid-disordered membrane fraction (Hui-ming, 2008). The mevalonate pathway, which leads to cholesterol synthesis, plays a key role in controlling cell proliferation by generating farnesyl and geranyl intermediates, These isoprenoids covalently alter and so modulate the biological activity of signal transducing proteins (Singh et al., 2003). Besides raised serum total cholesterol, mean LDL levels increased to some extent as a result of its enhanced ability to oxidation in PCa. Malondialdehyde (MDA) is an endogenous genotoxic product of enzymatic and oxygen radical-induced lipid peroxidation may cross-link DNA on the same and opposite strands via adenine and cytosine and contributes to carcinogenicity and mutagenecity in mammalian cells (Niedernhofer, 2003). Therefore, it can be concluded that elevated plasma cholesterol levels can be a risk for PCa.

Material and methods

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

Centrifugation by (genex /USA) of the blood 3000 round for 5 minutes to obtain the serum after 45 minutes.

Accent 200 chol diagnostic kits for determination of total cholesterol concentration (pz COMARY/Poland) by using (mindray automated /Germany)

Accent 200 HDL diagnostic kits for determination of total cholesterol concentration (pz COMARY/Poland) by using (mindray automated /Germany)

Accent 200 triglyceride diagnostic kits for determination of total cholesterol concentration (pz COMARY/Poland) by using (mindray automated /Germany)
PSA kits (biomerieux, france) for detection of total prostate specific antigen level by minVIDAS (USA).

Vit D kits (biomerieux, france) for detection of total vitamin D level by minVIDAS (USA)

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).

Results

Table (1) Prostate specific antigen, vitamin D, cholesterol, triglyceride and high density lipoprotein levels in prostate cancer patients and control group.

<table>
<thead>
<tr>
<th>Test</th>
<th>Prostate cancer patients with metabolic syndrome group /mean ±SE</th>
<th>Control group Mean ±SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA (ng/ml)</td>
<td>33.09 ± 6.01 b</td>
<td>2.93 ± 0.26 a</td>
</tr>
<tr>
<td>vitamin D (ng/ml)</td>
<td>17.34 ± 1.15 b</td>
<td>26.42 ± 1.05 a</td>
</tr>
<tr>
<td>high density lipoprotein (mg/dl)</td>
<td>35.61 ± 0.85 a</td>
<td>38.15 ± 1.20 a</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>129.63 ± 8.99 b</td>
<td>101.26 ± 3.50 a</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>184.47 ± 9.18 a</td>
<td>159.74 ± 4.96 a</td>
</tr>
</tbody>
</table>

Deferent letters indicate significant difference (p≤0.05).

There is significant difference (p≤0.05) in prostate specific antigen between PCa patients group and control group (3.309±6.01, 2.93±0.26)ng/ml respectively (Table-1). There is significant difference (p≤0.05) in vitamin D level between PCa patients group and control group (17.34±1.15, 26.42±1.05)mg/dl respectively (Table-1).

There is no significant difference (p>0.05) in cholesterol level between PCa patients group and control group (184.47±9.18, 159.74±4.96)mg/dl respectively (Table-1).

There is significant difference (p≤0.05) in triglyceride level between PCa patients group and control group (129.63±8.99, 101.26±3.50)mg/dl respectively (Table-1).

There is no significant difference (p>0.05) in high density lipoprotein level between PCa patients group and control group (35.61±0.85, 38.15±1.20) mg/dl respectively (table-1).

There is very weak negative correlation vitamin D with cholesterol (r=-0.24) in prostate cancer patients (figure -1). The correlation between Vit D and triglyceride (r=-0.07), HDL (r=0.049), is undetectable in prostate cancer patients (figure 2 and 3).
Figure (1) weak negative correlation between vitamin D and cholesterol in prostate Cancer patients.

Figure (2) weak negative correlation between Vit D and triglyceride in prostate cancer patients
Figure (3) weak positive correlation between Vit D and high density lipoprotein in prostate cancer patients

Discussion

Reduced PSA level was an important indicator for PCa diagnosis and follow up of the treatment of PCa; the data have showed high level of PSA which indicates they have PCa (Chen., et al., 2009) (table 1). Human prostate cells contain vitamin D receptor (VDR) for 1, 25-dihydroxyvitamin D, the active form of vitamin D to promotion of cell differentiation, apoptosis and Inhibition of cellular proliferation. PCa caused VDR decline in VDR number leading to less expression for 1, 25-hydroxyvitamin D which is converted locally within the prostate to 1, 25-(OH)2 D by 1α- hydroxylase and the activity of this enzyme decreased in cells derived from adenocarcinomas compared with cells derived from normal tissues or benign prostatic hyperplasia (BPH) (Hsu., et al 2001) in addition to VDR single Nucleotide polymorphisms (Hendrickson.,et al 2011 ) a Genetic heterogeneity ,all these factors lead to decrease in the level of vitamin D in PCa patients compared with healthy subjects(Donkena and Young, 2011) (table 1). Cholesterol essential component for 7-dehydrocholesterol in the skin is Converted to previtamin D which is then immediately converts by a heat dependent process to vitamin D (Holick, 2010). There is no significant difference (p>0.05) in HDLcholesterol and this indicate no effects of prostate cancer upon HDL and cholesterol while significant difference (p<0.05) in triglyceride level concerned with high-grade tumor (Chen et al., 2009). (table 1). There is weak negative correlation between Vit D and cholesterol because The fully active dihydroxylated Vitamin D induce the expression and possess Metabolism of vitamin D leads to decrease level 3-hydroxy-3-methyl-glutaryl-Coenzme A (HMG-CoA) reductase activity and low level of Vit D led to increased level of cholesterol (figure- 1)(Bhattacharyya.,et al 2012).
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