

Is the Good Cholesterol Bad for Prostate cancer?

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Abstract: The study was carried out to assess the association between HDL Cholesterol levels and Prostate cancer. In the present study the total cholesterol, Triglycerides, LDL, HDL and VLDL in Prostate cancer patients was assayed and compared with the same parameters in normal subjects. The blood lipid levels were assayed by Enzymatic CHOD/ POD method using commercially available assay kits supplied by Beacon Diagnostic Ltd.

A statically significant increase in total cholesterol, Triglycerides, HDL and VLDL was observed. The rise in HDL cholesterol, generally regarded as good cholesterol, seen in prostate cancer samples is a matter of concern. HDL cholesterol influenced tumor proliferation needs to be more researched for better understanding of tumorigenesis in prostate cancer.

Key words: Prostate cancer, HDL, LDL, VLDL, Blood lipids

I. Introduction

Prostate cancer is the most commonly diagnosed male cancer in the western world [17]. The morbidity and mortality of prostate cancer is significantly higher in western countries than in Asian countries [6]. Little is known about the etiology of Prostate cancer. Like most cancers, both genetic and environmental factors contribute to the pathogenesis of human Prostate cancer. Environment and life style (including diet) are likely to play a more dominant role than inheritance in the development of most Prostate cancer [9].

It has been hypothesized that blood lipid levels might be associated with Prostate cancer risk. Several findings have lead interest in lipid profiles as predictors of Prostate cancer risk [12, 4]. Epidemiological studies have described a positive correlation between high serum cholesterol level and prostate aggressiveness [13, 1].

Researchers at children hospital Boston have demonstrated that high blood cholesterol levels accelerate the growth of prostate tumors by promoting prostate tumor survival and growth by altering chemical signaling pathways within tumor cells.

Cholesterol plays a central role in steroidogenesis and is a substrate for *De novo* androgen synthesis and causes irregular growth of prostate cells. Excess intracellular cholesterol is incorporated in to membrane lipid rafts, thereby stabilizing the raft structure and enhancing AKT signaling in prostate cancer cells[2].

Hyper cholesterolemia is believed to contribute to higher serum prostate specific antigen (PSA) and hence to prostate cancer. However the mechanism is not yet understood [5]. In a study by Kok *et al.*, 2011 suggested that blood lipid levels may influence the risk of prostate cancer.

Furthermore the commonly used statins, Lovastatin, Fluvastatin and Simvastatin, induce apoptosis and inhibit the proliferation of prostate cancer cell lines in culture [18]. A significant chemoprotective effect of statins on prostate cancer has been shown *in vivo* [16].

II. Materials and methods

Patients

The cancer samples were collected from prostate cancer patients from V.S hospital, Chetpet, Chennai, India, after obtaining Institutional ethical clearance and informed consent from the patients to collect the same. The patients were aged between 60-80 years.

The control group consisted of healthy volunteers of similar age group.

Sample Collection

Randomly 30 Blood samples were collected from patients suffering from prostate cancer. Fasting blood samples were collected in plain vials. Serum was collected after centrifugation. Lipid parameters were measured freshly.

Lipid Profile Studies

The levels of TG, TC, HDL-Cholesterol and LDL cholesterol were determined by Enzymatic CHOD/POD method using commercially available assay kits supplied by Beacon Diagnostic Ltd. Tests were

performed according to the manufacturer’s protocol using a semi-autoanalyzer. The concentrations of serum lipid profile were expressed in milligram/ deciliter (mg/dl)

Statistical analysis

Statistical analyses were carried out using the SPSS statistical software. The results were expressed as mean±Standard deviation. The significance of differences between groups was determined by the Student unpaired t test. Values of p< 0.05 were considered as significant.

III. Results

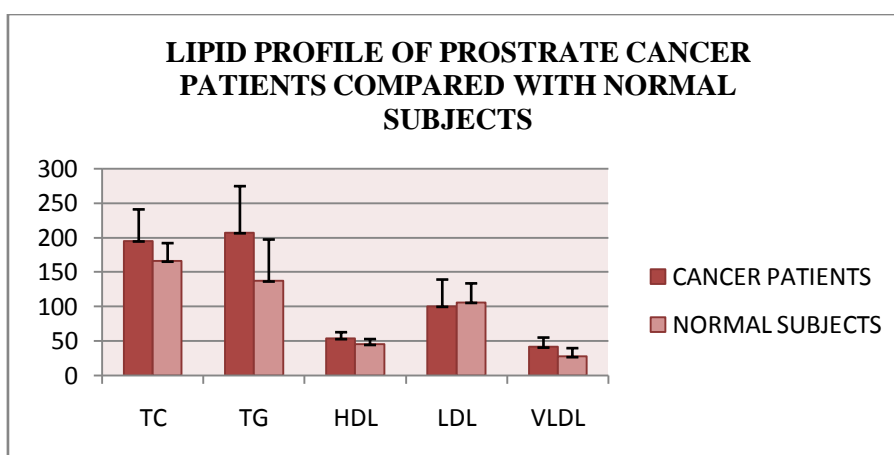
In prostate cancer samples a statistically significant increase in total cholesterol (p = 0.023) , triglycerides (p = 0.002) , HDL (p = 0.005) and VLDL (p= 0.002) was observed [Table :1 ; Graph : 1] .

TABLE : 1

| | PROSTATE CANCER | | | | |
|------------------------|----------------------|----------------------|----------------------------------|----------------------|---------------------|
| | CHOLESTEROL | TG | HDL | LDL | VLDL |
| CANCER PATIENTS | 195.44 ± 45.60 | 207.33 ± 67.42 | 53.67 ± 9.14 | 100.56 ± 38.67 | 41.44 ± 13.62 |
| NORMAL SUBJECTS | 166.11 ± 25.95 | 137.33 ± 59.99 | 45.28 ± 7.57 | 106.28 ± 27.39 | 27.56 ± 12.11 |
| P value | 0.023 | 0.002 | 0.005 | 0.611 | 0.002 |

Lipid profile of prostate cancer patients compared with normal subjects

GRAPH 1 :



IV. Discussion

Prostate cancer is the most common incidental cancer . During the past decade , several findings have led to an augmented interest in lipid profiles as predictors of prostate cancer risk[4].

It is thought that dietary fat intake might affect prostate cancer risk . Most population based studies researching on lipids and the risk of prostate cancer have focused on triglycerides (TG) and total cholesterol (TC) , but very few studies have investigated the role of HDL – cholesterol in patients with prostate cancer . Kok et al., 2011 reported serum TC, HDL – cholesterol , LDL-cholesterol and TG as potential risk factors for prostate cancer using multivariable COX proportional hazard regression models . Higher TC and higher LDL – cholesterol were significantly associated with an increased risk of prostate cancer [8].

HDL, which is generally viewed as beneficial, particularly for cardiovascular disease, but the effect of HDL on prostate cancer is unknown[15].

HDL increased serine 727 phosphorylation of STAT 3, but not tyrosine 705 only in DU145 cells. S1P and rHDL-S1P also induced the phosphorylation, but not rHDL without S1P. They also induced DU145 cells migration and invasion (14) . HDL induces the phosphorylation of STAT3 on both tyrosine 705 and serine 727 in ventricular cardio myocytes. [10].

The transcription factor signal transducer and activator of transcription 3 (STAT3) is activated in response to various growth factors, hormones, and cytokines, and has an important role in their signaling .When these ligands bind to the specific transmembrane STAT3 receptor, STAT3 becomes activated by JAK-mediated

tyrosine phosphorylation of a critical tyrosine residue (Tyr705) and dimerizes through reciprocal Src homology 2–phosphotyrosine interaction. The dimeric STAT3 translocates to the nucleus, where it binds to consensus STAT3 binding sequences within the promoter region of target genes and thereby activates their transcription [3].

In cardiac myocytes HDL and the HDL constituent sphingosine-1-phosphate (S1P) induce a concentration- and time-dependent increase in STAT3 activation. They also enhance extracellular signal-regulated kinases (ERK1/2) and p38 mitogen-activated protein kinase (MAPK) phosphorylation[10]. In endothelial cells, HDL suppress apoptosis. This is mediated via S1P3 and subsequent activation of intracellular signaling pathways involving ERK1/2, Akt and eNOS. [11, 7]

Dis regulation and manipulation of the STAT3 signaling pathway is important in tumorigenesis. HDL by an ABCA1-dependent mechanism can mediate signal transduction, leading to increased proliferation and migration of prostate cancer cells.[15].

The results obtained are in accordance with earlier studies .The significant increase in cholesterol levels especially HDL levels would form an important background in prostate cancer prevention.Our results are based on small number of cases (n=30) and require confirmation with increased sample size. Further the exact roles of different cholesterol fractions should also be evaluated.

V. Conclusion

Upon comparing the level of total cholesterol, Triglycerides, LDL, HDL and VLDL in Prostate cancer patients with the same parameters in normal subjects a statically significant increase in total cholesterol, Triglycerides, HDL and VLDL was observed. There is positive correlation between high serum cholesterol level especially HDL cholesterol and prostate cancer aggressiveness. Especially the rise in HDL cholesterol, generally regarded as good cholesterol, seen in prostate cancer samples is a matter of concern. This explains the possibility of cholesterol/ cholesterol fractions being a prognostic marker as well as a potential chemotherapeutic target for treating prostate cancer.HDL cholesterol influenced tumor proliferation needs to more researched for better understanding of tumorigenesis in prostate cancer.

Conflicts of Interest

No potential conflicts of interest were disclosed.

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