

Prediction of Prostate Cancer by Analyzing of Serum Trace Elements

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Abstract: Worldwide 1.1 million men were diagnosed with prostate cancer in 2012. In India, it is the second most widespread cancer in Indian males. Despite the far-reaching experimental and clinical studies over decades, the pathogenesis of Prostate cancer remains unidentified. The biochemical and molecular mechanisms accountable for and associated specifically with the development and progression of Prostate cancer are largely unidentified. The amalgamation of molecular/biochemical relationships is required to identify critical events in Prostate cancer process. Prostate cancer is a vital and potentially fatal disease in humans. Both genetic and environmental risk factors are associated with increased risk of prostate cancer among Asian populations. Previous observations have shown that trace elements play various roles in human health. The trace elements such as copper, iron and zinc are known to be associated with prostate cancer, but their functions are unclear. The aim of present study to evaluate the variation of serum trace mineral (iron, copper and zinc) and other special parameters (ferritin and ceruloplasmin) level with healthy men and those with prostate cancer. A total of 100 histopathologically proven prostate cancer patients participated in this study from the MGM medical college associated with MY Hospital; their age range was (50–75) years and 100 healthy men matched in age as a control group during the period from year 2014 to year 2015 after the diagnosis using a histopathological examination of the malignant tumour, the blood was centrifuged and serum samples resultant were unconnected and stored until the assay time. The analysis of the data showed that the mean values of serum copper were significantly increased ($P < 0.001$) and Serum Zinc were significantly decreased ($P < 0.001$) and serum iron is non-significant in prostate cancer patients as compared to normal healthy control. Other special parameters serum ferritin and ceruloplasmin were significantly increased in prostate cancer cases ($P < 0.01$) as compared to normal healthy male control. Serum PSA was significantly increasing ($P < 0.001$) in prostate cancer patients as compared to normal healthy controls and mean value progressively increase with the grades of cancer. In conclusion, serum ferritin, ceruloplasmin, zinc and copper is significantly associated with prostate cancer and may serve as a non-invasive biomarker to complement the PSA test in the diagnosis and prognostic assessment of prostate cancer.

Keywords: Prostate cancer, traces elements, copper, zinc, ferritin, ceruloplasmin.

INTRODUCTION

Prostate cancer is the second most common cancer in men. An estimated 1.1 million men worldwide were diagnosed with prostate cancer in 2012 [1, 2]. In India, it is the second most common cancer in Indian males as per the Indian Council of Medical Research (ICMR) and various state cancer registries. The incidence rate in India is 9-10/100000 population which is elevated than other parts of Asia and Africa but lower than USA and Europe. Prostate is the second foremost site of cancer amid males in large Indian cities [3], the data reveals that round about all regions of India are equally pretentious by this cancer. The incidence rates of this cancer are frequently and swiftly increasing in

all the Population Based Cancer Registries (PBCRs). Formerly it was thought, that prevalence of prostate cancer in India is far lower as compared to the western countries but with the increased migration of rural population to the urban areas, varying lifestyles, increased awareness, and easy access to medical facility, more cases of prostate cancer are being picked up and it is approaching to the knowledge that we are not very far behind the rate from western countries. The cancer projection statistics shows that the number of cases will turn into double by 2020 [4].

Despite the broad experimental and clinical studies over decades, the pathogenesis of Prostate

cancer remnants unfamiliar. The biochemical and molecular mechanisms accountable for and linked specifically with the development and progression of Prostate cancer are largely unidentified [5]. Coupled with this is the largely ignored function of altered cellular metabolism as an essential factor in Prostate cancer; although transformations of metabolism are concerned in virtually all malignant cells [6]. The combination of molecular/biochemical associations is required to make out critical events in Prostate cancer process.

Imbalance in the composition of trace metals, recognized to be essential to normal human homeostasis, besides the accumulation of potentially toxic or nonessential trace metals, may cause disease. Thus, there is a need for their analysis in cancerous and noncancerous human tissues to examine the relationship between cancer and these elements. The essential trace elements have four major functions as stabilizers, elements of structure, essential elements for hormonal function, and cofactors in enzymes. As a result, the lack of essential trace elements will influence structure alone or will alter function of structure through the lack of stabilization, change of charge properties, or allosteric configuration [7]. It may be expected that the deficiency of essential trace elements as cofactors of enzymes could severely impair the host's resistance against carcinogenic stress [8].

Serum ferritin is the storage type of iron, which is eminent in many diseases. Some recent reports have shown that serum ferritin expression was up-regulated in numerous tumor-associated diseases such as breast cancer, liver cancer, prostate cancer and lung cancer [9-12]. The result of several studies have recommended a correlation between ferritin and cancer. Certainly, although the lack of an increase in iron stores, (13) the serum ferritin level is significantly increased in patients with a diversity of neoplasms [13, 14].

Ceruloplasmin is an acute stage protein which increases in numerous malignancies and is a storage protein for copper in the liver. Increased levels of copper in serum of prostate & colon cancer patients may be due to the discharge of cytosolic and nuclear copper into the extracellular compartment. Secondaries in liver might be contributory to the high levels of ceruloplasmin [15].

In the present study, serum concentrations Copper, Iron, Zinc, Ferritin and Ceruloplasmin were determined relative to the PSA values of the patients.

AIM AND OBJECTIVES

1) To evaluate the variation of serum trace mineral (iron, copper and zinc) level with healthy men and those with prostate cancer.

- 2) To evaluate the variation of other special parameters serum ferritin and serum ceruloplasmin with healthy men and those with prostate cancer.
- 3) To assess the correlation between tumour marker PSA and all these metabolic parameters.
- 4) To evaluate the variation of serum copper /zinc ratio and copper ceruloplasmin ratio with healthy men and those with prostate cancer.

MATERIALS AND METHODS

This study was conducted in department of medical biochemistry, MGM medical college its associated MY hospital, from 2014 to 2016, On approval from ethical committee, 100 histopathologically proven prostate cancer cases were analysed in our study and they were compare 100 healthy age matched males controls . Five ml of venous blood was withdrawn from each individual using disposable syringes in blue vial. The samples were immediately centrifuged for 10 min at 3000 rpm, the serum obtained was removed and kept at -20°C till analysis. Biochemical parameters were done by fully automatic biochemistry analyser.

STATISTICAL ANALYSIS

Data were computed and analysed using Statistical Package for Social Science (IBM SPSS version 20.0) computer software. Student t-test, Pearson correlation analysis and One-way ANOVA were used. P. value at 0.05 was considered statistically significant.

RESULTS

In our study I was include 100 cases and 100 healthy control in which, Mineral profile included estimations of serum Iron, Copper, Zinc. The analysis of the data showed that the mean values of serum copper were significantly increased ($P < 0.001$) and Serum Zinc were significantly decreased ($P < 0.001$) and serum iron is non-significant in prostate cancer patients as compared to normal healthy control. Other special parameters serum ferritin and ceruloplasmin were significantly increased in prostate cancer cases ($P < 0.01$) as compared to normal healthy male control. Serum PSA were significantly increase ($P < 0.001$) in prostate cancer patients as compared to normal healthy controls and mean value progressively increase with the grades of cancer (Table-1).

Pearson correlation analysis between PSA and variables of interest among prostate cancer patients and showed that serum PSA significantly positively associated with serum copper ($r= 0.67$), ferritin ($r=0.74$), ceruloplasmin ($r=0.75$), Cu/Zn ratio ($r=0.73$) and significantly negatively associated with serum iron ($r = - 0.37$), zinc ($r=-0.47$)(Table 2).

All three stages of prostate cancer cases showed a higher concentration of copper ($P < 0.001$), ceruloplasmin ($P < 0.01$), PSA($P < 0.001$), Cu/Zn ratio and lowered concentration of serum zinc ($P < 0.01$)

compared to healthy control. The mean serum ceruloplasmin level were higher in stage II and advanced stage (III+ IV) (P < 0.001) if compare with stage I .The mean serum copper and ferritin level were

higher in advanced stage (III+ IV) (P < 0.001) if compare with stage I & II. The mean serum iron level were lower in advanced stage (III+ IV) (P <0.001) if compare with stage I and II.

Table-1: Comparison of Serum trace elements and tumour marker (PSA) in healthy control and prostate cancer patients

Parameters	Male Control (100)	Prostate Cancer(100)	T Value	P Value
	Mean±SD	Mean ±SD		
S Iron	104.33 ±19.56	102.46±25.36	0.56	Ns
S. Copper	106.09 ± 21.49	142.36±26.07	10.73	< 0.001
S. Zinc	93.06 ± 16.21	54.59±14.62	17.62	< 0.001
S. Ferritin	79.48 ± 22.05	91.54 ±44.2	2.43	< 0.05
S.Ceruloplasmin	31.27 ± 7.26	48.48 ±19.95.	8.08	< 0.001
S. PSA	2.96 ± 1.23	11.72± 5.27	16.18	< 0.001
Cu/Zn Ratio	1.18 ± 0.38	2.86±1.22	14.37	< 0.001

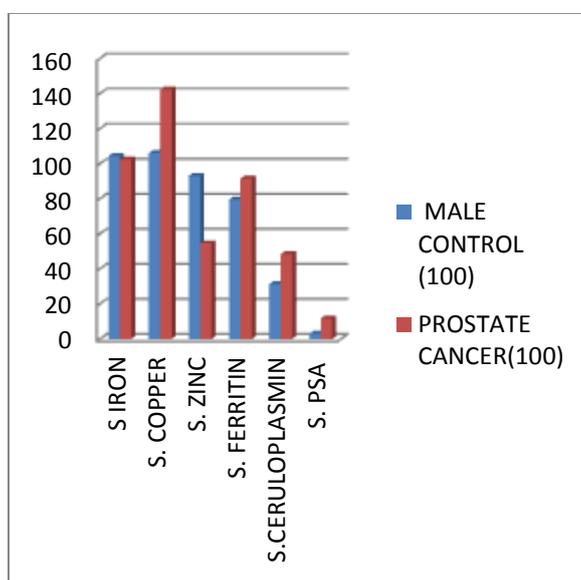
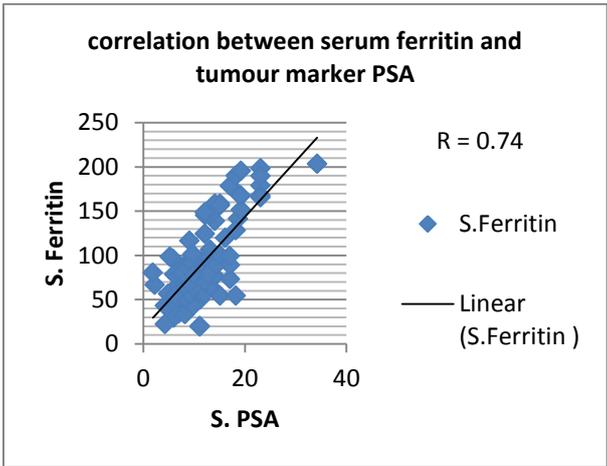
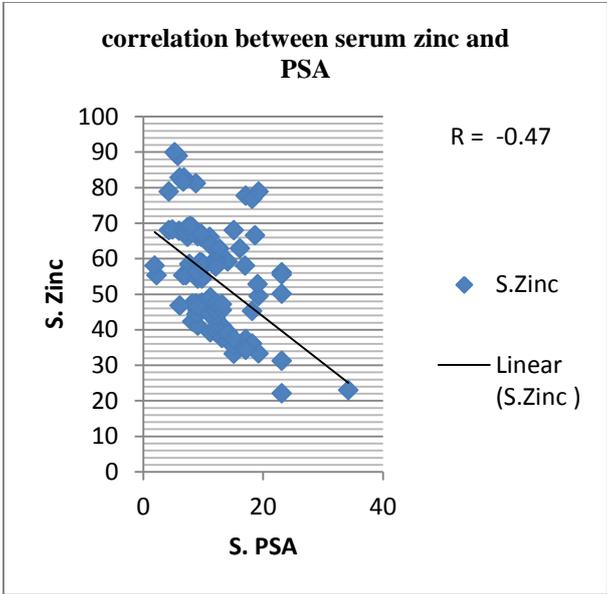
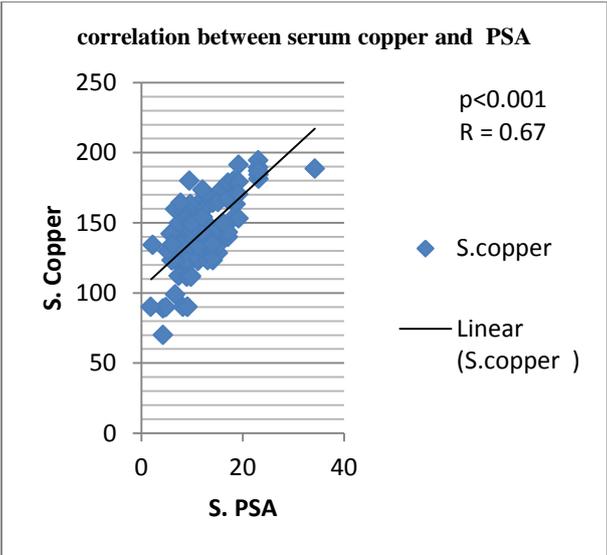
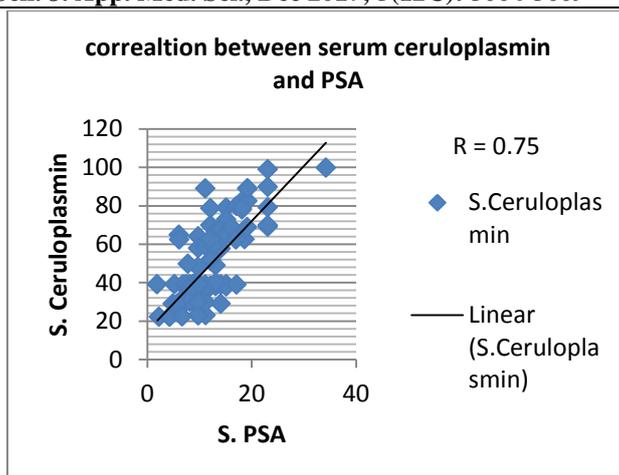


Table-2: Correlation of tumour marker with biochemical parameters in prostate cancer patients

Biochemical Parameters	R- Value	P- Value
Serum Iron	-0.45	<0.001
Serum Copper	0.67	<0.001
Serum Zinc	-0.47	<0.001
Serum Ferritin	0.74	<0.001
Serum Ceruloplasmin	0.75	<0.001





DISCUSSIONS

In patients with prostate cancer we were found significant increase of serum copper, ferritin, ceruloplasmin & Cu/Zn ratio with increased serum level of tumour marker PSA and significant decreased level of serum zinc. Fotiou K *et al.*, studied subjects with a prostate cancer, serum Cp values were higher than age-matched healthy controls [16]. Nayak S. *et al.*, were found copper and ceruloplasmin levels were increased significantly in the cancer patients as compared to controls [15]. Xijuan Wang *et al.*, found that high serum ferritin was significantly associated with increased serum total PSA levels ($p < 0.001$). In addition, increased serum ferritin was associated with increased Prostate Cancer risk [17]. Many studies shows lower serum zinc levels in prostate cancer patients compared to healthy controls [18, 19]. However, these studies measured zinc levels after cancer diagnosis, which could reflect the disease process. Some studies, conducted by Ozmen in Turkey, found that Zn values were significantly lower in patients with prostate cancer than in the controls [20]. Some small case-control studies indicate lower concentrations of zinc in plasma/serum [21-24]. When we measure the correlation between tumour marker PSA with different parameters of prostate cancer cases we found significant positive association with serum copper, ferritin, ceruloplasmin and Cu/Zn and significant negative association with serum zinc, iron and Cu/Cp ratio. The mean serum copper and ferritin level were higher in advanced stage (III+ IV) if compare with stage I & II. The mean serum iron level were lower in complex stage (III+ IV) if compare with stage I and II.

CONCLUSION

Our study strongly supports that the serum copper, ferritin and ceruloplasmin level were often increased and serum zinc is decreased in prostate cancer patients and suggests that all these trace elements can be used as a tumour marker for follow-up of prostate cancer patients. In a future study, serial determination of biochemical parameters (Copper, Zinc, Ferritin and Ceruloplasmin) and PSA in patients with the prostate cancer would be useful for evaluating the role of these

trace elements as a prognostic predictor. In conclusion, Serum Ferritin, Ceruloplasmin, Zinc and Copper is significantly associated with prostate cancer and may serve as a non-invasive biomarker to complement the PSA test in the diagnosis and prognostic evaluation of prostate cancer.

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