ORIGINAL ARTICLE

Estimation of Serum Copper Level in Benign & Malignant Prostate Disease & Correlation with Acid Phosphatase

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ABSTRACT

Objective: To estimate and compare the serum copper level in patients with benign prostatic hypertrophy and prostate carcinoma and their correlation with serum acid phosphatase.

Methods: This case control study was conducted at department of Biochemistry, Isra University Hyderabad from April 2016 to November 2016. A total of 100 individuals were divided into three groups. Group A consisted of 50 healthy individuals as Controls whereas; Group B and group C included 25 patients each with Benign Prostatic Hyperplasia (BPH) and Prostatic cancer respectively. Individuals taking copper supplements ,r any other trace elements and heavy metal supplements for the past three months were excluded from the study. Blood samples were collected from all cases and biochemical analysis for serum copper and prostatic acid phosphatase was performed in the Isra University Diagnostic and Research Laboratory, Hyderabad. All the results obtained were statistically analyzed.

Results: Prostatic acid phosphatase in Group A was 2.28± 0.99, Group B 16.03± 5.89 and Group C 46.43± 6.22 U/L respectively. P- value of 0.0001 was noted among all 3 groups. Serum copper levels in Group A was 106.88± 19.28, Group B 104.29± 17.40 and Group C 92.88± 11.28µg/L respectively. P value between groups A vs B, A vs C and B vs C were noted as 0.052, 0.001 and 0.022 respectively. Serum copper was reduced in group B compared to A but P value showed no significant difference (p=0.052). However, A vs C and B vs C showed statistically significant differences.

Conclusion: The present study reports the raised prostatic acid phosphatase, and decreased serum copper levels in carcinoma of prostate gland indicating their diagnostic and prognostic significance.

Key words: Benign Prostatic Hyperplasia, Prostate Carcinoma, Serum Copper Level, Prostate Acid Phosphatase.

INTRODUCTION:

Among different accessory glands of male reproductive systems, the Prostate gland is one of them, which adds secretions to semen. Prostate gland disorders are prevalent urinary disorders of senility. The gland is affected by a number of disorders such as infections, benign hypertrophy and malignant disorders. Benign prostatic hypertrophy (BPH) is most often encountered problem of urinary tract in old age. Whilst the Prostate gland cancer/malignancy is a serious health problem of old age. Prostate gland cancer is reportedly the 6th most common type of cancers the world over[1,2]. Prostate gland cancer is of diverse etiology; the genetic factors, environmental hazards and factors related to diet have been implicated in its aetiopathogenesis. Among various environmental factors, the alcohol addiction, smoking, pollutants, hormones and sexually transmitted diseases are important factors. Consumption of large quantities of fats, certain vitamin deficiency, trace elements and other micronutrients are suggested as dietary risk factors. All of the factors as mentioned are involve

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in the aetiopathogenesis of prostate gland cancer. These factors directly or indirectly interact with genes in causing abnormal glandular growth[3]. Carcinogenic agents of unknown origin may be present in diets, for example the heavy metals and also the endogenous hormones, both of which may induce carcinogenesis. Some of the heavy metals are essential for cellular functions while others are toxic and may be carcinogenic for human beings[4]. Various studies conducted on trace elements had suggested a possible role of heavy metals in the carcinogenesis. Heavy metals are suggested to interfere at the level of biochemical and metabolic enzyme levels of a cell. Extremes of heavy metal concentrations may be playing a role in carcinogenesis. However, a precise role of heavy metals in the initiation and promotion of cancer remains to be elucidated[5,6].

For better understanding, it is essential to identify the probability of heavy metals and its association with cancer of prostate gland. An alteration in the homeostasis of trace elements in common prostate gland disorders is worth to explore. Both of BPH and Prostate cancer have different histopathological characteristics, biological behavior and clinical findings with different metabolic alterations need to be evaluated. A change in serum concentrations of certain heavy metals/trace elements has been reported in previous studies[7,8] and needs further understanding. Previous studies had also reported low levels of zinc in Ca prostate gland have been implicated in the carcinogenesis. Similarly, the role of copper in carcinogenesis has also been reported, however other studies had reported contrary results[1,9]. Thus, the role of heavy metals/trace elements remains an ambiguity whether deficiency or excess is a risk factor in the pathogenesis of BPH and Prostate cancer[10]. Therefore, a research gap remains there to probe into the possible association and etiological role of heavy metals/trace elements; the selenium, copper and zinc in benign and malignant prostate disease which needs further elucidation[11]. The present study is proposed to evaluate the blood levels of serum selenium, copper and zinc in benign prostatic hypertrophy and prostate cancer and their correlation with acid phosphatase in patients presenting at tertiary care hospital of Isra University.

METHODS:

The current case control study was conducted at the department of Biochemistry, Isra University Hyderabad from April 2016 to November 2016. Serum Copper and Acid Phosphatase were estimated in 100 patients from Isra university Hospital, Hyderabad, samples were taken as purposive sampling and study was designed as a case control study, duration of study was 8 months , samples taken were analyzed in the Isra University Diagnostic and Research Laboratory, Hyderabad. A sample of 100 subjects selected according to inclusion and exclusion criteria and were divided into groups Group A = Control (n= 50), Group B = Benign Prostatic Hyperplasia (BPH) (n= 25), Group C= Prostatic cancer (PC) (n=25). The inclusion criteria was the diagnosed cases of BPH and Ca Prostate. The exclusion criteria was; individuals taking copper supplements or any other trace elements and heavy metal supplements for the past three months were excluded from the study, and after routine investigations the cases having anaemia and hypo-proteinemia were also excluded from the study since these two conditions are associated with low serum zinc level and high serum copper level[12]. All the patients and control subjects were informed about the purpose of taking blood samples and consent was taken. 5 ml of blood was collected by the vein puncture in specific bottles (zinc and copper free containers. In all cases, care was taken to prevent haemolysis of red blood cells as they contain might high zinc element[13]. The collected blood samples were centrifuged within one hour and the serum was refrigerated in polypropylene screw capped test tubes, and stored at -20 C. Two (2) ml of serum was diluted with deionized water and then 5ml of analar concentrated nitric acid was added. After mixing the samples well, they were allowed to stay at room temperature for three hours[14]. Then, they were centrifuged for 10 minutes at 2500 rpm[15]. The supernatant obtained was transferred to plastic bottles using chemically cleaned pipette; after adding double distilled water was preserved at room temperature[16]. The sample thus obtained was subjected to atomic absorption spectrophotometer (AAS) analysis technique for serum copper levels using GBC Aventa 2.01 equipment. Data was analysed on SPSS version 22.0 using student t-test and chi-square test at 95% confidence interval.

RESULTS

Age in controls, BPH and Ca prostate was noted as 61.39±5.88, 61.44± 5.27 and 64.58± 3.74 years respectively. Age showed no significant difference between groups A and B (p value 0.09), however, group C patients were older and a significant difference was noted, Group A vs. C (p value 0.016) and Group B vs. C (p value 0.038). Prostate acid phosphatase (PAP) was noted as 2.28± 0.99, 16.03± 5.89 and 46.43± 6.22 U/L respectively. P-value of 0.0001 was noted among 3 groups; A, B and C. Serum copper was noted as 106.88± 19.28, 104.29± 17.40 and 92.88± 11.28µg/L respectively. P value between groups A vs. B, A vs. C and B vs. C were noted as 0.052, 0.001 and 0.022 respectively. Serum copper was reduced in group B compared to A but P value showed no significant difference (p=0.052). However, A vs. C and B vs C. showed statistically significant differences. (Table I, Graph I & II)
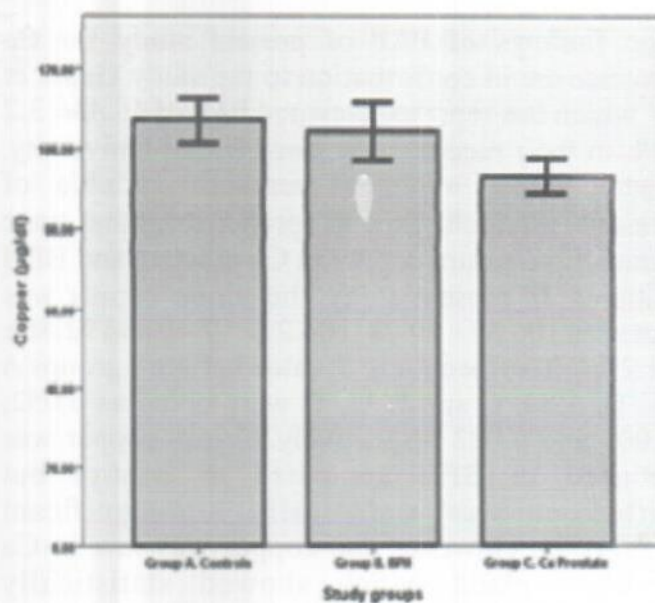
Graph II. Bar Graph Showing Serum Copper Levels in Controls and Cases

Table I: Showing Different Parameters in All Groups.

Variables	Group A. Controls	Group B. BPH	Group C. Prostate cancer		
	Mean± SD	Mean± SD	Mean± SD	F value	P value
Age (years)	61.39±5.88	61.44±5.27	64.58±3.74	13.37	0.038
Serum acid phosphatase levels (U/L)	2.28±0.99	16.03±5.89	46.43±6.22	869.6	0.0001
Serum copper levels (µg/dl)	106.88±19.28	104.20±17.40	92.88±11.28	5.76	0.0001
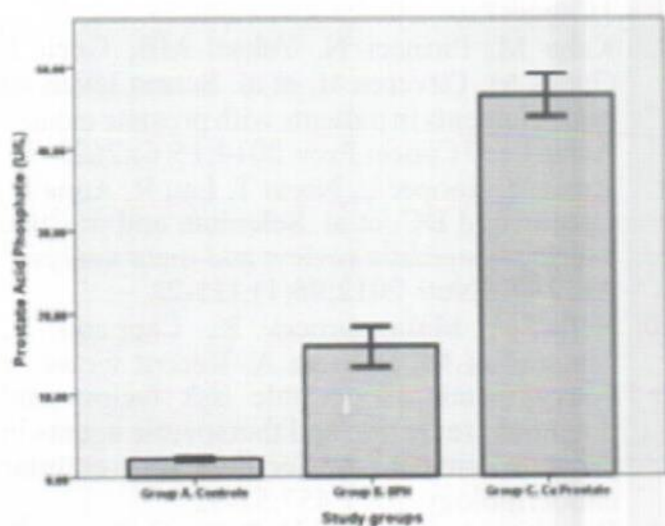
Graph I. Bar Graph Showing Serum Acid Phosphatase Distribution in controls and cases

DISCUSSION

The present study was conducted to evaluate the serum copper and prostate acid phosphatase (PAP) levels in normal controls, cases of benign prostatic hypertrophy (BPH), and carcinoma prostate (Ca Prostate).[17] Finding of age of 64.58± 3.74 years of Ca prostate is less compared to Famurewa et al, which has reported mean age of the Ca Prostate of 71.35±8.45 years which is slightly higher than the present study. However, the Famurewa et al[17] reported no significant differences for age between controls and Ca prostate (P<0.05). The reason for age difference may be various. One reason is that overall the mean age in Pakistan is on decline. Another reason may be the geographical differences, and age inclusion criteria of above study[17]. Age, an independent variable, has long been implicated as a risk factor for Ca Prostate among men[18]. It is reported that at the age of 5th decade, the prostate gland becomes enlarged as part of aging process, however, sometime this may be due to neoplastic growth. PAP is one of the tumor marker for Ca prostate, although its sensitivity is low. The PAP in present study was noted as 2.28± 0.99, 16.03± 5.89 and 46.43± 6.22 U/L in controls, BPH and Ca prostate subjects respectively (P- value 0.0001).

The findings of PAP of present study for Ca prostate are in confirmation to the study Gabra et al[19] which has reported elevated PAP of 45.43± 3.2 U/L in their recent study from Fedail University, Sudan. Most important research variable of present research was to probe into the trace mineral the serum copper in Ca prostate and BPH patients. In present study, the serum copper was noted as 106.88± 19.28, 104.29± 17.40 and 92.88± 11.28µg/L respectively. P value between groups A vs. B, A vs. C and B vs. C were noted as 0.052, 0.001 and 0.022 respectively. Serum copper was reduced in BPH compared to control but difference was statistically non-significant (p=0.052). However, the copper was low in Ca prostate gland which showed statistically significant differences. Finding of low serum copper level is in contradistinction to previous study of Karimi, et al,[7] which has reported high copper from nails and hair of Ca prostate gland patients. This contradistinction is most probably because of different samples i.e. serum of present study versus nails and hair of Karimi et al[7]. A recent study by Singh et al[1] has reported low serum copper levels in Ca prostate gland patients from India. The finding of Singh et al is a consistent finding to present study. Dunoyer[20], has recently reported that the Prostate cancerous tissue showed high copper content, but there was no change in serum copper concentrations in patients Ca prostate cancer compared to controls. The finding of Dunoyer[20] is in contradiction to present and previous study[7].The present study observed low serum copper in benign prostatic hypertrophy and carcinoma of prostate. Further studies will help to clarify whether, along with clinical diagnosis, serum copper is useful in the differential diagnosis of BPH and Ca prostate. Consideration of the biochemical evidence presented here ensures to the conclusion that altered copper metabolism may be playing a causal role in the benign prostate hypertrophy and Ca prostate.

CONCLUSION:

It is concluded that serum copper was decreased in both benign prostatic hyperplasia and carcinoma prostate. Acid phosphatase was significantly high in carcinoma prostate proving the diagnostic significance of both markers."

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