

Determination of Calcium and Iron in Prostate and Bladder Tumors by Atomic Absorption Spectrophotometer

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ABSTRACT

Background and Objectives: Serum calcium and iron were used as a biochemical markers for investigation of the neoplastic diseases ,since there is a growing concern about the possible links between these minerals and tumors of various organs and tissues ,the objectives of this study were to determine the changes in the serum levels of Ca & Fe ions in patients with benign prostatic hyperplasia and bladder cancer and to identify the role of these markers in diagnosis and prognosis of these patients .

Methods: This study was done in Baghdad at Al-Kadhemia Teaching Hospital between 10/9/2002 and 1/9/2003 .Serum samples were obtained for measurement of calcium and iron.,which were determined by flame atomic absorption spectrophotometer .

Results: Hypercalcemia affects up to 30% of patients with bladder and prostate cancers. In addition there were a decrease in the iron serum level as a result of tumor growth .

Conclusions: Hypercalcemia, is one of the most common metabolic disorders accompanying neoplasia.The cancers most often associated with hypercalcemia, in addition there were a reduction in serum level of iron this biochemical marker may be associated with the pathogenesis of cancer.

Key words: prostate cancer , bladder cancer , Iron ,Calcium.

INTRODUCTION:

Iron is essential for life¹, at the same time excess of iron has been implicated in cancer through increased iron –catalyzed free radical-mediated oxidative stress iron as a catalyst for the formation of the hydroxyl radical. These free radicals react with all biomolecules and are considered to be very toxic,causing structural damage to macromolecules(proteins &lipids) and breakage of DNA strands.Generation of these reactive oxygen species may deplete antioxidant². Oxidative processes are one of the mechanisms involved in both incidence & recurrence of bladder cancer, serum iron was significantly lower in patients than the control group. Iron is used in collagen synthesis by hydroxylation of proline and lysine by enzymes proline

hydroxylase& lysine hydroxylase that is lead to decrease iron level³, significantly in cancer patients, due to it's by tumors cells^{3,4}. The serum iron level was significantly lower in the patients with bladder cancer than the control group ($P < 0.001$)^{4,18}. Iron is essential for numerous enzymes and therefore it is reasonable to assume that variations in serum level of this biochemical marker may be associated with the pathogenesis of cancer¹⁹. Iron is an essential element carrying oxygen, forming part of the oxygen-carrying proteins hemoglobin in red blood cells and myoglobin in muscles¹⁹.Hypercalcemia, is one of the most common metabolic disorders accompanying neoplasia¹⁹. The cancers most often associated with hypercalcemia are those of the breast, lung, kidney, prostate, head and neck, as

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neoplasms particularly multiple myeloma. Normal, healthy kidneys are able to filter large amounts of calcium from the blood, excrete the excess not needed by the body, and retain the amount of calcium the body need. However, in the cases of hypercalcemia the blood calcium may increase to so high levels that kidneys become unable to excrete the excess¹⁹. Some tumors produce a substance similar to normal parathyroid hormone (such a parathormone-related peptide that drives the kidneys to increase calcium reabsorbtion) and it can mediate the kidneys to excrete too little calcium. This results in a large amounts of urine to produce, that then may cause dehydration. Dehydration may lead to appetite loss, nausea, and vomiting and make the general condition worse. Disability caused by weakness and tiredness may increase the blood calcium levels by increasing the amount of calcium resorbed from the bones¹⁹. Calcium deposits may be collected in the kidneys, causing permanent damage . Between 10 and 20 out of every 100 people with cancer (10 to 20%) develop hypercalcaemia. This usually happens in the advanced stages of cancer but it can happen in people with earlier stages.^{7 - 10} or it may be between 10% -30%^{13,14}. Decreasing the calcium levels in the blood can improve the symptoms in a few days¹⁰. Immobility, dehydration, anorexia, nausea and vomiting may also increase the calcium level^{12,13}.

AIMS OF THE STUDY : The aims of this study were to measure the changes in the serum levels of Ca & Fe ions in patients with benign prostatic hyperplasia and bladder cancer and to identify the role of

MATERIAL AND METHODS:

these markers in diagnosis and prognosis of these patients.

In this study we reviewed the personal ,clinical, histopathological data and calcium , iron levels in two groups of

age, sex, smoking ,alcohol, diseases, drugs, occupation, bilharziasis, residence and marital status , The date of diagnosis was the date of first admission for prostate & bladder cancer.

METHODS

Serum concentration of Ca and iron ions were determined by flame atomic absorption spectrophotometer.

RESULT:

In the current study, hypercalcemia recorded in up to 30% of patients with bladder and prostate cancers . In addition there were a decrease in the iron serum level as a result of tumor growth .

The mean value of serum Ca of the control group was 78 ± 11.12 ug /ml while the mean serum Ca levels of BPH group was 127 ± 10.11 ug/ml and the mean value of serum Ca levels of the patients with the bladder cancer was 95.5 ± 13.67 ug/ml .

ANOVA test showed the serum calcium level in the patients with BPH was marginally higher $P < 0.05$ than that of males, but highly significant than that of females of the bladder cancer ($p < 0.001$) . The difference between both sexes was also significant, the males showed higher mean than females ($p < 0.01$) The mean value of the Fe in the sera of the control group was 0.92 ug /ml ± 0.12 while the mean value of the serum Fe levels of the BPH & bladder cancer were 0.53 and 0.71 ug /ml respectively. ANOVA test showed that Iron level in BPH is significantly lower than that of males and females of the bladder tumors < 0.01 but the differences between both sexes was not significant > 0.05

STATISTICAL ANALYSIS (ANOVA , T-TEST & CORRELATION COFFICIENTS):

There are a significant difference in the level of serum iron & calcium between BPH & bladder cancer (males & females), while there is no significant difference in the level of serum iron in bladder cancer between males & females , additionally there is a significant difference in the level of serum calcium between

CORRELATION COEFFICIENTS:

Association between two variables (r) & the sign whether + or - indicates the direction of such association if both increased or decreased in the same direction then will be positive, if one of them increase and the other decrease that is the run in different direction then the correlation will be negative.

IN CASE OF (BPH): There was intermediate positive correlation between iron & calcium ions

IN CASE OF FEMAL WITH BLADDER CANCER: There was negative intermediate correlation between iron & calcium.

IN CASE OF MALE WITH BLADDER CANCER: There was no correlation

Table 1 : Group one, patients with benign prostatic hyperplasia average age 66 total 41.

Type of the disease	Average Age	No. of the patients	Kurdistan government	Middle of Iraq	South of Iraq
BPH	٦٦	٤١	٣٧.٥%	٣٧.٥%	.%٢٥

Table 2 : Group two Patients with bladder Tumor average ages 60.5 of both sexes, total number 47

Type of the disease	Average Age	No. of the patients	Kurdistan government	Middle of Iraq	South of Iraq
Bladder Cancer	٦٦.٥	٤٧	١٩.٤٤%	٥٠%	٣٠.٥٦%

Table 3: The mean (\pm SD) values of serum Ca in patients with BPH ,bladder cancer groups as compared to the control group

Ca ug /ml	NO.	Mean value ug/ml	(\pm SD)	P Value
control	٣٠	٧٨	± ١١.١٢	
BPH	٤١	١٢٧	± ١٠.١١	
Bladder cancer	٤٧	٩٥.٥	± ١٣.٦٧	
Males	٣٥	١٠٠	± ١٧.٢١	<٠.٠٥
Females	١٢	٩١	± ١٢.٨٨	<٠.٠٠١

Table 4: The mean (\pm SD) values of serum Fe in the patients with BPH, bladder cancer groups as compared to the control group

Fe ug /ml	No.	Mean value ug/ml	(\pm SD)	P Value
control	٣٠	٠.٩٢	± ٠.١٢	
BPH	٤١	٠.٥٣	± ٠.٠٤	
Bladder cancer	٤٧	٠.٧١	± ٢٩٧	<٠.٠١
Males	٣٥	٠.٧٣	± ٢٤٩	
Females	١٢	٠.٦٩	± ٠.٠١١	>٠.٠٥

Table 5 : The significant correlation between types of type of tumors and serum iron, calcium levels

Type of Tumors	Fe	Ca
BPH X Bladder cancer Males & Females	Significant difference	Significant difference
Bladder Cancer/ Males & Females	Not significant	Significant

Significant $P < 0.05$ Not significant , $P > 0.05$ **DISCUSSION:**

Iron play an important roles in biological processes⁵. Serum Iron levels are considered as biochemical indicators for nutritional assessment¹⁸. The result of serum iron in this study is combatable with other studies that shows the decrease in the iron value as a result of tumor growth . Iron is considered as nutritional & biochemical factors and it is necessary for proper cell growth that is utilized by tumors and normal tissues for growth since non-heme iron is necessary for proper cell growth , so the serum iron level was significantly lower in the patients than the control group ($P < 0.001$). Thus, our findings are in accordance with previous studies in developed countries³⁻⁵. Anemia in cancer patients has many etiologies, haemoglobin synthesis may be impaired by nutritional deficiency (iron, folic acid, coblamin) .Erythrocyte synthesis may be depressed by bone marrow inadequacy (metastasis, pure red cell aplasia, chemotherapy or radiotherapy). Erythrocyte quantity may be reduced by bleeding, ,haemolysis, or hypersplenism. Frequently, the anemia ensues from attempt of the host to raise an inflammatory response to defeat the neoplastic invader. This condition is known as anemia of chronic disorder (ACD)⁶. Our results are based on a small number of patients, so these findings require confirmation by other prospective studies on large number of patients . Sunali et al.¹⁸ reported that serum iron levels are considered as biochemical

hydroxylation of proline and lysine by the aid of the enzyme proline & lysine hydroxylase and this enzyme required a molecular oxygen, ferrous iron, alpha ketoglutarate and ascorbic acid lysine leads to decreased serum iron levels in cancer patients . Sunali et al.¹⁸ evaluated that there is a statistically significant reduction in the serum iron level in the pre-cancer group . In our study , there was a reduction in the serum iron levels of the cancer group, but our results are significantly higher than that of pre cancer groups that was published by Sunali et al.¹⁸ suggested that occurrence of iron deficiency is known to present in cancer, in addition this publisher was estimated that there were a statistically significant reduction in the serum iron level of the pre-cancer group. In a addition , in most cases clinical anemia may be a contributing factor so this is an additional factor to reduce serum iron .Additionally , serum iron and hemoglobin was probably due to utilization of iron by bone marrow and tumors¹⁸. Thus , this finding is in consistent with our study. More detailed studies on a large data base should be instituted to elucidate the exact role of iron. To our knowledge, this is the first study in Iraq to examine prostate & bladder cancers risk in relation to serum calcium. Hypercalcemia affects up to 30% of bladder and prostate cancer patients. In a review of the literature , identified that this finding is consistent with the study published by Dori¹⁵ but his results is lower than our results, he found that hypercalcemia affects up to 10% to 30% of cancer patients . Parathyroid

the growth and metastasis of prostate and bladder cancer cells¹⁴. These observations led us to ask whether men with high levels of serum calcium are at increased risk for prostate cancer. Increase in extracellular serum calcium cause a decrease in apoptosis and an increase in proliferation & migration of metastatic region. Thus, high serum calcium may promote the growth of potentially fatal cancers¹⁶. Many studies are in agreement with our finding that reported people with cancer get hypercalcemia, Dori et al.¹⁵ reported that the main pathogenesis of hypercalcemia in malignancy is increased osteoclastic bone resorption, which can occur with or without bone metastases, this is the main causes of cancer –mediated hypercalcemia are increase the amount of calcium resorbed from the bones because the cancer makes calcium leak out into the blood stream from the bones due to the secretion of parathyroid hormone related protein activating parathyroid hormone receptors in tissue, that increase the osteoclast of the bone these findings are concluded by Peter Fuszek et al.¹³ & increase intestinal absorption^{19,20} and finally increase the distal calcium reabsorption. Additionally, the kidneys cannot keep up with the elimination process., normally, the kidneys would eliminate excess^{11,15}, so this hypercalcemia make the kidney unable to get rid of calcium, so the level in the blood gets too high and an interfere with kidneys ability to excrete excess calcium. On the other hand, the dehydration from diarrhoea, urination and vomiting may also increase calcium levels^{11,15}. So our finding is consistent with the results of a large studies of serum calcium in relation to prostate & bladder cancers that is

CONCLUSION:

mentioned in the text.

This study has concluded that level of serum Ca were significantly increased in patients with benign prostatic hyperplasia,

level of serum iron were significantly decreased in patients with benign prostatic hyperplasia and bladder cancers. Further studies of the relationship between levels of body iron and cancer outcomes are needed because of our results based on a small number of prostate & bladder cancers, require confirmation by other prospective studies. Hypercalcemia is the most common life –threatening disorder associated with cancer, and correction of the hypercalcemia alleviate symptoms and improve patient's quality of life. Reduction in the serum iron level may be due to malnutrition caused by the tumor burden in cancer patients. In most cases clinical anemia may be a contributing factor.

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