Ferritin: A Complementary Tool to PSA in Diagnosis and Differentiation of Ca Prostrate with BPH

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Abstract: Prostate-specific antigen (PSA) has been widely used as a clinical diagnostic biomarker for prostate cancer. PSA is not necessarily specific for prostate cancer. To increase diagnostic accuracy and reduce the number of unnecessary screening procedures, biopsies, and treatments, new and complementary non-invasive biomarkers for prostate cancer are required. 25 diagnosed patients of carcinoma prostate and 25 patients with Benign Prostatic Hypertrophy were enrolled for this study done to estimate, evaluate, and compare the level of serum ferritin and PSA in prostate carcinoma and BPH patients. Serum ferritin level was significantly high in the carcinoma prostate patients compared to the BPH group.

Keywords: Ca prostrate, ferritin, PSA, BPH

1. Introduction

Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males worldwide. In Asia, the incidence and mortality associated with prostate cancer is increasing BPH typically begins after the age of 40.²

Prostate-specific antigen (PSA) has been widely used as a clinical diagnostic biomarker for prostate cancer. Prostate specific membrane antigen is a transmembrane carboxypeptidase and exhibits folate hydrolase activity. However, PSA is not necessarily specific for prostate cancer, and elevated PSA levels have also been reported in patients with benign prostatic hyperplasia (BPH), prostatitis, and following physical trauma to the prostate. Moreover, prostate cancer patients can have PSA levels ≤ 4 ng/ml, which is generally considered to be in the “normal” range, thereby contributing to misdiagnosis.³ Thus, PSA, due to its general lack of specificity and sensitivity may not be the most suitable biomarker for diagnosis of prostate cancer. To increase diagnostic accuracy and reduce the number of unnecessary screening procedures, biopsies, and treatments, new and complementary non-invasive biomarkers for prostate cancer are required.⁴⁻⁷

Ferritin serves to store iron in a non-toxic form, deposits it in a safe form, and transports it to areas where it is required. Serum ferritin expression has been found to be up-regulated in many tumor-associated diseases, such as breast cancer, liver cancer, and lung cancer.⁵⁻⁶. Current diagnostic testing for prostate cancer relies primarily on measuring serum levels of total prostate-specific antigen (PSA), which can lead to the over-diagnosis/overtreatment of prostate cancer. Therefore, further investigations; to check the feasibility of using serum ferritin levels as a complementary non-invasive biomarker are needed, thereby improving diagnostic specificity and clinical decision-making.

This cross-sectional, observational study was done to estimate, evaluate, and compare the level of serum ferritin and PSA in prostate carcinoma and BPH patients.

2. Material Methods

This cross-sectional, observational study was done in the department of Biochemistry, IGIMS, Patna, over a period of six months duration. 25 diagnosed patients of carcinoma prostate and 25 patients with Benign Prostatic Hypertrophy were enrolled for this study. All the study subjects were in the age group of 40-85 years. Subjects with any other cancer or chronic diseases were excluded from the study. 2ml of venous blood was collected from antecubital vein for biochemical analysis. Serum ferritin and PSA were estimated by Chemiluminescence immuno assay on Beckman Coulter Access2 machine.

All the Statistical calculations were done by SPSS software. Datas are expressed as mean ±1SD. p value <0.05 is considered significant.

3. Results

The mean age of patients diagnosed with carcinoma prostate was 72.3 ±10.8 years while that of BPH group was 68.5 ± 11.2 years. This difference in age in the two groups was not significant ( p value = 0.19).

Serum ferritin level in the carcinoma prostate patients was 268.4± 90.6 ng/ml. Among the BPH patients, level of ferritin was found to be 187.5 ± 62.4 ng/ml. Compared to BPH patients, serum ferritin was increased significantly in prostate cancer patients(p value<0.05).Its sensitivity and specificity was further improved at cut off value of serum ferritin >400ng/ml.

The level of PSA was 24.8 ± 12.5 ng/ml and 5.7 ± 1.2 ng/ml in the carcinoma prostate patients and BPH group respectively with significant difference (p value<0.001).
Table 1: Comparative analysis of parameters in Ca prostrate and BPH

<table>
<thead>
<tr>
<th></th>
<th>Ca prostrate</th>
<th>BPH</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>45</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Age(ys)</td>
<td>72.3 ±10.8</td>
<td>68.5 ±11.2</td>
<td>0.19</td>
</tr>
<tr>
<td>PSA</td>
<td>24.8 ± 12.5</td>
<td>5.7 ± 1.2</td>
<td>&lt;0.001</td>
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<tr>
<td>s.ferritin(nɡ/ml)</td>
<td>268.4±90.6</td>
<td>187.5 ± 62.4</td>
<td>&lt;0.001</td>
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Figure 1: Percentage of Ca prostrate and BPH patients with different ferritin level

4. Discussion

Serum ferritin level was significantly high in the carcinoma prostrate patients compared to the BPH group. Even the ferritin level showed increasing trend with staging and severity of carcinoma prostrate.

Similar results were obtained by Xijuan Wang et al., who found that compared to control patients with benign prostatic hyperplasia (BPH), the patients with prostate cancer had higher levels of total PSA and free PSA, as well as a lower ratio of free PSA to total PSA (Table 1). Moreover, the prostate cancer group contained significantly higher percentages of patients with high serum ferritin levels (i.e., > 300, > 400, and > 500 ng/ml; p < 0.001 for all three categories)10.

There are two possible mechanisms by which iron may increase the risk of cancer. The first is by increasing the production of free radicals thought to be carcinogenic and the second by regulating the activity of odivronucleotide reductase, the rate-limiting enzyme in the DNA synthesis pathway and, hence, cell proliferation. Indeed, iron chelation by deferoxamine inhibits the proliferation of tumor cells and normal lymphocytes, and also induces apoptosis.11-14

Increased levels of circulating ferritin, the body’s primary iron storage protein, have been reported in a wide range of malignancies; moreover, increased ferritin levels are often related to decreased survival time and more aggressive disease progression. For example, increased serum ferritin levels have been associated with the incidence, development, and metastasis of primary lung cancer. Moreover, serum ferritin level has also been shown to be a reliable prognostic indicator in hepatocellular carcinoma and other malignancies. Furthermore, serum ferritin measurements have been combined with more traditional cancer biomarkers such as CEA (carcinoembryonic antigen) and AFP (alpha-fetoprotein) for use as a diagnostic and/or prognostic marker in several types of cancer.15-24

However, Kuvibidila et al. reported an inverse correlation between serum ferritin levels and disease stage in prostate cancer patients.25

5. Conclusion

Serum ferritin may provide the additional sensitivity and specificity needed to improve the diagnostic and prognostic value of the PSA in prostrate carcinoma, and also in differentiation from BPH.

6. Conflict of Interest

None

References

[10]Xijuan Wang Serum ferritin in combination with prostate-specific antigen improves predictive accuracy
for prostate cancer Oncotarget. Advance Publications 2017


