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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 prostrate and 25 patients with Benign Prostratic Hypertrophy were enrolled for this study done to estimate, evaluate and compare the level of serum ferritin and PSA in prostrate carcinoma and BPH patients. Serum ferritin level was significantly high in the carcinoma prostrate 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[1, 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[3-5]. 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[6, 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[8, 9]. 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 prostrate 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 prostrate and 25 patients with Benign Prostratic 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 anticubital 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 prostrate 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 prostrate 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 prostrate 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 prostrate patients and BPH group respectively with significant difference (p value<0.001).

Table1: Comparative analysis of parameters in Ca prostrate and BPH

	Ca prostrate	BPH	p value
n	45	25	
Age(yrs)	72.3 ±10.8	68.5 ±11.2	0.19
PSA	24.8 ± 12.5	5.7 ± 1.2	<0.001
s.ferritin(ng/ml)	268.4± 90.6	187.5 ± 62.4	<0.001

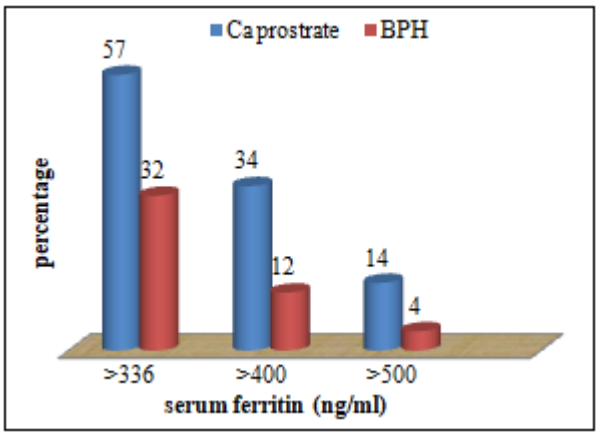

Figure 1: Percentage of Ca prostrate and BPH patients with different ferritin level

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 ofribonucleotide reductase, the rate-limitingenzyme 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

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman, D. Global cancer statistics. CA CanceJ Clin 2011;61:69-90.
[2] Ito K. Prostate cancer in Asian men. Nature Publishing Group. 2014; 11:197–212.
[3] Polascik TJ, Oesterling JE, Partin AW. Prostate specific antigen: a decade of discovery--what we have learned and where we are going. Journal of Urology. 1999; 162:293–306.
[4] Stamey TA, Caldwell M, McNeal JE, Nolley R, Hemenez M, Downs J. The prostate specific antigen era in the United States is over for prostate cancer: what happened in the last 20 years? Journal of Urology. 2004; 172:1297–1301.
[5] Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, Minasian LM, Ford LG, Lippman SM, Crawford ED, Crowley JJ, Coltman CA Jr. Prevalence of prostate cancer among men with a prostate-specific antigen level < or = 4.0 ng per milliliter. N Engl J Med. 2004; 350:2239–2246.
[6] Draisma G, Etzioni R, Tsodikov A, Mariotto A, Wever E, Gulati R, Feuer E, de Koning H. Lead Time and Overdiagnosis in Prostate-Specific Antigen Screening: Importance of Methods and Context. JNCI Journal of the National Cancer Institute. 2009; 101:374–383.
[7] Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RA, Schröder FH, de Koning HJ. Lead times andoverdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. J Natl Cancer Inst. 2003; 95:868–878.
[8] Wang W, KnovichM A, Coffman LG, Torti FM, Torti SV. Serum ferritin: Past, present and future. Biochim Biophys Acta 2010;1800:760-769.
[9] Jézéquel P, Campion L, Spyratos F et al. Validation of tumor-associated macrophage ferritin light chain as a prognostic biomarker in node-negative breast cancer tumors: a multicentric 2004 national PHRC study. Int J Cancer 2012;131:426-437.
[10] Xijuan Wang Serum ferritin in combination with prostate-specific antigen improves predictive accuracy

for prostate cancer Oncotarget, Advance Publications 2017
[11] Partin AW, Criley SR, Steiner MS, Hsieh K, Simons JW, Lumadue J, Carter HB, Marshall FF. Serum ferritin as a clinical marker for renal cell carcinoma: influence of tumor volume. Urology. 1995; 45:211–217.
[12] Facciorusso A, Del Prete V, Antonino M, Neve V, Crucinio N, Di Leo A, Carr BI, Barone M. Serum ferritin as a new prognostic factor in hepatocellular carcinoma patients treated with radiofrequency ablation. J Gastroenterol Hepatol. 2014; 29:1905–1910.
[13] Ji M, Li XD, Shi HB, Ning ZH, Zhao WQ, Wang Q, Zhu LN, Liu Y, Wu CP. Clinical significance of serum ferritin in elderly patients with primary lung carcinoma. Tumor Biol. 2014; 35:10195–10199.
[14] Kukulj S, Jaganjac M, Boranic M, Krizanac S, Santic Z, Poljak-Blazi M. Altered iron metabolism, inflammation, transferrin receptors, and ferritin expression in non-small-cell lung cancer. Med Oncol. 2010; 27:268–277.
[15] Yoh KA, Lee HS, Park LC, Lee EM, Shin SH, Park DJ, Ye BJ, Kim YS. The prognostic significance of elevated levels of serum ferritin before chemotherapy in patients with non-Hodgkin lymphoma. Clin Lymphoma Myeloma Leuk. 2014; 14:43–49.
[16] Wang SL, Cao S, Wu R, Chi F, Tang MY, Jin XY, Chen XD. Serum ferritin predicted prognosis in patients with locally advanced pancreatic cancer. Future Oncology. 2015; 11:2905–2910.
[17] Lee S, Song A, Eo W. Serum Ferritin as a Prognostic Biomarker for Survival in Relapsed or Refractory Metastatic Colorectal Cancer. J Cancer. 2016; 7:957–964.
[18] Uchino K, Tateishi R, Fujiwara N, Minami T, Sato M, Enooku K, Nakagawa H, Asaoka Y, Kondo Y, Yoshida H, Moriya K, Shiina S, Omata M, et al. Impact of serum ferritin level on hepatocarcinogenesis in chronic hepatitis C patients. Hepatol Res. March 2015.
[19] Dörner MH, Abel U, Fritze D, Manke HG, Drings P. Serum ferritin in relation to the course of Hodgkin's disease. Cancer. 1983; 52:2308–2312.
[20] Orlandi R, De Bortoli M, Ciniselli CM, Vaghi E, Caccia D, Garrisi V, Pizzamiglio S, Veneroni S, Bonini C, Agresti R, Daidone MG, Morelli D, Camaschella C, et al. Hepcidin and ferritin blood level as noninvasive tools for predicting breast cancer. Annals of Oncology. 2014; 25:352–357.
[21] Alkhateeb AA, Connor JR. The significance of ferritin in cancer: Anti-oxidation, inflammation and tumorigenesis. BBA-Reviews on Cancer. 2013; 1836:245–254.
[22] Lorenzi M, Lorenzi B, Vernillo R. Serum ferritin in colorectal cancer patients and its prognostic evaluation. Int J Biol Markers. 2006; 21:235–241.
[23] Song MK, Chung JS, Seol YM, Shin HJ, Choi YJ, Cho GJ. Elevation of serum ferritin is associated with the outcome of patients with newly diagnosed multiple myeloma. Korean J Intern Med. 2009; 24:368–373.
[24] Tatsuta M, Yamamura H, Iishi H, Kasugai H, Okuda S. Value of serum alpha-fetoprotein and ferritin in the diagnosis of hepatocellular carcinoma. Oncology. 1986; 43:306–310.
[25] Kuvibidila SR, Gauthier T, Rayford W. Serum ferritin levels and transferrin saturation in men with prostate cancer. J Natl Med Assoc. 2004; 96:641–649.