RESEARCH COMMUNICATION

Elevated Level of Prostate Specific Antigen Among Prostate Cancer Patients and High Prevalence in the Gangetic Zone of Bihar, India

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Abstract

Prostate cancer (CaP) is a common reproductive cancer among men. This study was conducted to correlate the cancer incidence with Gangetic zone and to correlate the tumor marker prostate specific antigen (PSA) level in serum with different age groups and stage of malignancy. Patients suffering from CaP in the pathology unit of Mahavir Cancer Sansthan (Hospital and Research Centre), Patna, Bihar, India were studied from June 2009 to May 2010. PSA level in the serum of CaP patients was estimated by ELISA method. CaP incidence was highly recorded in Gangetic zone than the non-Gangetic zone. Maximum patients were in the 56 – 75 years age group with a marked predominance. Results of PSA examination showed that serum PSA level was not correlating with the age of patient and stage of malignancy. Significantly, elevated level of more than 10 ng/ml of PSA was recorded among the studied cancer patients. In this study, it is concluded that Gangetic zone habitat have high risk of CaP and elevated level of PSA was marked in Bihar, India.

Keywords: PSA marker - prostate cancer - arsenic - environmental carcinogen - gangetic zone - cancer incidence

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Introduction

Cancer is a dreadful disease afflicting in human beings. Globally cancer incidence has increased every year. Nearly, 10 million new cases are reported each year worldwide out of which 5.5 million cases are from developing countries. In India, 5,50,000 deaths are occurring each year due to cancer related issues (Nandakumar, 1996). Prostate cancer (CaP) is a very common malignancy in men and its incidence varies worldwide. CaP disease is a reproductive disease and it is associated with aging. Prevalence of CaP has been reported to be associated with Prostate Specific Antigen (PSA) level in the serum of men. PSA is functionally and immunologically specific to prostate gland. In fact, it has been established that abnormal PSA value is a reliable indicator for CaP and PSA has been widely used as diagnostic marker for its detection. Elevated PSA has been associated with prostate malignancy and benign prostatic hyperplasia (Dennis et al., 2000; Christensen and Andriole, 2009).

Reproductive cancers are mostly caused due to hormonal carcinogenesis and also by endocrine disturbing chemicals (EDCs). According to Diamanti-Kandarakis et al., (2009), reproductive related cancer incidence increased due to the EDCs during the last 50 years in the industrialized world. It has been hypothesized that the significance of EDCs in carcinogenesis has increased in the current decade. CaP has also been associated with hormonal factors and EDCs. The growth and differentiation of the prostate is under androgen control, testosterone and estrogen are involved in the prostate function regulation. Elevated level of estrogen is a major risk factor for CaP (Modugno et al., 2001). Some of the EDCs especially xenoestrogens induce more production of estrogen and cause more risk of CaP.

Bihar is one of the poorest and least developed states in India. Reproductive cancer incidences continue to be an important public health hazard in Bihar. River Ganga flows across the state of Bihar in India, accounting for a high percent of water resource for a majority of its population. Due to high rate of population growth in this state and poor management of urbanization and industrial growth, the quality of resources has significantly deteriorated. This study was under taken for assessing the risk factors for CaP prevalence and to evaluate the PSA level in the serum of CaP patients.

Materials and Methods

CaP incidence in Bihar was analyzed from the patient's clinical registry maintained at the pathology unit of Mahavir Cancer Sansthan (Hospital and Research Centre), Patna, Bihar, India. This institute is the only 300-bed hospital for cancer care in Bihar, which is located in the capital city of Patna. According to hospital cases report most of the cancer cases were recorded from the different

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districts of Bihar. More than 8,000 new cases are being diagnosed every year in the hospital. A total of 280 prostate cancer patients files were chosen to assess the prevalence of cancer case in Bihar during June 2009 to May 2010. Collected data was categorized into different districts, age groups and stage of malignancy. The analyzed district wise data were classified into Gangetic zone and non-Gangetic zone. Estimated serum PSA levels were taken from untreated CaP patients from all the case files. PSA levels were assayed through ELISA technique using PSA kit (Himedia) during time the patients' were being treated at the institute.

One way ANOVA was used for statistical analysis for PSA level with age groups and stage of malignancy. Significant differences between PSA levels were determined using Tukey's multiple range tests ($P \leq 0.05$).

Results

The results revealed a high incidence of CaP in the districts of Begusarai, Buxar, Chapra, East Champran, Gaya, Khagaria, Muzaffarpur, Nalanda, Patna, Rohtas, Siwan and Vaishali (Figure 1). Out of the 38 districts in Bihar, over 5% of incidence rate was recorded from the districts of Begusarai, Buxar, Chapra, Muzaffarpur, Nalanda, Patna, and Vaishali. In the Gangetic zone, nearly 4% of CaP incidence was recorded and in non-Gangetic zone nearly 2% of CaP incidence was recorded (Figure 2). Figure 3 shows a comparison of CaP incidence with different age groups (36 to 45, 46 to 55, 56 to 65, 66 to 75 and 76 to 85 years). Age was a predominant factor in the CaP risk and its incidence was high in the age group of 56 to 75 years. Elevated level of more than 10 ng/ml of PSA in serum was recorded in the different age groups of prostate cancer cases (Table 1). Maximum 60 ng/ml mean value of PSA was recorded in 56 – 65 years of age group. Table 2 shows the serum PSA level with different stage of malignancy in 56 to 75 range age group. No correlation between the elevated serum PSA level and different age groups. Malignancy stage was also found to be uncorrelated with the elevated serum PSA level.

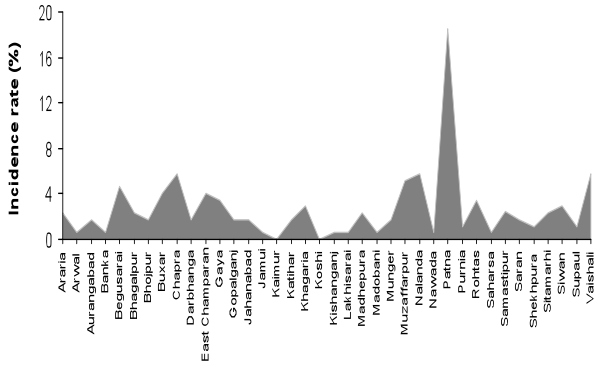

Figure 1. Prostate Cancer Incidence in Different Districts of Bihar

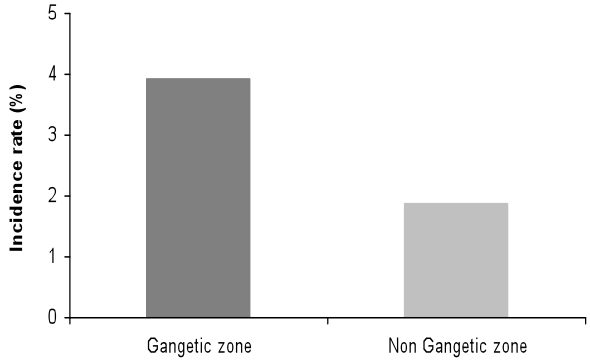

Figure 2. Prostate Cancer Incidence Variation Between Gangetic Zone and Non Gangetic Zone

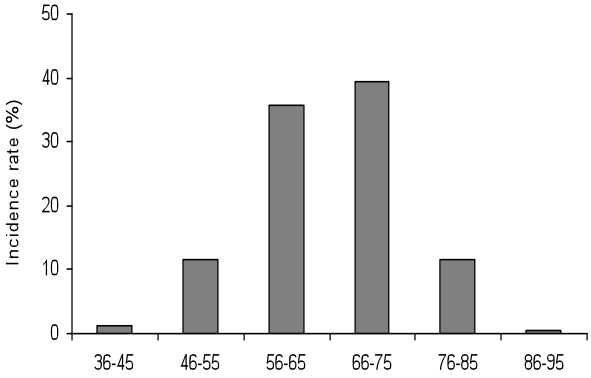

Figure 3. Prostate Cancer Incidence Among Different Age Groups

Table 1. Comparison of Serum PSA Level in Prostate Cancer Patients with Different Age Groups

Age range (Years)	PSA (ng/ml) Mean ± SD
36 - 45	23.40 ± 29.13[a]
46 - 55	17.16 ± 20.72[a]
56 - 65	60.03 ± 70.87[b]
66 - 75	54.04 ± 68.01[b]
76 - 85	54.79 ± 41.29[b]
86 - 95	23.36 ± 17.13[a]

[a,b]Within columns, mean ± SD followed by the same letter do not differ significantly using Tukey's test, P≤0.05

Table 2. Comparison of Serum PSA Level in Prostate Cancer Patients with Different Stages of Cancer

Age Range (Years)	Stage	PSA (ng/ml)
56-75	I	23.58 ± 12.33[a]
	II	46.08 ± 42.87[b]
	III	51.69 ± 49.36[b]
	IV	68.62 ± 70.89[b]

[a,b]Within columns, mean ± SD followed by the same letter do not differ significantly using Tukey's test, P≤0.05

Discussion

In this study a consistent pattern of high incidence of the disease was recorded from districts located closer to the Gangetic belt suggesting remarkably higher prevalence of CaP in this zone. Generally, the development of a malignant tumor involves complex interactions between several factors, both exogenous (environmental) and endogenous (genetic, hormonal, and immunological). Several studies suggest that arsenic (As), a non essential element causes increased risk of CaP. The level of As in

ground water in the districts in the Gangetic zone was found to be higher as compared to the areas from non Gangetic zone (Saha, 2009). Naturally, environmental carcinogens can enter into human body by accidental ingestion, inhalation or absorbed through skin contact from the environmental sources or through the food chain. It is very likely that the ingestion of water and food is primary exposure pathway for As entry. As is readily absorbed from gastrointestinal tract and via the lungs and has been observed to accumulate in liver, kidney, lungs and skin.

As is a well-known EDC and has been recently identified as a potential xenoestrogen (Diamanti-Kandarakis et al., 2009). Due to its xenoestrogenic nature, As may also causes reproductive cancer. This indicates that the ingestion of As could be causing more risk of CaP in male inhabitants of the region, possibly suggesting a gene-environment interaction in the area. Reports in literature suggest an association of As with reproductive hazards possibly due to disruption of the steroid hormone signalling pathway and disruption of the steroid hormone metabolism in human body. Because of prostate epithelial cell sensitivity, As reportedly plays a potential role in prostate carcinogenesis. It interacts with estrogen receptor and activates the estrogen-regulated genes due to which estrogen-signalling pathway is abrogated (Chatterjee and Chatterji, 2010) thereby producing elevated level of estrogen. This in turn is associated with increased risk of CaP (Modugno et al., 2001). Arsenate accelerates the rate of ITP (inosine triphosphate) hydrolysis and inhibits both Ca^{2+} and Sr^{2+} uptake. This perturbation of intracellular Ca^{2+} homeostasis activates protein kinase C (PKC) activity, which could potentially play an important role in arsenite-induced genotoxicity. Genotoxic effects of arsenic compounds may be associated with an inhibition of DNA repair and nucleotoxic effects. Present epidemiological study strongly suggests that As is a predominant factor causing CaP in As endemic regions.

Generally, 4 ng/ml of PSA in serum was considered as normal and more than 4 ng/ml of PSA indicated prostate malignancy or benign prostatic hyperplasia. Recently, Ezeiruaku et al., (2011) reported that serum PSA level increased from 4 ng/ml to 9 ng/ml with increasing age groups. However, in the present study, extremely elevated serum PSA morethan 10 ng/ml was recorded in all the cases. Hence, serum PSA does not seem to correlate with age and stage of malignancy. This is a remarkable finding and in disagreement to the previous reports. In conclusion, the study would recommend that men above 40 years of age inhabiting this region should be educated about the disease and should be motivated to go for regular prostate screening test. CaP cancer is a disease, with many aspects of management including the development of a sound data to support treatment recommendations, which can be specifically tailored for people belonging to different socio-cultural backgrounds and geo-ethnic groups.

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