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Research Article

RELATION BETWEEN LOW SERUM TESTOSTERONE AND PROSTATE CANCER BEHAVIOR

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ABSTRACT

Objectives: Prostate cancer is intensifying globally, including Asian countries also. There are numerous arguments still going on concerning the connection among endogenous testosterone levels and prostate ailments. The present research was performed to recognize the assessment of serum testosterone in identifying the threat and prostate cancer incidences.

Methods: Hundred cases were registered in the research, among that, the cases showing low testosterone value (<250 ng/dL) was considered A Group and cases with normal testosterone value (>250 ng/dL) was considered B Group. All cases those went radical prostatectomy were followed for post-operatively with histopathological analysis and variables, namely, Post-operative Gleason grade, pathological tumor status, pathological node status, surgical margin status, extracapsular extension of tumor, seminal vesicle invasion, and matched among groups. Variables were completed with the Student's t-test; $p<0.05$ was considered statistically significant.

Results: Serum testosterone levels was found to be reduced among 74% and regular among 34% prostate cancer cases. Patients in Group A showed greater complete tumor stage, advanced nodal stage, and widespread metastases on scientific assessment associated with Group B.

Conclusion: All the elderly men aged 60 and more should be screened for serum testosterone levels for timely prostate carcinoma diagnosis and for better prognosis in the management.

Keywords: Prostate cancer, Serum testosterone, Elderly men, Behavior, Testosterone.

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INTRODUCTION

Prostate cancer occurrences together with benign prostatic hyperplasia are intensifying globally. In our country, most of prostate carcinoma cases were detected during progressive phase, and therefore, morbidity rates were higher. Reasons of prostate carcinogenesis and its development were mysterious. Extensive research endorses together genetics and environmental parameters playing a significant impact in the beginning as well as the advanced ailments [1]. Etiology of prostate cancer is unclear, while several evidences suggest prostate cancer seems to be multifactorial. Age, ethnicity, heredities, surroundings, hormone, food habits, etc., mostly form the reason for prostate cancer [2]. Food intake and physical activities play a significant part in prostate cancer progress. Dietary influences are mostly connected with universally, indigenous changes in incidence rates of prostate cancer [3]. As per epidemiological researches, approximately 83% of prostatic cancer was related with benign prostatic hyperplasia in prostate, around 3 to 20% of males undergoing these transurethral prostatectomy (TURP) and/or open prostatectomy for benign prostatic hyperplasia later progress to prostate cancer [4]. Conversely, a proper and clear validation is missing for the part of endogenous testosterone in persuading the progress of prostate cancer among males [5].

Serum prostate-specific antigen analysis has transformed prostate cancer identification rate, it is a significant indicator in analyzing the concern research. Serum prostate-specific antigen (PSA) testing shows more in cases with confined prostate carcinoma and less in meta-static stage of cancer prostate. Serum PSA analysis results in further migration of disease and initial age during. Although PSA levels form the marker in the pathological status of prostate, it lacks sensitivity and does not rule out further non-prostatic reasons of raises in serum PSA values [6].

Considering all, the present research is aimed to evaluate the reasons for this testosterone with prostate cancer along with other variables performed to identify prostate diseases [1]. Leading aim of this current research is to define the link among low serum testosterone as well as prostate cancer patient's behaviors.

METHODS

Analysis of correlation among prostate cancer behavior having low serum testosterone and normal serum testosterone was performed as a prospective research during the period from August 2014 to December 2016 in the department of urology, SCB Medical College, Cuttack. Institutional ethical committee approval has been obtained before proceeding to the research initiation.

Inclusion criteria

This study included patients of altogether freshly analyzed prostate cancer (TRUS-Guided Biopsy proven) cases having the age of above 40 years in our research center.

Exclusion criteria

Cases previously consuming testosterone additional treatment, cases following any additional hormones treatment, males consuming medicines to decrease serum PSA values (like FINASTERIDE and/or DUTASTERIDE and/or testosterone reductase inhibitor, those with hypogonadism have been excluded. Informed consent was collected from all cases that were enrolled in to this research.

All TRUS BIOPSY confirmed cancer prostate cases are included to reach hundred. Complete set of all history were documented in the pro forma. Biochemical examinations including serum PSA, serum testosterone, and baseline studies were performed. Only at around 7 to 9.30 am, serum testosterone estimations were performed. Serum testosterone levels were estimated by standard procedure.

All the cases were grouped into two Groups constructed on the serum testosterone values. Cases showing less serum testosterone values that are

lesser than 250 ng/dL were considered as A Group: Cases showing standard range serum testosterone values more than 250 ng/dL were considered as B Group. Surgical procedure has been performed in these cases and these cases were followed-up for 1 month after the surgery period.

Completely all cases of the study were evaluated during admission time depending on elaborated clinical investigation, complete baseline plasma examinations, serum PSA, serum testosterone, Gleason grading (TRUS BIOPSY) including primary, secondary, total Gleason score (TGS), and imaging readings. Cases of restricted prostate tumors along with Clinical stage T1: stage T2 deprived of pelvic nodal contribution also metastasis was advised regarding choice of radical prostatectomy, remaining cases are in progressive stage of the disorder including experimental T3: T4 ailment, metastatic prostate cancer was accomplished by hormones treatment monitored through anti-androgen therapy.

Radical prostatectomy accomplished cases were followed post-operatively along with histopathological testing, variables, namely post-operative Gleason grade, pathological tumor (PT) status, pathological node (PN) status, surgical margin status (SMS), extracapsular extension (ECE) of tumor, seminal vesicle invasion (SVI), and are related among Groups A and B.

Statistical analysis

Interpretation was implemented by unpaired Students 't' test and $p<0.05$ was estimated as statistically significant. Chi-square test is done in associating the prostate cancer variables among Groups A and B.

RESULTS

Of 106 patients, 5 cases on five-α reductase inhibitors and one case on testosterone removal treatment were omitted in current research and 100 cases totally registered in the study; cases with low testosterone level (<250 ng/dL) were considered to be Group A; cases with normal testosterone level (>250 ng/dL) were considered to be Group B. The youngest age as 45 years, oldest documented age as 85 years.

Serum PSA values were estimated in cases and PSA values among Group A; Group B was investigated (Table 1). 74% of cases in Groups A showed a serum PSA of more than 20 values comparable with 34% of cases in Group B. p-values were found to be statistically significant (0.003).

Comparison of cases for TGS (low <7, intermediate 7, high 8–10) was done. Cases with 82.6% in Group A reported a greater Gleason grade (8–10) associated toward Group B. The relation among TGS and serum testosterone levels between Group A and B showed cases in Group A showed greater percentage of high Gleason score associated with Group B (Table 2).

Pre-operative clinical tumor (T) status, nodal status (N), and metastasis (M) status were examined (Table 3). Group A showed greater overall tumor stage, greater nodal stage, and widespread metastases on clinical assessment than Group B. 'P' value was found to be statistically significant (0.002).

Table 1: Serum PSA values among 2 groups

Serum PSA*serum testosterone	Serum testosterone		Total	p-value
	<250	>250		
Serum PSA				0.003
<10				
Count	1	16	17	
% within serum PSA	5	94	100	
% within serum testosterone	4	20	17	
10–20				
Count	5	35	40	
% within serum PSA	12	87	100	
% within serum testosterone	21	45	40	
>20				
Count	17	26	43	
% within serum PSA	39	60	100	
% within serum testosterone	73	33	43	
Total				
Count	23	77	100	
% within serum PSA	23	77	100	
% within serum testosterone	100	100	100	

PSA: Prostate-specific antigen

Table 2: Comparison of TGS among groups

TGS	Serum testosterone		Total	p-value
	<250	>250		
Serum TGS				
<7				
Count	0	30	34	<0.005
% within TGS	0	100	100	
% within serum testosterone	0	42	34	
7				
Count	4	39	43	
% within TGS	9	90	100	
% within serum testosterone	17	50	43	
8–10				
Count	19	4	23	
% within TGS	82	17	100	
% within serum testosterone	82	5	23	
Total				
Count	23	77	100	
% within TGS	23	77	100	
% within serum testosterone	100	100	100	

TGS: Total Gleason score

Table 3: Preoperative clinical tumour (T) statuses between 2 groups

TGS * serum testosterone	Serum testosterone		Total	p-value
	<250	>250		
Preoperative clinical tumor				<0.002
T2A				
Count	1	7	8	
% within TGS	12	87	100	
% within Serum Testosterone	4	9	8	
T2B				
Count	6	10	16	
% within TGS	37	62	5	
% within Serum Testosterone	26	13	100	
T2C				
Count	2	3	5	
% within TGS	40	60	28	
% within serum testosterone	8	3	100	
T3A				
Count	2	26	28	
% within TGS	7	92	39	
% within serum testosterone	8	33	100	
T3B				
Count	8	31	39	
% within TGS	20	79	2	
% within serum testosterone	34	40	100	
T4A				
Count	2	0	2	
% within TGS	100	0	2	
% within serum testosterone	8	0	100	
T4B				
Count	23	77	2	
% within TGS	23	77	100	
% within serum testosterone	100	100	100	

TGS: Total Gleason score

Patient's clinical Nodal statuses (N) were analyzed (Table 4). Group A showed a greater nodal participation than Group B. 'p' value was found to be statistically significant.

Patient management options among Group A and B were established, pathological tumor features were associated between the o groups. Although complete T staging is not statistically significant, cases in group A showed greater T3 disease than cases in group B. p-value was not statistically significant. Post-operative pathological nodal statuses among two groups were comparable (Table 6). Cases in Group A showed additional percentage of pathological lymph nodal participation than Group B. p-value was found to be statistically significant (p=0.015).

From prostatectomy specimen TGS of the 2 Groups was analyzed (Table 7). p value was found to be statistically significant.

SMS of the two groups was analyzed (Table 8). >60% of the cases in Group A showed positive surgical margin as compared to Group B. p-value was found to be statistically significant (p=0.026).

Table 4: Analysis of preclinical nodal status

Post-operative pathological nodal statuses	Serum testosterone		Total	p-value
	<250	>250		
Clinical stage N				
N0				
Count	7	68	75	<0.015
% within TGS	9	90	100	
% within serum testosterone	30	88	75	
N1				
Count	16	9	25	
% within TGS	64	36	100	
% within serum testosterone	69	11	25	
Total				
Count	23	77	100	
% within TGS	23	77	100	
% within serum testosterone	100	100	100	

Metastasis status (M) of the patients were analysed and the results between groups was found to be statistically significant [Table 5]. TGS: Total Gleason score

Table 5: Metastasis statuses of patients

Metastasis statuses of patients	Serum testosterone		Total	p-value
	<250	>250		
Clinical stages				
M0				
Count	9	64	73	<0.005
% within TGS	12	87	100	
% within serum testosterone	39	83	73	
M1A				
Count	0	1	1	
% within TGS	0	100	100	
% within serum testosterone	0	1.3	1	
M1B				
Count	11	12	23	
% within TGS	47.	52	100	
% within serum testosterone	47	15	23	
M1C				
Count	3	0	3	
% within TGS	100	0	100	
% within serum testosterone	13	0	3	
Total				
Count	23	77	100	
% within TGS	23	77	100	
% within serum testosterone	100	100	100	

TGS: Total Gleason score

ECE status between the 2 Groups are analyzed from post-prostatectomy specimen (Table 9). Groups A showed a higher number of ECE s than Group B. p-value was found to be statistically significant (p=0.036).

From post-prostatectomy specimen, SVI statuses between 2 groups were analyzed (Table 10). SVI seems to be greater in Group A than Group B. p-value was found to be statistically significant (p<0.026) Group A showed more SVI in comparison with Group B.

Table 6: Post-operative pathological nodal statuses

Post-operative pathological nodal statuses	Serum testosterone		Total	p-value
	<250	>250		
Nodal status				
PN0				
Count	1	6	7	<0.015
% within TGS	14	85	100	
% within serum testosterone	20	100	63	
PN1				
Count	4	2	4	
% within TGS	100	28	100	
% within serum testosterone	80	33	36	
Total				
Count	5	6	11	
% within TGS	45	54	100	
% within serum testosterone	100	100	100	

TGS: Total Gleason score

Table 7: Post-operative Gleason grade among 2 groups

Post-operative Gleason grade	Serum testosterone		Total	p-value
	<250	>250		
Grade				
7				
Count	0	4	4	<0.022
% within TGS	0	100	100	
% within serum testosterone	0	66	36.4	
8-10				
Count	5	2	7	
% within TGS	71	28	100	
% within serum testosterone	100	33	63.6	
Total				
Count	5	6	11	
% within TGS	45.5	54.5	100	
% within serum testosterone	100	100	100	

TGS: Total Gleason score

Table 8: SMS of the 2 Groups

SMS	Serum testosterone		Total	p-value
	<250	>250		
SMS				
Positive				
Count	3	0	3	<0.026
% within TGS	100	0	100	
% within serum testosterone	60	0	27.3	
Negative				
Count	2	6	8	
% within TGS	25	75	100	
% within serum testosterone	40	100	72	
Total				
Count	5	6	11	
% within TGS	45	54	100	
% within serum testosterone	100	100	100	

SMS: Surgical margin status, TGS: Total Gleason score

Table 9: ECE statuses between 2 Groups

ECE	Serum testosterone		Total	p-value
	<250	>250		
ECE				
Positive				
Count	4	1	5	<0.036
% within TGS	80	20	100	
% within serum testosterone	80	16	45	
Negative				
Count	1	5	6	
% within TGS	16	83	100	
% within serum testosterone	20	83	54	
Total				
Count	5	6	11	
% within TGS	45.5	54.5	100	
% within serum testosterone	100	100	100	

ECE: Extra capsular extension, TGS: Total Gleason score

Table 10: SVI statuses between 2 groups

SVI	Serum testosterone		Total	p-value
	<250	>250		
SVI				
Positive				
Count	3	0	3	<0.026
% within TGS	100	0	100	
% within serum testosterone	60	0	27	
Negative				
Count	2	6	8	
% within TGS	25	75	100	
% within serum testosterone	40	100	72	
Total				
Count	5	6	11	
% within TGS	45	55	100	
% within serum testosterone	100	100	100	

SVI: Seminal vesicle invasion, TGS: Total Gleason score

DISCUSSION

Prostate cancer forms the utmost communal malignancy among men, standing for 2nd afterward lung carcinoma [7]. Documentation of biomarkers, namely PSA, which is completely associated in the identification of prostate cancer has revolutionised epidemiology. Certainly, later, the PSA analysis arrival and successive biopsy, America enumerated two-fold rise of prostate cancer prevalence in late 1980s [8].

George *et al.* established among black men, low testosterone value seems to be independent bio-marker for high-grade prostate cancers [9]. Also, reported that in localized prostate carcinoma, high-grade carcinoma seems to be pragmatic with the cases of hypogonadism. Suggesting serum testosterone levels forms the chief impending biomarker for prediction in high-grade carcinoma prostate cases. Lesser, well-designed researches confirmed augmented prostate cancer threat in cases of lesser testosterone values [10]. Various reports suggested the positive connection, no association in addition null-hypothesis in connection to serum testosterone values [11].

Morgentaler *et al.* [12] done principal initiative to report the lesser testosterone values does not offers protection toward prostate cancer progress. Also, concluded asymptomatic males with less free, total serum testosterone values have great occurrence in carcinoma prostate rates. This study also showed an advanced prevalence of prostate carcinoma in cases having less serum testosterone. A supplementary report with Massachusetts aging research has stated no relationship among androgens plus serum testosterone, cancer prostate threat [13].

The correct reason for comparison among less testosterone value, high-risk prostate carcinoma is yet not documented. A possible cause is the destruction of discharge of testosterone by prostate cancer through the hypothalamic-pituitary-gonadal axis [14]. Miller *et al.* [15] determined prostate cancer subdues testosterone manufacture by generating inhibin and starts negative feedback on the hypothalamic-pituitary-gonadal axis. Similarly, it is also established that the testosterone values increase subsequently following radical prostatectomy.

Zang *et al*. [15] determined prostate cancer subdues testosterone manufacture by generating inhibin and starts negative feedback on the hypothalamic-pituitarygonadal axis. Similarly, it is also established that the testosterone values increase subsequently radical prostatectomy. Schatzl *et al*. [16]described low serum testosterone values in prostate cancer with high-grade tumors than temperate grade prostate tumors. Morgentaler *et al*. [17] too stated lesser testosterone, serum estradiol values of higher Gleason score in prostate cancers. Tumor-mediated destruction of gonadotrophins, among males with high-grade prostate carcinoma and androgen receptor expression seems to be increased in these cases. Therefore, this study also documented to consider the free testosterone diagnosing prostate cancer than total serum testosterone.

Relationship among serum testosterone, cancer prostate is not clearly documented till now. The relationship is because of the negative feedback mechanism of serum testosterone in hypothalamo pituitary axis. Miller *et al.* conducted a research [14] explained that prostate cancer hinders serum testosterone manufacture through inhibin. Relation among less serum testosterone value, high-risk cancer was mainly because of the changes which may occur in the hormonal levels. Specimen's Gleason total score, surgical margins status, ECE, and SVI were investigated with normal serum testosterone cases. Zhang *et al.* [15] have already documented the relationship among less serum testosterone values, greater Gleason grade prostate cancer. We observed better proportions of cases by low serum total testosterone levels when presented with great (≥8) TGSs.

The observed results were also obtained by another study done by Schatzl *et al.* cases showing low serum testosterone levels was documented showing greater Gleason total score if plotted versus normal serum testosterone [16]. Most of the documented studies reported serum testosterone values were significant, independent indicator to evaluate prostate biopsy. Post-prostatectomy histopathological specimen's Gleason score, pathological tumor stage, baseline serum PSA were connected to the threat of destructive prostate cancer. Hoffman *et al.* documented cases with low serum testosterone forms the indication in destructive cancer prostate [18].

CONCLUSION

Therefore, in considering pre-operative case, more precisely, free testosterone can be verified as a predictable examination with serum PSA levels towards prediction as well as improved treatment plan for prostate carcinoma. Low total serum testosterone is connected in greater percentage of Gleason pattern 4, an sign of prostate cancinoma. Cases with low testosterone undergone radical prostatectomy showed a greater percentage of positive surgical margin, ECE, SVI signifying destructive prostate cancer behaviors. Pre-operative total testosterone can be added to serum prostate-specific antigen determination progressing modalities of prostate cancer therapy.

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AUTHORS' CONTRIBUTIONS

Dr. Ghanashyam Meher and Dr. Pabitra Hembram - Design and Data collection of data, journal selection, literature analysis for the manuscript. Dr. Kshetra Mohan Tudu and Dr. Binod Kumar Sahu - Analysis or interpretation, literature search, manuscript writing and submission to the journal.

CONFLICT OF INTEREST

Nil.

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