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# CANCER PROSTATE;
## TREATMENT RESPONSE ON THE LEVEL OF PROSTATE SPECIFIC ANTIGEN (PSA)

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**ABSTRACT…** Prostate specific antigen was identified and characterized first time in 1977. There is no doubt that the PSA has significant role in prostate cancer diagnosis with help of Digital Rectal Examination and biopsy. **Study design:** This study was designed to assess the level of PSA in prostate cancer patients before and after the treatment given to patients. To determine the specific and precise finding regarding the tumors stages, the cancer biomarkers are handy and helpful. For this purpose researchers monitor changes in the cell on chromosomal level by comparing primary tumor with secondary tumor. The prostate-specific gene kallikrein 3 (KLK3), encodes PSA located on chromosome 19q13.4. KLK2 and KLK4 genes are also present here which are present in a family of fifteen closely related serine proteases. **Setting:** Allied Hospital, Faisalabad. **Period:** Jan 2014 to Dec 2014. **Material and methods:** We use the PSA (Human) CLIA Kit which is a solid phase two site immunoassay. One antibody was coated on the surface of the microtiter wells and another antibody (used as a tracer) was labeled with horseradish peroxidase. The PSA molecules present in the standard solution or serum were "sandwiched" between the two antibodies. **Results:** All prostate cancer patients had highly variable serum PSA values ranging from 12.90 ng/mL to 193.5 ng/mL. The post treatment PSA analysis revealed that the increase level of PSA (15%) which showed that the PSA level increased after the treatment. Whereas in all other 17 patients the PSA level was found to decreased. Our study also shows that sometime PSA level is increased by non-cancer associated benign prostatic hyperplasia (BPH), prostatitis, medications and environment and diet alterations. **Conclusions:** This study indicated that PSA serum level has a useful role in diagnosis of prostate cancer.

**Key words:** Prostate specific antigen, cancer biomarkers, KLK (Kallikrein)

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## INTRODUCTION

Globally 14.1 million new cases of cancer were reported in 2012. Of all human deaths it caused 14.6% deaths. According to the world cancer report, the most common types of cancer in females are breast cancer, colorectal cancer, lung cancer, and cervical cancer and in the males the most widespread types of cancers are lung cancer, prostate cancer, colorectal cancer, and stomach cancer. Prostate cancer is third in number among the cancer incidence and mortality stands at sixth position.[3] For prostatic cancer the commonly used and recognized biomarker is Prostate specific antigen (PSA).[4]

Different kinds of the biomarker are used for diagnosis and prognosis purposes like imaging epigenetic, proteomic and genetic biomarkers. The biofluids like blood or serum are used for assay of these biomarkers.[5,7] Many markers show promise but none seems poised to replace PSA, but rather may augment it. Prostate specific antigen (PSA) as a biomarker is very constructive tool for evaluating the prognosis, staging, effectiveness and recurrence in prostate cancer patients.[8]

PSA was identified and characterized in prostate in 1977 and 1979 respectively.[6] To determine the specific and precise finding regarding the tumors stages the cancer biomarkers are handy and helpful. For this purpose researchers monitor changes in the cell on chromosomal level by comparing primary tumor with secondary tumor. If alteration matches, then secondary tumor as metastatic or if differ, the secondary tumor can be

recognized as diverse primary tumor.[21]

The "epithelial cells of the prostate secrete" the "prostate specific antigen (PSA)" which is 33 serine protease (kallikrein-3). This PSA is released into the secretory ducts and play its role in the production of semen. PSA interferes into the circulation due to disorder of the basal cell layer then PSA level increases in the serum. PSA is present in the prostate and it is not always the sign of disease.[9] PSA has provided significant advancement in the diagnosis and prognosis of PCa. However, it does have limitations, including its lack of specificity and no seemingly safe level that confers a zero risk of a PCa diagnosis.[10] Further, its indiscriminate use has allowed for over diagnosis and overtreatment of low-risk PCa that would not have affected the longevity or quality of life.[11] These shortcomings have led many to investigate more optimized uses of PSA[12], in addition to the development of novel biomarkers using various tissue media. This paper describes the use of current biomarkers for PCa screening, surveillance, and future directions using blood. Our objective is to establish the effective role of "prostate specific antigen" level in the cancer patients before and after the chemotherapy treatment.

## MATERIALS AND METHODS

Research work was conducted in "Molecular Biochemistry Lab, Department of Chemistry and Biochemistry, University of Agriculture Faisalabad", Pakistan. This study was designed to assess the level of PSA in prostate cancer patients before and after the treatment given to patients at cancer ward Allied Hospital Faisalabad.

Using "standard venipuncture techniques", blood was drawn and the serum was separated from the RBCs as soon as feasible. Grossly turbid or hemolytic samples were avoided. Plasma samples collected in tubes contained anti-coagulants like oxalate, EDTA or heparin, may hamper the test procedures and were avoided. After capping the specimens were stored at 2-8 °C, before assaying. Specimens held for a longer time were frozen at -20°C. Thawed samples were mixed prior to testing. The PSA analysis was done by using the Acculit CLIA Microwells prostate specific antigen kit.

Upon receiving the new kits were stored at 2-8 °C. To minimize exposure to damp air the microtiter plate was kept in a sealed bag containing desiccants.

Contents of Wash Concentrate were diluted in a storage container to 1000 mL with deionized or distilled water. The diluted buffer was stored at room temperature 20-27 °C. The amount of reagent needed was determined and prepared in a clean container by mixing equal portions of "Signal Reagent A and B". For example, 1 ml of A and 1ml of B was added per two (2) eight well strips (A slight excess of solution was made in order to replicate the experiments later). If complete utilization of the reagents were expected, within the above time limit, the contents of "Signal Reagent B" were poured into "Signal Reagent A" and label therefore. After performing the assay according to the standard protocol and results were read within half an hour of adding the substrate solution

## RESULTS

Research work was conducted in "Molecular Biochemistry Lab, Department of Chemistry and Biochemistry, University of Agriculture Faisalabad", Pakistan. This study was designed to assess the level of PSA in prostate cancer patients before and after the treatment given to patients at cancer ward Allied Hospital Faisalabad. The blood samples were collected from the cancer unit Allied Hospital Faisalabad after the approval from the hospital ethical review committee. After chemotherapy of prostate cancer patients the same procedure was followed to evaluate the treatment response. Mortality is high in "prostate cancer" due to its frequent occurrence in elder population. Another reason for high mortality is its late identification in most of the cases. 20 patients were registered as "prostate cancer patients" in cancer unit Allied Hospital Faisalabad.

| Patients | Age | PSA (ng/mL |
|---|---|---|
| P1 | 75 | 168.1 |
| P2 | 70 | 176.0 |
| P3 | 43 | 90.6 |
| P4 | 60 | 130.0 |
| P5 | 79 | 134.8 |
| P6 | 73 | 12.90 |
| P7 | 65 | 100.3 |
| P8 | 70 | 124.4 |
| P9 | 80 | 17.40 |
| P10 | 55 | 62.11 |
| P11 | 70 | 136.7 |
| P12 | 69 | 15.5 |
| P13 | 69 | 56.10 |
| P14 | 68 | 13.4 |
| P15 | 58 | 49.0 |
| P16 | 60 | 83.0 |
| P17 | 60 | 44.0 |
| P18 | 62 | 92.15 |
| P19 | 62 | 193.15 |
| P20 | 56 | 121.3 |

Table-I. PSA level before treatment

All “prostate cancer patients” had highly variable “serum PSA” values ranging from 12.90 ng/mL to 193.5 ng/mL (Table-I). In these patients, 4 (20%) had “PSA levels” >10.0 ng/mL but less than 20 ng/mL (Mean 14.8ng/mL) and 2 (10%) had “PSA level” > 40 ng/mL (Mean 46.5 ng/mL) (Table-I) 3 (15%) patients had PSA level >50 ng/mL, PSA level > 60 ng/mL and PSA level > 80 ng/ml respectively. 2 (10%) patients had PSA level > 90. PSA values of 6 (30%) patients were in range of 100 to 150 ng/mL. PSA level was 150 ng/mL to 200 ng/mL in 3 (15%) cancer patients. There was also lab variation and 3 (15%) showed that the PSA level increased after the treatment. In all other 17 patients the PSA level decreased. Maximum decrease in PSA level was 34.5% after the treatment, PSA level before the treatment 130.0 ng/mL and after the treatment level of PSA reduce to 85.1ng/ml and the patient was 60 years old .The minimum decrease was 28.7% after the treatment in which PSA value before the treatment was 17.40 ng/mL and after the treatment it was reduce to 12.40 ng/mL, patient age was 80 years old. Minimum age recorded was 43 years (Range 43 to 80 years) and maximum number of patients was among the age group of 60- 80 years. The results indicate that the serum PSA level has useful role in diagnosis of prostate cancer. After treatment of prostate cancer patients the same procedure was followed to evaluate the treatment response.

| Patients | Age | PSA (ng/mL |
|---|---|---|
| P1 | 75 | 172.2 |
| P2 | 70 | 162.8 |
| P3 | 43 | 54.5 |
| P4 | 60 | 85.1 |
| P5 | 79 | 127.0 |
| P6 | 73 | 21.8 |
| P7 | 65 | 66.2 |
| P8 | 70 | 85.3 |
| P9 | 80 | 12.40 |
| P10 | 55 | 39.7 |
| P11 | 70 | 101.7 |
| P12 | 69 | 9.4 |
| P13 | 69 | 34.2 |
| P14 | 68 | 29.1 |
| P15 | 58 | 31.7 |
| P16 | 60 | 71.0 |
| P17 | 60 | 38.2 |
| P18 | 62 | 66.25 |
| P19 | 62 | 152.4 |
| P20 | 56 | 88.5 |

Table-II. PSA level after treatment

Approximately 80% of patients with a normal “digital rectal examination (DRE) and PSA Value” between 4 and 10 ng/mL have negative biopsy results for cancer.[14] According to this study if patients have PSA value above the normal range but normal digital rectal examination so unnecessary study should be avoided. The PSA level can increase for several reasons, including trauma, ejaculation, and rectal and urethral procedures. It can also increase because of diseases such as benign prostatic hyperplasia and prostatitis.[22]

## DISCUSSION

The use of PSA as a useful diagnostic marker in cancer patients was suggested in 1979. Before this, rectal examination was practiced. But this examination was not helpful as it shows

results after the cancer has been spread. Earlier observation showed that PSA was not a helpful tool for screening. But later it was proved that the increase level of PSA can be useful in diagnosis. Thompson and his coworkers in 2004 discussed that 22% of the men had prostate cancer who had the PSA level 4-9ng/ml and 67% had the cancer who had the PSA level 10ng/ml and above.[23] Our findings are also in accordance with this with a little bit change.

Our results shows that that 45% of these patients had PSA level >100 ng/ml. Other studies have provided similar estimates of specificity and sensitivity for PSA level with a cut-point of 4.0 ng/mL have been provided by other studies.[7] The reduction in PSA after hormonal treatment depends on the decrease in its production, fundamentally caused by the death of differentiated neoplastic cells of the tumor. An increase in PSA during hormonal treatment (therapeutic escape) begins 6 to 12 months before clinical and radiographical findings demonstrate the progression of the disease.[7,8] During this period, in accordance with the functional organic reserve of the patients, an alternative therapy may be indicated to reduce progression of the cancer (second-line therapy or experimental new protocols).

Kaygisiz and colleagues (2006) demonstrated that decrease in PSA levels after antibiotics was similar in patients with and without prostatitis, expressed by prostatic secretions. They detected PCa in 10.8% of the patients, and all of these patients had a PSA level >4 ng/mL. The study concluded that there was still a high risk for PCa in patients who have PSA levels > 4ng/mL after antibiotics, even if they have been diagnosed with prostatitis clinically. Serratta and coworkers found that there was a PSA duction in 59% of patients after a 3-week course of antibiotics. They reported that 40% and 20.3% of patients diagnosed with PCa had unchanged and decreased PSA levels, respectively. In addition, no cancer was detected in patients with a PS level below 4 ng/mL, and the study suggested that biopsy could be postponed if PSA levels decreased more than 50% or below 4 ng/ml.[17]

Research conducted in the early 1990s revealed that PSA shared with DRE is the most helpful screening and proved useful in early finding for prostate cancer.[18,19]

A study in the late 1980s concluded that as screenings became more widespread, the occurrence of prostate cancer appreciably increased and that PSA testing was related with the acceleration of the overall incidence of prostate cancer.[19,20]

## CONCLUSION

This study indicated that PSA serum level has a useful role in diagnosis of prostate cancer. Maximum decrease in PSA level was 35.5% after treatment. Also if the patients have PSA level above the normal range but normal digital rectal examination, so unnecessary study should be avoided.



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"The risk of a wrong decision is preferable to the terror of indecision."

Maimonides

## AUTHORSHIP AND CONTRIBUTION DECLARATION

| Sr. # | Author-s Full Name | Contribution to the paper | Author=s Signature |
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| 1 | Dr. Nighat Aslam | Writing of manuscript and compiling of results | |
| 2 | Khalid Nadeem | Data collection & writing of manuscript | |
| 3 | Dr. Razia Noreen | Statistical analysis & guidance in writing the manuscript | |
| 4 | Dr. Amer Jamil | Designing of project & guidance in writing the manuscript | |