Assessment of Vitamin A and D Status in Male Patients with Prostate Disorders in Lagos, Nigeria

**Abstract**

**Background:** Vitamin A and D are both fat-soluble vitamins that are crucial for maintaining overall health and are highly indispensable, despite their minimal daily requirements. Their involvement in cell proliferation, differentiation, and apoptosis has linked them to the development of various tumours, particularly those associated with an increased risk of benign prostatic hyperplasia (BPH) and cancer of the prostate (CAP).

**Objective:** This study aims to assess the levels of vitamin A and D among adult men with BPH and prostate cancers attending the clinic at the Lagos University Teaching Hospital, to establish any form of relationship between these vitamins and the disease conditions.

**Methods:** A total of one hundred thirty-eight consenting male subjects 50 years and above diagnosed with prostate enlargement (68) and prostate cancer (70) with Prostate Specific Antigen (PSA) above 4ng/ml and attended the urology clinic as well as healthy non-prostate diseased subjects’ men (69) attending general clinic all at the Lagos University Teaching Hospital, Idi-araba were recruited for the study. A 5 mL venous blood sample was collected from subjects and controls, and the samples were dispensed into specimen containers to determine the total PSA and Vitamins A and D levels using the ELISA method. Data generated were subjected to statistical analysis using SPSS version 20 with the application of mean, student’s test, one-way ANOVA and Pearson’s correlation coefficient, adopting a p-value less than 0.05 (p<0.05) as statistically significant.

**Results:** Vitamin D levels among individuals in the hyperplasia and prostate cancer group were significantly higher than those in the control subjects. In contrast, vitamin A levels showed no significant difference compared to the hyperplasia and prostate cancer group. Additionally, a positive correlation was observed between vitamin A and D, as well as between serum total PSA and both disease conditions. However, no correlation was found between the vitamins (A and D) and serum PSA in the control group.

**Conclusion**: Maintaining normal serum vitamin A and D levels among males will not only help to reduce the risk or severity of prostate cancer but also be of great benefit to prostate health.

**Key words :** **Vitamin A ,** **Prostate Disorders,** **prostate cancer,** **epithelial tissues**

**INTRODUCTION**

Vitamin A and D are both fat-soluble vitamins that are crucial for maintaining overall health and are highly indispensable, despite their minimal daily requirements (Nur et al., 2021). While Vitamin A is essential for maintaining healthy epithelial tissues, it has antioxidant properties that help protect cells from damage. Thus, Vitamin A and its derivatives play a role in regulating cell proliferation, differentiation, and apoptosis, which are important steps in various biological processes and cancer development. Natural and synthetic retinoids have been shown to inhibit the growth and development of various tumours, including those of the skin, breast, oral cavity, lung, liver, gastrointestinal tract, prostate, and bladder. (Bryan et al., 2011; Timoneda et al., 2018)

Vitamin D, on the other hand, is crucial for overall health, as it has been linked to immunomodulatory and antiproliferative properties, which could potentially protect against prostate cancer. Although Vitamin D helps regulate cell growth and differentiation, which can prevent the proliferation of cancerous cells in the prostate, its supplementation has been found to improve lower urinary tract symptoms and suppress the increase in prostate volume hence its deficiency is associated with an increased risk of benign prostatic hyperplasia (BPH) and prostate cancer (Prentice et al., 2006). Both conditions represent a significant burden of disease, particularly among men in developing countries (“The Global, Regional, and National Burden of Benign Prostatic Hyperplasia in 204  Countries and Territories from 2000 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019,” 2022). BPH, a non-cancerous condition, affects a substantial portion of the male population, while prostate cancer, a condition associated with uncontrolled growth of cells within the prostate gland, is also on the increase, becoming the most common cancer among Nigerian men (Glaser et al., 2022). Both conditions have been reported to increase significantly with age, with a high proportion of cases occurring in individuals above 50 years old (Launer et al., 2021). BPH can lead to a variety of lower urinary tract symptoms (LUTS), impacting quality of life and daily functioning (Parsons et al., 2020). Prostate cancer can have serious health consequences, including the development of metastatic disease and even death (Sung et al., 2021). Both BPH and prostate cancer pose significant health and economic burdens in Nigeria, impacting individuals, families, and the healthcare system (Iheanacho & Enechukwu, 2025). Both conditions have been primarily investigated and screened for using the PSA test, a generally accepted biomarker that indicates disease conditions when the serum PSA measurement is more than 4.0 ng/mL in combination with other clinical findings, such as the results of a digital rectal exam (Iyer et al., 2024).

 Establishing improved diagnostic and management strategies tailored to the relationship between these vitamins and the prostate may help to ameliorate the burden.

Several lines of evidence suggest a potential role of vitamin D in the development of BPH. Vitamin D3, one of the analogues of vitamin D, has been described as a potent regulator of cell growth and differentiation of prostatic cells (Espinosa et al., 2013). It acts by binding to the vitamin D receptor (VDR) of prostate cells, a member of the nuclear receptor superfamily, which may influence gene expression and potentially promote cell differentiation and apoptosis (programmed cell death) of abnormal cells. Vitamin D metabolites inhibit the growth of normal and malignant prostate cells as demonstrated in primary cultures, BPH, prostate cancer cell lines, xenograft models, and in vivo on rat prostate. Although relationships between diet and prostate cancer are not clearly defined, and specific recommendations to prevent the disease remain speculative, as it has been postulated that it correlates with affluent dietary patterns (Ghaderi et al., 2024). International and intra-country correlation studies indicate associations between prostate cancer mortality and the per capita intake of total fat (Loh et al., 2023). Similarly, several analytic epidemiologic studies and case-control studies have reported associations between total fat or the consumption of high-fat foods and prostate cancer, particularly saturated fats from animal products. As fat-soluble vitamins, such as vitamin D and A, require some dietary fat in the gut for absorption. Also, several epidemiological studies have implicated vitamin D deficiency as a risk factor for prostate cancer (Grace et al., 2024; Zhang et al., 2023)

 Although some studies (Arayici et al., 2023; Loh et al., 2023; Yin et al., 2009) have shown a link between vitamin D levels and prostate cancer, understanding the link will significantly impact the diagnosis and management of these conditions especially in our setting where most of these studies were scarce hence this study aims at assessing the levels of vitamin A and D among adult men with BPH and prostate cancers attending clinic in Lagos state teaching hospital, to establish any form of relationship between these vitamins and the disease conditions.

**HUMAN SUBJECTS**

A total of one hundred thirty-eight consenting male subjects, 50 years and above, who have been diagnosed with prostate enlargement or prostate cancer with PSA above 4ng/ml and attended the urology clinic in the Lagos University Teaching Hospital, Idi-Araba, were recruited for the study. Out of this number, 70 male subjects were diagnosed with prostate cancer, while 68 patients had BPH. Another 69 non-prostate diseased subjects within the same age group above were matched as negative controls.

**SAMPLE SIZE DETERMINATION**

Sample size determination was based on a local prevalence rate of 7.9% among men aged 50 years and older. The Armitage & Berry technique was used to calculate the sample size and significance at 5% level (Armitage et al., 2008)

**EXCLUSION CRITERIA**

* All male subjects below 50 years of age.
* Chronic renal failure resulting in tubular loss of calcium and non-formation of active vitamin D.
* Hyperthyroidism/thyrotoxicosis
* All subjects who had had their prostate gland examination before sample collection through Direct Rectal Examination (DRE) were excluded.
* All subjects on any form of vitamin A and D supplementation or treatment.

**INCLUSION Criteria**

All male subjects 50 years and above diagnosed with prostate cancer or BPH.

**SAMPLE COLLECTION AND METHODS.**

A 5 mL venous blood sample was collected from subjects and controls, and the samples were dispensed into specimen containers to determine total PSA and Vitamins A and D using the ELISA method. Samples were allowed to retract and spun at 3000 rpm for 5 minutes. The supernatant plasma was separated and stored at -20°C for batch analysis. Total PSA, Vitamins A and D were determined using the ELISA method with Elab Science products on an ELISA machine under standard conditions.

**Processing and Analysis**

The data generated were subjected to statistical analysis using SPSS version 20, with differences in the mean values between groups compared using the Student’s t-test and one-way ANOVA. The probability level was set at a 5% significance level (p < 0.05). The serum vitamin A and D levels for those with CAP and BPH and those without were expressed as Pearson’s correlation coefficient ‘r’ at 5% significance.

**ESTIMATION OF TOTAL PSA**

Principle

In this method, the PSA calibrator, patient specimen or control was first added to a streptavidin-coated well. Biotinylated monoclonal and enzyme-labelled antibodies (directed against distinct and different epitopes of PSA) were added, and the reactants were mixed. The reaction between the various PSA antibodies and native PSA forms a sandwich complex that binds to the streptavidin-coated well. After the completion of the required incubation period, the enzyme-PSA antibody-bound conjugate was separated from the unbound enzyme-PSA conjugate by aspiration or decantation.

The activity of the enzyme present on the surface of the well was quantified by reaction with a suitable substrate to produce colour. The use of several serum references with known prostate-specific antigen (PSA) levels allowed the construction of a dose-response curve relating activity to concentration. In comparison to the dose-response curve, the activity of an unknown specimen can be correlated with PSA concentration (Iheanacho & Enechukwu, 2025; Iyer et al., 2024)

ESTIMATION OF VITAMIN A

**Test Principle**

This ELISA kit employs a competitive ELISA method. The microtiter plate provided in this kit has been pre-coated with VA. During the reaction, VA in the sample or standard competed with a fixed amount of VA on the solid-phase supporter for sites on the Biotinylated Detection Antibody specific to VA. Excess conjugate and unbound samples or standards were washed from the plate, and Avidin conjugated to Horseradish Peroxidase (HRP) was added to each microplate well and incubated. Then, a TMB substrate solution was added to each well. The enzyme-substrate reaction was terminated by adding a sulphuric acid solution, and the colour change was measured spectrophotometrically at a wavelength of 450 nm + 2 nm. The concentration of VA in the samples was then determined by comparing the OD of the samples to the standard curve (Shastak et al., 2024)

ESTIMATION OF VITAMIN D3

**Test principle**

This ELISA kit employs a competitive ELISA method. The microtiter plate provided in this kit has been pre-coated with Dihydroxyvitamin D3 (DHVD3). During the reaction, DHVD3 in the sample or standard competes with a fixed amount of DHVD3 on the solid-phase supporter for sites on the Biotinylated Detection Antibody specific to DHVD3. Excess conjugate and unbound samples or standards were washed from the plate, and Avidin conjugated to Horseradish Peroxidase (HRP) was added to each microplate well and incubated. Then, a Tetramethylbenzidine (TMB) substrate solution was added to each well. The enzyme-substrate reaction was terminated by adding a sulfuric acid solution, and the colour change was measured spectrophotometrically at a wavelength of 450 nm ± 2 nm. The concentration of DHVD3 in the samples was then determined by comparing the optical density (OD) of the samples to the standard curve (Abd & Habeeb, 2023)

RESULTS

**Table 1: Concentrations of vitamins A and D in CAP, BPH and Control subjects.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | CAPn=70 | BPHn=68 | Controln=69 | fvalue | pvalue |
| Vit. A (µmol/l) | 3.65±2.84 | 2.52±2.29 | 3.10±3.11 | 0.53 | 0.596 |
| Vit. D3 (pmol/l) | 85.10±31.93b | 72.00±14.68 b | 65.43±14.75a | 3.76 | 0.029\* |
| Total PSA (µg/l) | 59.42±55.36f  | 15.13±9.49g | 1.22±0.68a  | 13.54 | 0.000\*\* |
|  |  |  |  |  |  |

Alphabets in superscripts denote significant difference at p < 0.05

\*\* denotes a significant difference at p < 0.01 \* denotes a significant difference at p < 0.05

CAP = cancer of the prostate. BPH = benign prostate hyperplasia

Vitamin D levels among individuals in the hyperplasia and prostate cancer group were significantly higher than those in the control subjects. In contrast, vitamin A levels showed no significant difference compared to the hyperplasia and prostate cancer group.

**TABLE 2:** Correlation of Vitamin A and D with total PSA among the CAP, BPH and control groups

Parameter N Disease r P

 Value

Vitamin A vs Total PSA 70 CAP 0.596 0.041

Vitamin D vs Total PSA 70 CAP 0.820\*\* 0.030

Vitamin A vs Total PSA 68 BPH 0.397\* 0.020

Vitamin D vs Total PSA 68 BPH 0.681\*\* 0.000

Vitamin A vs Total PSA 69 Control 0.172 0.331

Vitamin D vs Total PSA 69 Control 0.162 0.360

\*\* Correlation is significant at the level of 0.01 (2-tailed)

\* Correlation is significant at the level of 0.05 (2-tailed)

r = Pearson’s correlation coefficient

BPH: Benign prostate hyperplasia, CAP: Cancer of the prostate.PSA: Prostate-specific antigen.

A positive correlation was observed between vitamin A and D, as well as serum total PSA, in both disease conditions. However, no correlation was observed between the vitamins (A and D) and serum PSA in the control group.

**Discussion**

In this study, a random sample of 68 BPH, 70 CAP, and 69 controls was analyzed for vitamins A and D. The results showed significant differences between groups and within groups in the analysis of variance, P < 0.05. Although the mean serum concentration of vitamin A in the prostate cancer group was higher than that of the BPH and control groups, the increase in vitamin A in prostate cancer patients was not statistically significant. Thus, Vitamin A levels in control subjects showed no significant difference from those in hyperplasia and prostate cancer; p-value = 0.596. This may be because Vitamin A influences cell growth and apoptosis, which is more of a protective mechanism, as seen in a prospective study that found a protective effect of beta-carotene (Kirsh et al., 2006). This finding did not align with those of Loh et al. (2023) and Aghawegbehe et al. (2019), who reported significantly higher concentrations of vitamin A compared to controls. This difference may be because our study did not assay for the various forms of vitamin A, unlike Loh et al. (2023), who assessed all forms of Vitamin A, and Aghawegbehe et al. (2019), who studied a population without exclusion of Vitamin A supplementation. This factor would have caused an increase in the concentration of the vitamin.

Vitamin D, on the other hand, was found to be significantly higher in concentrations among the prostate cancer populations when compared to the controls; p = 0.029. This was also the finding of Holick (2007), who attributed it to the defensive mechanism mounted by the immune system in prostate cancer patients, involving vitamin D in a wide variety of biological processes and its activity mediated by the vitamin D receptor (VDR).

To establish a relationship between these vitamins (A and D) and the disease conditions (CAP and BPH), we sought a correlation between Vitamin A and D and total PSA, which served as an indicator of disease condition in the CAP, BPH, and control groups. A positive correlation was observed between vitamin A and D, as well as serum total PSA, in both disease conditions. However, no correlation was observed between the vitamins (A and D) and serum PSA in the control group. This indicates a positive linear relationship between the mean and standard deviation for both vitamins and the disease conditions. Specifically, it showed that vitamin A increased as vitamin D increased in both the CAP and BPH populations. This finding aligns with the results of a research study on the association between serum vitamin A and E levels and prostate cancer risk (Loh et al., 2023). Although the relationship exists between the two vitamins in our study, we observed that vitamin D had a stronger relationship (r = 0.82 and 0.681, respectively) than Vitamin A (r = 0.596 and 0.397, respectively) for both CAP and BPH.

Various school of thought surrounds the association of vitamin D with CAP and BPH. While some researchers (Arayici et al., 2023; Yin et al., 2009; Zhang et al., 2023) indicated a positive relationship between vitamin D and CAP, suggesting that high serum levels of vitamin D are associated with a lower risk of CAP and disease severity. Vitamin D exerts potent antiproliferative effects on both normal and cancer cells; therefore, it may slow the growth rate of prostate cells in both benign and malignant cell models (Holick, 2007). Other studies, in contrast, suggested that hypovitaminosis D is associated with a higher risk of death from prostate cancer (Tretli et al., 2009). However, the correlation coefficient reported in our study indicated a strong positive relationship between vitamin D and CAP. This agrees with Trump & Aragon-Ching (2018) and Holick (2017), who suggested that adequate vitamin D levels could reduce the risk or severity of prostate cancer.

**CONCLUSION**

Although the Serum values of both vitamins A and D were higher among the patients with CAP and BPH, as well as the normal range, when compared to the control population, vitamin D was significantly higher. We detected significant positive associations of serum vitamin A and D concentrations with prostate cancer and benign prostatic hyperplasia populations.

We can conclude that maintaining normal serum vitamin A and D levels among males will not only help to reduce the risk or severity of prostate cancer but also be of great benefit to prostate health.

LIMITATIONS OF THE STUDY

This includes the inability to classify the study population according to disease severity, as most participants may have more severe disease, which may influence the established relationship. We therefore recommend a more specific study in this regard in future. We also could not assay for the various forms of the vitamins, which would have added more specificity to the association established.

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

According to international standards or university standards, the author (s) have collected and preserved the participants' written consent.

**ETHICAL APPROVAL.**

Lagos University Teaching Hospital Idi-Araba's ethics committee approved this study after a detailed explanation of the research was provided in our application with **No:** **REF.NO.ADM/DCST/221**. We also obtained informed consent from the participating patients and subjects after thoroughly explaining the research to them.

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