Tuijin Jishu/Journal of Propulsion Technology
ISSN: 1001-4055
Vol. 44 No. 4 (2023)

To Estimate the Levels of Serum Vitamins A, E, And C in Cervical Cancer Patients

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Abstract

Background

Cervical cancer continues to be a leading cause of cancer-related mortality among women in developing nations, including India. Worldwide, cervical cancer is the third most frequent malignancy among women. In comparison to urban regions, cervical cancer is more common in rural communities. This investigation find the impact of vitamins (A, E, and C) on cervical cancer severity in SGT Hospital patients was the goal of this study.

Aim and Objectives

- To determine the levels of serum vitamin A,C and E in cervical cancer patients and healthy controls
- To compare the serum level of vitamin A,C and E in patients with cervical cancer and healthy control

Materials and Methods

This study is conducted in Department of Biochemistry in collaboration with Department of Pathology, and Department of Gynaecology at SGT Hospital, Budhera, Gurugram's Faculty of Medicine and Health Sciences, this is hospital-based cross-sectional case control study. Subjects are 50 healthy volunteers who are age-matched from the general population as the control group. A signed and informed permission is obtained from each individual in both groups once they have been fully informed of the study's objectives. Before beginning the sample collection, institutional ethical committee approval is soughted. Samples are centrifuged at 3000 rpm for 10 minutes; the serum is separated from the clot in the plain tube. The plasma obtained after centrifuging the blood in the lithium heparin tube at 3000 rpm is decanted. Vitamins A and E is examined on zaivik by HPLC method and Vitamin C is examined by ELISA method

Results

Patients with cervical cancer had a significantly lower level of a parameter, such as serum vitamin A, C and E when compare with controls. Our study shows that serum vitamin A levels in the patients were 30.2 ±4.0 mcg/dl and 54.7 ±10.6 mcg/dl,

respectively, with a p value of <0.05 which are lower when compared with controls. Vitamin E levels were also decreased in study group (4.5±1.5 mcg/dl) than controls (11.9±2.7 mcg/dl) having p value <0.05. Vitamin C levels in cases (1.83±0.3) mcg/dl were considerably lower than those in control groups 9.8±2.5 mcg/dl having p value <0.05.

Conclusion: Our results imply that lower antioxidant vitamin levels may contribute to the aetiology and development of cervical carcinoma, even if the precise mechanisms through which oxidative stress might cause cancer are still unclear.

Key Words: *Cervical cancer, Vitamin A, Vitamin E, Vitamin C and The human papillomavirus (HPV).*

Introduction:

Cervical cancer continues to be a leading cause of cancer-related mortality among women in developing nations, including India. The majority of women with cervical cancer in its early stages usually don't experience any symptoms, and patients only notice signs once the disease has progressed. (1) Worldwide, cervical cancer is the second most frequent malignancy among women. In comparison to urban regions, cervical cancer is more common in rural communities. Between the ages of 45 and 55, it dramatically increases before peaking. (2) In low-resource settings, women have a 2-4% lifetime risk of acquiring cervical cancer.(3,4) It is a condition that may be avoided, but it presents a problem in the majority of developing nations because of illiteracy, poverty, poor health seeking behaviour, late presentation, a delay in starting the right treatment based on histology, and inadequate treatment because of loss to follow-up. Women between the ages of four and six are affected with 80–90% of instances showing up in the last stages of the illness.(5) The human papillomavirus (HPV), a sexually transmitted infection with a high risk, is the main cause of cervical cancer. (4) Cervical cancer cannot be brought on only by persistent HPV infection. The carcinogenic potential of HPV has been demonstrated to be modulated by a number of cofactors, including smoking, low socioeconomic position, prolonged oral contraceptive usage, high parity, nutritional status, coinfection with other STDs, HIV, and immunosuppression.(6-8) Low dietary intakes of vitamin C, carotenoids, vitamin E, and folate are among the nutritional factors contributing to cervical neoplasia. (9) A variety of genetic alterations, including DNA strand breaks, chromosomal abnormalities, oxidative base modifications, and cellular transformation that could result in a mutagenic lesion leading to malignant transformation, have been demonstrated to be induced by reactive oxygen species (ROS) produced from biochemical reactions in vitro.(10) Oxidative stress is caused by an imbalance between the creation and detoxification of free radicals, which harms DNA, proteins, and lipids.(11) A number of dietary antioxidants have also demonstrated great promise in their ability to prevent cancer by lowering oxidative stress, which has been linked to the emergence of a number of disorders, including cancer. By quenching singlet oxygen, vitamin A (retinol) has a powerful antioxidant action. It promotes cell division and differentiation, controls immune function, hinders the growth of malignant cells, and has antimutagenic, antitumorigenic, immunostimulant, antiulcer, and degenerative effects on people. (12)Vitamin E (-tocopherol) has antioxidant properties by binding to free radicals and neutralising their unpaired electrons. It also scavenges lipid peroxyl radicals in both in vitro and in vivo systems and promotes wound healing. (13) Vitamin C, also known as ascorbic acid, functions as an antioxidant that breaks chains, a reducing agent, or an electron donor. It neutralises free radicals and prevents the oxidation of lipids. Additionally, it aids in the regeneration of -tocopherol. A vitamin C shortage may lead to illnesses.13. There have been several epidemiological and analytical investigations done to look into the connection between antioxidants and cervical cancer. (9,14) Therefore, the purpose of this study was to determine how vitamin levels affected individuals with various stages of cervical cancer. cervical cancer risk and antioxidant status. (15) This investigation find the impact of vitamins (A, E, and C) on cervical cancer severity in SGT Hospital patients was the goal of this study.

Materials and Methods:

A hospital-based case control study was conducted in the Departments of Biochemistry, Pathology, and Gynaecology at the SGT Medical College, Hospital & Research Institute in Gurugram, Delhi-NCR, India, from March 2021 to March 2023. Fifty patients with cervical cancer in the age range of 18 to 65 years who were undergoing care at SGT Hospital's Obs & Gyne OPD were identified based on information found in the MRD (medical records department) of the hospital. Histopathological analysis will serve as the foundation for case definition. In the study, 50 females who regularly visit the

gynaecology outpatient department and who have pap smear results that are NILM (negative for intra epithelial lesion or malignancy) will serve as the control group. All study participants in both groups completed written consent forms after discussing the study's purpose and scope. The study includes non-pregnant women, cases with a histopathologically confirmed diagnosis of cervical cancer, controls with a Papanicolaou smear result of NILM (negative for intra epithelial lesion/malignancy), and patients without a history of prior tumour treatment. Pregnant women, individuals who had undergone a prior hysterectomy, and individuals who had previously received any definitive therapy for a tumour were all excluded from the trial. The goal of the study will be clearly explained to both controls and patients, and then formal consent will be obtained. After that, participants will be venepunctured with a 5 ml sterile disposable syringe and needle to obtain a sample of venous blood in an aseptic environment. A 2.5 ml aliquot will be placed in a simple tube for the first time, and a second 2.5 ml aliquot will be placed in lithium heparin tubes. The patient's code for each tube will be written on it. By centrifuging the sample at 3000 rpm for 10 minutes, the serum will be separated from the clot in the plain tube. The plasma obtained after centrifuging the blood in the lithium heparin tube at 3000 rpm will be decanted. Vitamins A, C, and E will be examined. on zaivik by HPLC method

Statistical analysis

The generated results must undergo statistical analysis using SPSS. P-values ≤ 0.05 are deemed statistically significant. Non-parametric variables will be subjected to the chi square test. To compare the average between two groups, a student t-test will be utilised. To determine the relationship between the variables, Pearson's correlation coefficient will be used.

Results:

This investigation aimed to gauge vitamin A, vitamin E, and vitamin C levels.

Parameters		**Cases(mean+STD) n=50**	**control(mean+STD) n=50**	**t value**	**p value**	**Significance**
VITAMIN A (RETINOL)		30.2±4.0	54.7±10.6	-15.30	**<0.05**	Significant
VITAMIN E (ALPHA-TOCOPHEROL)		4.5±1.5	11.9±2.7	-17.00	**<0.05**	Significant
Vitamin C		1.8±0.3	9.8±2.5	-22.743	**< .05**	Significant

Table 1 showing the mean and Standard deviation of Vitamin A, E and C

Demographic Parameters:

50 instances of cervical cancer in women between the ages of 18 and 65, as well as 50 participants in the control group, were included in this study.

Figure 1 from our study shows that the mean and standard deviation of serum vitamin A levels in the patients were 30.2 ±4.0 mcg/dl and 54.7 ±10.6 mcg/dl (table 1), respectively, with a p value of <0.05 which are lower when compared with controls.

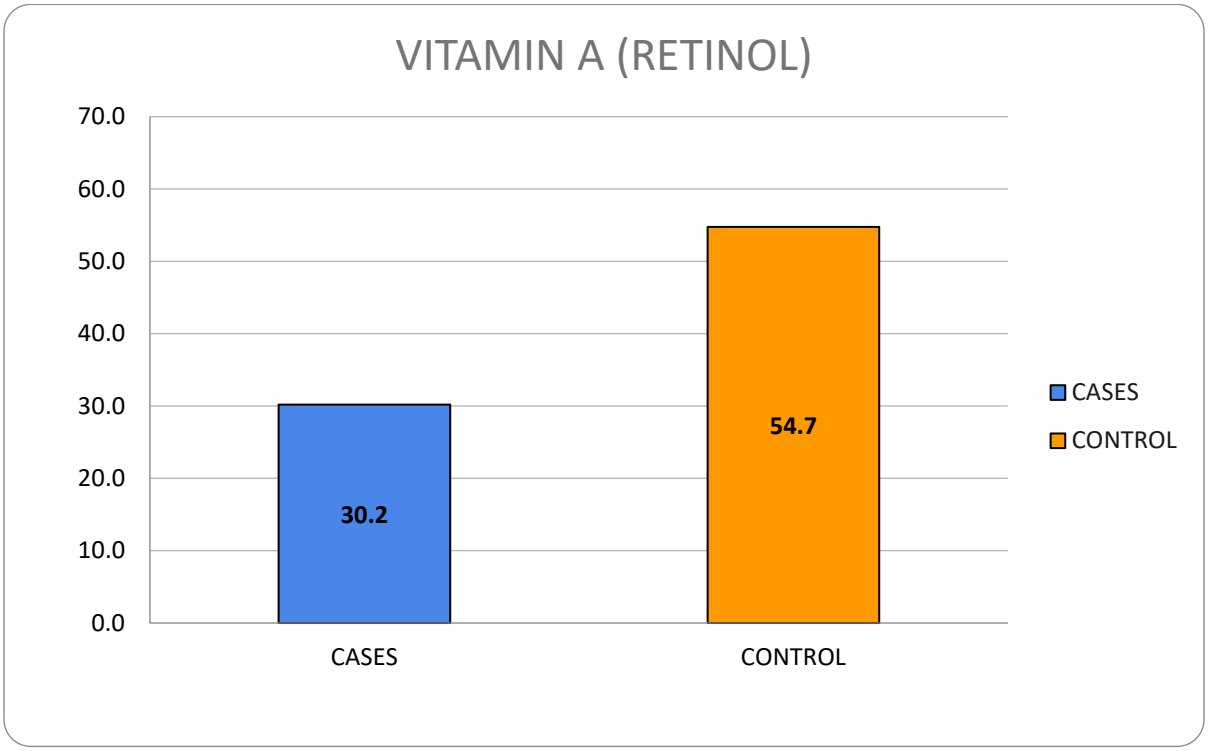

Figure 1: Graphical representation of serum Vitamin A in the cases and controls.

Figure 2 shown that vitamin E levels were also decreased in study group (4.5±1.5 mcg/dl) than controls (11.9±2.7 mcg/dl) (Table 1) having p value <0.05.

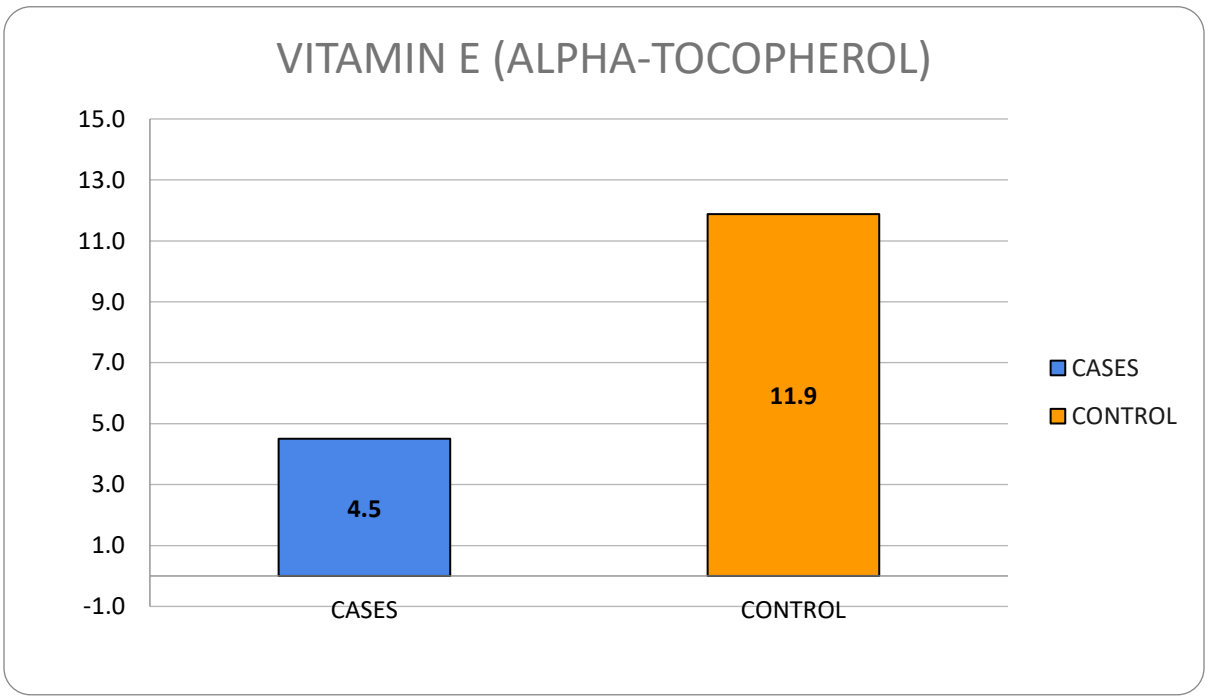

Figure 2: Graphical representation of serum Vitamin E in the cases and controls.

In our investigation, we find that mean and standard deviation of serum Vitamin C levels in cases (1.83±0.3) mcg/dl were considerably lower than those in control groups (9.8±2.5) mcg/dl having p value <0.05 shown in figure 3

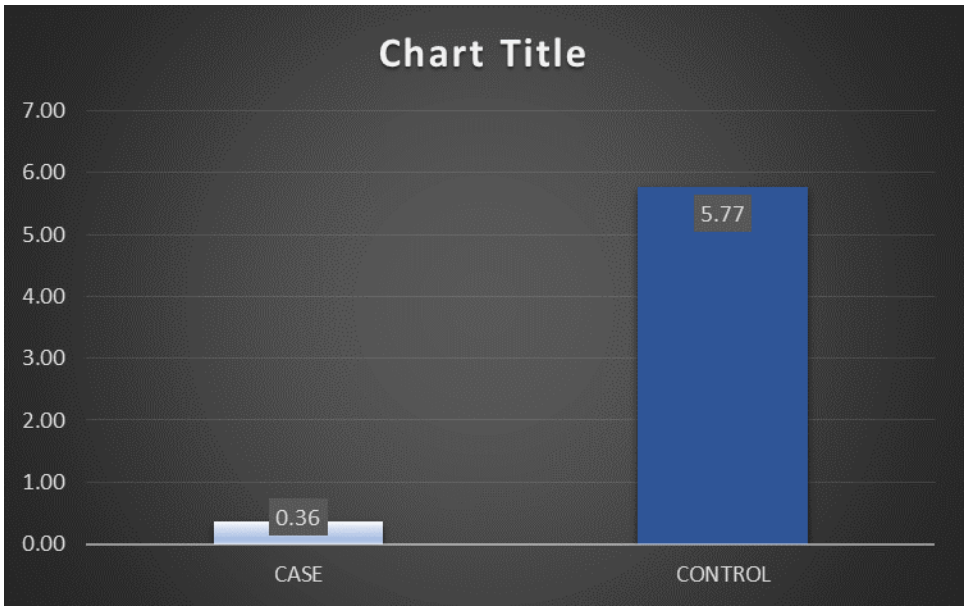

Figure 3: Graphical representation of serum Vitamin C in the cases and controls.

Discussion

Strong non-enzymatic antioxidants like vitamin A, E, and C are in charge of snatching free radicals, which stops oxidative chain reactions [16]. In this study, it was discovered that patients with cervical cancer in all four FIGO stages had significantly lower levels of vitamins A, E, and C than the controls. There are various explanations for why patients with cervical carcinoma had lower levels of the antioxidant vitamins A, E, and C in their bloodstreams prior to therapy; it could be a cause or an effect of the malignancy. (17) It is mentioned that cervical cancer is more common in women who are undernourished and who eat fewer fruits and vegetables. As a result, a significant portion of the decreased Vitamin A, E, and C levels found in cervical cancer patients can also be linked to a diet low in nutrition. According to the studies, a rise in free radicals may contribute to the emergence of cancer and other diseases (18). Therefore, antioxidant vitamins will have a greater burden to scavenge these extra free radicals because cancer may cause their depletion in circulation. It might also be brought on by tumour cells securing these vitamins for their own growth (12). According to reports, tumour cells scavenge vital antioxidants to meet the needs of the expanding tumour. ROS levels may rise when genetic abnormalities and the microenvironment are altered in the early stages of tumour development in cells. ROS can cause a tumour cell's growth to be arrested or to die, which will stop the growth of the tumour. In order to battle oxidative stress, which can encourage the growth of tumours by restoring the survival of sick, stressed tumour cells, it has been demonstrated that cellular drivers of tumour initiation and progression enhance their utilisation of antioxidants (19). A considerable drop in antioxidant is seen both during concomitant chemoradiotherapy and right after brachytherapy. Vitamins A, E, and C in people with cervical cancer. It can be accounted for by increased oxidative stress brought on by concomitant chemoradiotherapy, decreased food intake, or vomiting brought on by cisplatin. Radiation therapy is based on the fact that ionising radiation can kill cells. The creation of ROS is necessary for this therapy. These radicals—hydroxyl radicals, superoxide anion, and other organic radicals—increased the production of other ROS, such as peroxides, when oxygen was present. Therefore, these enhanced radicals would have an impact on the cellular antioxidant status, which would then have an impact on harmful radiation effects (20). A protective impact of antioxidants is seen against these free radicals.

The creation of building blocks for proteins and the replication of basal mucosa cells both require vitamin A. Thus, squamous metaplasia and HPV infection may both be made more likely by vitamin A deficiency (21). According to the current study, cervical cancer cases had low serum vitamin A levels (30.2±4.0 mcg/dl), which was significantly lower than the levels in the control groups (54.7±10.6 mcg/dl). Yeo et al. is similar clinic-based case-control study revealed that women with lower serum vitamin A levels had a higher probability of having CIN 1 than those with higher levels (odds ratio (OR) = 2.3). (21) Another case-control study revealed that there was no inverse relationship between serum levels of retinol and the risk of cervical cancer. Therefore, retinol (vitamin A) may prevent the early stages of cervical carcinogenesis, including HPV infection and CIN 1 development. (23)

The fat-soluble antioxidant vitamin E (tocopherol) prevents the oxidation of fat from releasing reactive oxygen species (ROS). Researchers are looking at whether vitamin E can help prevent or postpone the emergence of chronic conditions linked to free radicals. (24) It has also been suggested that vitamin E can shield cells against oxidative DNA deterioration and mutagenesis, hence halting the growth of some tumours. (25) In the current investigation, Vitamin E level are comparatively lower when compared with controls i.e (4.5±1.5 mcg/dl) and (11.9±2.7 mcg/dl). However, in a cross-sectional study of 230 women, patients with various stages of CIN and cervical cancer had significantly decreased mean plasma levels of alpha and gamma tocopherol compared to controls ($p < 0.001$ and < 0.001, respectively, by the Kruskal-Wallis test). (26) Manju et al. discovered that cervical cancer patients had considerably decreased levels of vitamin E compared to controls. (27) As mentioned above, vitamin E may significantly reduce the risk of HPV infection, CIN formation, and cervical cancer.

Ascorbic acid, often known as vitamin C, is known for its capacity to donate electrons, which prevents the aggregation of free radicals and oxidising agents. It is especially effective at getting rid of reactive nitrogen species, hydrogen peroxide, hydroxyl, and superoxide anion radicals (28). The mean±SD level of serum vitamin C was also decreased (1.83±0.3) mcg/dl and 9.8±2.5 mcg/dl in the current study's case and control groups. A low intake of vitamin C was linked to a higher risk of persistent HPV infection in a nested case-control study involving 433 women (adjusted OR, 0.50; 95% CI, 0.27-0.92 (highest vs. lowest quartile)).(29) Vitamin C intake was also found to be significantly linked with a lower risk of cervical neoplasia (from CIN to cervical cancer) in a meta-analysis (one prospective cohort trial and 11 case-control studies) (OR = 0.58; 95% CI: 0.44-0.75; $p<0.001$). (31) In addition, it was found that a 50 mg/day increase in vitamin C intake was associated with a lower incidence of CIN (OR = 0.92; 95% CI: 0.89-0.94; $p < 0.05$), demonstrating dose dependence. Additionally, Manju et al. showed that individuals with cervical cancer had considerably lower amounts of vitamin C compared to controls. (27) Cisplatin (CDDP) and vitamin C therapy, however, improved the induction of cell death by the overexpression of p53 and production of hydrogen peroxide in culture cells (SiHa cells), lowering the amount of CDDP needed to trigger cell death in cancer cells. (32) Therefore, vitamin C may lessen HPV infection and prevent the growth of CIN and cervical cancer.

Conclusion

It is also observed that individuals with cervical cancer receiving chemotherapy and radiation treatment reported a higher quality of life when receiving vitamin supplements. The majority of the patients had antioxidant levels that were below ideal. The addition of vitamins throughout therapy, improved food intake, and the absence of emesis may also contribute to the normalisation of vitamins after therapy. Our results imply that lower antioxidant vitamin levels may contribute to the aetiology and development of cervical carcinoma, even if the precise mechanisms through which oxidative stress might cause cancer are still unclear. It is also observed that individuals with cervical cancer receiving chemotherapy and radiation treatment reported a higher quality of life when receiving vitamin supplements. The majority of the patients had antioxidant levels that were below ideal. The addition of vitamins throughout therapy, improved food intake, and the absence of emesis may also contribute to the normalisation of vitamins after therapy. Our results imply that lower antioxidant vitamin levels may contribute to the aetiology and development of cervical carcinoma, even if the precise mechanisms through which oxidative stress might cause cancer are still unclear.

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