# Effect of Radiotherapy on Renal Function in Cervical Cancer Patients Treated at a Comprehensive Cancer Centre in Nigeria

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## Abstract

Background: Cervical cancer is the second commonest malignancy in women worldwide, and a leading cause of cancer-related death for women in Nigeria. Unfortunately, treatment for cervical cancer induces renalfunction injury due the nephrotoxicity of commonly used cytotoxic medications, as well as radiotherapy. Thus, this study seeks to evaluate the effect of radiotherapy on the renal function of cervical cancer patients.Objectives: 1) To examine if there will a positive of effect of radiotherapy on renal function in patients with cervical cancer after treatment. 2) To ascertain the statistical significance of the difference in renal function of cervical patients before and after treatment. Method:The study was an ex post facto research, used for retrospective evaluation of documented information on 220cervical cancer patients treated in the department of radiotherapy and oncology UDUTH, Sokoto. The study covered a five-year period, beginning from January, 2010 to December, 2015. Data was obtained from the patients' case notes using a semi-structured data extraction form. Percentage and analysis, independent t-test and chisquare statistics was used to determine the outcome of the findings.

***Index terms***— cervical cancer, chemotherapy, radiotherapy, renal function.

## 1 Introduction

ancer of the cervix (CC) is the second commonest cancer affecting women worldwide and about 86% of cervical cancer cases occur in developing countries (1) . According to statistical data, 8-30 new cases of cervical cancer occur in 100,000 females within a year, depending on the region and state (2) . Cervical cancer is recognized to be one of leading causes of illness and death among women worldwide, especially in developing countries 1 (including Nigeria) (3) . Unfortunately, most of the patients in Nigeria present at late stages and often have evidence of renal impairment at presentation (3) .The renal system is one of the first body systems to be directly affected by cancer of the cervix, especially in advanced cases (1) . Renal impairment was seen in more than a quarter of patients presenting with cancer of the cervix prior to commencement of treatment (4) . These complications are often preventable or reversible with prompt diagnosis and treatment (5) . Treatment of cervical cancer commonly requires the use chemotherapy, which can be given at the same time with radiotherapy (concurrent chemotherapy/radiotherapy-CRT), or alone as neo-adjuvant or adjuvant chemotherapy. The treatment is usually stratified by stage to include External Beam Radiation Therapy (EBRT), which is done by the use of CT-based treatment planning and conformal blocking, to complete the standard of care for EBRT (6) .

Regarding the effect and outcome of chemotherapy and radiation therapy on renal functioning in patients, it has been shown that these treatments have a mixed effect, based on the classification of the cancer stages. For example, Okadema et al showed that Radiotherapy and chemotherapy may have adverse effects on renal and urological function 3 . The same study showed that a relatively high percentage of women with pelvic radiotherapy and/or chemotherapy had a ?20% reduction in their estimated Glomerular Filtration rate (eGFR).Other studies report primarily that chemoradiation therapy has the negative effect of renal impairment (evidenced by a reduction in GFR) in patients with cervical or pelvic malignancy. Many studies have also shown that the presence of renal impairment in patients with carcinoma of the cervix is a poor prognostic indicator (7) . Patient with evidence of renal impairment relating to the cervical cancer are said to be stage 3b according to the widely

used International Federation of Obstetrics and Gynaecology (FIGO) staging for cancer of the uterine cervix (8) .Varlotto et al found that radiotherapy is associated with a rise in renal dysfunction (9) .

However, other reports based on comparison tests, have shown a significantly statistical difference between GFR values at the beginning vs. three months after using the therapy, while there was no difference between GFR values at three months into treatment vs. six months into treatment (2) . Specifically for patients with cervical cancer, studies have shown a significant statistical difference between the average values of GFR after therapy. This led Horan, McArdle, Martin, Collins & Faulto assert that pelvic radiation does not induce any deterioration of renal function or degree of hydronephrosis. Overall, the kidney function was found to improve at three and 6 months in the majority of patients (10) .

II.

# 2 Aim and Objectives

The primary aim of the study was to evaluate the effect of radiotherapy on the GFR of cervical cancer patients that underwent this treatment procedure at the department of Radiotherapy and Oncology, Usman Danfodiyo University Teaching Hospital (UDUTH) Sokoto state. The objectives are: 1. To determine the effect of radiotherapy on renal function in patients with cervical cancer after treatment. 2. To ascertain the statistical significance of the difference in renal function of cervical patients before and after treatment.

# 3 III.

Research Questions

1. Would there be a positive or negative effect of radiotherapy on renal function in patients with cervical cancer? 2. Would there be a significant difference in renal function of cervical cancer patients after radiotherapy, as compared to their renal function before radiotherapy?

IV.

# 4 Method a) Research design

The study adopted an ex post facto design for retrospective evaluation of cervical cancer patients that underwent radiotherapy treatment at the Department of Radio-Oncology, Usman Danfodiyo University Teaching Hospital (UDUTH), Sokoto. The study covered a 5-year period of treatment for patients with cervical cancer, starting from January 2010 and December 2015. In this context, the authors did not manipulate the independent variables (radiotherapy and chemotherapy) to observe their effect on the dependent variables (Renal function, eGFR).

# 5 b) Participants

Participants were cervical cancer patients that received radiotherapy treatment in the department of Radiotherapy-Oncology UDUTH, Sokoto. The sample consisted of 220selected case notes of cervical cancer patients that were exposed to radiotherapy treatment. The patients' demographic characteristics include sex, age, marital status, and occupation. Participants were both young and old patients, withe age ranging from 28-87years.

# 6 c) Materials

Data was collected from secondary sources. This comprised of patients case notes obtained in the archive of the department of Radio-Oncology UDUTH, Sokoto. The treatment information documented in patients' was obtained using a semi-structured data extraction form. For the radiotherapy procedure, patients were simulated in a computed tomography simulator with thermoplastic immobilization device and positioning devices such as knee-rests, to reproduce the same position during treatment. Three-dimensional conformal radiotherapy was planned using the Monaco treatment planning system (version 5.0). Radiation was delivered by linear accelerator with 6 MV or 10 MV photons. Four conformal fields were used in treating all carcinoma of cervix patients. Adequate coverage of target volumes and sparing of organs at risk was achieved. Treatment verification with Electronic Portal Imaging Devices (EPID) was done. The GFR values were calculated using Cocroft-Gault equation at first clinic visit, and repeated at first follow-up after treatment (radiotherapy).

# 7 d) Statistical Analysis

The data were analyzed using the Microsoft excel, then exported into SPSS version 20 (Chicago IL) for windows; for statistical analysis. The data were analyzed for frequency distribution, generated for all categorical variables. Mean and standard deviation were determined for quantitative variables. Comparison of the differences of the patients renal function status before treatment and after treatment was determined through the use independent t-test.

V.

# 8 Results

The purpose of the study was to evaluate the effect of radiotherapy of the GFR of cervical cancer patients. The GFR were calculated using Cocroft-Gault equation at first clinic visit, and repeated at first followup after treatment (radiotherapy). The results obtained from the statistical analysis is tabulated and interpreted as follows: The demographic distribution of patients on table 1shows that the peak age incidence occurred with age range of 40-49 year (31.4%), while the second most affected age group was 50-59 years (24.1%). The mean age of the cancer patients was 49.9, SD ± 11.9, and the age range of 24-87 years. Occupationally, 134(61.4%) were housewives, 35 (15.9%) were Civil servants, 31(14.1%) were traders/businesswomen, 14(6.4%) were farmers and 5(2.3%) had other occupations. The mean age of the cancer patients was 49.9, SD ± 11.9, and the age range of 24-87 years.

# 9

Table 3 shows that there is both positive and negative effect of radiotherapy on renal function of patients with cervical cancer after treatment. In analyzing these effect by percentages based on patients' disease stages, G1b indicates 63.6% negative effect and 36.4% positive effective. G2a 39.4% negative effect and 60.6% positive effect, G2b 49.0% negative effect and 51.0% positive effect. G3a 42.9% negative effect and 57.1% positive effect, G3b 43.5% negative effect and 56.5% positive effect. G4a 63.2% negative effect and 36.8% positive, G4b 72.7% negative effect and 27.3% positive effect. Overall, the finding shows 51.8% positive effect and 48.2% negative effect on renal function of the 220 patients. This result indicates that radiotherapy has both positive and negative effects on renal function of patients with cervical cancer after treatment. However, this effect of radiotherapy on renal function of the patients with cervical cancer was not found to be of statistically significant difference, with ?2 (1, N=220) = .284, P = 288. Table 4 shows the pattern of the eGFR status among the patients before and after completion of their treatments. The GFR measurement for the patients was done before and after radiotherapy.

Table 5 shows there was a marginal difference in the mean score of patients GFR before and after radiotherapy intervention. The mean scores (M= 69.67, SD=19.48, N=220) for GFR before treatment and the mean scores of (M=70.87, SD= 20.38, N=146) for GFR after treatment. However, there was no statistical significant difference in the patients GFR between before and after treatment as was(t (219) = -0.66, P< 0.5).

# 10 VI.

# 11 Discussion

Cervical cancer is the second most common malignancy in women and it is a leading cause of cancer-related death for women in Nigeria. Unfortunately, treatment for cervical cancer induces renal function injury due to the impact of high doses of ionizing radiation on the renal system in the course of radiotherapy. Following the known deleterious effect of radiotherapy on renal function, this study seeks to investigate the change in Glomerular Filtration Rate(GFR) among cervical cancer patients that have undergone radiotherapy in the department of Radio-Oncology UDUTH, Sokoto.

The mean age of the cancer patients in this study was 49.9 (SD ± 11.9), with an age range of 24-87years. The peak incidence of (31.4%) of the disease occurred in people age 40-49 years, just as it been established in previous researches done in Nigeria (11,12,13) .

The statistical analysis on table 2 shows the classification of cancer stages presented by patients. Stage1b 5%, stage2a 15%, and 2b 23.2%, stage3a 22.3%, and 3b 20.9%, stage4a 8.6%, and 4b was 5% respectively. This shows that there was 80%incidence of advanced disease (Stage 2b and above). This corresponds to other similar studies (15,16) which describe the late presentation of cervical cancer cases in Nigeria, compared to high-income countries where early presentation of cases predominates the disease (17) . This supports the importance of screening and early testing, which significantly reduces the incidence of cervical cancer and increases early detection of new cases, thereby improving prognosis for survival following treatment (19) .

Regarding the research questions which were put forward to be answered in this study, the statistical analysis for question one shows a bidirectional effect of radiotherapy on renal function of patients with cervical cancer. The bidirectional outcome of the result implies that application of radiotherapy as an intervention procedure in the treatment of cervical cancer has both negative and positive effects. This was established in the study from the derived findings which shows 51.8% positive effect of radiotherapy on renal function and 48.2% of its negative effect, in the 220 cervical cancer patients treated. These findings support the evidence from Okadema et al (3) , who assert that radiotherapy and chemotherapy may have adverse effects on renal and urological function. Their claim is supported by many prospective studies, which indicate that major genitourinary complications (or a significant rise in renal dysfunction) are associated with postoperative radiotherapy (3,9) .

On the contrary, despite the availability of extant literature showing that radiotherapy has a negative effect on renal function of the cervical cancer patients, there is also empirical evidence from studies that show the positive effect of radiotherapy on renal function of patients with cancer of the cervix, in tandem with the findings of this study. For example, Horan and his fellow researchers declared that pelvic radiation does not induce any deterioration of renal function or degree of hydronephrosis (10) . Another study also shows that kidney function was improved between the third and sixth months, in the majority of their patients (2) . Some studies have shown

that the dose (Gy) of radiation given and the Stage of the disease (especially among patients with stages III and IV cancer) are often responsible for the renal complication imposed by the use of radiotherapy in treatment of cervical cancer. For example, it found that that patients with KV 20Gy values < 10% retained significantly better renal function than did patients with KV 20Gy values > 10% (P = 0.002) (14) . The incidence of complications may be reduced to some extent by careful dose planning and continuous observation of the patient during the irradiation (9,16) .

Turning to the second research question, the findings show that there was a marginal difference in the mean score of patients' GFR before and after radiotherapy intervention. The mean scores were (M= 69.67, SD=19.48, N=220) for GFR before treatment and the mean scores were (M=70.87, SD= 20.38, N=146) for GFR after treatment. This marginal difference observed in the mean scores of the patients' GFR before and after treatment is a supportive evidence to the findings on question one, which shows a Year 2021 variance51.8% positive effect and 48.2% of negative effect in the 220 cervical cancer patients evaluated in the study. Despite the findings that radiotherapy has both negative and positive effect of renal function, it shows that there was no statistical significant difference in the patients GFR before and after treatment at (t (219) = -0.66, P< 0.5). Therefore, there was no statistical significant difference found regarding the effect of radiotherapy on renal function of patients with cervical cancer ?2 (1, N=220) = .284, P = 288. This supports findings from other studies, which showed that there was no statistical difference in the risk between patients treated with radical hysterectomy with postoperative radiotherapy and radiotherapy alone (15) . However, the latency period between radiotherapy and the manifestation of urological complications may be relatively long, as radiotherapy has both acute and chronic side-effects.

# 12 Global

# 13 VII.

# 14 Conclusion

Cervical cancer remains a disease of great public health importance in most of the developing world, Nigeria inclusive. The various modalities for managing this disease, have been associated with documented deleterious effects on the renal function of patients treated. Although this study shows a marginally predominant positive effect of radiotherapy on renal function of patients with cervical cancer, radiotherapy has been known to cause serious renal injury, especially due to the anatomical location of the cervix. The incidence of complications may be reduced to a large extent by careful dose planning and continuous observation of the patient during the irradiation. Consequently, it is necessary for the radiation oncologists to maintain the standard dose applications and procedures for treatment of cervical cancer patients, as well as to monitor patients closely so as to either prevent complications or identify them early. [1]

**1**

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Figure 1: Table 1 :

[1]

**2**

| Stage | Frequency | Percent |
|---|---|---|
| 1b | 11 | 5 |
| 2a | 33 | 15 |
| 2b | 51 | 23.2 |
| 3a | 49 | 22.3 |
| 3b | 46 | 20.9 |
| 4a | 19 | 8.6 |
| 4b | 11 | 5 |
| Total | 220 | 100 |

Table 2 shows the classification of cancer stages. Stage 1b accounted for 11(5 %), 2a 33(15%), 2b 51(23.2%), 3a 49 (22.3%), 3b 46(20.9%), 4a 19(8.6%), and 4b accounted for 11 (5%).

Figure 2: Table 2 :

**3**

Year 2021
35

Figure 3: Table 3 :

**4**

Year 2021
36

Figure 4: Table 4 :

**5**

| Variables | Group | N | M | SD | t | df | P = 0.05 |
|---|---|---|---|---|---|---|---|
| GFR: | Before | 220 | 69.67 | 19.48 | | | |
| | | | | | -0.66.2 | 219 | 0.505 |
| | After | 220 | 70.87 | 20.38 | | | |

Figure 5: Table 5 :

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