

To Evaluate the Association of Urinary Tract Infections in Patients Undergoing Pelvic Radiation for Cervical Cancers

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Abstract

Introduction: Radiation is an effective cancer treatment in cervical cancer due to its direct and indirect interaction with living cells. Damage to the basement membranes of blood vessels can lead to occlusion, thrombosis, and neovascularization followed by atrophy and contraction of tissue these result in significant urinary symptoms.

Methods: all are planned for concurrent chemoradiation having histopathology squamous cell carcinoma. We advised baseline urine culture and sensitivity analysis before starting radiation, with negative urine culture and sensitivity reports considered for chemoradiation and included in the study.

Results: It is a single-arm observational institutional study. The total number of patients taken is 100—patients with culture positive 28, and negative 72. The most common organism detected is *E.coli*. After one month of follow-up, completion of radiation, and after giving antibiotics, 93/100 patients are asymptomatic in their urine culture and sensitivity report. A total of 100 patients who underwent pelvic radiation were taken in the study. Urine culture was positive in 28% of individuals. Urinary tract infection can persist for months even after completion of pelvic radiation. Through this study, we can educate the patient about taking precautions, and prescribe antibiotics based on the culture and sensitivity reports. This follow-up can be continued for up to six months to assess the late complications like radiation-induced cystitis.

Keywords: Cervical Cancer, Radiation, Urine Culture, Radiation Cystitis

1. Introduction

Worldwide, cervical cancer remains the most common gynecologic cancer and the fourth most common malignancy in women, with over 526,000 women globally developing this tumor reported in 2015 and 239,000 dying of the disease every year. Cervical cancer is the second most common cancer among Indian women (As per GLOBOCON 2020). Adjusting population growth and aging, the global incidence rate for cervical cancer declined by 1.2% from 2005–2015. The majority of cases are in Africa because of the paucity of screening measures and the prevalence of immunodeficiency because of the human immunodeficiency virus (HIV). Unfortunately, it often affects young women, resulting in the loss of the ability to bear future children. An economic analysis from India demonstrates the financial benefit of treating women with cervical cancer with MR-based. Radiation is an effective cancer treatment due to its direct and indirect interaction with living cells. The direct interaction induces immediate cell death by damaging DNA

and tissue protein. The indirect interaction occurs by forming free radicals by ionizing radiation that interacts with enzymes leading to cell death and future mutation. These direct and indirect interactions lead to cellular injury by affecting division delay, reproductive failure, and interphase arrest, usually seen in rapidly dividing cells.

The radiation-induced damage to tissue architecture develops in a linear threshold model. Damage to blood vessels' basement membranes can lead to occlusion, thrombosis, neovascularization, and increased proliferation of fibroblasts. All these changes have the potential to cause significant urinary tract injury. Bladder damage and loss of capacity can cause significant urinary symptoms. Neovascularization is an essential factor for radiation cystitis and subsequent hemorrhagic cystitis. Replacement of the corpus spongiosum with fibrosis and subsequent occlusion of the urethral lumen is a critical factor in increased urethral strictures after RT. Late urinary adverse effects (AEs) grading using the

Radiation Therapy Oncology Group (RTOG) system grades AEs on a scale of 0-5. Grade 0 denotes no complications. Minor AEs like microscopic hematuria is labeled step 1. Grade 2 AEs include moderate urinary frequency, generalized telangiectasia, or intermittent macroscopic hematuria. Grade 1 and 2 AEs are commonly managed with observation or medical therapy and have minimal impact on life quality. Grade 3 and 4 AEs are considered severe.

These are often controlled with a procedure and have a significant effect on the quality of life. Adverse effects include intense frequency or dysuria, severe telangiectasia (often with petechiae) with hematuria, or reduced bladder capacity to less than 150 cc volume. We classify Severe hemorrhagic cystitis, reduced bladder capacity to less than 100 ccs volume, and necrosis as grade 4 toxicity. Sometimes, pelvic radiotherapy can

cause changes to the way the bladder works. In some people, these changes will not get better after treatment finishes. Others may not develop until months or years after treatment has finished.

Pelvic radiotherapy can cause scarring and hardening (fibrosis) of the bladder wall. It may also weaken the pelvic floor muscles. Blood vessels in the bladder may become fragile and bleed easily, and in some cases, pelvic radiotherapy may cause the urethra to narrow. These changes can lead to late effects, such as passing urine more often or difficulty passing urine, leaking urine, and blood in the urine. For some people, these changes start during treatment and do not get better. Nevertheless, sometimes, bladder changes may develop months or years after treatment has finished. Changes also happen as the bladder muscles age, so the symptoms below are more common as people age.

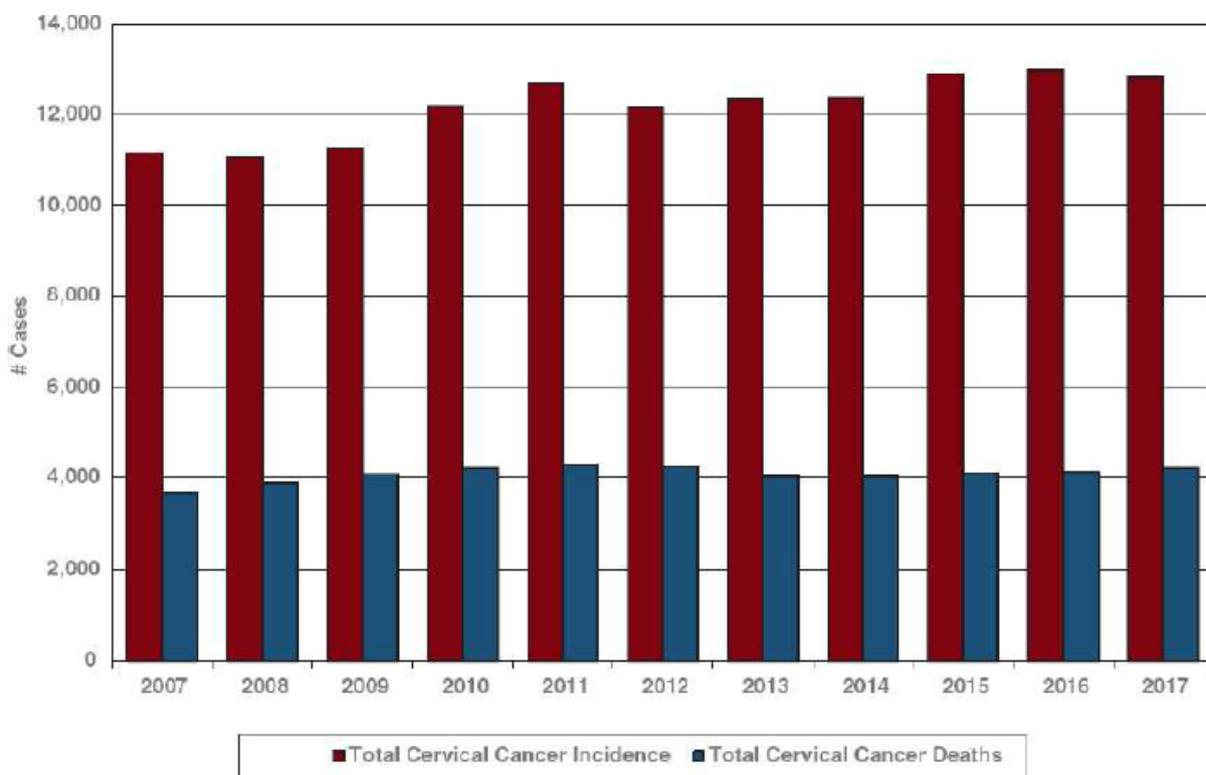


Figure 1:

- A: Lymph vessels and lymph nodes of the cervix and the body of the uterus. (Anatomical Chart Company, Lexington, SC.)
- B: Three-dimensional reconstruction of pelvic and common iliac lymph nodes' location outlined on CT scans in patients with carcinoma involving the distal vagina, requiring inguinal node coverage.
- C: The incidence of cervical cancer increased slightly in the United States from 2007 to 2017.

The purpose of this study was to diagnose the etiological factors in urinary tract infection and to determine the drug sensitivities of bacteria causing UTI in patients with malignant neoplasms of the reproductive system.

2. Aims and Objectives

Evaluate the association of urinary tract infections in patients undergoing pelvic radiation and observe the effect of radiation on cervical carcinoma and the association of radiation with urinary tract infections.

2.1. Inclusion Criteria

- We have histologically proven squamous cell carcinoma of the cervix.
- Consent of the patient.
- KPS 70 and above
- Adequate bone marrow reserve hemoglobin >10,wbc >4000, platelet count>1 lakh.
- Age 18 to 65 years
- Average values of renal, cardiac, and liver function tests.
- Staging of the patient who indicates radiation (concurrent chemoradiation).

2.2. Exclusion Criteria

- History of a second malignancy.
- previously of a concurrent patient having any concurrent illness (hypertension, diabetes)
- Prior treatment in the form of surgery, chemotherapy, radiotherapy, or chemoradiation.
- Patients enrolled in the study and left the treatment in between radiation are excluded from the study.

3. Materials and Methods

This research is a single-arm observational study. We have excluded patients with urine culture-positive results and included those patients who have sterile urine cultures. Hence, we took the patients in a single arm. All the patients enrolled in the study are taken from our radiotherapy OPD, which are new cases of carcinoma cervix, sent to us from the Gynecology department with the histopathological report of squamous cell carcinoma. All the patients were newly diagnosed carcinoma cervix cases that were only indicative of chemoradiation. We advised those patients a baseline urine sample for urine culture and sensitivity and routine microscopy. The technique for taking the urine sample was correctly explained to the patients. They have to collect an early morning clean-catch midstream urine sample. We advise patients to collect the urine sample after removing the first urine flow, cleaning the perineal area, and soaking it with a clean cloth. We have provided them with two sterile urine containers—one sample for routine microscopy and another sample for culture and sensitivity. The patients enrolled in the study should have a sterile report in their urine culture and sensitivity to see the effects of radiation when the external beam radiation therapy starts.

So, we have included patients in the study who are having culture sterile in urine reports before the start of radiation.

4. Results

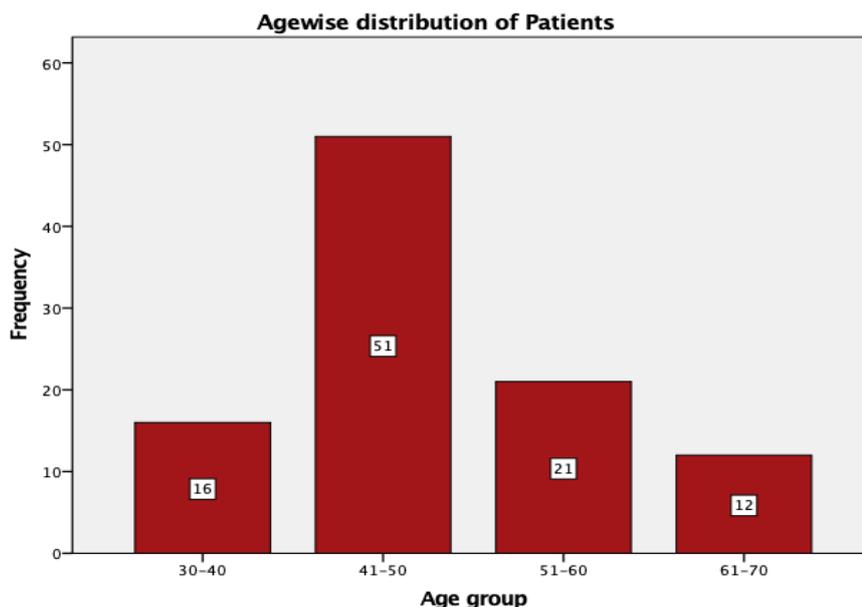


Figure 2: We Took A Total Of 100 Patients with Cervical Cancer Who Were Undergoing Pelvic Radiation for Study.

Samples are taken from the patient in the second week and third week of radiation when they come for follow-up. On analysis of the patient's urine sample in the second week and third week of radiation, certain microorganisms are found, in the culture and sensitivity report, along with patients' developing symptoms of burning micturition and urgency and increased frequency of micturition. We have prescribed antibiotics based on the culture and sensitivity report and assess for improvement within 5 to 7 days. If the patient is still having urinary complaints like burning micturition or increasing in frequency and urgency, then those antibiotics were given for 14 days.

Patients are also advised to drink plenty of fluids and hold urine before going for radiation according to the bladder protocol in which we have to advise the patient to drink 4-5 cups of 200 ml each just 5 minutes after emptying their bladder. We advise them to follow the same bladder protocol each day before going for radiation. Similarly, another sample is taken in the third week to assess the presence of urinary tract infections. The urine culture reports are collected by each patient and advised antibiotics accordingly. Some patients are planned by conventional technique and some by conformal technique, but the comparison of techniques is not related to urinary tract infections. After completing external beam radiation therapy, they were with a urine culture. We again assess them for their complaints.

Initially, patients are also considered for pus culture sensitivity while undergoing intracavitary brachytherapy, but later on, the source has become depleted, so we have excluded those patients from the study. We have completed a one-month follow-up with these patients. Even after one month of follow-up, if the patient's urine culture is positive for microorganisms, we prescribe antibiotics accordingly and a cystoscopy to determine the presence of infection growth or anything irritating the bladder.

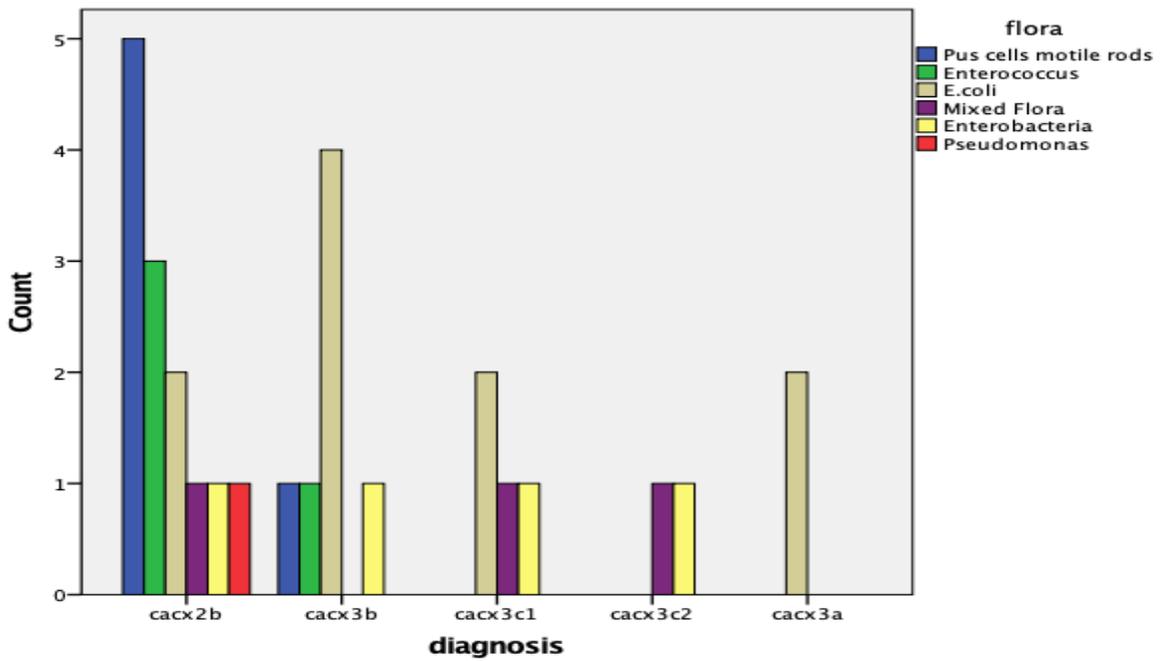


Figure 3: Most of The Cases Were of Carcinoma Cervix Figo 2b Stage Followed by Carcinoma Cervix 3b.

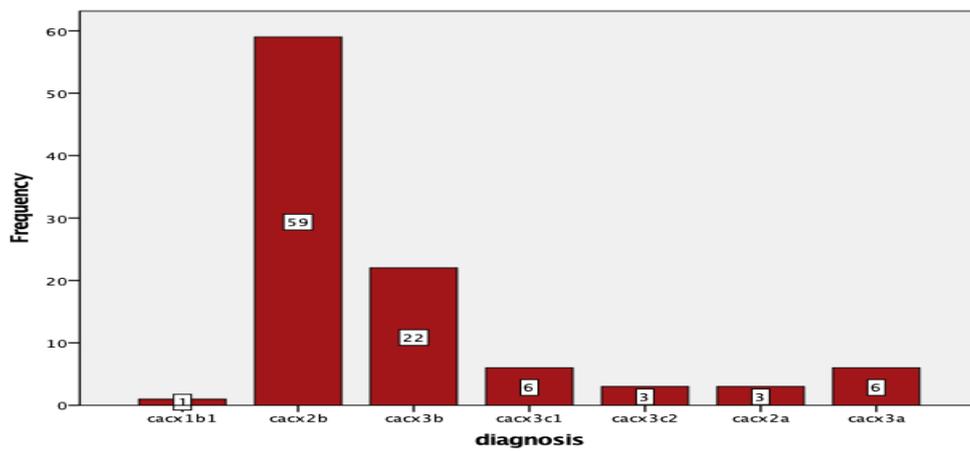


Figure 4: Histopathological Stage of The Tumor at The Time of Presentation. After the Radiotherapy Intervention, 28% Of Patients Were Found Positive with A Urine Culture.

culture	Frequency
negative	72
positive	28
total	100

Table 1: Distribution / Diagnosis of Microorganism in Culture Positivity Samples After Radiotherapy

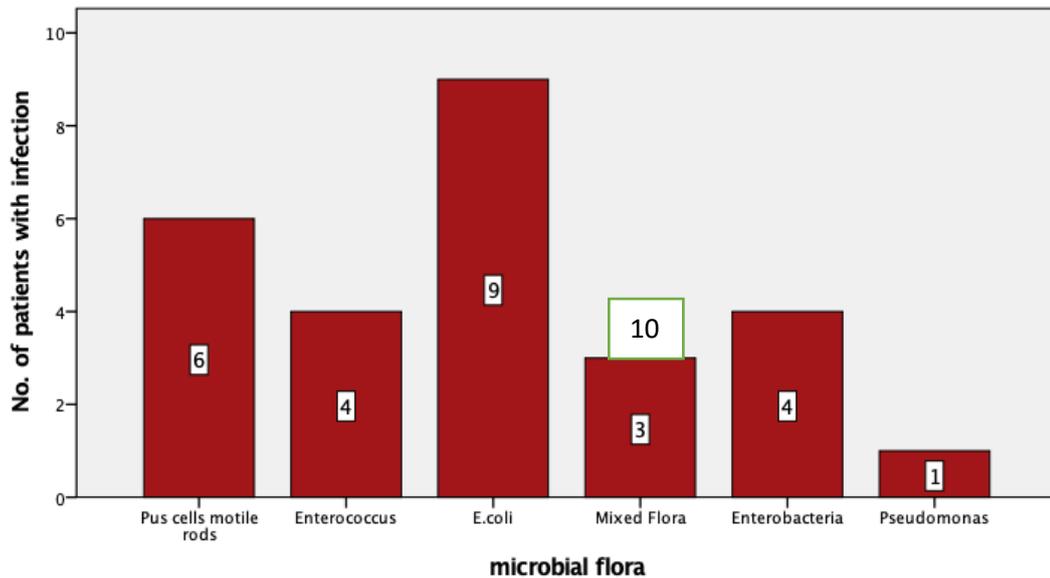


Figure 5: No Significant Correlation Was Seen Between Different Microbial Infections with Pathological Stages of The Lesion.

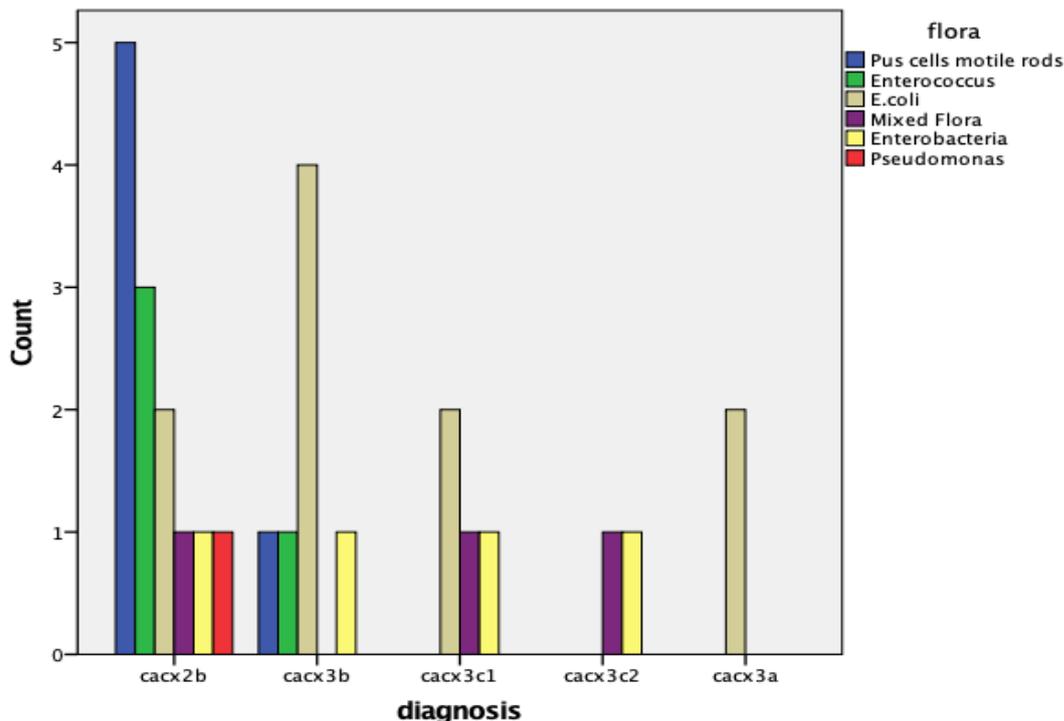


Figure 6:

5. Conclusion

Total number of patients =100 Patients with culture positive=28, negative=72 The age group in which most patients were between 41-50 years of age. The most common organism detected is E.coli in 10 patients. The most common stage is ca cervix 2b, associated with UTI, followed by ca cervix 3b. After 1 month of follow-up, completion of radiation, and after giving antibiotics, 93/100 patients become asymptomatic.

6. Discussion

We took 100 patients in the study who underwent pelvic radiation. Urine culture was positive in 28% of individuals, with the most common organism detected E.coli observed in 10 patients,

followed by pus cells and motile rods in 6 individuals, followed by Enterococcus species Enterobacteriaceae. In the study done by Shuford et al., Escherichia coli was the most commonly grown in culture, isolated from 19 (22.6%) of specimens in 134 women receiving pelvic radiotherapy retrospectively analyzed a total of 241 urine specimens. In this study, based on the age group taken in the study, UTI is developing in patients more commonly in the age group 41-50 years, followed by 51-60.

Most of the cases included in this study belonged to carcinoma cervix 2b stage followed by ca cervix 3b. The total number of microorganisms detected in stage 2b is 13, followed by 7 in ca cervix 3b (since more cases are getting enrolled in the

study area of carcinoma cervix 2b). There was no significant correlation observed between different microbial infections with pathological stages of the lesion. Authors have described in an article published in *Gynecological Oncology* in July 1995 a higher percentage (33.3%) of infections in patients with stage III cervical cancer in comparison to patients with stage II disease (16.7% UTI). In this study, based on urine culture and sensitivity reports, we got the results, that is the standard gold test for diagnosing UTI, but in the study done by Kupelian et al., they have performed dipstick, urine microscopy, and urine culture tests and categorized patients on that basis.

While acute radiation cystitis tends to resolve shortly after therapy, radiation can induce several changes within the bladder urothelial, which vary over time. We chose to include samples till 1 month from the completion of EBRT. The studies that have taken patients who received EBRT and underwent urine culture sensitivity with confirmatory culture during or within six months of radiotherapy completion were included in this analysis. Those patients who are positive for E coli in their culture report they are sensitive to tab nitrofurantoin, which was given in a dose of 100 mg twice for 5-7 days depending upon the symptoms, while the study done by Kupelian et al. symptoms of acute uncomplicated cystitis in the primary care setting 15% of positive culture were resistant to trimethoprim/ sulphamethoxazole. Only 2% were resistant to nitrofurantoin [1-20].

7. Limitation

It includes a relatively small sample size from a single institution. Antibiotic susceptibility data were not available for each positive culture because we had to order tests according to our laboratory protocol.

Patients for intracavitary brachytherapy are initially taken for the study but then excluded later on as the source is depleted and reduces the number of patients.

Intracavitary brachytherapy is not included in this study because of the instrumentation that we apply during brachytherapy itself is the source of infection for the patients, and the reports of culture sensitivity will be a false negative.

Those who received intracavitary brachytherapy are also not included in the study because of the instrumentation used to do the procedure as it is the source of added infection.

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