Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Impact of Prostate Radiotherapy on Urinary Bacterial Profiles and the Emergence of Multidrug-Resistant Organisms: A Prospective Study

Hassan Yamine

dr.hassanyam@gmail.com

Centre Hospitalier Universitaire Hassan II

S. Khalfi

Centre Hospitalier Universitaire Hassan II

W. Hassani

Centre Hospitalier Universitaire Hassan II

K. Soussy

Centre Hospitalier Universitaire Hassan II

F. Farhane

Centre Hospitalier Universitaire Hassan II

Z. Alami

Centre Hospitalier Universitaire Hassan II

T. Bouhafa

Centre Hospitalier Universitaire Hassan II

Research Article

Keywords: Prostate cancer, Radiotherapy, Urinary tract infection, Multidrug-resistant bacteria, Urinary microbiome, Radiation cystitis

Posted Date: March 22nd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9035707/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Radiotherapy represents a major therapeutic modality for localized prostate cancer. Despite technological advances, pelvic irradiation remains associated with urinary complications including radiation cystitis and urinary tract infections (UTIs). Emerging evidence suggests that radiation may alter urinary microbiota and promote antibiotic resistance.

Objective

To evaluate the impact of prostate radiotherapy on urinary bacteriological profiles and the emergence of multidrug-resistant bacteria.

Methods

This prospective study included 120 patients treated for prostate cancer between March 2024 and February 2026 at the Radiation Oncology Department of Hassan II University Hospital, Fez. All patients received 3D conformal radiotherapy with or without androgen deprivation therapy. Urine cultures and antibiograms were performed before radiotherapy, weekly during treatment, and during follow-up at 1, 3 and 6 months. Infection rates and antibiotic resistance profiles were analyzed.

Results

Urinary infection incidence was 24% before radiotherapy, 18% during treatment, and increased to 40% after treatment. Escherichia coli (48%) and Enterococcus faecalis (32%) were the most common pathogens before radiotherapy. Multidrug-resistant bacteria increased from 10% before treatment to 28% after radiotherapy. Multivariate analysis identified radiotherapy as the only independent factor significantly associated with the emergence of resistant strains ($p < 0.01$).

Conclusion

Prostate radiotherapy significantly modifies the urinary bacteriological ecosystem and promotes the emergence of multidrug-resistant organisms. Systematic microbiological monitoring is recommended during and after radiotherapy.

Introduction

Prostate cancer is the most common malignancy among men in many regions of the world and represents a major public health concern. Radiotherapy plays a central role in the management of localized and locally advanced prostate cancer, either as a primary treatment or in combination with androgen deprivation therapy. Advances in radiation techniques such as intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) have significantly improved tumor control while reducing treatment toxicity.

Despite these improvements, pelvic irradiation remains associated with genitourinary toxicity. Among these complications, radiation cystitis and urinary tract infections are frequently observed and may significantly affect patient quality of life.

The pathophysiology of radiation-induced cystitis remains incompletely understood. Access to irradiated bladder tissue is limited, which restricts histopathological studies. However, recent research suggests that alterations in the urinary microbiome may play a role in post-radiotherapy urinary complications.

Ionizing radiation can disrupt microbial ecosystems, modify host immune responses, and induce genetic mutations in bacterial populations. These mechanisms may promote the emergence of multidrug-resistant organisms and increase susceptibility to urinary infections.

The objective of this prospective study was to evaluate the impact of prostate radiotherapy on urinary bacteriological profiles and the development of multidrug-resistant bacteria in patients treated for prostate cancer.

Materials and Methods

Study Design

This prospective observational study was conducted at the Department of Radiation Oncology of Hassan II University Hospital, Fez.

Study Population

A total of **120 patients** with localized prostate cancer treated between **March 2024 and February 2026** were included.

Inclusion criteria

- histologically confirmed prostate cancer
- indication for curative radiotherapy
- availability of urine cultures before and after treatment

Exclusion criteria

- active systemic infection at baseline
- incomplete microbiological data

Treatment Protocol

Treatment Protocol
All patients received **3D conformal radiotherapy (3D-CRT)** according to institutional protocols.

Radiotherapy was delivered using linear accelerators with standard fractionation schedules. Androgen deprivation therapy was administered when indicated according to risk stratification.

Microbiological Evaluation

Urine samples were collected using **midstream urine collection**.

The following tests were performed:

- urine culture (ECBU)
- bacterial identification
- antibiogram sensitivity testing

Clinical Data Collection

Clinical data included:

- age
- diabetes mellitus
- history of recurrent urinary infections
- urethral catheterization
- immunosuppression
- prior antibiotic exposure

Patients were monitored weekly during treatment using the **International Prostate Symptom Score (IPSS)**.

Follow-up visits occurred at:

- 1 month
- 3 months

- 6 months after radiotherapy

Results

Urinary infection incidence was 24% before radiotherapy, 18% during treatment, and increased to 40% after treatment. Escherichia coli (48%) and Enterococcus faecalis (32%) were the most common pathogens before radiotherapy. Multidrug-resistant bacteria increased from 10% before treatment to 28% after radiotherapy. Multivariate analysis identified radiotherapy as the only independent factor significantly associated with the emergence of resistant strains ($p < 0.01$).

Patient Characteristics

A total of 120 patients with localized prostate cancer were included in this prospective study. The mean age of the patients was 68.5 years (range 55–82 years). Baseline clinical characteristics are summarized in Table 1.

Table 1. Patient Characteristics (n=120)

Variable	Value	Percentage
Number of patients	120	—
Mean age (years)	68.5	—
Diabetes mellitus	26	21.6%
History of recurrent UTI	19	15.8%
Urethral catheterization	11	9.1%
Immunosuppression	6	5.0%
Associated hormone therapy	72	60.0%

These baseline characteristics indicate that a significant proportion of patients presented risk factors potentially associated with urinary infections, particularly diabetes mellitus and prior urinary tract infections.

Incidence of Urinary Tract Infections During Radiotherapy

The incidence of urinary tract infections (UTIs) varied throughout the treatment course.

Before the initiation of radiotherapy, 24% of patients presented positive urine cultures. During radiotherapy, the infection rate slightly decreased to 18%, while a significant increase was observed after treatment completion, reaching 40%.

These findings indicate a delayed increase in infection incidence following radiotherapy, suggesting a potential relationship between radiation-induced bladder changes and urinary infections.

Bacterial Spectrum

The bacterial profile identified in urine cultures before radiotherapy revealed a predominance of Gram-negative organisms.

Table 2. Bacterial Distribution Before Radiotherapy

Bacteria	Frequency (%)
Escherichia coli	48
Enterococcus faecalis	32
Other Gram-negative bacilli	20

These findings are consistent with previously reported epidemiological patterns of urinary infections in prostate cancer patients.

Emergence of Multidrug-Resistant Organisms

A major finding of this study was the significant increase in multidrug-resistant bacteria following radiotherapy.

Before treatment, only 10% of infections were caused by multidrug-resistant organisms (MDR). After radiotherapy, this proportion increased significantly to 28%.

This represents a nearly threefold increase in multidrug-resistant bacterial strains following radiotherapy.

Risk Factor Analysis

Potential risk factors associated with urinary infection were analyzed, including:

diabetes mellitus

urethral catheterization

recurrent urinary infections

immunosuppression

prior antibiotic exposure

In univariate analysis, diabetes and catheterization showed a trend toward association with urinary infection. However, multivariate logistic regression analysis demonstrated that radiotherapy exposure

remained the only independent statistically significant factor associated with the emergence of multidrug-resistant organisms (OR = 3.6, 95% CI 1.8–7.2, p = 0.001) (Table 3, Figure 3).

These results suggest that radiotherapy plays a central role in modifying the urinary microbial ecosystem and promoting the development of antibiotic resistance.

Table 3 – Risk factor analysis

Factor	Univariate p	Multivariate p	OR	CI95
Diabetes	0.08	0.18	1.3	0.7–2.5
Catheterization	0.06	0.12	1.4	0.8–2.9
Age	0.12	0.25	1.02	0.98–1.06
Radiotherapy	**0.004**	**0.001**	**3.6**	**1.8–7.2**

Discussion

This prospective study demonstrates that prostate radiotherapy is associated with significant alterations in the urinary bacteriological profile, with a particularly high cumulative incidence of urinary tract infections observed in our cohort and a marked increase in infections during the post-treatment period. Interestingly, although the incidence of infection remained relatively modest during radiotherapy itself, it increased substantially after treatment completion, suggesting that radiation-associated urinary infections may not be exclusively related to acute inflammatory processes but rather to progressive radiobiological changes affecting the bladder environment. Radiation-induced urothelial injury typically evolves through several pathological stages including acute epithelial inflammation, microvascular damage, submucosal fibrosis, and progressive impairment of mucosal barrier integrity [2,11].

These structural and functional alterations may create a favorable environment for bacterial colonization and persistence within the urinary tract, particularly during the early post-irradiation phase. In our study, the microbiological profile was characterized by a predominance of Gram-negative bacilli, accounting for the majority of isolated pathogens, which is consistent with the classical epidemiology of urinary tract infections [15]. However, exposure to ionizing radiation may also influence bacterial virulence and resistance patterns. Experimental studies have demonstrated that gamma radiation can induce modifications in bacterial gene expression, promote enhanced resistance phenotypes, and increase the capacity of microorganisms to form biofilms [5].

In addition, radiation-induced oxidative stress generates reactive oxygen species that can damage microbial DNA and trigger stress-response mechanisms that facilitate bacterial adaptation and survival under hostile environmental conditions. These mechanisms may contribute to the emergence of multidrug-resistant strains, as observed in our cohort, where the proportion of resistant bacteria increased significantly after radiotherapy. Moreover, radiation exposure may facilitate horizontal gene

transfer between bacterial species, accelerating the dissemination of resistance determinants such as blaTEM, blaCTX-M, and blaSHV genes, which encode extended-spectrum β-lactamases [13,14]. This phenomenon has been described by El-Zawahry et al., who demonstrated that radiation exposure may induce genetic mutations and promote the expression of beta-lactamase enzymes, thereby increasing bacterial resistance to β-lactam antibiotics [5].

Beyond its direct microbiological effects, pelvic irradiation may also disrupt the urinary microbiome, a complex microbial ecosystem that plays a crucial role in maintaining urological health. Emerging evidence suggests that the urinary tract is not sterile but hosts a dynamic microbial community whose balance contributes to mucosal defense mechanisms [15]. According to Maślak et al., patients undergoing prostate radiotherapy exhibit a reduction in urinary microbial diversity, a condition that may predispose to dysbiosis and opportunistic infections [4].

Pelvic irradiation may disrupt this microbial equilibrium through multiple mechanisms including direct microbial DNA damage, alterations in urinary metabolites, modifications in local pH and oxygen tension, and changes in immune responses. Recent metabolomic studies have demonstrated persistent alterations in urinary and plasma metabolic profiles following pelvic irradiation, which may impair host–microbial homeostasis and contribute to long-term urinary complications [3].

In addition to microbiological and metabolic factors, immune modulation may also play an important role in the development of post-radiotherapy infections. Radiotherapy is known to induce both local and systemic immune alterations, including radiation-induced lymphopenia, decreased mucosal immune surveillance, and modifications in cytokine signaling pathways [6]. Lymphocyte depletion may impair bacterial clearance mechanisms and increase susceptibility to infection, particularly in elderly patients who already exhibit reduced immune reserve.

Although traditional risk factors such as diabetes mellitus, smoking, catheterization, or previous urinary tract infections are well-known contributors to infection risk, our analysis did not demonstrate a statistically significant association between these comorbidities and infection incidence in our cohort, suggesting that radiation exposure itself may represent the dominant determinant of urinary microbiological changes in this specific clinical setting.

From a clinical perspective, the high incidence of urinary tract infections observed after radiotherapy has several important implications. Pre-treatment screening for urinary infections should be systematically performed, as the identification and adequate treatment of pre-existing infections may reduce the risk of post-treatment recurrence. Furthermore, systematic microbiological surveillance during the early post-radiotherapy period, particularly within the first three months after treatment completion, may facilitate early detection and management of infections.

Another important clinical challenge is the differentiation between radiation cystitis and infectious cystitis, as both conditions share overlapping symptoms such as dysuria, urgency, frequency, and hematuria [2,11]. In addition, recurrent infections following radiotherapy may contribute to increased

antimicrobial exposure, potentially promoting further emergence of antibiotic-resistant strains, thereby emphasizing the importance of appropriate antibiotic stewardship strategies [13,14].

Our findings are consistent with several reports in the literature describing microbiome alterations following pelvic radiotherapy, increased susceptibility to infections related to radiation-induced lymphopenia, and persistent metabolic perturbations affecting host–microbial interactions after irradiation [3,6]. Nevertheless, few prospective studies have specifically investigated serial urine cultures in patients undergoing prostate radiotherapy, highlighting the relevance and originality of our work.

Despite these findings, several limitations should be acknowledged. This study was conducted at a single institution and included a relatively moderate sample size, which may limit the generalizability of the results. In addition, molecular characterization of the urinary microbiome using high-throughput sequencing techniques was not performed, and the follow-up period remained relatively limited.

Future research should therefore integrate advanced microbiome analyses such as 16S rRNA sequencing or metagenomic profiling, longer follow-up periods exceeding twelve months, and correlations between microbiological findings and radiation dose–volume parameters. The integration of microbiome science into radiation oncology represents an emerging and promising research field that may improve our understanding of radiation-induced toxicity and identify potential preventive or therapeutic strategies.

Potential future directions include the identification of predictive microbial signatures associated with radiation cystitis, the evaluation of probiotic or microbiome-modulating interventions, and comparative analyses of different radiotherapy techniques such as IMRT, VMAT, or stereotactic radiotherapy in relation to urinary microbiota alterations [7–10].

Overall, the results of this prospective study suggest that prostate radiotherapy is associated with dynamic and clinically relevant modifications of urinary bacteriological profiles, particularly during the early post-treatment period, and support the hypothesis that radiation-induced dysbiosis may contribute to post-irradiation bladder morbidity.

Conclusion

Prostate radiotherapy is associated with significant alterations in urinary bacteriological profiles and a notable increase in multidrug-resistant organisms. These findings suggest that radiation-induced changes in the bladder microenvironment may contribute to post-treatment urinary infections. Systematic microbiological monitoring during and after radiotherapy may facilitate early detection and appropriate management of urinary infections in patients with prostate cancer.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Hassan II University Hospital, Fez, Morocco.

Consent for publication

Written informed consent was obtained from all participants for publication of the study data.

Funding

This research received no external funding.

Author Contribution

HY designed the study, collected the clinical data and wrote the manuscript. SK, KS and WH contributed to data collection and microbiological analysis. FF and ZA performed the statistical analysis and interpretation of the results. TB supervised the research project and critically revised the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. Dearnaley DP et al. Radiotherapy for prostate cancer. Lancet Oncology.
2. Delobel JB et al. Radiation-induced cystitis. Urology.
3. Reis Ferreira M et al. Impact of pelvic radiation therapy on metabolic profiles and microbiota. Cancer Research.
4. Maślak E et al. Microbiome identification in prostate cancer patients undergoing radiotherapy.
5. El-Zawahry YA et al. ESBL production after gamma radiation exposure.
6. Mohamad O et al. Genitourinary toxicity after prostate radiotherapy. Radiotherapy and Oncology.
7. Michalski JM et al. Toxicity after IMRT for prostate cancer. Journal of Clinical Oncology.
8. Zelefsky MJ et al. Long-term toxicity of IMRT for prostate cancer. Int J Radiat Oncol Biol Phys.
9. De Meerleer G et al. Radiotherapy toxicity in prostate cancer. Lancet Oncology.
10. Fonteyne V et al. Urinary complications after prostate radiotherapy.
11. Hamstra DA et al. Radiation cystitis: pathophysiology and treatment.
12. Muls AC et al. Urinary complications following pelvic radiation therapy.
13. Falagas ME et al. Multidrug-resistant Gram-negative bacteria infections.

14. Ventola CL. Antibiotic resistance crisis. Pharmacy and Therapeutics.
15. Flores-Mireles AL et al. Urinary tract infections: epidemiology and mechanisms. Nature Reviews Microbiology.

Figures

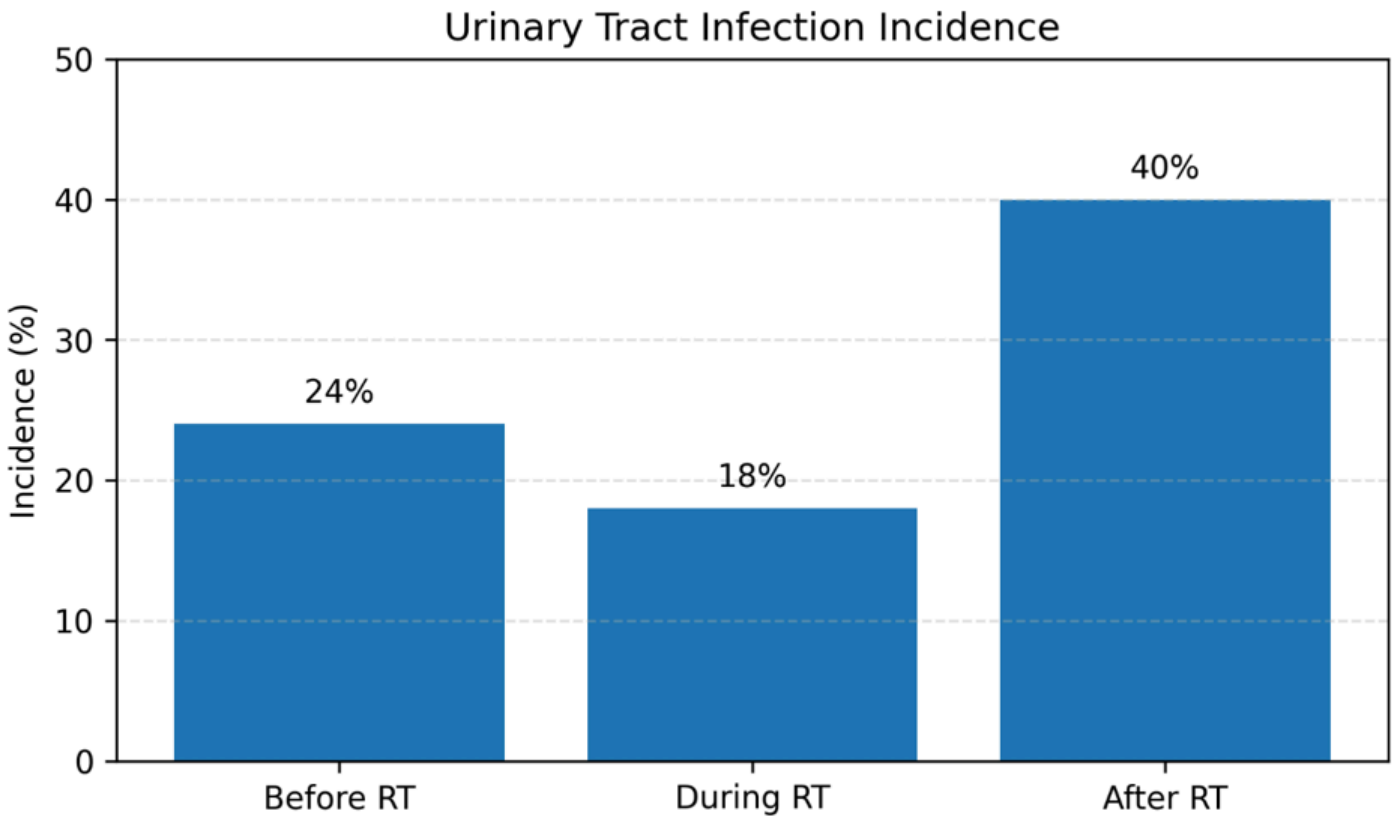


Figure 1

Incidence of urinary tract infections during treatment

The figure illustrates the increase in infection rates after radiotherapy, highlighting the post-treatment vulnerability period.

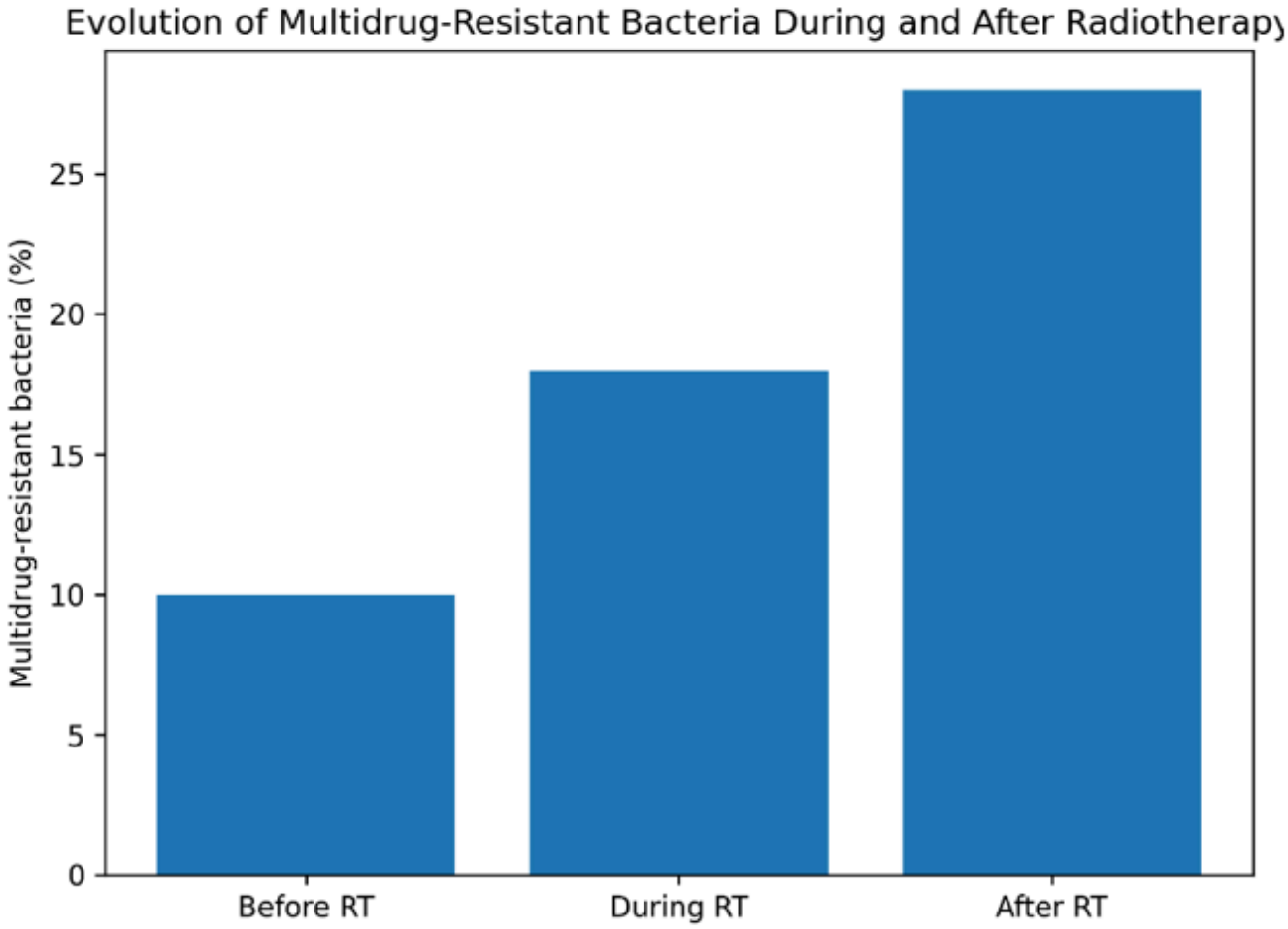


Figure 2

Evolution of multidrug-resistant bacteria before, during and after prostate radiotherapy

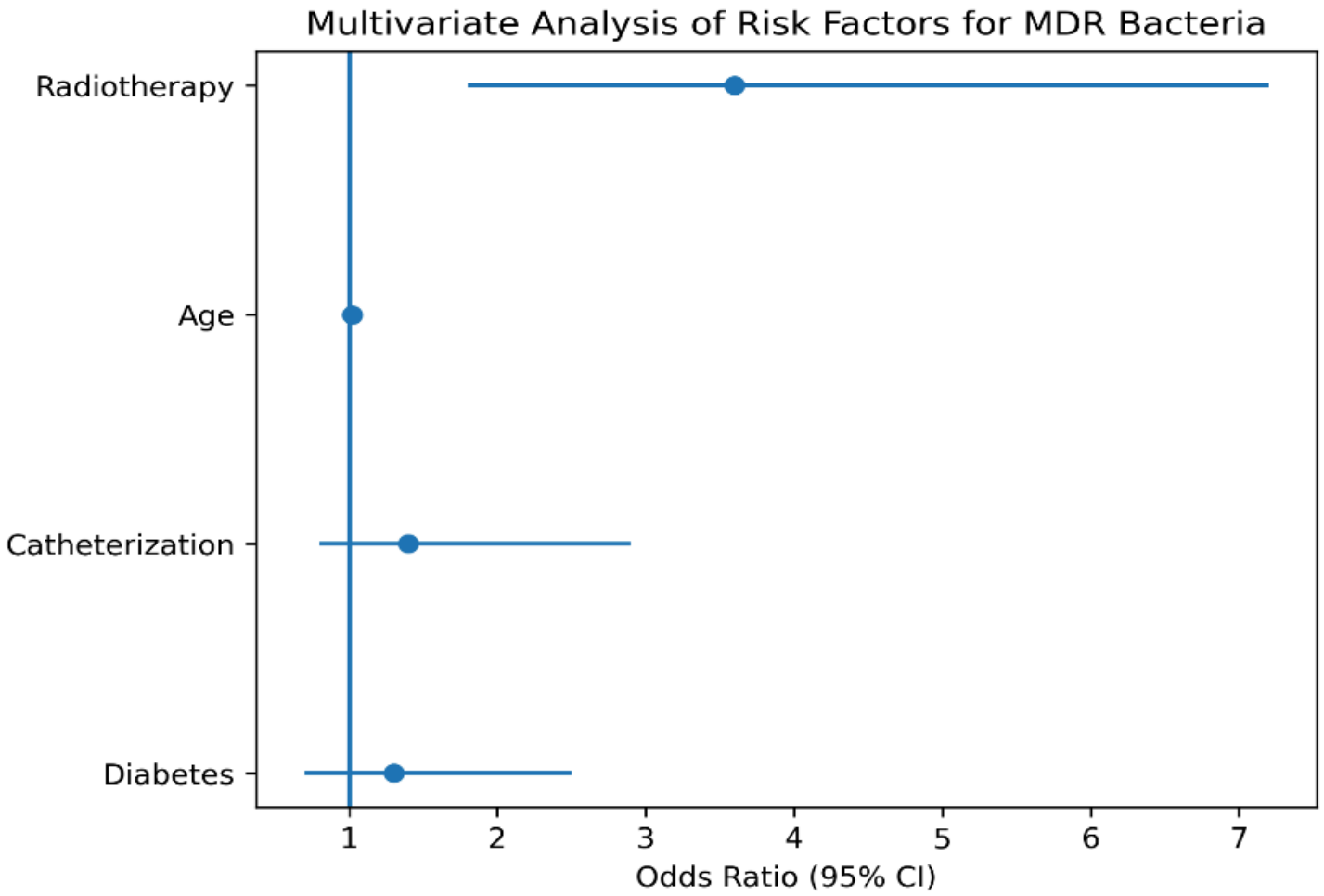


Figure 3

Forest plot showing multivariate logistic regression analysis of risk factors associated with multidrug-resistant bacterial emergence