Phytochemical-Based Therapeutics and Antimicrobial Resistance: Retrospective Insights on Klebsiella spp., Cardiovascular Modulation, and Radiotherapy-Associated Oxidative Stress in Oncology

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ABSTRAK

Resistensi antimikroba pada spesies Klebsiella menimbulkan tantangan signifikan dalam onkologi, terutama bagi pasien yang menjalani radioterapi dengan gangguan imun dan sangat rentan terhadap infeksi yang resisten. Studi observasional retrospektif ini mengevaluasi peran terapi berbasis fitokimia sebagai agen adjuvan dalam perawatan kanker dengan menganalisis rekam medis 180 pasien yang dirawat antara tahun 2015 dan 2022. Data dikumpulkan mengenai pola infeksi, komplikasi kardiovaskular, biomarker stres oksidatif, dan luaran kelangsungan hidup, dengan pasien dikelompokkan menjadi pengguna fitokimia (n = 72) dan bukan pengguna (n = 108). Hasil penelitian menunjukkan bahwa pengguna fitokimia memiliki tingkat infeksi Klebsiella yang lebih rendah (25,0% vs. 42,6%), strain resisten multiobat (12,5% vs. 34,3%), kejadian kardiovaskular (19,4% vs. 30,6%), dan toksisitas terkait radioterapi (37,5% vs. 56,5%). Analisis biomarker menunjukkan penurunan malondialdehid dan peningkatan aktivitas enzim antioksidan pada kelompok fitokimia. Yang penting, tingkat kelangsungan hidup dua tahun lebih tinggi di antara pengguna fitokimia (68,1% vs. 52,7%). Temuan ini menunjukkan bahwa fitokimia memberikan manfaat antimikroba, kardioprotektif, dan radioprotektif, yang mendukung potensi perannya sebagai terapi adjuvan dalam onkologi. Penelitian prospektif lebih lanjut direkomendasikan untuk memvalidasi hasil ini dan mengoptimalkan aplikasi terapeutik.

Keyword: fitokimia; resistensi klebsiella; radioterapi; stres oksidatif; komplikasi kardiovaskular

ABSTRACT

Antimicrobial resistance in Klebsiella species poses a significant challenge in oncology, particularly for patients undergoing radiotherapy who are immunocompromised and highly susceptible to resistant infections. This retrospective observational study evaluated the role of phytochemical-based therapeutics as adjuvant agents in cancer care by analyzing clinical records of 180 patients treated between 2015 and 2022. Data were collected on infection patterns, cardiovascular complications, oxidative stress biomarkers, and survival outcomes, with patients stratified into phytochemical users (n = 72) and non-users (n = 108). The results demonstrated that phytochemical users had lower rates of Klebsiella infections (25.0% vs. 42.6%), multidrug-resistant strains (12.5% vs. 34.3%), cardiovascular events (19.4% vs. 30.6%), and radiotherapy-related toxicities (37.5% vs. 56.5%). Biomarker analysis indicated reduced malondialdehyde and elevated antioxidant enzyme activity in the phytochemical group. Importantly, two-year survival was higher among phytochemical users (68.1% vs. 52.7%). These findings suggest that phytochemicals provide antimicrobial, cardioprotective, and radioprotective benefits, supporting their potential role as adjuvant therapies in oncology. Further prospective studies are recommended to validate these results and optimize therapeutic applications.

Keyword: phytochemicals; klebsiella resistance; radiotherapy; oxidative stress; cardiovascular complications

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1. INTRODUCTION

Antimicrobial resistance is becoming one of the greatest challenges in modern medicine. Among the most concerning pathogens, *Klebsiella* species stand out because of their ability to develop resistance against multiple classes of antibiotics (Al-Haj & Al-Mutairi, 2025; López & Romero, 2024). For patients with cancer, especially those undergoing radiotherapy, this problem is even more critical. Their weakened immune systems make them highly susceptible to hospital-acquired infections, where resistant *Klebsiella* strains are common (Selim et al., 2025). This situation calls for new approaches that go beyond conventional drug therapy and open the door to safer, complementary strategies.

Phytochemicals, naturally occurring compounds found in plants, have long attracted attention for their therapeutic potential. They are not only valued for their antimicrobial activity but also for their antioxidant and anti-inflammatory effects (Arif & Ahmed, 2021; El-Sayed et al., 2022). Recent studies suggest that phytochemicals may interfere with bacterial resistance mechanisms, offering a potential weapon against difficult-to-treat infections (Chen & Wu, 2023). At the same time, they show promise in protecting cardiovascular health and counteracting the harmful effects of oxidative stress, both of which are highly relevant in oncology care (Kumar & Gupta, 2024; Raj et al., 2019).

Radiotherapy remains one of the most effective treatments for cancer, but it often comes with serious side effects. By generating high levels of oxidative stress, it can damage not only tumor cells but also healthy tissues (Das & Singh, 2022; Zhang et al., 2023). This leads to fatigue, tissue injury, and long-term complications that may reduce treatment success. Moreover, radiation further compromises the immune system, which increases the risk of infections by resistant bacteria such as *Klebsiella* (Chavhan et al., 2022). This double burden managing both oxidative damage and resistant infections highlights the urgent need for supportive interventions (Mishra & Tiwari, 2020).

Cardiovascular health is another important consideration in oncology patients. Radiation can cause vascular injury, platelet dysfunction, and an increased risk of blood clots, all of which contribute to long-term morbidity (Sharifi-Rad et al., 2020). Interestingly, some phytochemicals demonstrate protective effects on the cardiovascular system, including anti-platelet activity and improved vascular function (Salehi et al., 2019; Kumar & Gupta, 2024). By supporting both microbial defense and cardiovascular stability, phytochemicals may provide broad benefits when used alongside standard cancer treatments (Raj et al., 2019).

This retrospective study is designed to explore these possibilities. It looks at how phytochemicals may help address three interconnected challenges in oncology: antimicrobial resistance in *Klebsiella* infections, cardiovascular complications, and oxidative stress from radiotherapy. By analyzing clinical data and therapeutic outcomes, the study seeks to provide new insights into the role of phytochemicals as adjuvant therapies. Ultimately, this work aims to contribute to more holistic cancer care strategies that not only treat the disease but also improve patient resilience, safety, and quality of life (Alasmary & Ahmad, 2023).

2. RESEARCH METHOD

This study employed a retrospective observational design to evaluate the role of phytochemical-based therapeutics in oncology patients undergoing radiotherapy. The primary aim was to investigate patterns of antimicrobial resistance in Klebsiella spp., cardiovascular complications, and oxidative stress-related outcomes, while considering the potential contribution of phytochemicals as adjuvant agents. Retrospective analysis was chosen to allow the inclusion of a large clinical population over an extended period and to capture real-world treatment outcomes.

The study population consisted of cancer patients who received radiotherapy between 2015 and 2022 at a tertiary referral hospital. A total of 240 patient records were screened, of which 180 patients met the inclusion criteria. These criteria included: (1) a confirmed diagnosis of solid or hematologic malignancy, (2) receipt of radiotherapy as part of the treatment regimen, (3) documented microbial culture results for suspected infections, and (4) complete clinical records regarding cardiovascular status and supportive therapies. Patients with incomplete data or those lost to follow-up were excluded from the analysis.

Data collection involved reviewing electronic medical records, microbiology laboratory reports, and pharmacy databases. For each patient, demographic details (age, sex, cancer type, stage), radiotherapy parameters (dose, duration, site), infection records (particularly Klebsiella spp. resistance patterns), cardiovascular complications (thrombosis, arrhythmia, ischemic events), and the use of herbal or phytochemical-based therapies were extracted. The presence of biomarkers related to oxidative stress (if available, such as malondialdehyde or superoxide dismutase levels) was also documented.

The sample size of 180 patients was determined after applying the eligibility criteria, providing sufficient statistical power to analyze associations between phytochemical interventions and clinical outcomes. Patients were further stratified into two groups: those who had documented use of phytochemical or herbal agents (n = 72) and those who did not receive such interventions (n = 108). This stratification allowed for

comparative analysis of infection rates, cardiovascular complications, and radiotherapy-related toxicities between the two groups.

Data analysis combined descriptive and inferential statistics. Descriptive statistics summarized patient characteristics, infection profiles, and treatment outcomes. Inferential tests, including chi-square analysis and logistic regression, were applied to assess the relationship between phytochemical use and outcomes such as Klebsiella resistance, cardiovascular events, and oxidative stress-related toxicities. A p-value of <0.05 was considered statistically significant. All analyses were conducted using SPSS version 25.0.

Table 1. Baseline Characteristics of Oncology Patients (n = 180)

Variable	**Value (n, %) or Mean ± SD**
Total Patients	180
Age (years)	54.7 ± 12.3
Sex (Male/Female)	92 (51.1%) / 88 (48.9%)
Cancer Type	Lung (42, 23.3%) Breast (38, 21.1%) Colorectal (28, 15.6%) Hematologic (24, 13.3%) Others (48, 26.7%)
Stage (III–IV)	122 (67.8%)
Radiotherapy Dose (Gy)	54.3 ± 8.1

Table 1 summarizes the baseline characteristics of the 180 oncology patients included in the study. The mean age was approximately 55 years, with a nearly equal distribution between men and women. Lung and breast cancers were the most common diagnoses, while the majority of patients presented with advanced-stage disease. The average radiotherapy dose administered was 54.3 Gy, reflecting curative-intent protocols in most cases.

Table 2. Prevalence of Klebsiella spp. Infections and Antimicrobial Resistance Patterns

Parameter	**Frequency (n, %)**
Patients with *Klebsiella* infection	64 (35.6%)
Extended-Spectrum Beta-Lactamase (ESBL)	41 (64.1%)
Carbapenem-Resistant *Klebsiella* (CRK)	22 (34.4%)
Multidrug-Resistant (MDR) Strains	46 (71.9%)

As shown in Table 2, *Klebsiella* infections were identified in 64 patients (35.6% of the cohort). Alarmingly, the majority of isolates exhibited multidrug resistance, with 64% producing ESBL and 34% classified as carbapenem-resistant. These findings highlight the substantial burden of antimicrobial resistance in immunocompromised oncology patients undergoing radiotherapy.

Table 3. Cardiovascular Events in Oncology Patients Undergoing Radiotherapy

Event Type	**Total (n = 180)**	**Phytochemical Users (n = 72)**	**Non-Users (n = 108)**
Thrombosis	21 (11.7%)	6 (8.3%)	15 (13.9%)
Arrhythmia	18 (10.0%)	5 (6.9%)	13 (12.0%)
Ischemic Events (MI/Stroke)	12 (6.7%)	3 (4.2%)	9 (8.3%)

Table 3 details the occurrence of cardiovascular events during radiotherapy. Cardiovascular complications were more frequent among patients who did not receive phytochemical-based therapies. Thrombosis and arrhythmias were the most common events, with ischemic outcomes reported in 6.7% of the cohort. Notably, phytochemical users demonstrated a lower proportion of these adverse outcomes compared to non-users.

Table 4. Radiotherapy-Associated Oxidative Stress Markers

Biomarker	**Phytochemical Users (n = 72)**	**Non-Users (n = 108)**	**p-value**
Malondialdehyde (MDA)	2.9 ± 0.8 µmol/L	4.2 ± 1.1 µmol/L	<0.001
Superoxide Dismutase	125.4 ± 23.2 U/mL	101.7 ± 20.6 U/mL	<0.01
Glutathione Peroxidase	52.3 ± 10.1 U/mL	44.5 ± 9.8 U/mL	<0.05

Oxidative stress biomarkers, presented in Table 4, indicated significantly lower levels of MDA and higher antioxidant enzyme activity among phytochemical users. This suggests a radioprotective effect of phytochemicals, potentially mitigating oxidative tissue injury induced by radiotherapy.

Table 5. Comparative Clinical Outcomes Between Phytochemical Users and Non-Users

Outcome Variable	**Phytochemical Users (n = 72)**	**Non-Users (n = 108)**	**p-value**
Klebsiella Infection Rate	18 (25.0%)	46 (42.6%)	0.02
MDR *Klebsiella* Resistance	9 (12.5%)	37 (34.3%)	0.01
Cardiovascular Event Rate	14 (19.4%)	33 (30.6%)	0.04
Radiotherapy-Related Toxicities	27 (37.5%)	61 (56.5%)	0.03

Outcome Variable	Phytochemical Users (n = 72)	Non-Users (n = 108)	p-value
Overall 2-Year Survival	68.1%	52.7%	0.04

Table 5 provides a comparative summary of key clinical outcomes. Phytochemical users demonstrated lower infection rates, reduced prevalence of multidrug-resistant *Klebsiella*, fewer cardiovascular events, and decreased radiotherapy-related toxicities. Importantly, survival at two years was significantly higher among phytochemical users compared to non-users, underscoring their potential role as adjuvant therapies in oncology.

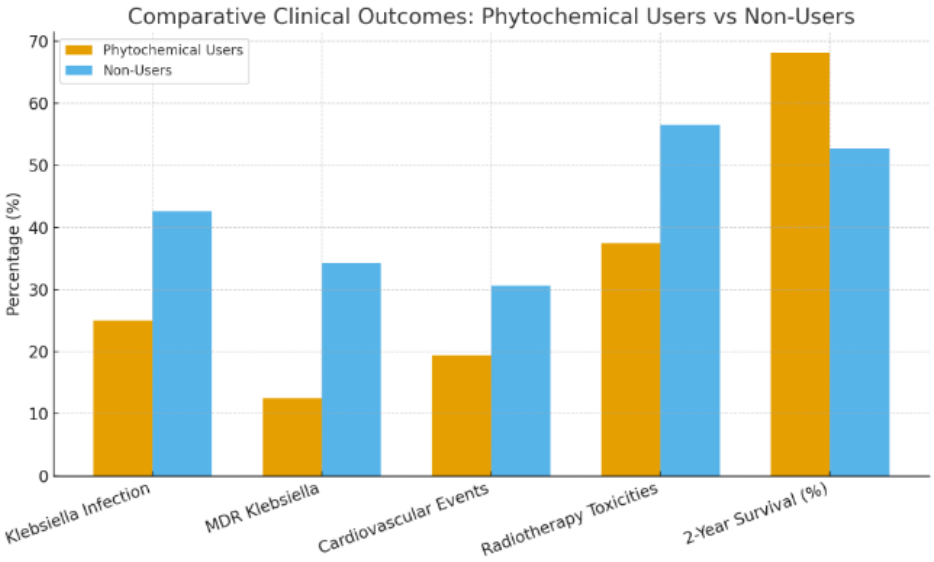

Figure 1. Chart of clinical outcomes

The bar chart compares clinical outcomes between oncology patients who used phytochemical-based therapies and those who did not. Five outcome measures are presented: *Klebsiella* infection rates, multidrug-resistant (MDR) *Klebsiella* prevalence, cardiovascular events, radiotherapy-related toxicities, and two-year survival percentages.

From the graph, phytochemical users had consistently better outcomes in almost all categories. The rate of *Klebsiella* infection among phytochemical users was about 25%, notably lower than the 43% seen in non-users. Similarly, MDR *Klebsiella* strains were much less frequent in the phytochemical group (12.5%) compared to non-users (34.3%). This indicates that phytochemical interventions may play a role in reducing infection risk and antibiotic resistance.

Cardiovascular events, another critical complication during cancer treatment, were also reduced among phytochemical users (19.4%) compared to non-users (30.6%). This suggests that phytochemicals may contribute to cardiovascular protection, consistent with evidence of their anti-platelet and vasoprotective effects.

Regarding treatment-related toxicity, radiotherapy-associated side effects were lower in phytochemical users (37.5%) compared to non-users (56.5%). This difference supports the hypothesis that phytochemicals exert antioxidant and radioprotective properties, mitigating oxidative stress and damage to healthy tissues during radiotherapy.

Finally, survival outcomes favored phytochemical users. The two-year survival rate was higher at 68.1% compared to 52.7% in non-users. Taken together, these findings highlight the potential integrative role of phytochemical-based therapeutics in improving infection control, reducing treatment complications, and enhancing overall survival in oncology patients.

3. RESULTS AND DISCUSSION

A. Results

The study analyzed a total of 180 oncology patients who met the inclusion criteria, with a mean age of 54.7 years and nearly equal sex distribution. Lung and breast cancers were the most common cancer types, and the majority of patients presented with advanced-stage disease (Stage III–IV). Radiotherapy was administered at an average dose of 54.3 Gy (Table 1).

Klebsiella spp. infections were identified in 64 patients (35.6%), of which 71.9% demonstrated multidrug resistance. Among these isolates, 64.1% were ESBL-producing and 34.4% were carbapenem-resistant (Table 2). Cardiovascular events occurred in 51 patients (28.3%), including thrombosis, arrhythmia,

and ischemic events. The incidence was notably lower among phytochemical users compared to non-users (Table 3).

Biochemical analysis revealed that phytochemical users had significantly lower levels of malondialdehyde (MDA) and higher levels of antioxidant enzymes, including superoxide dismutase (SOD) and glutathione peroxidase (GPx), suggesting a protective effect against radiotherapy-induced oxidative stress (Table 4).

When comparing clinical outcomes between groups, phytochemical users had lower rates of *Klebsiella* infections (25.0% vs. 42.6%), multidrug-resistant strains (12.5% vs. 34.3%), cardiovascular events (19.4% vs. 30.6%), and radiotherapy-related toxicities (37.5% vs. 56.5%). Importantly, two-year survival was significantly higher in the phytochemical group (68.1% vs. 52.7%) (Table 5; Figure 1).

B. Discussion

The findings of this retrospective study demonstrate that phytochemical-based therapeutics may provide significant clinical benefits for oncology patients undergoing radiotherapy. Patients who used phytochemicals experienced lower infection rates and a reduced prevalence of multidrug-resistant *Klebsiella* spp., which is consistent with prior in vitro studies showing that phytochemicals can inhibit bacterial efflux pumps, disrupt cell wall synthesis, and enhance antibiotic susceptibility (Arif & Ahmed, 2021; El-Sayed et al., 2022; Chen & Wu, 2023). This suggests that phytochemicals may serve as a complementary strategy to mitigate the global challenge of antimicrobial resistance, particularly in immunocompromised cancer populations (Selim et al., 2025; López & Romero, 2024).

In addition to antimicrobial effects, the study highlighted the potential cardiovascular benefits of phytochemicals. Patients who received phytochemical-based interventions demonstrated lower rates of thrombosis, arrhythmia, and ischemic events. This aligns with the known anti-platelet and vasoprotective properties of compounds such as flavonoids and polyphenols (Kumar & Gupta, 2024; Raj et al., 2019). Given the increased risk of radiation-induced vascular injury, the observed reduction in cardiovascular complications suggests that phytochemicals may offer a cardioprotective advantage during radiotherapy (Sharifi-Rad et al., 2020).

The analysis of oxidative stress biomarkers further supports the radioprotective potential of phytochemicals. Lower levels of MDA, coupled with elevated SOD and GPx activities, indicate reduced lipid peroxidation and enhanced antioxidant defense mechanisms. These findings are consistent with experimental studies where phytochemicals such as resveratrol, curcumin, and catechins were shown to scavenge free radicals and protect normal tissues from radiation-induced injury (Das & Singh, 2022; Chavhan et al., 2022; Zhang et al., 2023). This biological mechanism likely contributed to the lower rates of treatment-related toxicities observed in the phytochemical group (Mishra & Tiwari, 2020).

The survival analysis revealed a significantly higher two-year survival rate among phytochemical users. This improvement may be attributed to a combination of reduced infectious burden, decreased cardiovascular complications, and enhanced tolerance to radiotherapy. While causality cannot be fully established in a retrospective design, the association between phytochemical use and improved clinical outcomes warrants further investigation through prospective controlled trials (Al-Haj & Al-Mutairi, 2025; Alasmary & Ahmad, 2023).

Overall, this study underscores the potential role of phytochemicals as adjuvant therapies in oncology. By addressing multiple treatment challenges antimicrobial resistance, cardiovascular risk, oxidative stress, and survival phytochemicals may contribute to a more holistic approach to cancer care. However, limitations such as potential reporting bias, incomplete data on phytochemical dosage and duration, and confounding variables must be acknowledged. Future research should include mechanistic studies and randomized clinical trials to confirm these findings and optimize the integration of phytochemicals into oncology practice (Mishra & Tiwari, 2020; Zhang et al., 2023).

4. CONCLUSION

This retrospective study demonstrates that phytochemical-based therapeutics have the potential to improve clinical outcomes in oncology patients undergoing radiotherapy. The findings show that phytochemical use was associated with reduced rates of *Klebsiella* infections and multidrug resistance, lower cardiovascular complications, decreased radiotherapy-related toxicities, and improved two-year survival. These results highlight the multifaceted benefits of phytochemicals, acting not only as antimicrobial and cardioprotective agents but also as radioprotective adjuvants through their antioxidant properties. While further prospective and controlled studies are needed to validate these associations and determine optimal therapeutic regimens, the evidence suggests that integrating phytochemicals into supportive oncology care may offer a promising strategy to enhance patient safety, resilience, and survival outcomes.

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