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ASSESSMENT OF ADVERSE EVENTS IN CANCER PATIENTS UNDERGOING RADIATION THERAPY - LONGITUDINAL OBSERVATIONAL STUDY

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ABSTRACT

Background: Radiation therapy is a cornerstone in cancer treatment but is often accompanied by radiation-related adverse events (RRAEs), which can impair quality of life, particularly in settings with limited technological advancement. This study aimed to evaluate the frequency and severity of RRAEs in cancer patients undergoing radiotherapy or chemoradiotherapy.

Methods: This prospective observational study was conducted over six months in a tertiary cancer care hospital, KLE's Cancer Hospital, Belagavi. A total of 93 patients receiving radiotherapy or Concurrent chemoradiotherapy were monitored for RRAEs by a radiation oncologist along with clinical pharmacists, using Radiation Therapy Oncology Group (RTOG) criteria, and were documented.

Results: Major RRAEs included radiation dermatitis (59.1%), oral mucositis (56.9%), neutropenia (92.47%), haemoglobin toxicity (93.5%), and radiation enteritis (63.4%). Symptoms peaked during the fifth week. Post-treatment issues like nausea and fatigue increased. Multiple concurrent toxicities were common.

Conclusion: RRAEs are frequent and can significantly impact quality of life and also therapy outcomes. Involving clinical pharmacists in monitoring and reporting can help mitigate risks. Continuous monitoring during and after treatment are recommended. Clinical pharmacists can play a crucial role in detecting, reporting, and managing these adverse effects in collaboration with radiation oncologists. Implementing structured reporting systems and preventive strategies may improve patient outcomes and enhance the safety of cancer treatment.

KEYWORDS: Radiation therapy (RT), Radiation-related adverse events (RRAEs), Quality of life(QOL), Adverse events, Clinical pharmacists, Toxicity monitoring

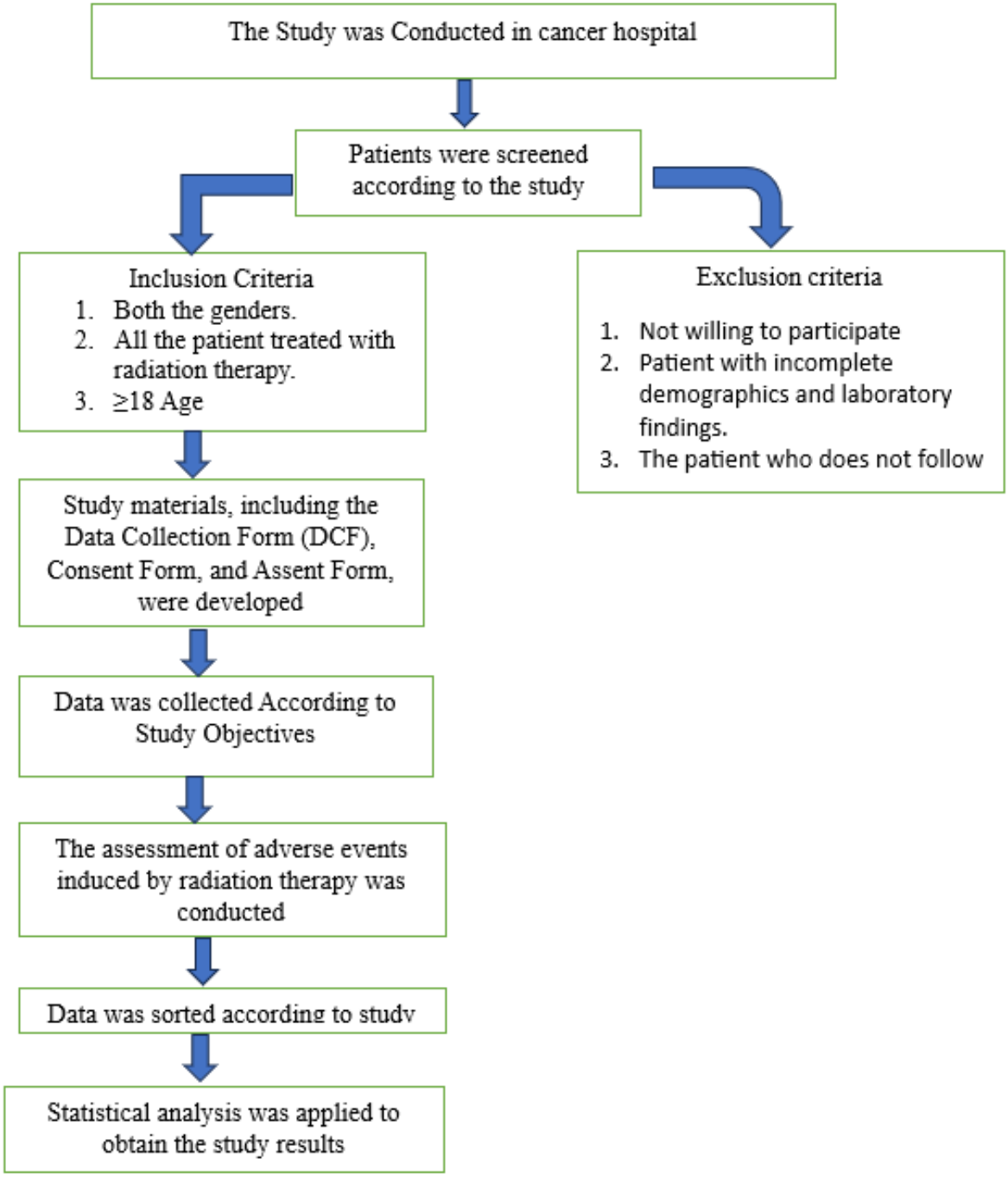
INTRODUCTION

Radiation therapy (RT) is a critical component in the treatment of various cancers, with an estimated 50–60% of patients receiving RT at some stage during their cancer care journey [1,2]. While RT effectively targets malignant cells, it also impacts surrounding healthy tissues, often resulting in radiation-related adverse events (RRAEs) such as oral mucositis, radiation dermatitis, gastrointestinal toxicity, and bone marrow suppression [3,4]. These toxicities can significantly reduce patients' quality of life (QOL), increase treatment costs, and sometimes lead to treatment interruptions [5]. The severity of RRAEs varies with radiation dose, treatment duration, cancer site, and chemotherapy. In high-burden settings such as India, limited resources hinder effective monitoring, leading to underreporting and delayed management. [7]. Clinical pharmacists, along with Radiation Oncologists, with proper training, could play a vital role in detecting and documenting RRAEs, enhancing the safety and effectiveness of cancer care, thereby improving the quality of care in these cancer patients [8]. This longitudinal observational study aims to assess the frequency, progression, and clinical impact of RRAEs in cancer patients receiving RT, and to emphasize the importance of timely detection, multidisciplinary collaboration, and close monitoring and reporting systems.

METHODOLOGY

Study Design and Setting: A six-month prospective longitudinal observational study was conducted (August 2024 – January 2025) at a cancer hospital in Belagavi. Ethical approval was obtained from the Institutional Ethics Committee (Ref No. KLECOPBGMEC/D016-2024).

Fig.1 Study methodology flow chart



The study included 93 cancer patients, mostly aged over 35 and predominantly male (69.9%). Self-payment/insurance 64.5% of treatments. Head and neck cancer (43.01%) was the most common. IMRT (45.16%) was the most common technique used in the majority of patients, and the latest TrueBeam (55.91%) machine was used for this technique. Most patients had early-stage cancer and were married, 72.04% . **(Table – 1)**

Table -1 Demographic details (N=93)

Characteristics	**Category**	**Frequency (%)**
Age	0-18	1(1.08%)
	19-35	2(2.15%)
	35-60	**48(51.61%)**
	Above 60	42(45.16%)
Gender	Male	**65(69.9%)**
	Female	28(30.1%)

Payment Scheme	Self-payment/insurance	**60(64.5%)**
	Govt. schemes	33(35.4%)
Occupation	Professional	**29(31.18%)**
	employed	24(25.8%)
	Unemployed	17(18.27%)
	Housewife	15(16.12%)
	Others	8(8.6%)
Marital Status	Single	26(27.95%)
	Married	**67(72.04%)**
Stages of Cancer	Stage 0	6(6.45%)
	Stage 1	**54(58.06%)**
	Stage 2	21(22.58%)
	Stage 3	9(9.67%)
	Stage 4	3(3.22%)
Type of Cancer	Head & Neck	**40(43.01%)**
	Breast cancer	16(17.20%)
	Oesophageal cancer	13(13.9%)
	Cervical cancer	6(6.45%)
	Malignant neoplasm cancer	5(5.3%)
	Others cancer	7(4.3%)
Type of Radiation therapy	(IMRT)-Intensity Modulated Radiation Therapy.	**42(45.16%)**
	(VMAT) -Volumetric modulated Arc Therapy.	30(32.25%)
	(SBRT) - Stereotactic Body Radiation Therapy.	12(12.9%)
	(SRS) - stereotactic radiosurgery.	6(6.45%)
	Others	3(3.22%)

Radiation-related adverse events increased during treatment. Radiation dermatitis rose from 5.37% to 59.1%, while oral mucositis peaked at 56.9% in week five. Neutrophil and haemoglobin toxicities worsened significantly, reaching over 90% by week five, then declined to 63.4% one-month post-treatment, indicating recovery.

Radiation enteritis followed a gradual upward trend, affecting 15.05% of patients in the first week and rising to 41.9% by the fifth week. After radiation therapy, its prevalence further escalated to 63.4%, indicating prolonged effects. Overall, most adverse events reached their peak by the fifth week of treatment, with some persisting or worsening after therapy**. (Table – 2)**

Table – 2: Incidence of Radiation-Related Adverse Events in 1st week, 3rd Week, 5th Week, and Post Radiation Therapy for major Events (comparing which time has got more Adverse events) (n = 93)

Adverse Events	**During Radiation Therapy**			**Post Radiation therapy (After One Month)**
	1st week	**3rd week**	**5th week**	
Radiation dermatitis	5 (5.37%)	16(17.20%)	45(48.38%)	**55(59.1%)**
Oral mucositis	49(52.68%)	50(53.76%)	**53(56.9%)**	48(51.61%)
Haematological-Toxicity (Neutrophils)	36(38.7%)	71(76.3%)	**86(92.47%)**	59(63.4%)
Haematological Toxicity (HB)	37(39.7%)	71(76.3%)	**87(93.5%)**	59(63.4%)
Radiation Enteritis	14(15.05%)	24(25.08%)	39(41.9%)	**59(63.4%)**

Minor radiation-related adverse events varied across treatment phases. Hair loss increased from 55.9% during therapy to 64.51% post-treatment, while skin discoloration slightly declined. Pain and insomnia showed minimal change. Burning sensation and loss of taste increased after therapy, as did fatigue, dehydration, and gastrointestinal symptoms like nausea and vomiting. Notably, nausea rose from 7.53% to 19.35%. These findings indicate that while some side effects peak during treatment, others worsen or emerge more prominently in the post-radiation period. **(Table – 3)**

Table 3: Incidence of Radiation-Related Adverse Events Pre-Radiation Therapy and Post-Radiation Therapy for Minor Events (n = 93)

Minor adverse events	During Radiation therapy	Post Radiation therapy
Hair loss	52(55.9%)	**60(64.51%)**
Skin black in colour	**75(80.64%)**	70(75.26%)
Pain	**59(63.4%)**	55(59.13%)
Insomnia	51(54.8%)	**53(56.98%)**
Burning sensation	61(65.5%)	**64(68.8%)**
Nausea & vomiting	7(7.53%)	**18(19.35%)**
Dehydration	10(10.75%)	**15(16.13%)**
Fatigue	3(3.23%)	**12(12.90%)**
Loss of taste	23(24.73%)	**31(33.33%)**

Radiation-related adverse events progressively worsened over time, with some persisting beyond treatment. **Radiation Dermatitis & Oral Mucositis:** The incidence of dermatitis increased from 3.23% (Grade 1) in the first week to 44.09% by the fifth week, with 36.56% of cases advancing to Grade 2 post-treatment. Oral mucositis peaked in the fifth week, with 53.76% of cases classified as Grade 1, while Grade 2 cases rose to 33.33% after radiation therapy.

Haematological Toxicity: Neutrophil and haemoglobin toxicity reached their highest levels in the fifth week, affecting 64.52% and 66.67% of patients (Grade 1), respectively, before showing partial improvement post-treatment (41.94% and 43.01%).

Radiation Enteritis: Cases steadily increased, with Grade 1 rising from 2.15% in the first week to 38.71% by the fifth week. Notably, Grade 3 enteritis emerged post-radiation, affecting 9.68% of patients.
Adverse events peaked during radiation therapy, with some persisting or worsening after treatment, emphasizing the need for continued post-treatment care and monitoring. **(Table – 4)**

Table 4: Grading of Adverse Events Incidence During and After Radiation Therapy

Pre radiation therapy (1st week, 3rd week and 5th week), Post Radiation therapy					
Adverse Event	**Grades**	**During Radiation therapy**			**Post Radiation therapy (After one month)**
		1st week	**3rd week**	**5th week**	
Radiation dermatitis	Grade - 0	88**(94.62%)**	77**(82.80%)**	48**(51.61%)**	38(40.86%)
	Grade - 1	3**(3.23%)**	15**(16.13%)**	41**(44.09%)**	21(22.58%)
	Grade - 2	1**(1.08%)**	1**(1.08%)**	4**(4.30%)**	34(36.56%)
	Grade - 3	1**(1.08%)**	0(0%)	0(0%)	0(0%)
	Grade - 4	0(0%)	0(0%)	0(0%)	0(0%)
	Total	**93(100%)**	**93(100%)**	**93(100%)**	**93(100%)**
Oral mucositis	Grade - 0	44**(47.31%)**	43**(46.24%)**	40**(43.01%)**	45(48.39%)
	Grade - 1	9**(9.68%)**	18**(19.35%)**	50**(53.76%)**	13(13.98%)
	Grade - 2	37**(39.78%)**	32**(34.41%)**	3**(3.23%)**	31(33.33%)
	Grade - 3	3**(3.23%)**	0(0%)	0(0%)	4(4.30%)
	Grade - 4	0(0%)	0(0%)	0(0%)	0(0%)
	Total	**93(100%)**	**93(100%)**	**93(100%)**	**93(100%)**
HT (Neutrophils)	Grade - 0	57**(61.29%)**	22**(23.66%)**	7**(7.53%)**	34(36.56%)
	Grade - 1	21**(22.58%)**	49**(52.69%)**	60**(64.52%)**	39(41.94%)
	Grade - 2	13**(13.98%)**	20**(21.51%)**	24**(25.81%)**	20(21.51%)
	Grade - 3	1**(1.08%)**	1**(1.08%)**	1**(1.08%)**	0(0%)
	Grade - 4	1**(1.08%)**	1**(1.08%)**	1**(1.08%)**	0(0%)
	Total	**93 (100%)**	**93(100%)**	**93(100%)**	**93(100%)**
Haematological Toxicity (HB)	Grade - 0	56**(60.22%)**	22**(23.66%)**	6**(6.45%)**	34(36.56%)
	Grade - 1	23**(24.73%)**	50**(53.76%)**	62**(66.67%)**	40(43.01%)
	Grade - 2	12**(12.90%)**	19**(20.43%)**	23**(24.73%)**	18(19.35%)
	Grade - 3	1**(1.08%)**	1**(1.08%)**	1**(1.08%)**	1(1.08%)
	Grade - 4	1**(1.08%)**	1**(1.08%)**	1**(1.08%)**	0(0%)
	Total	**93(100%)**	**93(100%)**	**93(100%)**	**93(100%)**

Radiation Enteritis	Grade - 0	79**(84.95%)**	69**(74.19%)**	54**(58.06%)**	34(36.56%)
	Grade - 1	2**(2.15%)**	17**(18.28%)**	36**(38.71%)**	18(19.35%)
	Grade - 2	11**(11.83%)**	7**(7.53%)**	3**(3.23%)**	32(34.41%)
	Grade - 3	1**(1.08%)**	0(0%)	0(0%)	9(9.68%)
	Grade - 4	0(0%)	0(0%)	0(0%)	0(0%)
	Total	**93(100%)**	**93(100%)**	**93(100%)**	**93(100%)**

DISCUSSION

The involvement of clinical pharmacists in detecting, overseeing, and improving the safe administration of medications for cancer patients is well acknowledged and broadly endorsed. However, their role in identifying, tracking, and reporting radiation-induced toxicities in cancer patients has not yet become a standard practice. In the present study, male patients experienced a higher incidence of radiation-related adverse events, likely due to the greater number of head and neck cancer cases. Similarly, a previous study reported a higher occurrence of radiation-related adverse events in female patients, primarily due to the prevalence of cervical cancer cases [10]. Both studies reported more adverse events in middle-aged and older patients. Our study had 96.77% of patients over 35, while Rohit et al. observed 84.5% in the 41–80 range. Their study had more younger patients (13.5%) compared to ours (5.38%), indicating a slightly older cohort in our study [8] . Most adverse events in our study were acute, peaking during later treatment weeks, similar to the referenced study. Common toxicities included dermatitis, mucositis, and haematological issues. Long-term effects like fibrosis and GI toxicity emerge later. Both studies emphasize the need for extended follow-up to assess delayed radiation toxicities. Both studies showed a progressive worsening of oral mucositis. Our study saw Grade 1 peaking at week 5 (53.76%), while the referenced study reported higher Grade 2 (60.4%) and Grade 3 (13.2%) cases. Lower high-grade mucositis in our cohort may reflect differences in treatment protocols or supportive care. [11]. Both studies showed a higher prevalence of adverse events among older patients. Our study had 96.77% of patients over 35, similar to the referenced study's majority in the 41–80 age range. Haematological toxicity increased over time, with normal neutrophil counts dropping from 61.29% to 7.53%. Gastrointestinal toxicity also worsened, with Grade 0 enteritis cases decreasing significantly. These trends highlight the cumulative impact of radiation and the importance of supportive care [12].

CONCLUSION

The study emphasizes the substantial effects of radiation-related adverse events (RRAEs) on cancer patients, particularly those undergoing radiotherapy or combined chemo-radiotherapy. Frequent side effects—such as skin irritation, mucosal inflammation, and gastrointestinal problems—significantly diminish patients' quality of life. Proper management depends on prompt monitoring, active participation of pharmacists, and systematic reporting. In countries with high patient volumes like India, educating patients and providing supportive care are crucial. Additional research is necessary to evaluate long-term outcomes and to design effective preventive measures.

Conflict of Interest: The authors declare no conflict of interest.

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Authors' contribution:
SK - Conceptualization; Data curation; Formal analysis; Methodology; Writing-original draft;
MG - Data curation; Formal analysis; Writing review & editing.
RS - Conceptualization; Data Curation; Formal analysis; Methodology;
MS - Supervision; Validation; Visualization,

Data availability: No datasets were generated or analysed during the current study.

Consent: Informed consent was obtained from the patients for publication.

Competing interests: The authors declare no competing interests.

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