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Original Research Paper

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ADVERSE EFFECTS ASSOCIATED WITH IMMUNOTHERAPY AND BIOLOGICAL AGENTS IN PATIENTS WITH MALIGNANCY: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Immunotherapy and biological agents have transformed the treatment of malignancy but are associated with a broad spectrum of treatment-related toxicities affecting multiple organ systems. **Objective:** To study the spectrum and severity of adverse effects associated with immunotherapy and biological agents in adult patients with malignancy. **Methods:** This hospital-based prospective observational study was conducted in the Department of Medicine, Command Hospital Western Command, Chandimandir, from April 2023 to March 2024. Adults with proven malignancy receiving immunotherapy or biological therapy were enrolled consecutively. Clinical evaluation and relevant laboratory/imaging investigations were performed, and adverse effects were graded using Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Data were analyzed using SPSS version 21; $p<0.05$ was considered statistically significant. **Results:** A total of 152 patients were included. The 41–50-year age group was most represented (32.9%), and the study narrative reported male predominance (77%). Breast cancer (16.4%), bladder cancer (14.5%), and head-and-neck squamous cell carcinoma (13.8%) were the leading malignancies. Atezolizumab (20.4%), pembrolizumab (17.1%), and nivolumab (14.5%) were the most frequently used agents. Common adverse effects included abdominal pain (48.03%), eczema (46.05%), hypopituitarism (40.13%), hypothyroidism (39.47%), acute respiratory distress syndrome (38.16%), and nausea/vomiting (36.84%). Drug-specific patterns included atrial arrhythmias with bevacizumab, endocrine and respiratory toxicities with pembrolizumab/atezolizumab, and akathisia with lenalidomide. **Conclusion:** Adverse effects of immunotherapy and biological agents are multisystem and drug-specific. Structured surveillance—particularly endocrine, respiratory, gastrointestinal, dermatological, cardiac, and neurological monitoring—may facilitate earlier recognition and management of clinically significant toxicity.

KEYWORDS : immunotherapy; biological agents; immune-related adverse events; malignancy; immune checkpoint inhibitors; CTCAE.

INTRODUCTION

Cancer immunotherapy has altered the therapeutic landscape by harnessing immune mechanisms rather than relying solely on direct cytotoxicity. Immune checkpoint inhibitors targeting CTLA-4 and PD-1/PD-L1, monoclonal antibodies, cellular therapies, and other biological agents have expanded treatment options across solid and hematological malignancies. However, activation or modulation of immune pathways can produce adverse effects that differ from conventional chemotherapy toxicity and may involve virtually any organ system.

Reported toxicities include endocrine dysfunction, dermatological reactions, gastrointestinal inflammation, pneumonitis and other pulmonary injury, neurological syndromes, and cardiovascular complications. Some events are mild and self-limited, whereas others may be severe, life-threatening, and require interruption of anticancer therapy or intensive supportive care. As use of these therapies increases, recognition of the spectrum and severity of adverse events in routine clinical practice becomes increasingly important.

The present study prospectively evaluated adverse effects associated with immunotherapy and biological agents among patients with malignancy treated at a tertiary care centre.

AIMS AND OBJECTIVES

- **Aim:** To study the adverse effects associated with immunotherapy and biological agents in patients with malignancy.
- **Primary objective:** To characterize the spectrum and severity of adverse effects associated with these therapies.

MATERIALS AND METHODS

Parameter	Details
Study design	Hospital-based prospective observational study
Setting	Department of Medicine, Command Hospital Western Command, Chandimandir, Haryana
Study period	April 2023 to March 2024
Sample size	152 patients
Sampling	Convenience/consecutive enrolment of eligible patients
Adverse-event grading	CTCAE version 5.0
Statistical software	SPSS version 21

Study population and eligibility

Adults (>18 years) with a proven diagnosis of cancer who were receiving immunotherapy or biological therapy in the outpatient, ward, ICU, hematology, or oncology services were considered eligible. The thesis excluded pregnant/ postpartum women within 30 days, patients younger than 18 years, and selected neurological conditions that could independently cause weakness, including head trauma, neuroinfection, venous stroke, CNS tumor with weakness, subdural hemorrhage, and hemorrhagic stroke.

Clinical assessment and investigations

After written informed consent, detailed history and physical examination were recorded using a predesigned format. Assessment included vital signs and cardiovascular, respiratory, neurological, oral/fundus, genitourinary, and skin examination. Investigations included complete blood count, renal and liver function tests, electrolytes, calcium and phosphorus, lipid profile, viral markers, ECG, chest radiograph, and additional imaging or specialized investigations as clinically indicated. Medication exposure and system-wise adverse effects were documented.

Outcome measures

Adverse events were categorized and graded using CTCAE v5.0 from Grade 1 (mild) to Grade 5 (death). The study focused particularly on cardiac, endocrine, respiratory, dermatological, neurological, and gastrointestinal toxicities.

Statistical analysis and ethics

Descriptive statistics were used for study variables. The thesis reports use of the Shapiro–Wilk test for distribution testing, chi-square testing for categorical variables, and a significance threshold of $p<0.05$. The study was conducted after Institutional Ethics Committee approval, in accordance with Good Clinical Practice, the Declaration of Helsinki, and ICMR ethical principles. Written informed consent and confidentiality safeguards were maintained.

RESULTS

Patient Profile

Age group	n (%)
18–30 years	20 (13.2%)
31–40 years	31 (20.4%)
41–50 years	50 (32.9%)
51–60 years	36 (23.7%)
61–70 years	9 (5.9%)
≥71 years	6 (3.9%)

The mean age of the cohort was 45.76±12.64 years. The thesis narrative reports 117 males (77%) and 35 females (23%); mean age did not differ significantly by sex ($p=0.603$).

Malignancies and Treatment Exposure

Common malignancy	Proportion
Breast cancer	16.4%
Bladder cancer	14.5%
Head and neck squamous cell carcinoma	13.8%
Renal cell carcinoma	10.5%
Glioblastoma	9.9%
Non-Hodgkin lymphoma	8.6%

Agent	Proportion treated
Atezolizumab	20.4%
Pembrolizumab	17.1%
Nivolumab	14.5%
Durvalumab	10.5%
Ipilimumab	10.5%
Avelumab	9.2%
Lenalidomide	7.9%

Spectrum of Adverse Effects

System	Adverse effect	Observed frequency
Gastrointestinal	Abdominal pain	48.03%
Dermatological	Eczema	46.05%
Endocrine	Hypopituitarism	40.13%
Endocrine	Hypothyroidism	39.47%
Respiratory	ARDS	38.16%
Gastrointestinal	Nausea/vomiting	36.84%
Respiratory	Allergic rhinitis	34.21%
Gastrointestinal	Constipation	30.92%
Gastrointestinal	Gastritis	29.61%
Dermatological	Alopecia	17.11%
Neurological	Akathisia	13.16%
Neurological	Amnesia	10.53%
Cardiac	Atrial fibrillation	3.95%
Cardiac	Atrial flutter	3.29%

Drug-specific Observations

Bevacizumab showed a notable association with atrial arrhythmias in the thesis analysis, including atrial fibrillation and atrial flutter, supporting the need for cardiac surveillance. Pembrolizumab and atezolizumab were associated with a broader burden of endocrine and respiratory toxicity, including hypothyroidism, hypopituitarism, and ARDS. Pembrolizumab also showed frequent nausea/vomiting. Lenalidomide demonstrated a prominent association with akathisia. Avelumab and bevacizumab were associated with substantial abdominal pain in the drug-wise analysis.

DISCUSSION

This prospective cohort demonstrates that toxicity associated with contemporary anticancer immunotherapy and biological agents is multisystem and heterogeneous. The most frequent problems in this study involved the gastrointestinal, dermatological, endocrine, and respiratory systems. This broad pattern is consistent with the established concept that immune-related adverse events may affect almost any organ system and may vary considerably according to the therapeutic class and individual agent.

Endocrine abnormalities were particularly prominent, with hypothyroidism and hypopituitarism reported in approximately two-fifths of patients. The thesis discussion links these findings particularly with PD-1/PD-L1 pathway inhibition and emphasizes the need for baseline and interval endocrine assessment. Respiratory toxicity was also clinically important, with ARDS reported in 38.16% of the cohort and prominent associations described with atezolizumab and pembrolizumab. Such pulmonary adverse effects can deteriorate rapidly and may require escalation of respiratory support.

Gastrointestinal and cutaneous adverse effects were among the most frequent. Abdominal pain, nausea/vomiting, constipation, gastritis, and eczema were common enough to warrant structured symptom review at each treatment contact. Although neurological and cardiac toxicities were less frequent overall, their potential severity is important. The observed association of bevacizumab with atrial arrhythmias suggests a need for targeted cardiovascular monitoring, while the reported relationship between lenalidomide and akathisia supports active neurological assessment.

The findings reinforce a practical principle: toxicity surveillance should be tailored to the drug rather than limited to a generic checklist. Baseline assessment, patient education, early symptom reporting, CTCAE-based grading, and rapid multidisciplinary evaluation may reduce treatment interruption and severe complications.

LIMITATIONS

The study was single-centre and used convenience/ consecutive sampling, which may limit generalizability. Several

malignancies and therapeutic agents were represented by relatively small subgroups, making some drug-specific percentages sensitive to sample size. The study was observational and therefore identifies associations rather than causality. The thesis dataset also contains a labeling inconsistency in one gender-frequency table; the manuscript follows the repeated narrative and age-by-gender table reporting 117 males and 35 females.

CONCLUSION

Immunotherapy and biological agents used in malignancy are associated with a wide range of adverse effects, most prominently gastrointestinal, dermatological, endocrine, and respiratory complications in this cohort. Atezolizumab and pembrolizumab showed broader endocrine/respiratory toxicity patterns, bevacizumab was associated with cardiac arrhythmias, and lenalidomide showed a notable neurological signal. Individualized, organ-directed monitoring and CTCAE-based severity grading should be integrated into routine care to enable early recognition and management of treatment-related toxicity.

DECLARATIONS

- **Ethics approval and consent to participate:** Institutional Ethics Committee approval was obtained before study initiation. Written informed consent was obtained from participants.
- **Funding:** No funding source was specified in the thesis.
- **Conflict of interest:** No conflict-of-interest statement was specified in the thesis; authors should confirm before submission.
- **Data availability:** Data availability statement to be completed as per the target journal's policy.
- **Author contributions:** To be finalized according to the target journal's authorship requirements.

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