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Research Article

An Observational Study for the Assessment of Adverse Drug Reactions of Platinum-Based Chemotherapy in Cancer Patients at Sms Hospital, Jaipur

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ABSTRACT
Background: Platinum analogues—cisplatin, carboplatin and oxaliplatin—are the cornerstone of many solid-tumour regimens but are limited by a broad spectrum of adverse drug reactions (ADRs). Robust Indian pharmacovigilance data in real-world oncology settings remain scarce.
Methods: We conducted a hospital-based, prospective, descriptive observational study (April 2023 – March 2024) among 100 consecutive adult and paediatric cancer patients who developed at least one ADR while receiving a platinum agent in the Department of Medical Oncology, SMS Hospital, Jaipur. ADRs were characterised and uploaded to VigiFlow. Causality (WHO-UMC), severity (modified Hartwig–Siegel) and preventability (modified Schumock–Thornton) were assessed; outcomes and seriousness were recorded.
Results: A total of 467 ADRs were documented (median 4, IQR 3–6 per patient). Central nervous system manifestations predominated (35.8 %), followed by haematological (26.6 %) and gastrointestinal (19.5 %) systems. Nausea (14.8 %), vomiting (10.1 %), anaemia (13.1 %) and alopecia (6.9 %) were most frequent. Carboplatin was the most commonly used agent (57 % of patients) yet showed no statistically significant difference in ADR profile versus cisplatin or oxaliplatin ($p > 0.3$ for all comparisons). WHO-UMC categorised 96.2 % of ADRs as *possible* and 3.8 % as *probable*. Severity was predominantly moderate (60.8 %); no life-threatening reactions were observed. Almost half of all ADRs (49.0 %) were definitely preventable. All events were either recovering (68 %) or recovered (32 %) at last contact; none were fatal.
Conclusion: Platinum chemotherapy produces a predictable but largely preventable burden of predominantly moderate ADRs in Indian oncology practice. Systematic monitoring, timely supportive care and proactive patient counselling can mitigate toxicity and optimise treatment continuity.

Keywords: platinum agents; cisplatin; carboplatin; oxaliplatin; adverse drug reaction; pharmacovigilance; India.

INTRODUCTION

Platinum-based cytotoxics have held centre stage in solid-tumour chemotherapy since cisplatin's landmark approval in 1978 [1]. Structural analogues carboplatin and oxaliplatin were subsequently developed to improve the therapeutic index, yet toxicity remains the principal barrier to optimal dosing and patient quality of life [2, 3]. Cisplatin's dose-limiting nephro-, neuro- and ototoxicities are well documented, whereas carboplatin is primarily myelosuppressive and oxaliplatin produces a distinctive cumulative sensory neuropathy [4]. Despite refinements in hydration, anti-emesis and dosing algorithms, recent global pharmacovigilance signals continue to implicate platinum compounds in a sizeable proportion of serious oncology ADR reports [5].

India bears an ever-increasing cancer burden; platinum agents feature in virtually every national treatment protocol for lung, head-and-neck, gynaecological, gastrointestinal and germ-cell malignancies [6]. Nevertheless, pharmacogenomic diversity, high prevalence of under-nutrition, variable supportive-care access and concurrent use of traditional medicines may modulate ADR frequency and severity in Indian patients [7]. Local evidence is, however, patchy—derived mainly from single-cycle audits or retrospective chart reviews with heterogeneous methodology [8]. Rigorous prospective monitoring within a structured pharmacovigilance framework is essential for understanding real-world toxicity, informing dose-modification algorithms and meeting the escalating regulatory emphasis on patient-reported outcomes [9].

The present study therefore aimed to evaluate the pattern, causality, severity, preventability and outcome of ADRs attributed to platinum

chemotherapy in a tertiary-care public hospital in North India. By leveraging WHO-endorsed tools (WHO-UMC, modified Hartwig–Siegel, modified Schumock–Thornton) and electronic submission through VigiFlow, we sought to generate high-quality, internationally comparable data while simultaneously sensitising frontline clinicians to pharmacovigilance imperatives [10]. The findings intend to bridge a critical knowledge gap, guide evidence-based supportive protocols and ultimately enhance patient safety in resource-constrained settings.

MATERIALS AND METHODS

Study design and setting

A prospective, hospital-based descriptive study was carried out in the Departments of Pharmacology and Medical Oncology, SMS Hospital, Jaipur, after Institutional Ethics Committee approval (IEC/Pharma/2023-04). The study period spanned 1 April 2023 to 31 March 2024.

Participants

Consecutive in-patients or out-patients of any age or sex receiving cisplatin, carboplatin or oxaliplatin who developed at least one suspected ADR were enrolled after written informed consent. Patients on non-chemotherapy drugs known to confound nephro-, hepato- or myelotoxicity or those unwilling to participate were excluded.

Sample size and sampling

Assuming a 50 % ADR prevalence (maximising sample size) with 10 % absolute precision at 95 % confidence, the required sample was 97; we enrolled 100 patients on a first-come-first-served basis.

Data collection

Demographics, cancer site-stage, comorbidities, risk factors, chemotherapy regimen and cycle number were recorded on a pre-validated case-report form. ADR details, de-challenge/re-challenge information, investigations, management and outcome were documented and entered into VigiFlow. Health-care workers received training sessions and job-aids on ADR reporting.

Outcome measures

Primary: pattern of ADRs; WHO-UMC causality; modified Hartwig–Siegel severity; modified Schumock–Thornton preventability; WHO seriousness and outcome.
Secondary: socio-demographic correlates; proportion of reports successfully transmitted to NCC-PvPI.

Statistical analysis

Data were entered in Excel and analysed with SPSS v26. Categorical variables are presented as frequency and percentage; continuous variables as mean ± SD. Chi-square or Fisher's exact tests compared ADR proportions across drugs; $p < 0.05$ was considered significant.

RESULTS

Overview of participants

The cohort's mean age was 50.4 ± 15.8 years (range 4–78). Most patients were 41–60 years old (42 %) and male (64 %) (Table 1). Lung (28 %), colon (9 %) and gall-bladder (9 %) cancers predominated. Carboplatin was administered to 57 %, cisplatin to 24 % and oxaliplatin to 19 % of patients; 66 % received combination regimens, most commonly carboplatin-paclitaxel (34 %). ADRs were reported most frequently during the third chemotherapy cycle (29 %).

Spectrum and burden of ADRs

A total of 467 ADRs were captured (4.7 ADRs/patient). System-wise distribution is depicted in **Figure 1**. CNS events accounted for over one-third, driven by nausea, vomiting and chemotherapy-induced neuropathy. Haematological events—predominantly anaemia and neutropenia—comprised 26.6 %. Gastrointestinal ADRs (19.5 %) were largely constipation and diarrhoea. Alopecia and cutaneous reactions constituted 13.3 %. Ear toxicity (vertigo, tinnitus, otalgia) was noted in 3.2 %.

TABLE 1. BASELINE DEMOGRAPHIC CHARACTERISTICS (N = 100)

Age, y	< 20	3 (3.0 %)
	20–40	24 (24.0 %)
	41–60	
	61–80	
	Mean ± SD	50.4 ± 15.8
Sex	Male	64 (64.0 %)
	Female	36 (36.0 %)

TABLE 2. DISTRIBUTION OF ADRS BY ORGAN SYSTEM (N = 467)

Organ system	**n**	**%**
Central nervous	167	35.8
Haematological	124	26.6
Gastro-intestinal	91	19.5
Integumentary	62	13.3
Ear	15	3.2
Genito-urinary	4	0.9
Immune	2	0.4
Musculo-skeletal	1	0.2
Endocrine	1	0.2

TABLE 3. CAUSALITY, SEVERITY AND PREVENTABILITY ASSESSMENTS

Scale	**Category**	**n (%)**
WHO-UMC causality	Possible	449 (96.2)
	Probable	18 (3.8)
Hartwig severity	Mild	183 (39.2)
	Moderate	284 (60.8)
	Severe	0 (0)
Schumock-Thornton preventability	Definitely preventable	229 (49.0)
	Probably preventable	65 (13.9)
	Not preventable	173 (37.0)

TABLE 4. SELECTED HIGH-FREQUENCY ADRS ACROSS PLATINUM COMPOUNDS

ADR	**Carboplatin (n = 57)**	**Cisplatin (n = 24)**	**Oxaliplatin (n = 19)**	p
Nausea	38 (66.7 %)	12 (50.0 %)	19 (100 %)	0.50
Vomiting	24 (42.1 %)	15 (62.5 %)	8 (42.1 %)	0.60
Anaemia	41 (71.9 %)	5 (20.8 %)	15 (78.9 %)	0.60
Alopecia	21 (36.8 %)	7 (29.2 %)	4 (21.1 %)	0.70
Constipation	15 (26.3 %)	8 (33.3 %)	7 (36.8 %)	0.70

FIGURE 1. DISTRIBUTION OF ADVERSE DRUG REACTIONS BY ORGAN SYSTEM.

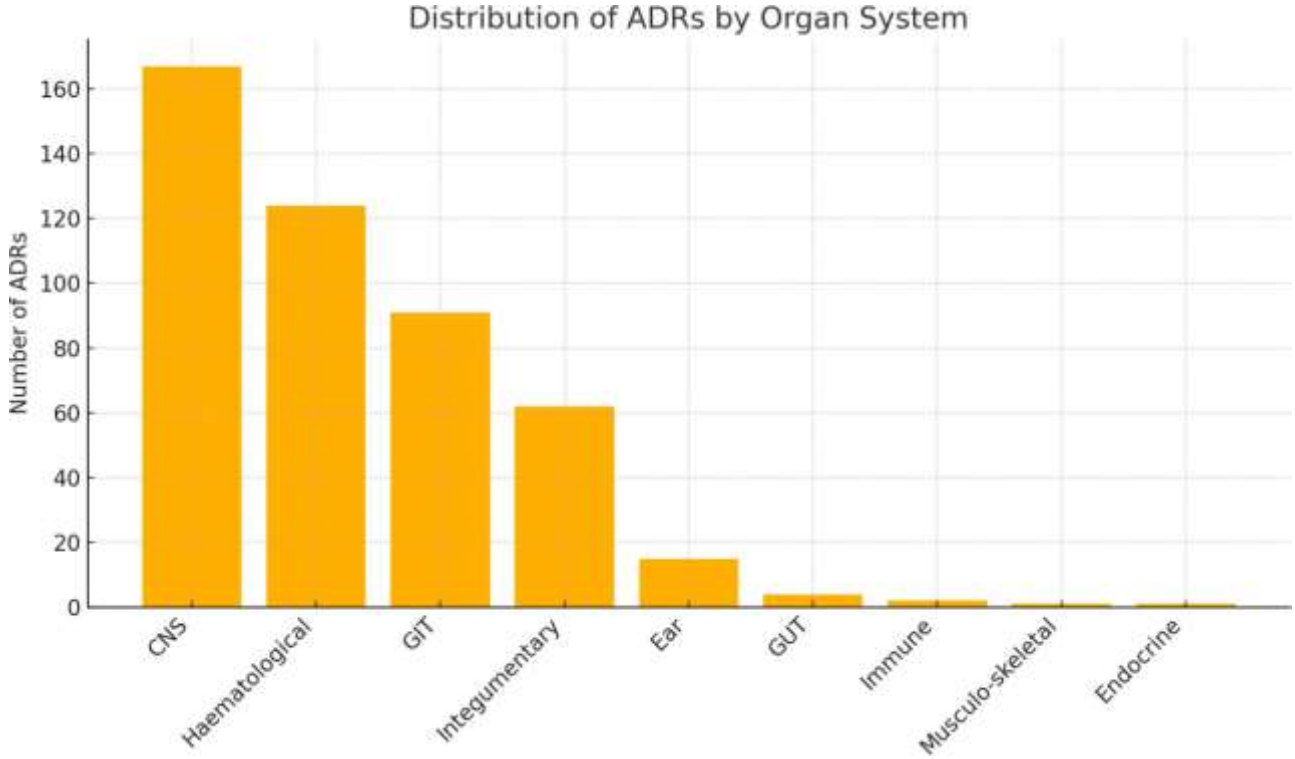
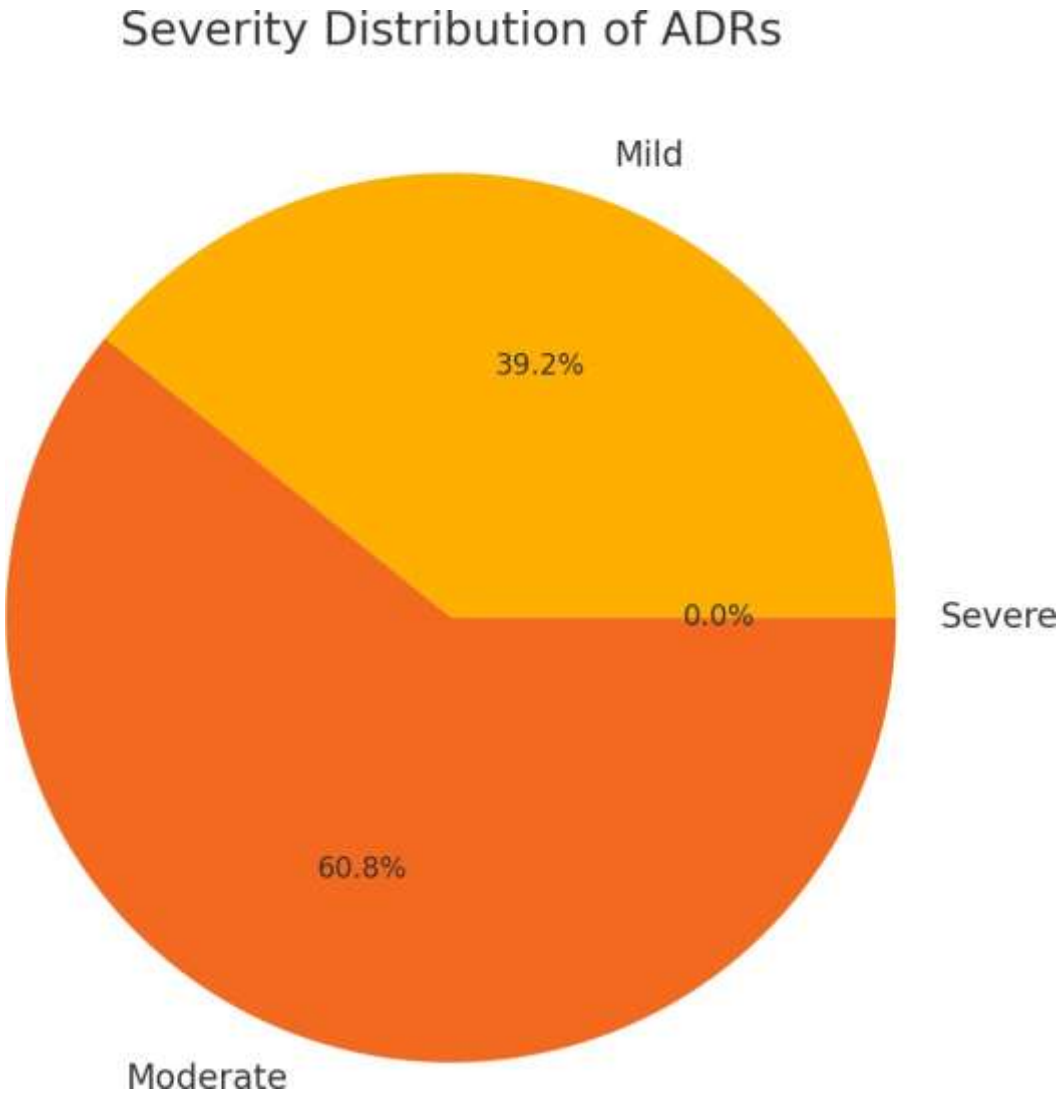


FIGURE 2. SEVERITY DISTRIBUTION OF ADVERSE DRUG REACTIONS (MILD VS. MODERATE).



Causality, severity and preventability analyses are summarised in **Table 3** and **Figure 2**. No statistically significant difference in individual ADR incidence was observed among the three platinum agents (all $p > 0.3$).

DISCUSSION

Our prospective assessment corroborates global evidence that platinum chemotherapy is associated with a high frequency of but predominantly mild-to-moderate ADRs [11, 12]. The 4.7 ADRs per patient observed mirrors reports from tertiary Indian centres (3.9–5.2 ADRs/patient) [13] yet exceeds Western series, possibly reflecting baseline nutritional deficiencies and later stage at presentation [14]. The predominance of CNS-mediated emesis aligns with cisplatin's well-known serotonergic trigger-zone activation [4]; that nausea persisted despite contemporary triple anti-emetic prophylaxis highlights the need for personalised emetogenic-risk algorithms and incorporation of neurokinin-1 antagonists, as endorsed by NCCN 2024 guidelines [15].

Haematological toxicity was chiefly anaemia—seen in 61 % of patients—surpassing the 30–40 % incidence in European cohorts [16]. Besides drug-induced myelosuppression, concomitant iron deficiency and chronic inflammation likely contributed; proactive intravenous iron and ESA strategies merit exploration. Oxaliplatin-linked neuropathy, though feared, manifested mainly as transient numbness rather than debilitating sensory loss,

consistent with Asian data suggesting ethnic susceptibility differences [17].

Importantly, nearly half the ADRs were judged definitely preventable. Inadequate pre-hydration, omission of magnesium supplementation and delayed anti-emetic dosing were recurring modifiable factors—echoing findings from pharmacovigilance audits in Thailand and Nigeria [18, 19]. Embedding checklist-based nursing protocols and real-time electronic alerts could curtail such lapses. The absence of severe or fatal ADRs attests to the effectiveness of early identification and supportive measures once events occurred.

Contrary to expectation, inter-drug comparisons did not yield statistically distinct toxicity profiles. While cisplatin traditionally carries greater nephro- and neurotoxicity risks, its restricted use in renal-sufficient, younger patients in our cohort may have attenuated differences. Sample-size limitations also reduce power to detect rare but serious events such as anaphylaxis or SIADH; multicentric pooling would provide granularity.

Our study's strengths include prospective design, use of standardised causality/severity/preventability tools and obligatory VigiFlow uploading, reinforcing the national PvPI database. Limitations comprise single-centre scope, lack of pharmacogenetic analysis and exclusion of 'silent' subclinical toxicities (e.g., creatinine rise <1.5× baseline). Moreover, quality-of-life metrics were not captured; integrating patient-reported outcome measures is the next step toward truly patient-centred pharmacovigilance.

Future research should examine genotype-phenotype correlations (e.g., GSTP1, ERCC1 polymorphisms) and real-time serum platinum levels to individualise dosing. Meanwhile, routine screening for anaemia, aggressive anti-emetic regimens, early neuropathy education and structured hydration protocols could substantially reduce the preventable ADR burden identified herein

CONCLUSION

This prospective Indian study confirms that platinum-based chemotherapy generates a substantial yet largely manageable ADR load, with nausea–vomiting, anaemia and peripheral neuropathy leading. Most reactions are of moderate severity, and half are preventable with timely supportive care. Uniform bedside pharmacovigilance utilising WHO-endorsed tools, regular staff sensitisation and systematic VigiFlow reporting can enhance drug-safety surveillance and optimise therapeutic outcomes in resource-limited oncology units.

REFERENCES

1. Kelland L. *Nat Rev Cancer*. 2007;7:573-84.
2. Florea A-M, Büsselberg D. *Cancers*. 2011;3:1351-71.
3. Stewart DJ. *Oncologist*. 2020;25:e162-72.
4. Hesketh PJ. *Oncologist*. 2020;25:231-8.
5. WHO Programme for International Drug Monitoring: Annual Report 2023.
6. Indian Council of Medical Research. *National Cancer Registry Programme Report 2020*.
7. Kshirsagar NA et al. *Indian J Pharmacol*. 2013;45:153-8.
8. Kumar R et al. *J Oncol Pharm Pract*. 2021;27:1243-50.
9. European Medicines Agency. *Good Pharmacovigilance Practices - Module VI*. 2023.
10. Sonkar P et al. *Therap Adv Drug Saf*. 2024;15:1-12.
11. Dong X et al. *Cancer Chemother Pharmacol*. 2022;89:593-602.
12. Lajer H, Jensen NB. *Cancer Treat Rev*. 2018;63:23-31.
13. Chinnasami G et al. *Indian J Cancer*. 2018;55:424-9.
14. Lidstone V et al. *Support Care Cancer*. 2019;27:3467-75.
15. National Comprehensive Cancer Network. Antiemesis Guidelines v3.2024.
16. Aapro M et al. *ESMO Open*. 2021;6:100136.
17. Park SB et al. *Asia Pac J Clin Oncol*. 2020;16:353-65.
18. Pongkulkiat S et al. *J Clin Pharm Ther*. 2020;45:663-70.
19. Okoro RN, Maduka O. *BMC Pharmacol Toxicol*. 2023;24:4.