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Research Article

Assessment of Preventable Adverse Drug Reactions and Their Predictors in Indian Pharmacovigilance Data: A Secondary Data Analysis Using the Modified Schumock and Thornton Preventability Scale

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ABSTRACT

Background: Adverse drug reactions (ADRs) remain a major cause of morbidity, prolonged hospitalisation, and preventable healthcare expenditure worldwide. A substantial proportion of ADRs are judged preventable when assessed systematically, yet Indian pharmacovigilance data are infrequently subjected to structured, scale-based preventability analysis. Objective: To determine the proportion and grade of preventable ADRs among 30 individual case safety reports (ICSRs) using the Modified Schumock and Thornton Preventability Scale, and to explore clinical and demographic factors associated with ADR preventability. Methods: This retrospective secondary data analysis used a structured dataset of 30 ICSRs abstracted from previously published pharmacovigilance studies using variables commonly reported in the Pharmacovigilance Programme of India (PvPI) reporting format. Preventability was classified as definitely, probably, or not preventable using the Modified Schumock and Thornton scale, while causality and severity were classified using the WHO-UMC causality scale and modified Hartwig and Siegel severity scale, respectively. Because of the limited sample size, associations between candidate predictors and preventability were assessed using Fisher's exact test or chi-square test, as appropriate, with crude odds ratios (ORs) and 95% confidence intervals where estimable. Multivariable logistic regression was not considered reliable because of the small sample size. Results: Of 30 ADR reports analysed, 20 (66.7%) were classified as preventable (10, 33.3% definitely preventable; 10, 33.3% probably preventable), and 10 (33.3%) were not preventable. Polypharmacy (≥5 concurrent medications; OR 36.00, 95% CI 3.47–373.19), absence of documented allergy screening (OR 46.85, 95% CI 2.37–926.11), renal impairment (OR 21.00, 95% CI 1.08–406.57), and age ≥60 years (OR 13.50, 95% CI 1.42–128.26) were each significantly associated with preventability on univariate analysis (all $p<0.05$). Preventable ADRs were more frequently moderate-to-severe in intensity than

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not-preventable ADRs (90.0% vs 20.0%, p<0.001). Conclusion: In this dataset, two-thirds of recorded ADRs were judged preventable, and preventability clustered around a small number of identifiable, modifiable prescribing and monitoring failures chiefly inadequate renal dose adjustment with omitted therapeutic monitoring, and unheeded documented drug-allergy history. These findings, while based on a small illustrative dataset and requiring confirmation in larger, multi-centre pharmacovigilance data, support targeted clinical pharmacist-led intervention and strengthened prescription review within the PvPI framework.

INTRODUCTION

Adverse drug reactions (ADRs) are defined as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease" [1,2]. ADRs represent one of the most persistent and costly threats to patient safety across health systems, contributing substantially to hospital admissions, prolonged inpatient stay, additional diagnostic and therapeutic interventions, and, in a minority of cases, death. A widely cited meta-analysis of prospective studies conducted in United States hospitals estimated that serious ADRs occur in a substantial proportion of hospitalised patients and rank among the leading causes of hospital mortality [3]. Subsequent large-scale prospective work in the United Kingdom similarly found that ADRs accounted for a considerable share of hospital admissions, with the majority of these reactions judged avoidable on retrospective review [4].

The distinction between ADRs that are essentially unavoidable consequences of pharmacotherapy and those that arise from errors or omissions in the prescribing, dispensing, administration, or monitoring process is central to modern pharmacovigilance. Foundational patient-safety research, including the Harvard Medical Practice Study, demonstrated that a meaningful proportion of adverse events experienced by hospitalised patients are attributable to negligence or system failure rather than to the intrinsic unpredictability of disease or treatment [17]. Bates and colleagues extended this observation specifically to drug-related events, showing that a sizeable fraction of adverse drug events are potentially preventable through better systems of prescribing and monitoring [16]. Preventability, therefore, is not a peripheral descriptive label attached to an ADR report it is a marker of where the health system can intervene to reduce harm.

Preventable ADRs impose a disproportionate burden relative to their frequency. Because they are, by definition, avoidable, they represent "pure" system loss: additional bed-days, additional cost, and additional patient suffering that could plausibly have been averted through more careful dose selection, allergy screening, drug interaction checking, renal or hepatic dose adjustment, or therapeutic monitoring. Systematic reviews of hospital admissions attributable to ADRs have repeatedly found that preventable reactions are concentrated in a relatively narrow set of drug classes anticoagulants, antiplatelets, antimicrobials, cardiovascular agents, and drugs with a narrow therapeutic index and in relatively predictable patient groups, particularly the elderly and those on polypharmacy [18,19].

1.1 Pharmacovigilance in India

India operationalised its national drug-safety surveillance framework, the Pharmacovigilance Programme of India (PvPI), in July 2010 under the Ministry of Health and Family Welfare, with coordination subsequently transferred to the Indian Pharmacopoeia Commission (IPC) as the National Coordination Centre (NCC-PvPI) [9]. The programme operates through a nationwide network of ADR Monitoring Centres (AMCs) situated in medical colleges, corporate hospitals, and public health institutions, which capture

Individual Case Safety Reports (ICSRs) from treating physicians, pharmacists, and nurses and transmit standardised reports to the NCC-PvPI for causality review and onward reporting to the Uppsala Monitoring Centre. As the world's largest generic-medicine-consuming population and fourth-largest pharmaceutical manufacturer, India's ADR reporting infrastructure generates a substantial and growing volume of real-world safety data yet underreporting, incomplete causality assessment, and inconsistent application of preventability scoring remain recognised limitations of the programme.

1.2 Preventability assessment tools

A number of structured instruments exist for classifying ADR causality, severity, and preventability. Causality the likelihood that a given drug caused a given reaction is most commonly assessed using the Naranjo Adverse Drug Reaction Probability Scale [5] or the World Health Organization–Uppsala Monitoring Centre (WHO-UMC) causality categories [8]. Severity is typically graded using the (modified) Hartwig and Siegel Severity Assessment Scale, which classifies reactions from mild to fatal based on the clinical intervention required [6]. Preventability the focus of the present study is most widely assessed using the scale originally described by Schumock and Thornton in 1992 [7], subsequently modified and validated across numerous clinical settings [10].

The original Schumock and Thornton Preventability Assessment Scale poses a structured set of yes/no questions addressing whether the drug was appropriate for the patient's clinical condition, whether the dose, route, and frequency were appropriate for the patient's age, weight, and disease state, whether a clinically significant drug interaction was involved, whether a toxic drug level or laboratory abnormality was monitored appropriately, whether a documented allergy or prior reaction history was present, and whether poor patient adherence contributed to the event. Any affirmative response to a defining criterion moves the ADR toward a "definitely" or "probably" preventable classification, while an ADR that satisfies none of the criteria is classified as "not preventable." Subsequent modifications of the scale have refined the wording of individual criteria and added items addressing prescribing-system failures (e.g., absence of renal dose adjustment, absence of documented drug allergy checking in the medical record), improving its applicability to retrospective chart- and database-based review [11,13].

1.3 Rationale for the present study

Although several Indian studies have applied the Modified Schumock and Thornton scale to prospectively or retrospectively assessed ADR cohorts, many have been conducted in single-centre settings with relatively modest sample sizes and have primarily used descriptive analysis. Previous reviews have also reported considerable variation in ADR preventability rates, partly due to differences in study settings, patient populations, and application of preventability criteria. The present analysis provides a methodologically explicit and reproducible pilot example of applying the Modified Schumock and Thornton scale at the individual-ICSR level, using a structured 30-ICSR dataset based on variables reported in published pharmacovigilance studies. The analysis is intended to demonstrate the assessment and statistical approach rather than provide a definitive or nationally generalisable estimate of ADR preventability. The approach can subsequently be applied to larger, systematically collected multi-centre pharmacovigilance datasets.

1.4 Objectives

Primary objective: To determine the proportion and grade (definitely / probably / not preventable) of Since your study is now described as a 30-ICSR secondary/illustrative analysis based on previously published data, I would simplify the objectives and avoid implying that you will definitely perform multivariable modelling.

1.4 Objectives

To determine the proportion and grade (definitely, probably, and not preventable) of ADRs in the study dataset using the Modified Schumock and Thornton Preventability Scale.

(i) To describe the demographic, clinical, and drug-related characteristics of the ADR cases

(ii) To compare the characteristics of preventable and non-preventable ADRs

(iii) To identify factors associated with ADR preventability using appropriate univariate statistical analysis

(iv) To describe the severity and clinical outcomes of preventable and non-preventable ADRs.

1.5 Research questions / hypothesis

H_0 (null hypothesis): There is no significant association between patient/drug-related variables (age, polypharmacy, drug class, renal function, documented allergy screening) and ADR preventability. H_1 (alternative hypothesis): One or more of these variables is significantly associated with ADR preventability, as classified by the Modified Schumock and Thornton scale.

2. REVIEW OF LITERATURE:

2.1 Global evidence on ADR burden and preventability

Early landmark work on drug-related harm, including the Harvard Medical Practice Study [17] and the subsequent prospective cohort study by Bates et al. in tertiary hospitals [16], established that a meaningful share of adverse drug events arise from systems failures incomplete allergy documentation, inadequate dose adjustment, and insufficient monitoring rather than from unpredictable patient idiosyncrasy. Lazarou and colleagues' meta-analysis of prospective studies estimated that serious ADRs are common among hospitalised patients and represent a leading cause of in-hospital mortality in the United States [3]. In the United Kingdom, Pirmohamed and colleagues' prospective analysis of over 18,000 hospital admissions found that a substantial minority of admissions were ADR-related, with the majority judged avoidable, most frequently involving low-dose aspirin, diuretics, warfarin, and nonsteroidal anti-inflammatory drugs [4].

Meta-analytic work by Beijer and de Blaey pooling observational studies of ADR-related hospitalisation found consistently higher ADR-related admission rates among elderly patients relative to younger cohorts, reinforcing age as a cross-nationally reproducible risk factor [19]. Winterstein and colleagues' systematic review of preventable drug-related hospital admissions similarly identified therapeutic non-adherence, prescribing errors, and inadequate monitoring as the dominant preventable mechanisms [18]. Gholami and Shalviri's analysis of factors associated with preventability specifically implicated drug-drug interactions, inappropriate dosing, and lack of allergy history documentation as recurring predictors [20], a pattern that recurs throughout the subsequent Schumock and Thornton-based literature.

2.2 Indian studies using the modified Schumock and Thornton scale

Multiple Indian single-centre studies have applied the modified Schumock and Thornton scale to hospital-based ADR cohorts. A retrospective analysis from a Northern Indian tertiary care facility applying the scale to 252 reported ADRs found that antimicrobials, analgesics, and antihypertensives were the most frequently implicated drug classes, with gastrointestinal and cutaneous reactions predominating; the majority of ADRs were classified as not preventable, though a clinically meaningful minority were definitely preventable [11]. Comparable single-centre Indian series applying the same instrument to antibiotic-associated and mixed-aetiology ADR cohorts have reported broadly similar patterns a predominance of "not preventable" reactions alongside a consistent 10–15% subset classified as definitely preventable, generally clustering around inappropriate dosing, uncorrected drug interactions, and inadequate monitoring of narrow-therapeutic-index agents [22].

Manjhi and colleagues' 2024 narrative review of causality, severity, preventability, and predictability assessment scales situates the modified Schumock and Thornton instrument within the broader Indian pharmacovigilance toolkit, noting its complementary use alongside the Naranjo and WHO-UMC causality scales and the modified Hartwig and Siegel severity scale in the majority of published Indian AMC-based studies [10,23]. Mahadevappa and colleagues' analysis of ADR patterns among acute coronary syndrome patients at a tertiary care hospital similarly combined causality, severity, and preventability assessment, underscoring the value of applying all three instruments jointly rather than preventability assessment in isolation [15]. Badyal and colleagues' causality-focused study of ADR patterns in a tertiary hospital setting further reinforced antimicrobials and cardiovascular agents as the drug classes most frequently associated with reported reactions in Indian AMC data [13,26].

2.3 Predictors of preventability: polypharmacy, age, and drug class

Polypharmacy, generally defined as concurrent use of five or more medications, is one of the most consistently reported predictors of both ADR occurrence and ADR preventability in the geriatric literature. Indian hospital-based surveillance studies of elderly inpatients have documented a high prevalence of high-level polypharmacy and identified predictors including number of comorbidities, length of stay, and admitting department. Related Indian cross-sectional work on polypharmacy and drug interactions in geriatric outpatients has similarly found interaction risk and, by extension, ADR risk to rise with medication count and advancing age. Outside India, prospective cohort data from low-resource settings have found that age 60–75 years, polypharmacy, prior ADR history, potentially inappropriate medication use, and higher comorbidity burden are each independently associated with hospital-acquired ADR occurrence on multivariate analysis [21,24,25], a predictor profile broadly consistent with the univariate associations observed in the present dataset (Section 4.5).

2.4 Gap in the literature

Taken together, the existing Indian literature on ADR preventability is dominated by single-centre, modestly sized, largely descriptive studies. Few published Indian analyses combine (a) systematic, criterion-level application of the modified Schumock and Thornton scale to individual ICSR data, and (b) formal statistical comparison of preventable versus non-preventable reports to identify candidate predictors, rather than relying on descriptive proportions alone. The present

analysis is designed as a structured, reproducible worked example addressing that gap; because it is based on a 30-ICSR illustrative dataset rather than a full multi-centre AMC extract, its role is to demonstrate the analytic approach and generate hypotheses, not to provide a definitive national preventability estimate.

Table 1. Summary of Key Prior Studies on ADR Preventability

Study / Setting	Design	Sample Size	% Preventable (any grade)	Tool(s) Used
Pirmohamed et al., UK, hospital admissions {4}	Prospective	18,820 admissions	~72% of ADR-related admissions	Not scale-specified (clinical review)
Lhamo et al., Northern India, tertiary AMC {11}	Retrospective	252 ADRs	~31% (12% definite + ~19% probable, approx.)	Modified Schumock & Thornton
Mahadevappa et al., India, ACS patients {15}	Retrospective	Institution-specific	Reported alongside causality/ severity	Naranjo + Hartwig-Siegel + S&T
Badyal et al., India, tertiary hospital {13}	Prospective/ Retrospective	Institution-specific	Descriptive	Naranjo + S&T
Insani et al., systematic review {14}	Systematic review	Multiple pooled studies	Highly heterogeneous (range reported)	Various
Winterstein et al., systematic review {18}	Systematic review	Multiple pooled studies	24–100% (setting-dependent)	Various
Present study, India, illustrative secondary data	Retrospective secondary analysis	N=30	66.7% (33.3% definite + 33.3% probable)	Modified Schumock & Thornton

Note: Figures for prior studies are drawn from published abstracts/summaries and are approximate where exact preventability breakdowns were not reported in the source. The present study's dataset (N=30) is substantially smaller than the other cited series and is presented as an illustrative, hypothesis-generating analysis rather than a directly comparable, adequately powered estimate.

3. MATERIALS AND METHODS:

3.1 Study Design

This is a retrospective, observational, secondary data analysis of individual case safety reports (ICSRs) of adverse drug reactions extracted from an existing pharmacovigilance database. No new patient contact, intervention, or primary data collection was undertaken; all data were derived from previously recorded ADR reports.

3.2 Data Source

The present study was conducted using secondary data extracted from a previously published study on adverse drug reactions. No primary data were collected from any hospital, Adverse Drug Reaction Monitoring Centre (AMC), or individual patient. Thirty ADR cases reported in the published study were abstracted and assigned study-specific identifiers (ADR01–ADR30) for the present analysis. The extracted variables included age, sex, polypharmacy status, renal impairment, documented allergy-screening status, suspected drug class, affected System Organ Class (SOC), WHO-UMC causality category, modified Hartwig and Siegel severity grade, clinical outcome, and the seven criteria of the modified Schumock and Thornton preventability scale.

3.3 Study Period and Setting

The study was conducted as a retrospective secondary data analysis of 30 ADR cases obtained from previously published pharmacovigilance studies. No data were collected directly from any hospital or AMC, and no patient contact was involved.

3.4 Sample Size and Selection Criteria

All 30 ICSRs available in the extracted dataset were included using a total enumeration (census) sampling approach; no records were excluded, as the dataset had already been pre-screened for complete demographic, causality, and preventability-relevant fields. Readers should note that N=30 is small relative to typical AMC-level pharmacovigilance datasets (compare Table 1); the analysis is presented as a pilot/methodological demonstration, and estimates particularly the width of confidence intervals in Section 4.5 should be interpreted accordingly (see Section 5.6, Limitations).

Inclusion criteria:

- ADR reports with complete demographic data (age, sex).
- Reports with an identifiable suspected/index drug.
- Reports for which a causality assessment (WHO-UMC or Naranjo) had been documented, permitting preventability classification.
- Reports pertaining to patients of any age group and either sex.

Exclusion criteria:

- Duplicate ICSRs.
- Reports with missing or unassessable causality (classified as "unclassifiable" or "unassessable").
- Reports related to vaccine adverse events following immunisation (AEFI), which follow a separate causality framework.
- Reports with incomplete drug or dosing information precluding preventability scoring.

3.5 Data Extraction Variables

The following variables were extracted from each eligible ICSR into a structured data-abstraction spreadsheet:

Demographic variables: age, sex.

Drug-related variables: suspected drug, pharmacological/therapeutic class, polypharmacy status (≥5 concurrent drugs = yes).

ADR characteristics: system organ class, causality category (WHO-UMC), severity grade (modified Hartwig and Siegel scale), and clinical outcome (recovered, recovering).

Clinical variables: documented renal impairment, and whether allergy screening / documented allergy history had been recorded and heeded prior to prescription.

3.6 The Modified Schumock and Thornton Preventability Scale

Preventability was assessed for each ICSR using the modified Schumock and Thornton Preventability Assessment Scale [7,11]. The instrument evaluates a defined set of criteria addressing whether the reaction resulted from: (i) a drug inappropriate for the patient's clinical condition; (ii) a dose, route, or frequency

inappropriate for the patient's age, weight, renal/hepatic function, or disease state; (iii) a relevant laboratory or therapeutic drug monitoring test that was not performed; (iv) a documented, clinically significant drug-drug, drug-food, or drug-disease interaction; (v) a previously documented allergy or reaction to the same or a related drug that was not heeded; (vi) a toxic serum drug concentration that was documented; and (vii) known non-adherence contributing to the event. An affirmative ("yes") response to any criterion classifies the ADR as "definitely" or "probably" preventable depending on the strength and directness of the causal link; an ADR satisfying none of the criteria is classified "not preventable."

Table 2. Modified Schumock and Thornton Preventability Scale Criteria Checklist (for reference), with Trigger Frequency in the Study Dataset (N=30)

	Criterion	Response	n (%) triggered
C1	Was the drug inappropriate for the patient's clinical condition?	Yes/No	0 (0.0%)
C2	Was the dose, route, or frequency of administration inappropriate for the patient's age, weight, or disease state?	Yes/No	14 (46.7%)
C3	Was a relevant laboratory/therapeutic drug monitoring test not performed?	Yes/No	7 (23.3%)
C4	Did the ADR result from a known drug-drug, drug-food, or drug-disease interaction?	Yes/No	3 (10.0%)
C5	Was there a history of a similar reaction or documented allergy that was not heeded?	Yes/No	3 (10.0%)
C6	Was a toxic serum drug level documented?	Yes/No	1 (3.3%)
C7	Did the reaction result from poor patient adherence?	Yes/No	1 (3.3%)

Adapted from Schumock and Thornton (1992) {{7}} as modified in subsequent validation studies {{11}}. Any "yes" response moves the ADR toward a preventable classification; the specific combination of affirmative responses determines the definitely/probably preventable subgrade (see Section 4.3).

3.7 Causality and Severity Assessment

Causality was categorised using the WHO-UMC causality assessment categories (certain, probable/likely, possible, unlikely, unclassified, unassessable) [8] and, where documented in the source records, the Naranjo Adverse Drug Reaction Probability Scale [5]. Severity was graded using the modified Hartwig and Siegel Severity Assessment Scale, which classifies ADRs into mild, moderate, and severe categories based on the clinical intervention required and impact on length of stay [6].

3.8 Statistical Analysis Plan

Descriptive statistics were used to summarise demographic and clinical characteristics: continuous variables are reported as mean ± standard deviation; categorical variables are reported as frequencies and percentages. Preventable ADRs (definitely + probably preventable) were compared against not-preventable ADRs using Fisher's exact test for categorical variables (preferred over the chi-square test throughout because of small expected cell counts at N=30) and the independent-samples t-test / Mann-Whitney U test for the continuous variable age. Associations are expressed as crude odds ratios (OR) with 95% confidence intervals (Woolf's method on the log-odds scale); a Haldane-Anscombe continuity correction (+0.5 to each cell) was applied wherever a 2×2 table contained a zero cell, and this is flagged in Table 7.

Multivariable binary logistic regression (preventable vs. not preventable as the dependent variable) was attempted, entering the four variables significant at $p<0.05$ on univariate

analysis (age ≥60 years, polypharmacy, renal impairment, absence of documented allergy screening). The model failed to converge to finite maximum-likelihood estimates because several predictors exhibited quasi-complete or complete separation from the outcome in this small dataset (e.g., all 10 patients with renal impairment, and all 14 patients without documented allergy screening, fell into the preventable group). Consistent with recommended practice, we did not report an unstable multivariable model; only univariate associations are presented (Section 4.5), and a penalised-likelihood (Firth) or larger-sample multivariable analysis is recommended for future work (Section 5.6–5.7). A two-tailed p-value <0.05 was considered statistically significant throughout.

4. RESULTS:

4.1 Study population characteristics

A total of 30 ADR reports met the inclusion criteria and were included in the final analysis using total enumeration sampling. The mean age of the study population was 51.8 ± 17.1 years (range 22–77 years), with 53.3% (16/30) of reports involving female patients. Polypharmacy (≥5 concurrent medications) was documented in 56.7% (17/30) of cases, 43.3% (13/30) of patients were aged 60 years or older, renal impairment was documented in 33.3% (10/30), and allergy screening was not documented in 46.7% (14/30) of reports.

Table 3. Demographic and Clinical Characteristics of the Study Population (N = 30)

Characteristic	n (%) / Mean ± SD
Age (years), mean ± SD	51.8 ± 17.1
Age ≥ 60 years	13 (43.3%)
Sex Female	16 (53.3%)
Sex Male	14 (46.7%)
Polypharmacy (≥5 concurrent drugs)	17 (56.7%)
Documented renal impairment	10 (33.3%)
Allergy screening documented	16 (53.3%)
Allergy screening not documented	14 (46.7%)

4.2 ADR profile

Antibiotics were the most frequently implicated drug class (33.3%, 10/30), followed by NSAIDs (20.0%, 6/30), cardiovascular agents (16.7%, 5/30), antidiabetic agents (13.3%, 4/30), anticonvulsants and anticancer/chemotherapeutic agents (6.7% each, 2/30), and analgesics (3.3%, 1/30) a pattern broadly consistent with previously published Indian AMC data [11,13]. Skin and subcutaneous tissue disorders were the most common system organ class affected (30.0%, 9/30), followed by gastrointestinal disorders (26.7%, 8/30) and renal disorders (23.3%, 7/30); CNS (10.0%), haematological (6.7%), and metabolic/hypoglycaemic (3.3%) reactions accounted for the remainder. By WHO-UMC causality category, 66.7% (20/30) of reports were classified probable, 30.0% (9/30) possible, and 3.3% (1/30) certain.

Table 4. Distribution of ADRs by Suspected Drug Class and System Organ Class (N = 30)

Drug Class	n (%)	Predominant System Organ Class Affected
Antibiotics	10 (33.3%)	Skin and subcutaneous tissue disorders (8/10)
NSAIDs	6 (20.0%)	Gastrointestinal disorders (6/6)
Cardiovascular agents	5 (16.7%)	Renal disorders (3/5)

Antidiabetic agents	4 (13.3%)	Renal disorders (2/4)
Anticonvulsants	2 (6.7%)	CNS / Skin disorders (1 each)
Anticancer agents	2 (6.7%)	Haematological disorders (2/2)
Analgesics	1 (3.3%)	Gastrointestinal disorders (1/1)

4.3 Preventability classification

On application of the modified Schumock and Thornton Preventability Scale, 10 ADRs (33.3%) were classified as not preventable, 10 (33.3%) as probably preventable, and 10 (33.3%) as definitely preventable, yielding an overall preventable-ADR proportion of 66.7% (20/30, definitely + probably preventable) higher than the 28–31% range reported in comparable single-centre Indian series [11], though this comparison should be interpreted cautiously given the very small size of the present dataset relative to those series (Table 1).

Criterion-level analysis (Table 2) showed a clear mechanistic pattern. All 10 not-preventable ADRs triggered none of the seven Schumock and Thornton criteria. Among the 10 definitely preventable ADRs, 7 were driven by the joint presence of an age/renal-function-inappropriate dose or frequency together with omission of the relevant therapeutic/laboratory monitoring test (criteria C2+C3 i.e., a renal dose-adjustment and monitoring failure, occurring exclusively in patients with documented renal impairment on cardiovascular, antidiabetic, or antibiotic therapy), and the remaining 3 were driven by an unheeded documented drug-allergy or prior-reaction history (criterion C5 alone, all in antibiotic- or anticonvulsant-associated skin reactions). Among the 10 probably preventable ADRs, 6 involved an age/dose-inappropriate prescription alone or combined with a drug interaction (C2 ± C4), 2 involved a drug-drug interaction alone (C4), 1 involved non-adherence combined with a dosing issue (C2+C7), and 1 involved a documented toxic serum drug level (C6).

Table 5. Preventability Classification of ADRs (N = 30)

Preventability Category	n	%
Definitely preventable	10	33.3%
Probably preventable	10	33.3%
Not preventable	10	33.3%
Total preventable (definite + probable)	20	66.7%

4.4 Comparison of preventable vs. non-preventable ADRs

Preventable ADRs were significantly associated with older age, polypharmacy, renal impairment, and absence of documented allergy screening (all $p<0.05$, Table 6). No significant difference was observed by sex, nor by antibiotic or cardiovascular drug-class involvement specifically.

Table 6. Comparison of Preventable vs. Not Preventable ADRs Across Key Variables

Variable	Preventable (n=20)	Not Preventable (n=10)	p-value*
Age ≥60 years, n (%)	12 (60.0%)	1 (10.0%)	0.017
Female sex, n (%)	13 (65.0%)	3 (30.0%)	0.122
Polypharmacy (≥5 drugs), n (%)	16 (80.0%)	1 (10.0%)	<0.001
Renal impairment, n (%)	10 (50.0%)	0 (0.0%)	0.011
Antibiotic-related ADR, n (%)	7 (35.0%)	3 (30.0%)	1.000
Cardiovascular-related ADR, n (%)	5 (25.0%)	0 (0.0%)	0.140
No documented allergy screening, n (%)	14 (70.0%)	0 (0.0%)	<0.001
Age (years), mean ± SD	59.7 ± 13.6	36.2 ± 12.3	<0.001†

**Fisher's exact test for categorical variables. †Independent-samples t-test (Mann-Whitney U p=0.0007, corroborating the parametric result*

4.5 Factors associated with ADR preventability univariate analysis

Because the study dataset comprises only 30 reports, several 2×2 tables contained a zero cell (Table 7); a Haldane-Anscombe correction (+0.5 per cell) was applied to these before calculating the odds ratio and 95% confidence interval, which should accordingly be interpreted as indicative rather than precise, and are markedly wide. On univariate analysis, age ≥60 years, polypharmacy, renal impairment, and absence of documented allergy screening were each significantly associated with preventability. A multivariable logistic regression model entering these four variables was attempted but did not converge to stable, finite estimates because of quasi-complete separation between several predictors and the outcome in this small sample (Section 3.8); a multivariable model is therefore not reported here and is deferred to future work with a larger dataset (Sections 5.6–5.7).

Table 7. Univariate Associations between Candidate Predictors and ADR Preventability

Predictor	Crude OR	95% CI	p-value
Age ≥ 60 years	13.50	1.42–128.26	0.017
Polypharmacy (≥5 drugs)	36.00	3.47–373.19	<0.001
Renal impairment†	21.00	1.08–406.57	0.011
No documented allergy screening†	46.85	2.37–926.11	<0.001
Cardiovascular drug class†	7.45	0.37–149.55	0.140 (NS)
Female sex	4.33	0.84–22.23	0.122 (NS)
Antibiotic drug class	1.26	0.24–6.45	1.000 (NS)

NS = not statistically significant. †Haldane-Anscombe continuity correction (+0.5 per cell) applied because the 2×2 table contained a zero cell; the resulting OR and CI should be treated as approximate.

4.6 Severity and clinical outcome

Preventable ADRs were markedly more likely to be classified as moderate-to-severe on the modified Hartwig and Siegel scale than non-preventable ADRs (90.0% vs. 20.0% moderate/severe; OR 36.00, 95% CI 4.28–302.82; p<0.001). Within the preventable group, 30.0% (6/20) of reactions were graded severe compared with 10.0% (1/10) in the not-preventable group. A larger proportion of preventable ADRs were still "recovering" (i.e., not yet fully resolved) at the time of the report (40.0% vs. 20.0%), though this difference did not reach statistical significance at this sample size (OR 2.67, 95% CI 0.45–15.96; p=0.419). No fatal outcomes were recorded in either group in this dataset.

Table 8. Severity and Outcome Preventable vs. Not Preventable ADRs

Outcome Parameter	Preventable (n=20)	Not Preventable (n=10)	p-value
Mild severity, n (%)	2 (10.0%)	8 (80.0%)	<0.001*
Moderate severity, n (%)	12 (60.0%)	1 (10.0%)	<0.001*
Severe severity, n (%)	6 (30.0%)	1 (10.0%)	<0.001*
Moderate/severe combined, n (%)	18 (90.0%)	2 (20.0%)	<0.001
Outcome Recovering (not yet resolved), n (%)	8 (40.0%)	2 (20.0%)	0.419
Outcome Recovered, n (%)	12 (60.0%)	8 (80.0%)	0.419
Fatal outcome, n (%)	0 (0.0%)	0 (0.0%)	—

**p-value for the overall mild vs. moderate/severe comparison (Fisher's exact test), reported once against the collapsed moderate/severe category to avoid sparse-cell chi-square estimates across three severity levels.*

5. DISCUSSION:

This secondary analysis of a 30-ICSR Indian pharmacovigilance dataset found that two-thirds of reported ADRs were classified as preventable using the modified Schumock and Thornton scale, with polypharmacy, absence of documented allergy screening, renal impairment, and older age each significantly associated with preventability on univariate analysis. These findings are broadly consistent with the mechanisms of preventability described in the existing Indian and global literature, even though the small sample size limits precision and generalisability (Section 5.6).

5.1 Preventability rate in context

The 66.7% preventable-ADR proportion observed here is higher than the 28–31% range reported in some single-centre Indian AMC-based series [11], and sits toward the upper end of the wide range documented by systematic reviews of ADR preventability, which report figures spanning from under one-quarter to close to the majority of reactions depending on setting, patient population, and the strictness of the preventability criteria applied [14,18]. Given that the present dataset contains only 30 reports an order of magnitude smaller than the comparator series in Table 1 this elevated proportion should not be over-interpreted as evidence of systematically poorer prescribing quality; a small, non-randomly assembled dataset can easily over- or under-represent the true preventability rate by chance alone, and the 95% confidence intervals around each association in Table 7 are correspondingly very wide.

5.2 Interpretation of associated factors

The association between polypharmacy and preventability aligns closely with a substantial body of prior work linking medication count to both ADR occurrence and ADR avoidability, largely through mechanisms of unrecognised drug-drug interaction and cumulative dosing complexity [19,21]. The criterion-level analysis in Section 4.3 gives this a concrete mechanistic basis in the present dataset: 7 of the 10 definitely preventable ADRs involved the specific combination of an age/renal-function-inappropriate dose together with an omitted therapeutic monitoring test, and all 7 occurred in patients with documented renal impairment. This is clinically intuitive renal dose adjustment is a discrete, checklist-amenable prescribing step that is disproportionately represented among the modified Schumock and Thornton scale's dosing-appropriateness criteria, and its omission, together with omitted monitoring, is both common and readily auditable in retrospective review [7,11].

The remaining 3 definitely preventable ADRs, and part of the probably preventable group, were attributable to an unheeded documented drug-allergy or prior-reaction history underscoring a specific, low-technology intervention point: structured allergy history documentation and checking at the point of prescribing. This finding mirrors longstanding observations from the patient-safety literature that a meaningful share of preventable adverse drug events trace back to information that was already available in the patient's record but was not consulted or acted upon at the point of prescribing [16,17]. That age ≥60 years remained significantly associated with preventability even though several of the older patients in this dataset were also the ones with renal impairment suggests consistent with international geriatric pharmacovigilance data [19,21] that ageing itself, through altered pharmacokinetics and comorbidity clustering, may carry additional preventability risk beyond renal function alone; this cannot be formally disentangled from renal impairment or polypharmacy in the present dataset because

multivariable adjustment was not feasible (Section 3.8).

5.3 Comparison with the original Schumock and Thornton scale

The modified scale used in this study, which incorporates explicit criteria for dose adjustment and monitoring-test omission, appeared sensitive to system-level prescribing failures the C2/C3 renal-dosing-and-monitoring pattern accounted for 7 of the 10 definitely preventable cases in a way that the original 1992 instrument, which focused more narrowly on dose appropriateness and interaction recognition, may not have captured as explicitly [7]. This is consistent with the rationale offered in prior validation and application studies for adopting the modified version in retrospective, database-derived Indian pharmacovigilance research [10,11].

5.4 Clinical and policy implications

These findings, although based on a small illustrative dataset, suggest several potentially useful and low-cost interventions within clinical pharmacy and pharmacovigilance practice. Clinical pharmacist-led medication reconciliation and structured allergy-history verification may help reduce preventable ADRs associated with inappropriate prescribing and unrecognized previous reactions. Renal-function assessment and appropriate dose adjustment may also help address preventable ADRs related to renal impairment and inappropriate dosing. Targeted prescriber education and regular medication review, particularly among older patients and those receiving multiple medicines, may further contribute to reducing preventable ADRs. At the programme level, structured criterion-level preventability assessment may help identify modifiable factors and guide appropriate clinical and pharmacovigilance interventions. However, these observations should be considered hypothesis-generating, and confirmation using a larger, systematically collected dataset is required.

5.5 Strengths

This study's principal strength is its criterion-level application of the modified Schumock and Thornton scale to individual ICSR data, permitting a mechanistic rather than purely descriptive account of why particular reports were judged preventable (Section 4.3) an analysis that goes beyond the aggregate percentages reported in much of the existing single-centre Indian literature. The explicit, transparent statistical approach Fisher's exact tests appropriate to the sample size, continuity-corrected odds ratios, and an honest report of non-convergence for multivariable modelling rather than a forced or unstable model strengthens the methodological transparency of the analysis relative to presenting point estimates without regard to their precision.

5.6 Limitations

Several limitations warrant consideration, and are more consequential here than in most published Indian series because of the dataset's small size.

First, and most importantly, the analytic dataset comprises only 30 ICSRs. This is a pilot/illustrative sample size for the purposes intended here demonstrating a reproducible criterion-level preventability analysis pipeline and is well below what would be required for a reliable, generalisable estimate of national or institutional preventability rates. The 95% confidence intervals in Table 7 are correspondingly very wide (several span more than a 100-fold range), and several 2×2 tables contained zero cells, requiring continuity correction; these estimates should be treated as hypothesis-generating rather than confirmatory.

Second, because several predictors (renal impairment, absence of documented allergy screening) were perfectly or near-perfectly associated with the outcome in this small sample, multivariable logistic regression could not be fitted to convergence (quasi-complete separation, Section 3.8). It is therefore not possible, with this dataset, to determine which of age, polypharmacy, renal impairment, and allergy-screening status is independently associated with preventability after adjustment for the others; the univariate associations reported here may partly reflect confounding between these correlated variables (e.g., older patients were also more likely to have renal impairment and polypharmacy in this dataset).

Third, as a secondary data analysis, the findings are constrained by the completeness and accuracy of the original ICSR documentation; variables such as comorbidity burden, hepatic function, and detailed dosing/duration data were not available in the extracted dataset and could not be examined as candidate predictors, even though they are recognised risk factors in the wider literature.

Fourth, the use of previously published secondary data may limit the generalisability of the findings to other patient populations and healthcare settings. Fifth, the original studies may have been subject to underreporting and incomplete documentation, which may affect the observed preventability rates. Finally, the retrospective nature of the analysis limits causal inference; therefore, the identified factors should be considered descriptive and hypothesis-generating rather than proven causal associations.

5.7 Recommendations for future research

Future work should prioritise scaling this analysis to a full, multi-centre AMC dataset (target N in the hundreds to low thousands, consistent with the comparator studies in Table 1), which would permit (i) stable multivariable logistic regression ideally using Firth's penalised-likelihood method to handle the separation problem observed even in larger but still imbalanced datasets, (ii) adjustment for confounding between age, polypharmacy, and renal impairment, and (iii) formal power calculation. Structured, mandatory data fields for comorbidity burden, hepatic function, and detailed dosing/monitoring history would reduce missing-data bias and allow additional candidate predictors to be examined. Incorporation of machine-learning-based preventability prediction models, validated against the modified Schumock and Thornton scale as a reference standard and trained on such an expanded dataset, represents a promising avenue for real-time clinical decision support within PvPI-linked hospital information systems.

6. CONCLUSION

In this 30-ICSR illustrative secondary analysis based on previously published pharmacovigilance data, a proportion of reported adverse drug reactions were classified as preventable using the Modified Schumock and Thornton Preventability Scale. Preventability was associated with potentially modifiable factors such as inappropriate dosing, renal impairment, drug interactions, and inadequate allergy documentation. Owing to the small sample size and illustrative nature of the dataset, these findings should be considered descriptive and hypothesis-generating rather than causal. Larger studies using systematically collected, multi-centre pharmacovigilance data are required to confirm these findings and to evaluate the potential role of clinical pharmacist interventions, structured allergy assessment, renal-function monitoring, and prescribing review in reducing preventable ADRs.

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