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The Compounding Effect of Polypharmacy and Comorbidities on Adverse Drug Reaction Severity in Critically Ill Patients

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Abstract

Background: Adverse drug reactions (ADRs) present a profound clinical challenge in the intensive care unit (ICU), where multi-organ dysfunction and complex pharmacotherapy are prevalent. This study investigates the compounding effects of polypharmacy and baseline comorbidities on the severity of ADRs in critically ill patients.

Methods: A prospective observational study was conducted over six months in a 1009-bedded multi-speciality tertiary care teaching hospital. A cohort of 174 patients who developed an ADR during ICU admission was evaluated. Severity was assessed using Hartwig's scale, while causality and preventability were measured using the Naranjo and Schumock-Thornton scales, respectively.

Results: Among the 174 patients, 109 (62.64%) presented with pre-existing comorbidities. Polypharmacy was extensive, with 120 patients (68.97%) prescribed 10 or more concurrent medications. Severity assessment revealed 93 (53.44%) mild, 78 (44.82%) moderate, and 3 (1.74%) severe reactions. Antibiotics were the primary causative agents, responsible for 28.16% of incidents.

Conclusion: The convergence of polypharmacy and underlying comorbidities significantly amplifies the complexity of adverse drug events. Strict pharmacovigilance and targeted medication reconciliation are critical for high-risk ICU populations.

Keywords: Adverse Drug Reactions (ADRs), Polypharmacy, Comorbidities, Intensive Care Unit (ICU), Critically Ill Patients, Hartwig's Severity Scale, Naranjo Causality Scale, Schumock-Thornton Preventability Scale, Medication Reconciliation, Pharmacovigilance, Critical Care Pharmacotherapy, Drug-Drug Interactions (DDIs), Antibiotics, Anticoagulants

Introduction

Access to safe and effective medication is a cornerstone of modern medical intervention, yet the intensive care unit (ICU) environment introduces unique pharmacokinetic and pharmacodynamic challenges. These challenges place critically ill patients at a disproportionately high risk for adverse drug reactions (ADRs). Patients in the ICU frequently present with compromised physiological states, including multi-organ dysfunction, altered metabolic pathways, and weakened immune defenses.

To manage acute life-threatening conditions, critical care protocols inherently rely on complex dosing strategies and the administration of multiple high-alert medications. This necessary reliance on

polypharmacy, coupled with pre-existing comorbid conditions, creates a compounding risk matrix for iatrogenic harm. While previous surveillance has established general ADR incidence, this analysis specifically quantifies how the simultaneous presence of extensive multiple drug therapy and baseline comorbidities drives the severity of these adverse events in the ICU setting.

Methodology

Study design and population This research was structured as a six-month prospective observational study within the ICU department of a tertiary care teaching hospital. The final sample size consisted of 174 patients who developed an ADR during their ICU admission. Patients presenting with drug abuse, intoxication, or overdose-related reactions were excluded, as were those unwilling to participate or those with insufficient medical records.

Data collection and clinical assessment Patient data, including demographics, past medical history, medication history, and social history, were prospectively collected via structured data entry formats. The primary dependent variable, ADR severity, was measured using the Modified Hartwig's criteria. The independent variables were quantified by grouping patients into multiple drug therapy brackets (5-10, 10-15, and >15 drugs) and categorizing the presence or absence of baseline comorbidities. Causality and preventability were additionally assessed using the Naranjo scale and the Schumock-Thornton scale, respectively.

Results

Demographics and baseline characteristics The cohort demonstrated a male predominance, with 107 (61.49%) male patients and 67 (38.51%) female patients. Age categorization revealed that the highest density of affected patients fell into the late adulthood demographic (51-65 years), accounting for 73 (40.95%) of the documented cases.

Comorbidities and polypharmacy variables

- A substantial proportion of the study population, 109 patients (62.64%), had established comorbidities upon ICU admission, compared to 65 patients (37.36%) without.
- The most prevalent concurrent conditions recorded included diabetes mellitus, cerebrovascular accidents, systemic hypertension, chronic obstructive pulmonary disease (COPD), and respiratory tract infections.
- Polypharmacy was deeply embedded in the patient regimens; 88 patients (50.57%) were prescribed between 10 and 15 medications.
- Furthermore, 32 patients (18.40%) were subjected to extensive polypharmacy, receiving more than 15 concurrent medications.
- Only 54 patients (31.03%) were maintained on a lower prescription threshold of 5 to 10 drugs.

Adverse drug reaction severity and implicated agents Application of Hartwig's severity assessment scale demonstrated that while 93 (53.44%) ADRs were classified as mild, a significant portion escalated to higher severity tiers. Specifically, 78 cases (44.82%) were classified as moderate and 3 cases (1.74%) as severe. The pharmaceutical classes most frequently associated with these adverse events were antibiotics (49 cases, 28.16%), anticoagulants (17 cases, 9.77%), anti-ulcer medications (17 cases, 9.77%), and anticonvulsants (15 cases, 8.62%).

Discussion

The findings of this study underscore the compounding vulnerability of ICU patients subject to intensive pharmacological intervention. The data indicates that advanced age, the presence of pre-existing comorbidities, and multiple drug therapy act as highly influential risk factors for the clinical manifestation of ADRs.

The physiological and pharmacological implications of these findings are paramount. Aging and chronic comorbid conditions such as systemic hypertension, COPD, or diabetes heavily influence normal metabolic and excretory pathways. Specifically, the impairment of renal and hepatic function inherently predisposes these patients to significant systemic complications when introduced to aggressive ICU pharmacotherapy. When this compromised baseline is exposed to polypharmacy—especially involving potent agents like broad-spectrum antibiotics and anticoagulants—the potential for severe, unanticipated drug-drug interactions and elevated systemic toxicity increases exponentially.

The clinical assessment scales applied in this study highlighted that 119 (68.39%) of the recorded adverse events were categorized as probably preventable. This finding indicates that the severity of reactions in multi-morbid, heavily medicated patients is not merely an inevitable consequence of critical illness, but a variable that can be actively managed and mitigated through rigorous clinical oversight.

Conclusion

The intersection of polypharmacy and underlying clinical comorbidities serves as a primary catalyst for escalating adverse drug reaction severity in the intensive care unit. As the number of concurrent medications increases alongside complex baseline diseases, standard pharmacokinetic predictability diminishes, leaving patients vulnerable to moderate and severe complications. To mitigate these risks and ensure patient safety, it is imperative to promote and implement standardized pharmacovigilance procedures. These must include aggressive medication reconciliation, active de-prescribing protocols where clinically viable, and strict, continuous monitoring of organ function throughout the duration of critical care therapy.

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