

ORIGINAL ARTICLE

Polypharmacy in critically ill children: A prospective cross-sectional study from a Tertiary PICU in Pakistan.

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ABSTRACT... Objective: To determine the frequency and patterns of polypharmacy from the PICU of a tertiary care children's hospital in Karachi, Pakistan. **Study Design:** Prospective Cross-sectional Observational study. **Setting:** PICU at Korangi Children Hospital, Karachi, Pakistan. **Period:** Three months: March–May 2025. **Methods:** All admitted children aged 1 month to 15 years were included. Patients with PICU stay of less than 48 hours were excluded. Data on clinico-demographic characteristics and prescribed medications were collected. Polypharmacy was defined as ≥ 5 medications, while hyper-polypharmacy was defined as ≥ 10 . Descriptive statistics were used to summarize demographics, prescribing patterns, and the frequency of polypharmacy. **Results:** Among 499 patients included in the analysis, polypharmacy was observed in 46.9% of patients, while 26.3% had hyper-polypharmacy. The median number of medications per patient per day was 7 (interquartile range 4-10). Anti-infective agents were the most prescribed class of drugs; ceftriaxone (41%) and meropenem (15%) were the most frequently used. Other commonly prescribed drug classes included sedatives, vasoactive agents, and corticosteroids. Most medications were administered intravenously. **Conclusion:** Polypharmacy is highly prevalent among critically ill pediatric patients in this setting. These findings highlight the need for rational prescribing practices, pharmacovigilance, and the integration of clinical pharmacists into PICU care to optimize medication safety.

Key words: Critical Illness, Drug Utilization, Polypharmacy, Pediatric Intensive Care Unit, Prescription Patterns.

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INTRODUCTION

Polypharmacy (PP) is defined as the concurrent use of five or more medications in adults and two or more distinct medications in the pediatric population.¹ However, multiple definitions have been described in the different studies.^{1,2} PP is a multifaceted concept, with its definition often influenced by factors such as the number and duration of medications, therapeutic classes involved, clinical appropriateness, underlying medical conditions, and the healthcare setting. These varying considerations have led to the emergence of multiple definitions across the literature. According to previous studies, reported PP prevalence ranges from approximately 42% to 74%, while hyperpolypharmacy (HP) ranges from about 32% to 47.5%.³

PP may alter drug metabolism and increase the risk of medication errors and drug–drug interactions, which have been extensively reviewed in the literature.^{4,5} PP in children is an emerging concern, particularly

due to limited pediatric-specific drug safety data and increased risk of adverse outcomes.³ Efforts to ensure safer pediatric prescribing practices have been reinforced through regulatory initiatives such as the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), which mandates the study of drug effects in children and promotes evidence-based medication use.⁶ Caring for acutely ill children in the PICU often necessitates multiple medications due to multi-organ dysfunction, which is common among critically ill patients, while sepsis and septic shock remain major contributors to the global burden of pediatric critical illness.⁷

Data on inpatient pediatric drug use, particularly in intensive care settings, remain limited.^{1,8} As healthcare systems in high-income countries increasingly focus on cost-effectiveness and efficient use of available resources, similar efforts are essential in low- and middle-income countries (LMICs), where resource constraints are often more

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pronounced. Few adult pharmacy research reports are available from Pakistan.^{9,10} This study aims to assess the frequency of PP in a tertiary care PICU in Karachi, Pakistan. The secondary objectives are to identify commonly prescribed drug classes and the clinical conditions associated with high medication use.

METHODS

This prospective cross-sectional observational study was conducted at the closed multidisciplinary PICU of the Children's Hospital, Korangi, Karachi, a tertiary care pediatric facility operating under the administrative framework of the Sindh Institute of Child Health and Neonatology (SICHN), a provincial government initiative of the Government of Sindh, Pakistan. The 28-bed PICU is equipped with advanced medical technology and is staffed by a dedicated team providing round-the-clock care, offering services free of charge to all admitted patients. The study was approved by the Institutional Review Board of the Sindh Institute of Child Health and Neonatology (SICHN) (IRB no. SICHN/IRB-008/2024). Written informed consent was obtained from parents/guardians of all enrolled patients. All data were anonymized. This study report has followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies.¹¹

The study population comprised all patients admitted to the PICU of the Sindh Institute of Child Health and Neonatology (SICHN), Karachi, during the study period (March–May 2025).

All patients admitted to the PICU aged 1 month to 15 years were included in the study, regardless of their admitting diagnosis or clinical condition. Patients with a PICU stay of less than 48 hours were excluded to ensure sufficient observation time and the reliability of data collection. Intravenous fluids, emergency, and PRN (as-needed) medications were excluded from the analysis.

The sample size was calculated using OpenEpi software version 3.01¹², assuming an expected prevalence of 45%, derived from a prior study conducted in similar pediatric intensive care settings.¹³ Using a 95% confidence interval and a

5% margin of error, the required sample size was estimated to be 499 participants. Consecutive eligible patients admitted during the study period were enrolled until the target sample size was achieved.

Study Definitions

Pediatric Polypharmacy

PP was defined as the concurrent use of five or more medications, a commonly used clinical threshold in clinical research, although definitions in pediatric populations vary.¹

Hyper-polypharmacy

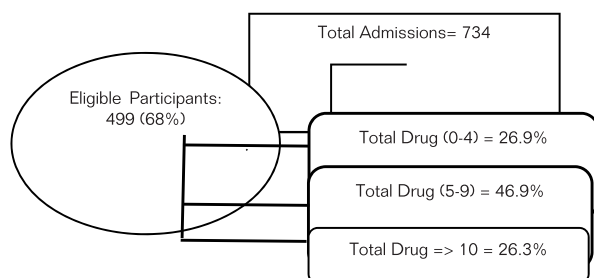
It refers to the use of more than ten distinct medications in a day.¹⁴

Patient demographics (age, gender), clinical parameters (diagnosis, comorbidities), and drug-related data were prospectively recorded using a structured electronic form. Pharmacological related variables included all medications administered for a duration exceeding 48 hours, specifying their route of administration and total duration of use. Descriptive statistics were used to summarize demographic, clinical, and prescribing data. Data were analyzed using SPSS version 26. IBM Corp. Continuous variables were presented as means with standard deviations (SD) or medians with interquartile ranges (IQR), while categorical variables were summarized as frequencies and percentages. In addition to statistical analysis, drug-related data were classified according to the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) system, with major categories including anti-infectives for systemic use (ATC J), nervous system drugs (ATC N), cardiovascular system drugs (ATC C), mineral supplements (ATC A12), and systemic hormonal preparations such as corticosteroids (ATC H02).¹⁵

RESULTS

This study included 499 (68%) patients admitted to the PICU. The minimum age was 1 month, while the maximum age was 168 months, with a median of 11 and an IQR of 7-24 months. Of the 499 patients, 288 (57.7%) were males, while 211 (42.3%) were females. The most common admitting diagnosis was respiratory disorders 30.7% followed by central nervous system (CNS) disorders (10.4%)

and cardiovascular (CVS) conditions (3.4%). The majority (55.5%) were admitted with diagnoses classified under the “Other” category. Detailed demographic characteristics are presented in Table-I.



Among 499 PICU admissions that were included in the drug exposure analysis, 134 (26.9%) received 0–4 drugs (non-polypharmacy), while 365 (73.2%) were exposed to PP. Specifically, 46.9% received 5–9 drugs, and 26.3% experienced HP (≥10 drugs). (Figure-1) Patients received a median of 6 drugs per day (interquartile range [IQR], 4–10), with values ranging from 1 to 21 (Figure-2). The intravenous (IV) route was the most common, accounting for approximately 70% of all prescriptions. (Table-I)

According to the WHO ATC classification, Anti-infectives accounted for the largest proportion of prescriptions (Figure-3). Nervous system drugs (analgesics/opioids, sedatives, and antiepileptics) constituted the next largest group. The remaining prescriptions were from cardiovascular system drugs and alimentary tract and metabolism drugs. Among nervous system agents, nalbuphine (22.6%) and levetiracetam (23.8%) were the most common opioids and antiepileptics respectively. In the cardiovascular group, epinephrine (25.3%) and furosemide (24.8%) were the most frequently prescribed, while zinc (32.5%) was the most common mineral supplement. Ceftriaxone (41%) and meropenem (15%) were the most frequently used antibiotics, followed by vancomycin (14%) and tazobactam–piperacillin (10%). The detailed distribution of drug classes is shown in Tables-II and III. The ten most prescribed antibiotics and drugs are shown in Figures-3 and 4, respectively.

A statistically significant association was observed between diagnostic categories (Respiratory, CVS, CNS, Others) and the utilization patterns of key

drugs ($p < 0.001$).

Ceftriaxone was the most frequently prescribed antibiotic across all groups, with the highest usage in patients with CNS (82.7%) and respiratory (73.9%) diagnoses. (Table-V)

FIGURE-1

Distribution of polypharmacy among PICU patients

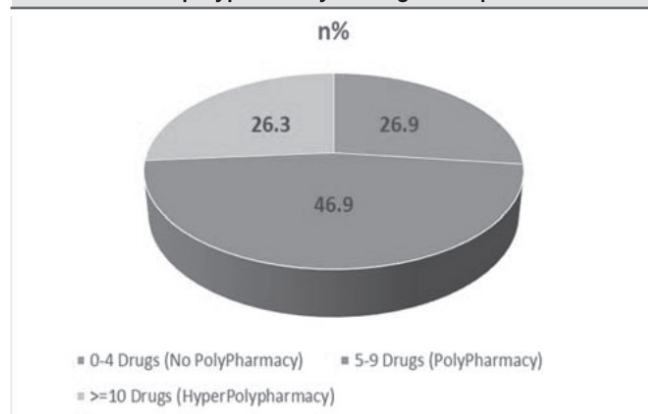


FIGURE-2

Number of drugs prescribed per patient per day

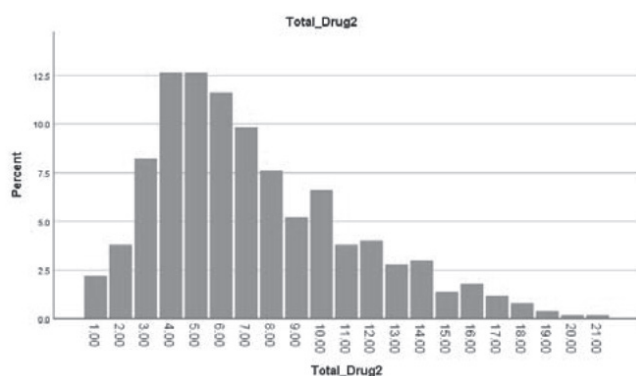


FIGURE-3

Distribution of prescribed antibiotics by ATC classification
Percentages are calculated from the total number of patients (n=499).

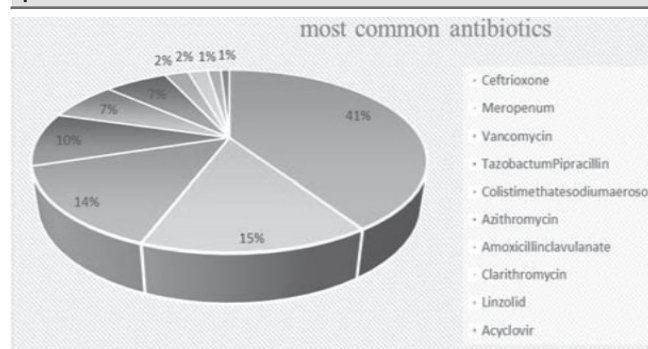
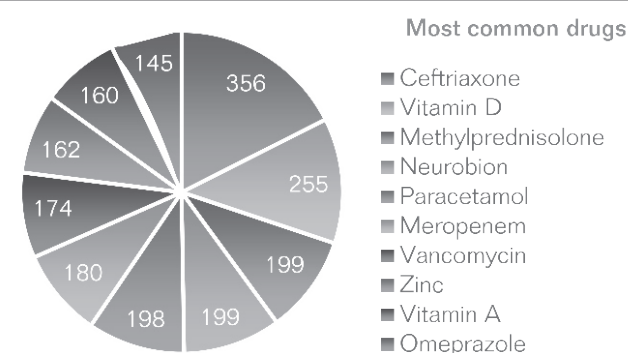


FIGURE-4

Most common drugs



Percentages are calculated from the total number of patients (n=499).

TABLE-I

Characteristics of study participants (n=499)

Gender	n%
Male	288(57.7)
Female	211(42.3)
Total	499(100)
Diagnosis	n%
Respiratory	153(30.7)
CVS	17(3.4)
CNS	52(10.4)
Other	277(55.5)
Weight Kg	
Weight Kg	7.6(5.6-11)
Min-Max	2-40
Age Months	
Median(IQR)	11(7-24)
Min-Max	1-168
Routes of Administration:	
Route of Adm (Total)	n%
IV	2647(72.7)
Oral	947(26)
IV+Oral	47(1.3)

DISCUSSION

The high prevalence of PP (46.9%), HP (26.3%), and the mean number of used drugs (7.3±3.9) in our study aligns with previous reports from PICU settings. Dai et al reported 89% and 68.2% of patients were exposed to PP and H-PP in the cohort of almost 60,000 PICU admissions from 42

children's hospitals of United States.¹⁶ Gaetani et al observed the frequency of PP in 71% of children admitted in a quaternary PICU in Canada.¹⁷ The mean number of drugs per day utilized varied from 5-9 drugs in a few published reports.^{16,17} There is a very significantly high rate of drug utilization in PICUs worldwide.^{16,17} PP has also been reported in children with neuro-psychiatric disorders and children with chronic complex conditions.¹⁸ Studies in general pediatric populations have also reported high rates of polypharmacy, with a substantial proportion of prescriptions associated with potential drug-drug interactions, underscoring the importance of medication review and stewardship.⁵

Infection-related illnesses, including sepsis and septic shock, are frequently admitted to the PICU worldwide.⁷ Anti-infectives for systemic use (ATC J), particularly antibiotics, are among the most frequently prescribed medications in pediatric critical care units.^{17,19} The high usage of ceftriaxone in our research reflects patterns observed in similar settings, where empiric broad-spectrum coverage is often prioritized over pathogen-directed therapy.^{20,21} Polypharmacy in PICU's increases the risk of potential drug-drug interactions.¹⁶ The need for advanced organ support in PICU patients inherently drives the administration of multiple complex drug therapies, increasing the risk of interactions and adverse events.^{16,22} Sedation, analgesia, and hemodynamic support must be used appropriately and with vigilant oversight during mechanical ventilation to maintain patient stability and comfort.²³ Opioid-based therapy predominated, with nalbuphine as the primary agent, while midazolam and dexmedetomidine were used less frequently.²³ These patterns are consistent with multicenter data, which show benzodiazepine-opioid combinations as the preferred first-line sedation strategy, with ketamine and dexmedetomidine used selectively.²³ The predominance of epinephrine as a vasoactive agent likely reflects its broad efficacy across cardiovascular, CNS, and respiratory support indications.²⁴ A need for the administration of vasoactive drugs during pediatric critical care transport has been documented in 14.5% of cases, highlighting the frequent need for hemodynamic support during inter-facility transfer.²⁵

TABLE-II

Medications characteristics

ATC Main Group	Subgroup	Drug (ATC Code)	n (%)
N – Nervous System	Analgesics, opioids	Nalbuphine (N02AF02)	113 (22.6%)
		Paracetamol (N02BE01)	198 (39.7%)
	Hypnotics and sedatives	Midazolam (N05CD08)	17 (3.4%)
		Dexmedetomidine (N05CM18)	11 (2.2%)
	Antiepileptics	Levetiracetam (N03AX14)	119 (23.8%)
		Lacosamide (N03AX18)	41 (8.2%)
		Phenobarbital (N03AA02)	32 (6.4%)
		Topiramate (N03AX11)	3 (0.6%)
		Phenytoin (N03AB02)	1 (0.2%)
C – Cardiovascular System	Adrenergic and dopaminergic agents	Epinephrine (C01CA24)	126 (25.3%)
		Dopamine (C01CA04)	35 (7%)
		Norepinephrine (C01CA03)	9 (1.8%)
		Milrinone (C01CE02)	17 (3.4%)
	Diuretics	Furosemide (C03CA01)	124 (24.8)
	ACE Inhibitors	Captopril (C09AA01)	17 (3.4%)
A – Alimentary Tract and Metabolism	Mineral supplements	Calcium Gluconate (A12AA20)	66 (17.3)
		Magnesium Sulphate (A12CC02)	58 (15.2)
		Potassium Chloride (A12BA01)	46 (12.1)
		Zinc (A12CB01)	162 (32.5%)
	Vitamins	Vitamin A (A11CA01)	160 (32.1%)
		Vitamin D (A11CC05)	255 (51.1%)
	Proton Pump Inhibitors	Omeprazole (A02BC01)	145 (29.1%)
	Serotonin (5-HT ₃) receptor antagonists	Ondansetron (A04AA01)	44 (8.8%)
H- Systemic hormonal preparations	Glucocorticoids	Hydrocortisone (H02AB09)	13 (2.6%)
		Methylprednisolone (H02AB04)	199 (39.9%)
		Prednisolone (H02AB06)	48 (9.6%)
		Dexamethasone (H02AB02)	87 (17.4%)
J -Anti-infectives for systemic use	Antibacterials	Ceftriaxone (J01DD04)	356 (71.3%)
		Linezolid (J01XX08)	17 (3.4%)
		Meropenem (J01DH02)	180 (36.1%)
		Vancomycin (J01XA01)	174 (34.9%)
		Piperacillin–Tazobactam (J01CR05)	116 (23.2%)
		Colistimethatesodiumaerosol (J01XB01)	87 (17.4%)
		Co amoxiclav(Amoxicillin Clavulanate) (J01CR02)	30 (6%)
		Azithromycin (J01FA10)	79 (15.8%)
	Antivirals	Acyclovir (J05AB01)	11 (2.2%)
P- Antiparasitic products, insecticides and repellents	Artemisinin and derivatives	Artesunate (P01BE03)	5 (1%)

TABLE-III

Distribution of commonly prescribed drugs according to system involvement
Percentages are calculated within each diagnostic subgroup (Respiratory n=93, CVS n=13, CNS n=33, Other n=242).

Drugs	Diagnosis			
	Respiratory Frequency (%)	CVS Frequency (%)	CNS Frequency (%)	Other Frequency (%)
Nalbuphine	22(14.4)	10(58.8)	17(32.7)	64(23.1)
Paracetamol	28.80%	47.10%	55.80%	39.70%
Phenobarbitone	6(3.9)	2(11.8)	15(28.8)	9(3.2)
Levetiracetam	8(5.2)	4(23.5)	46(88.5)	61(22)
Lacosamide	4(2.6)	-	18(34.6)	19(6.9)
Epinephrine	26(17)	11(64.7)	19(36.5)	70(25.3)
Dopamine	4(2.6)	7(41.2)	11(21.2)	13(4.7)
Milrinone	3(2)	8(47.1)	1(1.9)	5(1.8)
Captopril	6(3.9)	5(29.4)	2(3.8)	4(1.4)
Furosemide	33(21.6)	17(100)	11(21.2)	63(22.7)
MagSulphate	56(36.6)	4(23.5)	8(15.4)	29(10.5)
PotassiumChloride	5(3.3)	3(17.6)	9(17.3)	35(12.6)
CalciumGluconate	14(9.2)	8(47.1)	8(15.4)	48(17.3)
Hydrocortisone	3(2)	4(23.5)	1(1.9)	5(1.8)
Methylprednisolone	98(64.1)	12(70.6)	10(19.2)	79(28.5)
Prednisolone	25(16.3)	5(29.4)	4(7.7)	14(5.1)
Dexamethasone	14(9.2)	1(5.9)	35(67.3)	35(12.6)
Omeprazole	37(24.2)	10(58.8)	22(42.3)	75(27.1)
Ondansetron	12(7.8)	1(5.9)	5(9.6)	26(9.4)

Electrolyte and mineral disturbances are common in critical illness, explaining the frequent use of mineral supplements (ATC A12) such as calcium gluconate, magnesium sulfate, and potassium chloride.¹⁵ These agents are essential for correcting metabolic imbalances and preventing complications in critically ill children.¹⁴ Peripheral administration of vasoactive drugs, though feasible, requires central line conversion in a subset of patients, particularly at higher doses, highlighting practical considerations in resource-limited PICUs.²⁴ In our study, methylprednisolone was the most frequently used corticosteroid, primarily for respiratory diagnoses, followed by dexamethasone, prednisolone, and hydrocortisone. These drugs fall under systemic hormonal preparations (ATC H02). This pattern contrasts with report on use of corticosteroids in PICUs, where dexamethasone is often the preferred agent, used in approximately one-third of critically ill children.²⁶ The variation may reflect local prescribing practices, availability, or patient characteristics, emphasizing that corticosteroid selection should

be guided by both clinical indications and evidence-based protocols.²⁶ In a cohort of pediatric septic shock cases, corticosteroid administration was associated with a 42% reduction in the likelihood of prolonged intensive care stays exceeding six days.²⁷ Intravenous administration predominated, reflecting the need for rapid therapeutic effects and highlighting the importance of line management and vigilance for potential complications in the PICU, like other reports.^{20,21}

LIMITATIONS

This study has several limitations. The single-center design may restrict the applicability of our findings to other PICUs with varying clinical practices and resource availability. Most patients had short-term admissions, and a limited spectrum of local prevalence of diseases. Those with complex chronic conditions were excluded, potentially underestimating the prevalence, as chronic patients often require multiple concurrent medications. The absence of advanced therapies in our setting

may have influenced medication choices, limiting the applicability of the findings to resource-rich PICUs. The study focused only on scheduled medications used during the hospital stay and excluded intravenous fluids and emergency drugs. We did not analyze drug-drug interactions, adverse events of prescribed drugs, and this study did not assess whether the prescribing was appropriate or inappropriate in this study. Without evaluating PICU length of stay or clinical outcomes, the impact of PP on patient prognosis remains unclear. Despite these limitations, a high prevalence of PP was observed. The absence of a clinical pharmacist likely limited real-time assessment of potential drug interactions, highlighting the need for integrated pharmacy services in PICUs.

To the best of our knowledge, this is the first epidemiological study from a resource-constrained setting, assessing the prevalence of PP and the pattern of drug utilization in critically ill pediatric patients from the PICU. Further multicenter studies are required to better understand prescribing patterns, rational drug use, and the role of pharmacy services in improving medication safety in critically ill pediatric populations.

CONCLUSION

This study demonstrates a high prevalence of PP, including HP, in a tertiary-care PICU of public-sector children in Pakistan. The findings underscore the urgent need for rational prescribing practices, strengthened pharmacovigilance, and integration of clinical pharmacy services in critical care. Multicenter studies are warranted to evaluate prescribing appropriateness, drug-drug interactions, and strategies to optimize medication safety in critically ill children.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Khizra Saleem: Conceptualization, Literature review, drafting.
2	Tasmina Panhwer: Contributed to writing and editing the manuscript.
3	Muhammad Waqas: Curated patient data.
4	Kanza Shakir: Critical revisions.
5	Aqsa Majeed: Interpreted data.
6	Anwar ul Haque: Supervised the project, Critical revisions.