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Drug utilization patterns and drug-related problems in pediatric bacterial meningitis: A prospective observational study from a tertiary care hospital in Pakistan

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Abstract

Background: Bacterial meningitis is a neurological emergency associated with substantial mortality and long-term disability in children, particularly in low- and middle-income countries where ward-based clinical pharmacy oversight is scarce. The multidrug regimens required for its management create ample opportunity for drug-related problems (DRPs).

Objective: To evaluate the rationality of pharmacotherapy, characterize DRPs and describe antimicrobial prescribing patterns in children hospitalized with bacterial meningitis at a tertiary care hospital.

Methods: A prospective, observational, single-centre study was undertaken over 90 days in the pediatric ward of Lady Reading Hospital, Peshawar, Pakistan. Twenty consecutive children aged 0–12 years with clinically and/or laboratory-confirmed bacterial meningitis were assessed for demographic and clinical characteristics, prescribed medicines and DRPs (drug–drug interactions, contraindications, adverse drug reactions, dosing and route errors) using a structured proforma. Prescriptions were audited against standard pediatric meningitis treatment guidelines. Data were summarized descriptively and reported in accordance with the STROBE statement.

Results: Fourteen children (70%) were male and 8 (40%) were infants aged under 2 years. Guideline-concordant therapy was documented in 17 patients (85%). Ceftriaxone was the most frequently prescribed antibiotic (11; 55%), followed by meropenem (5; 25%), ampicillin (4; 20%) and ciprofloxacin (2; 10%); vancomycin (12; 60%) and aciclovir (5; 25%) were used adjunctively, and dexamethasone in 19 (95%). DRPs were identified in 5 patients (25%): drug–drug interactions in 2 (aciclovir–vancomycin; phenytoin–dexamethasone), adverse drug reactions in 2 and a contraindication in 1. Comorbidity was present in 16 (80%), most commonly epilepsy (13; 65%). No deaths occurred and length of stay was 5–9 days.

Conclusion: Although most children received rational pharmacotherapy, DRPs affected one quarter of patients. These findings underscore the value of clinical pharmacy services, standardized treatment protocols and systematic interaction screening in pediatric wards in resource-limited settings.

1. Introduction

Acute bacterial meningitis remains one of the most serious infectious emergencies of childhood, capable of causing death within hours of onset and leaving survivors with permanent neurological sequelae such as sensorineural hearing loss, epilepsy, motor deficit and cognitive impairment.[1,2] Despite advances in antimicrobial chemotherapy, conjugate vaccination and neurocritical care, the disease continues to impose a disproportionate burden in low- and middle-income countries (LMICs), where delayed presentation, constrained diagnostic capacity and limited clinical pharmacy support all contribute to preventable morbidity and mortality.[2,3]

The microbiological etiology of childhood bacterial meningitis is strongly age-dependent, with Streptococcus pneumonia, Neisseria meningitidis and Haemophilus influenza type b predominating beyond the neonatal period.[3,4] Because outcome is tightly coupled to the timeliness and appropriateness of empirical therapy, guidelines emphasize the prompt administration of an agent with reliable cerebrospinal fluid (CSF) penetration, chosen according to the patient's age, the likely pathogens and local resistance epidemiology.[5] Every hour of delay to effective antimicrobial therapy is associated with a measurable increase in mortality and neurological disability.[5,6]

Contemporary meningitis care is rarely confined to a single antibiotic. Adjunctive dexamethasone, anticonvulsants, osmotic agents and empirical antiviral cover are frequently co-prescribed to address seizures, cerebral oedema and diagnostic uncertainty.[6,7] While often clinically necessary, these complex regimens broaden the surface for drug-related problems (DRPs) - drug–drug interactions, inappropriate dosing, adverse drug reactions and contraindicated prescribing - which constitute a recognized and largely preventable source of iatrogenic harm in hospitalized children.[7,8]

Although the epidemiology of DRPs is well characterized in high-income settings, comparatively few studies have examined prescribing quality and drug utilization in pediatric meningitis within LMICs, where practice may diverge from international standards owing to formulary limitations, heavy clinical workloads and the near-absence of ward-based clinical pharmacy services.[8,9] In such environments, structured medication review is frequently unavailable, allowing interactions and dosing errors to proceed undetected until they manifest clinically.[9,10]

Pakistan, and the province of Khyber Pakhtunkhwa in particular, carries a heavy burden of childhood central nervous system infection, yet local data on the rationality of meningitis pharmacotherapy remain scarce. To address this gap, we prospectively evaluated the rationality of prescribing, characterized DRPs and described antimicrobial utilization among children admitted with bacterial meningitis to a large tertiary care hospital. We hypothesized that, despite broadly guideline-concordant antibiotic selection, a clinically important proportion of patients would harbour preventable DRPs attributable to the absence of routine clinical pharmacy review.

The specific objectives were to:

1. Document the demographic and clinical characteristics of children admitted with bacterial meningitis;
2. Audit prescribed medicines against standard paediatric meningitis treatment guidelines;
3. Identify and classify drug-related problems (drug–drug interactions, contraindications, adverse drug reactions and dosing or route errors);
4. Describe antibiotic prescribing patterns and treatment durations; and
5. Explore the relationship between comorbidity and prescribing complexity.

2. Materials and Methods

2.1. Study design and setting

A prospective, observational, single-centre study was conducted in the pediatric ward of Lady Reading Hospital, Peshawar - a 1,200-bed tertiary care teaching hospital serving Peshawar city and the wider Khyber Pakhtunkhwa province, and receiving referrals from surrounding districts. The study is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for cross-sectional/observational research.

2.2. Study period, population and eligibility

Over a continuous 90-day period, all consecutively admitted children aged 0–12 years with bacterial meningitis - diagnosed clinically and supported by cerebrospinal fluid (CSF) examination and/or positive blood culture - were eligible for inclusion. Patients with incomplete medical records, or those transferred to another facility before completing the treatment course, were excluded.[10]

2.3. Sample size

Given the descriptive, audit-based objectives and the fixed enrolment window on a single ward, a formal a priori sample-size calculation was not undertaken; instead, every eligible patient presenting during the study period was enrolled, yielding a final analytic sample of 20 children. The resulting sample is modest and is treated as a limitation (Section 4.6).

2.4. Data collection and variables

For each patient, data were abstracted from medical records and medication charts onto a standardized, pilot-checked proforma. Variables comprised: demographic and clinical data (age, sex, geographic origin, presenting features, confirmed diagnosis and causative organism where available, comorbidities, laboratory investigations including complete blood count and CSF analysis where performed, length of stay and clinical outcome); and medication data (every prescribed medicine by generic and proprietary name, dose, frequency, route and duration; timing of the first antibiotic dose relative to admission; and all adjunctive therapies including anticonvulsants, osmotic agents and corticosteroids).

2.5. Operational definitions and DRP assessment

Each regimen was screened systematically for the following categories of drug-related problem: overdose (dose above the recommended maximum); sub-therapeutic dose (below the recommended range); wrong route; clinically significant drug-drug interaction (pharmacokinetic or pharmacodynamics); adverse drug reaction; contraindication (a medicine prescribed despite a patient factor precluding its use); and inappropriate renal or hepatic dose adjustment. Rational therapy was defined a priori as pharmacotherapy consistent with standard guidelines - appropriate to the patient's age and the suspected or confirmed pathogen, at correct dose and interval, and with appropriate monitoring. Irrational therapy denoted prescriptions that deviated from guidelines, contained a significant DRP, or lacked documented justification for the deviation.

2.6. Guideline-concordance audit

Prescribed regimens were audited against standard pediatric bacterial meningitis guidelines with respect to age band (neonate; infant 1–3 months; child 3 months–7 years; older child), the identified or suspected pathogen, the correct agent, dose and dosing interval, the recommended duration of

therapy (typically 7–10 days), and the indicated use of adjunctive dexamethasone, anticonvulsants and osmotic agents.[5,11]

2.7. Bias and data quality

A single trained abstractor completed all proformas, cross-checking each entry against the primary chart to reduce transcription error; ambiguous entries were resolved by re-inspection of the source record. As an observational audit, data collection was not blinded to treatment decisions, and this is acknowledged among the limitations.

2.8. Statistical analysis

Analysis was descriptive, in keeping with the study objectives and sample size. Categorical variables (sex, age band, comorbidity, DRP category, and rational vs. irrational therapy) are presented as frequencies and percentages, and continuous variables as means with standard deviations or as medians with ranges, as appropriate. Denominators are stated where available-case reporting was used for incompletely documented fields. Data were tabulated and summarized using standard spreadsheet software; no inferential testing was performed.

2.9. Ethical considerations

The study was conducted as an observational clinical-pharmacy audit of routinely collected, de-identified medical-record data; no intervention was administered and no directly identifying patient information was used in analysis. In accordance with institutional policy governing service evaluation and audit, formal ethics-committee review was not mandated. Confidentiality was preserved throughout by the use of medical-record numbers in place of patient names.

3. Results

3.1. Demographic and clinical characteristics

Twenty children with bacterial meningitis were evaluated during the study period (Table 1). Fourteen (70%) were male and 6 (30%) female, a male predominance consistent with the recognized epidemiology of invasive bacterial disease. Eight children (40%) were infants aged under 2 years and 12 (60%) were older children aged 2–12 years. Eleven patients (55%) originated from Peshawar city and 9 (45%) were referred from surrounding districts, reflecting the hospital's tertiary referral role.[3]

Presenting features were typical of meningitis: fever was universal (100%), followed by headache (85%), neck stiffness (80%) and irritability or altered consciousness (75%); four children (20%) presented with seizures or in a critical condition requiring immediate stabilization. Comorbidity was present in 16 patients (80%), most frequently epilepsy (13; 65%) and pneumonia (6; 30%); some children had more than one comorbid condition (Table 1).

Table 1. Demographic and clinical characteristics of the study population (n = 20).

Characteristic	n	%
Sex		
Male	14	70
Female	6	30
Age band		
Infants (< 2 years)	8	40
Children (2–12 years)	12	60
Geographic origin		
Local (Peshawar)	11	55
Referred (other districts)	9	45
Comorbidity[a]		
Epilepsy	13	65
Pneumonia	6	30
None	4	20
Clinical presentation[a]		
Fever	20	100
Headache	17	85
Neck stiffness	16	80
Irritability / altered consciousness	15	75
Seizures / critical condition	4	20

[a] *Categories are not mutually exclusive; some patients had more than one comorbidity or clinical feature, so percentages within these groupings may exceed 100%.*

3.2. Rationality of pharmacotherapy

Seventeen children (85%) received rational, guideline-concordant pharmacotherapy, characterized by age-appropriate empirical antibiotic selection, correct weight-based dosing, appropriate parenteral administration, adequate treatment duration (≥ 7 days) and judicious adjunctive therapy without a significant DRP. Three children (15%) received irrational therapy, in which prescriptions contained a significant drug–drug interaction without documented justification, or a sub-optimal antimicrobial choice was made despite an available safer alternative (Table 4).

3.3. Antibiotic prescribing patterns

Ceftriaxone was the most frequently prescribed antibiotic, administered to 11 children (55%) as first-line empirical therapy - consistent with guideline recommendations for a third-generation cephalosporin on account of its excellent CSF penetration and broad-spectrum activity (Table 2, Figure 1). Meropenem was used in 5 children (25%), typically where cephalosporin resistance was suspected or a beta-lactam allergy was documented; ampicillin in 4 (20%), chiefly for Listeria monocytogenes cover in infants; and ciprofloxacin in 2 (10%) as an alternative for children unable to tolerate beta-lactams.[12,13]

Vancomycin was co-prescribed in 12 children (60%), a rational response to the rising prevalence of penicillin-non-susceptible S. pneumonia and a standard component of empirical combination therapy given its CSF penetration across inflamed meninges.[12] Empirical acyclovir was given to 5 children (25%) as cover for herpes simplex encephalitis pending its exclusion. Notably, no aminoglycoside was used as meningitis monotherapy, in keeping with current best practice given the poor CSF penetration of this class.[13]

Table 2. Antimicrobial prescribing patterns (n = 20).

Antimicrobial agent	Frequency	%[a]
First-line / definitive antibacterials		
Ceftriaxone	11	55
Meropenem	5	25
Ampicillin	4	20
Ciprofloxacin	2	10
Adjunctive antimicrobials		

Antimicrobial agent	Frequency	%[a]
Vancomycin	12	60
Aciclovir	5	25

[a] *Percentages are of all 20 patients and sum to more than 100% because most children received combination therapy.*

3.4. Adjunctive medication and comorbidity management

Dexamethasone was prescribed to 19 children (95%), reflecting evidence-based practice supporting corticosteroid administration with, or shortly before, the first antibiotic dose to reduce neurological sequelae; doses and durations were generally appropriate (typically 10 mg daily in divided doses for 2–4 days).[11] Anticonvulsants were used in 15 children (75%) — phenytoin in 8, valproate in 4 and levetiracetam in 3 - for seizure prophylaxis or the treatment of breakthrough seizures, the heterogeneous selection reflecting physician preference rather than a standardised protocol. Osmotic therapy with mannitol (typically 20%, 200 mL once daily for 3–5 days) was given to 9 children (45%) for cerebral oedema.[14]

3.5. Drug-related problems

At least one DRP was identified in 5 children (25%) (Table 3). Drug–drug interactions were documented in 2 patients (10%): a clinically significant aciclovir-vancomycin combination, in which additive nephrotoxicity and reduced vancomycin clearance warrant renal monitoring; and a phenytoin–dexamethasone combination, in which corticosteroid-mediated enzyme induction can lower phenytoin exposure and jeopardize seizure control.[15] Adverse drug reactions occurred in 2 patients (10%) - blurred vision (attributed to phenytoin) and nausea with vomiting - both mild and not requiring discontinuation. A contraindication was identified in 1 patient (5%). No overdose, sub-therapeutic dosing or wrong-route error was detected, and all patients received appropriate intravenous therapy.

Table 3. Drug-related problems identified (n = 20).

Drug-related problem	n	%	Description
Drug–drug interactions	2	10	Aciclovir–vancomycin (×1); phenytoin–dexamethasone (×1)
Adverse drug reactions	2	10	Blurred vision (×1); nausea and vomiting (×1)

Drug-related problem	n	%	Description
Contraindication	1	5	Medicine prescribed despite a documented contraindication
Overdose	0	0	—
Sub-therapeutic dose	0	0	—
Wrong route	0	0	All intravenous — appropriate for meningitis
Patients with ≥ 1 DRP	**5**	**25**	—

DRP, drug-related problem. Counts are per patient; the two interaction types were each observed in a single patient.

3.6. Outcomes and dosing appropriateness

All 20 children completed their treatment course with documented clinical improvement, and no in-hospital deaths occurred; the length of stay ranged from 5 to 9 days (mean 7.2 days). Long-term neurological outcomes beyond discharge were not systematically followed. Renal and hepatic dose adjustment was not required, as no patient had significant organ dysfunction on available biochemistry, and all prescribed doses fell within the recommended ranges for age and weight (Table 4).

Table 4. Overall rationality of pharmacotherapy (n = 20).

Category	n	%
Rational (guideline-concordant) therapy	17	85
Irrational (guideline-discordant) therapy	3	15
Total	**20**	**100**

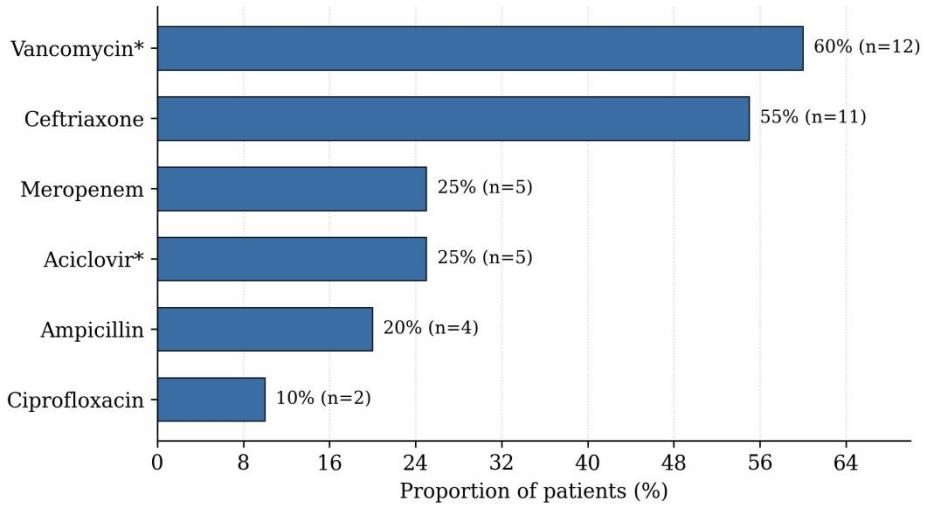

Figure 1. Antimicrobial utilisation in children hospitalised with bacterial meningitis (n = 20). Bars show the proportion of patients receiving each agent; asterisks denote adjunctive antimicrobials (vancomycin, aciclovir). Proportions sum to more than 100% because most patients received combination therapy.

4. Discussion

In this prospective audit of paediatric bacterial meningitis at a Pakistani tertiary care hospital, most children (85%) received guideline-concordant pharmacotherapy, yet one quarter harboured a drug-related problem. To our knowledge, this is among the first systematic evaluations of prescribing quality and medication safety in childhood meningitis from a resource-limited South Asian setting, and it offers a practical benchmark for quality-improvement efforts.

4.1. Rational drug use

The 85% concordance rate indicates that prescribers possessed sound working knowledge of meningitis treatment principles — age-appropriate agent selection, correct weight-based dosing, parenteral administration and adequate duration. Nevertheless, the 15% of prescriptions that deviated from guidelines, and the interactions detected within otherwise appropriate regimens, indicate clear scope for improvement through structured pharmacy oversight and protocolised prescribing.[8]

4.2. Antibiotic selection

The predominance of ceftriaxone (55%) mirrors international recommendations that position third-generation cephalosporins as empirical agents of choice, given their CSF penetration and broad activity against the principal meningeal pathogens.[5] Adjunctive vancomycin in 60% represents an appropriately conservative response to penicillin non-susceptibility,[12] while empirical aciclovir in 25% reflects prudent cover for a treatable but potentially fatal herpetic aetiology. Reserved use of meropenem, ampicillin and ciprofloxacin, and the complete avoidance of aminoglycoside monotherapy, are all consistent with contemporary practice.[9,13]

4.3. Drug-related problems and medication safety

The two interactions identified are clinically meaningful. Concurrent acyclovir and vancomycin -both renally eliminated - can act additively to precipitate acute kidney injury, mandating baseline and serial renal monitoring, adequate hydration and dose review should function decline. Dexamethasone, a potent inducer of hepatic CYP3A4 and CYP2C9, accelerates phenytoin metabolism and can reduce its concentration substantially, threatening seizure control in a population already at heightened risk; therapeutic-drug monitoring, dose adjustment, or a less interaction-prone agent such as levetiracetam are reasonable mitigations.[15] Although neither interaction produced documented harm in this cohort, both were preventable and would ordinarily be intercepted by routine clinical-pharmacy review - a service largely absent from many LMIC pediatric wards.[7,8]

4.4. Comorbidity and prescribing complexity

The high prevalence of comorbidity (80%), dominated by epilepsy (65%), materially complicated prescribing: background anticonvulsant therapy must be reconciled with meningitis treatment, and meningitis itself lowers the seizure threshold, so interactions between antiepileptic and adjunctive agents assume clinical importance. Pneumonia co-infection (30%) is consistent with the respiratory origin of many meningeal pathogens and necessitated dual cover, again enlarging the potential for interaction.

4.5. Adjunctive therapy

Near-universal dexamethasone use (95%) aligns with trial evidence that early corticosteroid reduces neurological sequelae, notably hearing loss, in

childhood bacterial meningitis, and signals good guideline awareness.[11] The heterogeneous choice of anticonvulsant, by contrast, suggests an opportunity to standardize seizure management, while appropriate mannitol use (45%) reflects sound handling of raised intracranial pressure.[14]

4.6. Strengths and limitations

Strengths include the prospective design, the use of a standardized proforma and the explicit, guideline-anchored definitions of rationality and DRPs. Several limitations temper interpretation. First, the sample of 20 patients from a single centre limits precision and generalizability, and no inferential testing was appropriate. Second, the observational design and unblinded, single-abstractor data collection may introduce information bias. Third, long-term neurological outcomes were not followed, so the downstream clinical impact of the identified DRPs cannot be quantified. Fourth, CSF and culture data were incomplete, constraining confirmation of etiology and of susceptibility-guided appropriateness. Finally, the absence of a comparator regimen precludes formal benchmarking of prescribing quality. These constraints define a clear agenda for larger, multicenter work.

4.7. Comparison with the literature

The 85% rate of appropriate prescribing sits within the 70–90% range reported by pediatric medication-appropriateness studies across varied settings,[8] while the 25% DRP frequency is congruent with estimates that 5–25% of hospitalized patients experience a preventable adverse drug event.[6] The ceftriaxone-led, vancomycin-supported pattern accords with international guidance,[5,9] and the specific interactions detected add to a growing literature on medication-safety hazards in meningitis therapy that argues for systematic interaction screening.[15]

4.8. Implications for practice and policy

The findings make a concrete case for embedding clinical pharmacists in pediatric wards, where prospective medication review could intercept the interactions documented here and lift concordance towards ceiling. Standardized, age-banded meningitis protocols would reduce prescribing variability; computerized order entry with interaction alerts would provide an automated safety net; and targeted prescriber education, interdisciplinary rounds and structured efficacy- and safety-monitoring would consolidate these gains.

5. Conclusion

Most children hospitalized with bacterial meningitis at this tertiary centre received rational, guideline-concordant pharmacotherapy, and empirical antibiotic selection was broadly sound. However, drug-related problems affected one quarter of patients, including two clinically important drug–drug interactions. Integrating clinical pharmacy services, standardized treatment protocols and electronic interaction screening into pediatric care offers a realistic route to fewer preventable adverse events and safer meningitis treatment in resource-limited settings. Larger multicenter studies with linked outcome data are needed to confirm these observations and to quantify the clinical benefit of pharmacist-led review.

6. Recommendations

- Clinical: Institute prospective clinical-pharmacist review of every paediatric meningitis regimen, with mandatory renal monitoring when nephrotoxic combinations (e.g. aciclovir–vancomycin) are unavoidable.
- Research: Extend this work to adequately powered, multicentre cohorts with documented aetiology, susceptibility data and post-discharge neurological follow-up.
- Hospital: Adopt standardised, age-banded meningitis order sets and deploy computerised prescriber order entry with automated drug-interaction alerts.
- Educational: Deliver targeted prescriber and trainee education on paediatric meningitis guidelines, dosing and high-risk interactions.
- Policy: Support the establishment and reimbursement of ward-based clinical pharmacy services within national paediatric-care and antimicrobial-stewardship frameworks.

Declarations

Ethics approval and consent to participate. This observational clinical-pharmacy audit used routinely collected, de-identified medical-record data and administered no intervention; under institutional policy for service evaluation/audit, formal ethics-committee review was not required, and the requirement for individual informed consent was waived. Confidentiality was maintained using medical-record numbers.

Consent for publication. Not applicable; no individually identifiable patient data are reported.

Availability of data and materials. The de-identified datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests.

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