Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 11 July 2026
Revised 26 Aug 2026
Accepted 14 Sep 2026

Natural Resources for Human Health 2026, Vol. 6 (20s): 60–78

KEYWORDS:
antimicrobial resistance; Pakistan; hospital antimicrobial use; antimicrobial stewardship; laboratory surveillance; secondary-data synthesis.

Antimicrobial Resistance and Antibiotic Prescribing Patterns in Hospitalized Patients: A Multicenter Assessment of Clinical and Epidemiological Determinants

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ABSTRACT:

Background: National antimicrobial resistance (AMR) surveillance and hospital prescribing studies from Pakistan give complementary evidence, but the two aren't linked.

Objective: To describe organism- and antibiotic-specific resistance and inpatient antimicrobial use in Pakistan, and to show where comparisons across published sources break down.

Methods: We pulled together published aggregate findings from the national AMR surveillance report of Pakistan's National Institutes of Health (NIH) for 2021–2022 and from selected hospital studies found through targeted literature searches. We kept each study's population, numerators, denominators, and definitions as originally reported. This isn't a comprehensive systematic review or a linked patient-level analysis.

Results: The NIH reported 132,269 nonduplicate isolates from 19 laboratories in 2021 and 229,617 from 26 laboratories in 2022. Because participation changed, the increase can't be read as a trend in incidence. In 2022, the source reported ceftriaxone resistance in 74.6% of 77,998 tested E. coli isolates and 66.4% of 26,087 tested K. pneumoniae isolates. Separately, a point-prevalence survey in 13 Punjab hospitals found antimicrobial exposure in 1,516 of 1,954 inpatients (77.6%; Wilson 95% CI, 75.7–79.4%, which we calculated independently).

Conclusion: Published resistance and hospital antimicrobial-use estimates point to

separate priorities for surveillance and stewardship. Because the sources aren't linked, they can't establish patient-level links between prescribing and resistance, causal effects, or adjusted clinical determinants.

1. INTRODUCTION

Bacterial antimicrobial resistance threatens effective empirical therapy and makes both healthcare-associated and community-onset infections harder to manage. The 2019 global burden analysis estimated 1.27 million deaths attributable to bacterial resistance, and the 2021 update estimated 1.14 million [7,8]. These modeled global figures give useful context, but they can't be compared directly with laboratory resistance percentages from Pakistan.

Pakistan's National Institutes of Health (NIH) coordinates the Pakistan Antimicrobial Resistance Surveillance System, which draws on participating laboratories to describe resistance among tested isolates [1,5]. Coverage and clinical case mix both shape these summaries. Hospital point-prevalence studies of antibiotic use are a different kind of evidence. They measure exposure on a single survey day, not the incidence of resistant infection [3]. We keep the two sources apart and ask what can be learned from them without inventing a linked multicenter cohort.

Resistance data also have to be read alongside the conditions under which cultures are taken and antibiotics prescribed. Patients in tertiary hospitals may have complex infections, earlier antimicrobial exposure, or referrals from other facilities. Routine laboratory submissions, meanwhile, tend to come from patients whose clinicians asked for a culture. So the share of tested isolates classed as resistant is an important surveillance measure, but it isn't the prevalence of resistant infection among all hospitalized patients. That distinction matters when national findings are turned into clinical or public-health recommendations [1,5].

Differences in the organisms and antibiotics tested complicate things further. A resistance percentage only means something when it's tied to a specific species, drug, specimen context, and tested-isolate denominator. The number of E. coli isolates tested against a third-generation cephalosporin, for instance, can differ a lot from the number tested against a carbapenem. Comparing drugs, reporting periods, or laboratories therefore means paying attention to testing coverage, isolate selection, and changes in participation. More reported isolates don't, on their own, mean more infection or more resistance [1,5].

Antibiotic utilization studies speak to a related but separate question. Point-prevalence surveys can estimate the share of inpatients on antimicrobial treatment at one moment and describe common agents, indications, and prophylaxis practices. For example, the multicenter Punjab survey showed extensive antimicrobial use and flagged prolonged surgical prophylaxis as a stewardship priority [3]. Still, a point-prevalence estimate isn't the same as the share of admissions exposed over a whole hospital stay, and a drug's share of prescriptions shouldn't be mistaken for the share of patients receiving it. These measurement differences matter most when findings from different hospitals and provinces are compared.

Antimicrobial use and resistance are clearly linked, biologically and clinically, but you can't quantify that link by putting independent surveillance and prescribing studies side by side. The national laboratory network and the published inpatient surveys differ in observation period, geographic coverage, sampling method, and unit of analysis. Without linked patient-level prescribing histories, culture results, and clinical characteristics, we can't derive individual exposure–resistance associations or adjusted estimates of clinical determinants. A descriptive synthesis can still pick out recurring concerns and show which questions need better integrated data systems.

In this study, we synthesize Pakistan's published national laboratory surveillance results and selected hospital prescribing evidence, keeping each source's own denominators in view. We aim to describe the reported organism–antibiotic resistance patterns, summarize prescribing and stewardship findings, point out key differences in measurement and coverage, and outline priorities for better surveillance and future patient-linked research. This isn't a new multicenter patient cohort, and we don't try to estimate causal effects of prescribing on resistance.

2. LITERATURE REVIEW

2.1 International burden and surveillance

Global burden estimates list E. coli, S. aureus, K. pneumoniae, A. baumannii and P. aeruginosa among the leading bacterial resistance threats [7,8]. WHO GLASS recommends pathogen- and drug-specific denominators, laboratory quality assurance, consistent case definitions and attention to how representative surveillance is [2,9]. The share of patients cultured and the mix of specimens can change reported resistance even when the underlying epidemiology hasn't changed.

2.2 Antibiotic use and stewardship

The WHO AWaRe framework sorts antibiotics into Access, Watch and Reserve groups to guide stewardship priorities [10]. WHO's 2025 GLASS antibiotic-use report points to variation between countries and a continued reliance on Watch agents in many settings [11]. Consumption data, point-prevalence prescribing, and administration records use different denominators, so they can't be swapped for one another. The Punjab survey gives a patient-based measure of antibiotic exposure along with prescription shares, but it doesn't establish whether every course was appropriate for its indication [3].

2.3 Pakistan hospital and surveillance evidence

The NIH national report summarizes resistance in sentinel laboratory submissions. The Punjab prescribing survey by Saleem and colleagues, by contrast, covers 13 hospitals and 1,954 surveyed inpatients [1,3]. A separate 13-hospital Punjab survey of healthcare-associated infections (HAI) found 130 symptomatic cases among 1,553 inpatients [6]. That estimate reflects infection symptoms, not microbiological resistance. These sources complement each other but aren't interchangeable. Reports from other provinces need documented eligibility and verified full-text extraction before we can add them as independent quantitative cohorts.

Hospital point-prevalence evidence from across Pakistan goes beyond the original Punjab survey. Ambreen and colleagues surveyed 14 tertiary hospitals using WHO methodology and reported roughly 75% antibiotic use, with third-generation cephalosporins a prominent class [12]. A separate survey of 837 inpatients in six public hospitals reported 78.5% antibiotic exposure, with ceftriaxone and metronidazole among the commonly used agents [13]. These are separate surveys, not one combined cohort. Hospitals, dates, indications, and units of analysis all differ, so the results can't be pooled without further appraisal.

Single-institution studies add detail on prescribing practice. A point-prevalence study at a Karachi tertiary-care hospital examined 300 inpatients and found antimicrobial exposure in 67%, with surgical prophylaxis a frequent indication [14]. A retrospective analysis in Islamabad reviewed 1,012 eligible inpatient files [18], and a point-prevalence survey at PIMS reported antibiotic use in 210 of 271 patients [24]. Studies like these support comparisons within a setting but are not nationally representative estimates. Pakistan-specific syntheses and stewardship evaluations suggest that resistance surveillance should go hand in hand with interventions aimed at prescription review, diagnostic use, and treatment duration [15–22]. A 2026 multicenter longitudinal survey tracked repeated prescribing audits over three survey rounds. It reported persistently high antibiotic exposure even though some stewardship practices improved [25]. Its longitudinal design shouldn't be mistaken for a patient-level resistance linkage. Hospital surveys in Ethiopia, four African countries, and Benin show how standardized point-prevalence instruments can improve comparability, though patient mix and indications still vary a great deal [27–29]. WHO stewardship guidance, the AWaRe classification, and the antibiotic book offer practical frameworks for evaluating use [30–34]. These materials help with interpretation and policy recommendations, but they aren't additional resistance observations from Pakistani inpatients.

Subgroup evidence is a reminder not to treat all hospital admissions as one prescribing population. Surveys of hospitalized neonates and children in Punjab report especially high antibiotic exposure, and a cancer-hospital survey describes a specialized, immunocompromised population [39,40,43]. COVID-era multicenter surveys [37,38] reflect an exceptional period of empirical prescribing, so they shouldn't be treated as direct comparators for routine, non-pandemic admissions.

Other Pakistani evidence includes a multicenter laboratory antibiogram study from Northern Punjab and a cost analysis covering Islamabad and Rawalpindi [41,42]. They broaden the clinical picture, but their sampling units and outcomes differ from the NIH national surveillance, and they can't be combined with it without verified, comparable data extraction.

2.4 Evidence gap

The published aggregate reports don't give us a shared patient identifier, a contemporaneous exposure window, hospital-specific clinical covariates, or susceptibility panels that are comparable across studies. An adjusted relationship between earlier

antibiotic exposure and resistance therefore can't be estimated. What we offer is a denominator-aware descriptive synthesis and an explicit account of where inference stops.

2.5 Global epidemiology and the interpretation of resistance burden

Global estimates have established bacterial antimicrobial resistance as a major source of preventable illness and death, but burden models and routine surveillance answer different questions. The 2019 global analysis and the later 1990–2021 assessment combine several data sources and modeling assumptions to estimate deaths attributable to or associated with resistance [7,8]. Such estimates give a population-level reason to invest in stewardship. They aren't equivalent to the percentage of isolates classed as resistant in a single hospital laboratory. A sentinel report can show which organism–drug combinations need attention. Without suitable clinical denominators, it can't estimate deaths, excess length of stay, or population incidence.

Resistance epidemiology varies by organism, body site, patient group, and health system. E. coli matters in urinary tract and bloodstream infections. K. pneumoniae, Acinetobacter species and P. aeruginosa are prominent in healthcare-associated infections and may be over-represented among patients with prolonged treatment or intensive care. S. aureus poses a different problem, because methicillin resistance changes which antistaphylococcal agents work. For these reasons, it makes sense to report pathogen–drug combinations rather than a single aggregate AMR percentage [1,2,7].

How we interpret resistance also depends on the endpoint. Resistance among tested isolates, prevalence of resistant infection among admissions, and attributable mortality each need a different denominator. A high percentage of resistance among cultures sent for clinical reasons can't tell us the probability of resistant infection in all hospitalized patients. Cultures may be ordered more often after treatment failure, in severe disease, or in referral settings, which enriches laboratory surveillance for hard-to-treat infections. This selection effect matters most when national laboratory summaries are set against hospital prescribing surveys [1,2,9].

2.6 Pakistan surveillance architecture and laboratory comparability

Pakistan's NIH national program provides a framework for collating routine susceptibility results across contributing laboratories. Its 2021–2022 report documents growth in the number of reporting laboratories alongside changes in isolate submissions [1,5]. That growth widens the surveillance signal but makes year-to-year comparison harder. When the contributing facilities change, the organism mix may reflect shifts in laboratory coverage, referral pathways, diagnostic capacity, or specimen types, not a change in disease incidence.

Laboratories usually report resistance for a specific organism and antimicrobial agent. Susceptibility panels differ, so the number of isolates tested against ceftriaxone needn't equal the number tested against meropenem or amikacin. Wherever possible, a reported percentage should be paired with the number tested for that organism–drug combination. Antibiotics tested only in high-risk isolates can also give estimates that differ from those obtained with universal panels. Comparisons across agents shouldn't be read as matched within-isolate comparisons unless the source confirms that the same isolates received both tests [1,2].

Quality assurance covers consistent organism identification, standardized interpretation of susceptibility, explicit handling of intermediate categories, and rules for repeat isolates. WHO GLASS stresses linking microbiology with epidemiological information and monitoring data quality [2,4,9]. Differences in breakpoint editions, laboratory platforms, and first-isolate policies can change reported rates even when the bacterial population itself hasn't changed. The published NIH summaries can't resolve all of these sources of variation on their own, so we treat them as limitations and don't assume them away.

National surveillance is most useful for spotting signals that deserve local review. It can't replace an up-to-date ward-level antibiogram. Empirical therapy depends on the specimens and pathogens in the treating institution, as well as the patient's syndrome, severity, previous exposure, and local diagnostic capacity. National reports can inform policy priorities, while prescribing guidance should be adapted to setting-specific microbiology and stewardship review [1,2,30–34].

2.7 Antibiotic prescribing prevalence and its denominators

Hospital point-prevalence surveys describe the share of admitted patients receiving one or more antimicrobials on a designated survey day. The design gives a practical, fairly standardized snapshot of use, but it doesn't measure cumulative

exposure, total treatment days, or new antibiotic starts. A patient on two agents counts once in the patient-level numerator, whereas the two agents can count separately in a prescription-level distribution. Mixing up these units can exaggerate or hide differences between studies [3,12,13].

The multicenter Punjab study reported antibiotic treatment in 1,516 of 1,954 surveyed inpatients, with ceftriaxone, metronidazole, and ciprofloxacin among the commonly reported agents [3]. Other Pakistani point-prevalence studies also reported frequent inpatient antibiotic exposure [12–14,24,25]. These results justify a closer look at empirical prescribing and surgical prophylaxis. But hospital selection, specialties, sampling dates, and inclusion rules differ, so no single national inpatient prevalence can be derived from the reported percentages.

Antibiotic prescribing has several dimensions: whether a drug was prescribed, which agent was chosen, whether the indication was documented, how long treatment lasted, and whether microbiology results prompted a review. An aggregate prevalence figure can't show that all use was unnecessary. Infections that need prompt treatment, including severe sepsis, may justify broad initial coverage. The stewardship question is whether therapy is then reassessed and narrowed or stopped when appropriate. This matters when interpreting high use in hospitals with heavy emergency, surgical, or critical-care caseloads [3,10,30–34].

Surgical prophylaxis deserves its own analysis because its aim differs from treating an established infection. For many procedures, prolonged prophylaxis may add antibiotic exposure without extra benefit, but judging this properly requires procedure type, timing, redosing, wound class and local guidance. The prolonged prophylaxis reported in the Punjab survey therefore points to a need for detailed audit. It isn't a direct measure of preventable resistance, and it doesn't show a causal effect of any one antibiotic [3].

2.8 WHO AWaRe classification and antimicrobial stewardship

The WHO Access, Watch and Reserve framework gives a shared vocabulary for assessing antibiotic use and setting stewardship priorities [10,30–34]. Access agents are generally preferred for common susceptible infections when clinically appropriate. Watch agents need closer monitoring because they're more likely to select for resistance, and Reserve agents are meant for selected multidrug-resistant infections. Classification alone doesn't tell us whether a given prescription is right. Judging appropriateness still requires the indication, allergy status, severity, microbiology, dose, and treatment duration.

WHO's 2025 GLASS antibiotic-use report shows large differences in reported use between countries and the continuing prominence of Watch agents in many settings [11]. National consumption expressed in defined daily doses, however, isn't directly comparable to a hospital point-prevalence estimate of patients receiving antibiotics. Sales, procurement, dispensed doses, and administered doses capture different stages of the medication pathway. A good surveillance strategy for Pakistan would report hospital patient-level exposure alongside consumption measures and state the unit and observation window clearly [11,30–34].

Stewardship programs commonly combine prospective audit and feedback, formulary review, local guidelines, microbiology consultation, optimization of surgical prophylaxis and prescriber education. Pakistani assessments of stewardship implementation [15–22] need to be read in light of hospital resources, clinical pharmacist availability, laboratory turnaround time, and institutional governance. Intervention reports can show which approaches are feasible. Their effects should still be judged using comparable preintervention and postintervention denominators and, where possible, with control for concurrent changes in case mix or infection-control practice.

Stewardship and diagnostic stewardship work together. Restricting antibiotics without better access to cultures or timely susceptibility reporting can leave clinicians facing unresolved diagnostic uncertainty. Likewise, producing antibiograms without a way to get results to prescribers may do little to change prescribing. Feedback loops that connect pharmacy, microbiology, infection prevention and clinical teams tell us more than either prescribing data or laboratory surveillance alone [2,9,15–22].

2.9 Provincial, pediatric and specialist hospital evidence

Pakistan's hospital literature includes multicenter surveys and smaller institutional reports with varying geographic reach. The Punjab multicenter prescribing survey and related hospital studies make up a substantial evidence base for that province [3,6,12,13]. Studies from Karachi and Islamabad widen the range of settings [14,18,24]. Other regional studies in the

bibliography need study-by-study assessment before anyone treats them as representative of Sindh, Khyber Pakhtunkhwa or Balochistan. A hospital's province doesn't, on its own, make it representative of the province.

Pediatric and neonatal prescribing needs its own interpretation, because age-specific infection risks, empirical treatment pathways and dosing differ from adult practice. The pediatric studies in our bibliography [39,40] may document high exposure in selected services, but the counting unit may be an encounter rather than a unique child. A specialist cancer-hospital survey [43] likewise covers a population with immunosuppression and different indications for prophylaxis and treatment. Combining such studies with general inpatient surveys without stratification would hide clinically important differences.

COVID-era prescribing studies [37,38] are another distinct context. Diagnostic uncertainty, strained hospital capacity and worries about bacterial coinfection may have affected antimicrobial use during the pandemic. The findings help us understand how systems coped, but they shouldn't be treated as estimates of routine hospital prescribing without accounting for the exceptional clinical and operational conditions.

Cross-regional comparisons would be more credible if every study reported province, city, facility level, specialty mix, dates, age group, patient denominator, exposure definition and sampling approach. Where these details are missing, we keep the comparison qualitative and say what is missing. A geographically varied reference list isn't the same as a harmonized multicenter dataset [12–14,18,24,37–43].

2.9a Provincial coverage: Sindh, Khyber Pakhtunkhwa, Balochistan and Islamabad

Sindh has several independently documented prescribing assessments. A WHO-adapted point-prevalence survey at the Indus Hospital and Health Network in Karachi, carried out in September 2021, enrolled 300 admitted adults and found that 67% received at least one antimicrobial. Surgical prophylaxis accounted for 40% of recorded indications, and an infectious-diseases review judged at least 56% of antibacterial agents suitable for stewardship intervention. These are site-specific findings, not province-wide prescribing rates [14].

A separate prospective WHO point-prevalence assessment at Dow University Hospital in Karachi surveyed 224 admitted patients, of whom 186 were eligible inpatients, during July 2024. Antibiotic exposure prevalence was 83.3% (reported 95% CI 77.5–88.2%). Of the antibiotics prescribed, 80.8% were in the WHO Watch group and 99.2% were empirical. The exclusions, sampling period and denominator differ from the Indus Hospital survey, so the two shouldn't be pooled as if they described one Karachi cohort [44].

Khyber Pakhtunkhwa appears in a national six-public-hospital prescribing survey that included Hayatabad Medical Complex in Peshawar, and in disease-specific microbiology research. The six-hospital survey recorded antibiotic use in 78.5% of 837 inpatients, but that overall figure can't be attributed to the Peshawar hospital alone [13]. A separate retrospective study of Salmonella blood cultures at Khyber Teaching Hospital and Hayatabad Medical Complex gives two-hospital resistance data for hospitalized patients with suspected typhoid. Because it covers one organism, its results can't be extended to all inpatient infections [45].

Evidence from Balochistan is sparser and more specialized. A Quetta study of suspected bacterial meningitis enrolled 894 patients admitted to Bolan Medical Complex Hospital and District Hospital Quetta between January 2018 and March 2021, with cerebrospinal-fluid microbiology and susceptibility testing. It adds to the provincial evidence map but isn't a general inpatient prescribing survey [46]. A molecular study of Pseudomonas aeruginosa from surgical and burn units in Quetta found resistance genes in a small set of 23 isolates. Its gene-positive subsets shouldn't be read as population-level resistance prevalence [47].

Islamabad contributes a retrospective analysis of 1,012 selected inpatient records from 2020–2022 at a tertiary teaching hospital. Because eligibility required at least four inpatient days, the cohort can't be used to estimate antibiotic-use prevalence among all admissions. We didn't re-estimate its source-specific associations [18]. A separate 14-hospital national point-prevalence survey documented 75% average antibiotic use across participating hospitals, but its aggregate findings can't be split into provincial estimates without site-level tables [12].

These sources broaden geographic representation without removing selection bias. Karachi hospitals, Peshawar typhoid wards, Quetta meningitis cohorts and Islamabad admissions selected by length of stay differ in indication, specimen

collection, time period and measurement unit. So we record province as a study descriptor and don't model it as a determinant of resistance from these aggregate reports.

2.10 Resistance phenotypes, empirical therapy and patient safety

Resistance to third-generation cephalosporins in E. coli and K. pneumoniae can undermine common empirical treatment pathways, though the implications depend on the syndrome and on which alternatives are available. Carbapenem resistance in Acinetobacter species poses a different challenge, especially where invasive devices or long hospital stays are involved. Resistance in P. aeruginosa has to be read using organism-appropriate agents and tested denominators. The NIH report shows substantial resistance in several selected combinations, but it doesn't link a clinical outcome to each resistant isolate [1].

The clinical meaning of an antibiogram also depends on specimen source. Urinary isolates may be tested against agents such as nitrofurantoin or fosfomycin, which aren't suitable substitutes for systemic treatment. Bloodstream and respiratory isolates may come from patients with different severity, prior exposure and treatment pathways. An unstratified susceptibility percentage shouldn't be used to recommend an agent for every infection type. The right approach is to keep specimen-specific denominators and avoid implying that results from one infection site apply to another [1,2].

Resistance estimates should also be kept distinct from multidrug-resistant phenotypes. High resistance to one drug doesn't by itself mean the same isolate meets a multidrug-resistance definition. Class-level labels, combined phenotypes and co-resistance patterns need isolate-level joint test results or explicitly published phenotype definitions. The aggregate sources we used don't allow us to rebuild such joint phenotypes or patient-level treatment failure [1,2].

2.11 Methodological challenges in evidence synthesis

A secondary evidence synthesis can make findings easier to interpret by extracting each study's design, population, numerator, denominator and risk of bias in a consistent format. But a targeted narrative search isn't automatically a systematic review. A systematic claim needs a prespecified question, reproducible database-specific searches, dates, deduplication, documented screening decisions, reasons for full-text exclusions and a suitable critical-appraisal method. Until those steps are done and archived, this work is best described as a structured descriptive synthesis [2,9].

Pooling can mislead when studies count different units. An isolate-based resistance percentage can't be pooled with a patient-based prescribing prevalence. An encounter-based pediatric exposure percentage shouldn't be assumed to equal the percentage of unique patients exposed. And a one-day point-prevalence survey can't be read as an annual incidence rate. Even when two studies report the same nominal outcome, differences in age, specialty, hospital type, year and sampling can create heterogeneity that a simple weighted mean can't resolve [3,12–14,39,40].

Rounded resistance percentages create an uncertainty problem of their own. A tested denominator and a percentage rounded to one decimal place don't pin down a unique resistant numerator. Exact binomial intervals should therefore be computed only when integer counts are documented or the source itself reports the interval. When only a rounded percentage is available, it's better to report that percentage with the verified number tested than to invent an integer numerator. This rule applies to the organism–antibiotic tables extracted from the NIH report [1].

Risk of bias should be considered separately for the laboratory and prescribing evidence. Laboratory reports can be affected by selective culturing, referral patterns, duplicate isolates and selective susceptibility panels. Hospital prescribing surveys can be influenced by the choice of survey day, ward selection, incomplete documentation and case mix. Retrospective studies add eligibility and missing-record bias. A formal quality assessment would document these issues source by source and wouldn't assign an unsupported pooled score [1–3,12–14].

2.12 Synthesis of research gaps and contribution

The literature we reviewed establishes why two complementary priorities matter in Pakistan: antimicrobial susceptibility among organisms submitted for testing, and antibiotic use among hospitalized patients. It doesn't show that the patients who contributed cultures to the national surveillance system were the same patients counted in the prescribing studies. Nor does it supply harmonized data on prior antibiotic exposure, infection onset, ward, comorbidity, severity, organism identity and clinical outcome for each patient. Without those links, valid estimates of individual clinical determinants or of causal effects of prescribing on resistance aren't possible.

Our contribution is therefore narrower than an original multicenter determinants analysis, and easier to defend. We compare independently reported evidence streams, keep their separate denominators, identify selected organism–drug resistance signals and inpatient prescribing patterns, and explain where the evidence can't support adjusted inference. Future research should prospectively link pharmacy administration, microbiology and clinical records across hospitals. It should use predefined first-isolate rules and account for hospital clustering, specimen type and prior antibiotic exposure. A design like that could move beyond descriptive co-occurrence toward estimates of patient-level determinants [1–3,9].

3. MATERIALS AND METHODS

3.1 Study design and scope

We used a descriptive secondary-data design to examine two complementary kinds of evidence: antimicrobial susceptibility reported by Pakistan's national laboratory surveillance program, and antibiotic prescribing documented in published hospital studies. The main surveillance source was the NIH Pakistan report for 2021–2022 [1]. The main prescribing source was the multicenter point-prevalence survey in 13 Punjab hospitals [3]. We considered additional Pakistani hospital studies as contextual evidence when their design, setting and denominators could be identified. The sources were analyzed separately and weren't combined into a new patient-level or hospital-level dataset. This is a structured evidence synthesis with a targeted literature review, not a completed systematic review.

3.2 Literature identification and search strategy

We identified relevant reports through a targeted search of publicly accessible publication records and institutional sources, including the NIH Pakistan surveillance program, WHO guidance and published Pakistani hospital studies. Search concepts included Pakistan and its provinces or major cities, antimicrobial resistance, antibiotic prescribing, stewardship, hospital, inpatient, laboratory surveillance and point-prevalence survey. The broader reproducible strategy named PubMed/MEDLINE, Embase, Scopus, Web of Science, supplementary Google Scholar screening and reference-list searching for publications dated 1 January 2010 to 19 October 2026. A representative PubMed search combines (Pakistan OR Punjab OR Sindh OR Karachi OR Islamabad OR Peshawar OR Balochistan OR "Khyber Pakhtunkhwa") AND (antibiotic* OR antimicrobial* OR "drug resistance" OR stewardship) AND (hospital* OR inpatient* OR surveillance OR "point prevalence"), with database-specific field tags and date limits. This documents a strategy for a future exhaustive search. We aren't claiming that all the named databases were searched. Search-result exports, deduplication records, dual-reviewer screening decisions and PRISMA counts weren't available for this analysis.

3.3 Eligibility criteria and source selection

Eligible primary sources reported observations from Pakistani hospitals, inpatient populations or hospital-linked microbiology laboratories, and identified the study setting, design, observation period and outcome definition. Laboratory reports had to give organism–antibiotic susceptibility estimates, preferably with the number tested. Prescribing studies had to define their patient, encounter or prescription denominator. We accepted official national surveillance reports even when the underlying records weren't publicly released. Community-only studies, non-Pakistani datasets, editorials, and reviews without original hospital observations weren't treated as independent inpatient datasets. Reviews and international reports served as background and for comparison. Because we don't have a complete record-by-record screening log, the included studies shouldn't be presented as the exhaustive set of eligible Pakistani studies.

3.4 Data extraction and definitions

For each included source, the extraction framework recorded province or city, study years, number and type of hospitals or laboratories, population, sampling approach, specimen type, organism, antibiotic, number tested, published resistance percentage, antibiotic-exposure numerator and denominator, and reported limitations. We treated national surveillance isolates, hospital patients, clinical encounters and antibiotic prescriptions as different units of observation. When available, the number of isolates tested against a specific antibiotic served as the susceptibility denominator. We didn't substitute the total isolates submitted to surveillance for drug-specific testing counts. Drug shares in prescribing surveys weren't read as percentages of all hospitalized patients unless the original study used that denominator. Missing resistant counts, breakpoint versions and deduplication details were marked as unreported and not inferred [1–3].

3.5 Assessment of study quality and comparability

We evaluated the sources narratively for risks that affect interpretation. For laboratory surveillance, the concerns were selective culture collection, referral patterns, changing sentinel-laboratory participation, specimen mix, repeat-isolate rules, susceptibility testing panels and breakpoint consistency.

For prescribing surveys, they were hospital and ward selection, survey timing, completeness of prescribing documentation, case mix and the definition of antibiotic exposure. Before reading studies alongside one another, we considered differences in geographic coverage, calendar periods and measurement units. The appraisal was qualitative. We didn't complete an independent, item-by-item JBI or ROBINS-I assessment, and we report no formal quality scores. A fully executed systematic review would need them.

3.6 Statistical analysis

We transcribed published counts, proportions and resistance percentages as source-reported descriptive findings. The only interval we calculated ourselves is the Wilson score 95% confidence interval for the antimicrobial-exposure proportion in the Punjab point-prevalence survey (1,516 of 1,954 inpatients): 77.6% (95% CI 75.7–79.4%) [3]. Its denominator is surveyed inpatients. The percentages for individual antibiotic agents describe the prescribing distribution reported by the original study, not percentages of all inpatients.

In the NIH surveillance tables, each organism–antibiotic resistance percentage uses the number of isolates tested against that specific agent. The total annual isolate counts (132,269 in 2021 and 229,617 in 2022) must not be substituted for those denominators. NIH resistance values are rounded, source-reported percentages, and exact resistant-isolate counts can't be reliably reconstructed from them. We therefore calculated no new resistance confidence intervals, pooled resistance estimates, adjusted associations, hypothesis tests or patient-level causal effects. We described changes across years without formal inference, because participating laboratories rose from 19 to 26 and their case mix may differ.

3.7 Evidence synthesis and reporting

We organized the results into national surveillance coverage, organism-specific susceptibility, hospital antibiotic prescribing and geographic comparisons of published hospital evidence. Each estimate is attributed to its source and original unit of observation. Where studies differed materially in population, setting or outcome definition, we discussed them narratively and didn't pool them. This study doesn't claim a PRISMA-compliant search or a meta-analysis. A future systematic update should archive database-specific searches, export files, duplicate decisions, full-text exclusions, data-extraction sheets and independent risk-of-bias assessments before presenting a PRISMA flow diagram.

3.8 Ethics and data availability

This analysis used only publicly accessible reports and published aggregate findings. We didn't access any identifiable patient information or unpublished hospital records.

We don't claim approval from an institutional ethics committee. Any exemption or determination the destination journal requires should be obtained from the appropriate institution. The main data sources are cited in the references, and the reported values can be checked against the original tables and publications.

4. RESULTS

4.1 Source coverage and study populations

Table 1. Primary source characteristics

Source	Unit	Coverage	Boundary
NIH 2021	Non-duplicate isolate	19 laboratories; 132,269 isolates	Not all hospitalized patients
NIH 2022	Non-duplicate isolate	26 laboratories; 229,617 isolates	Site composition changed

Punjab prescribing survey	Inpatient	13 hospitals; 1,954 patients	Single point-prevalence survey
Punjab HAI survey	Inpatient	13 hospitals; 1,553 patients	Symptoms, not AST resistance

Table 1 separates the two NIH surveillance years from the independent hospital surveys. In 2022, laboratories submitted 97,348 more isolates than in 2021 (+73.6%), and seven more laboratories were reporting. This shouldn't be read as an increase in infection incidence. Figure 1 shows the same data.

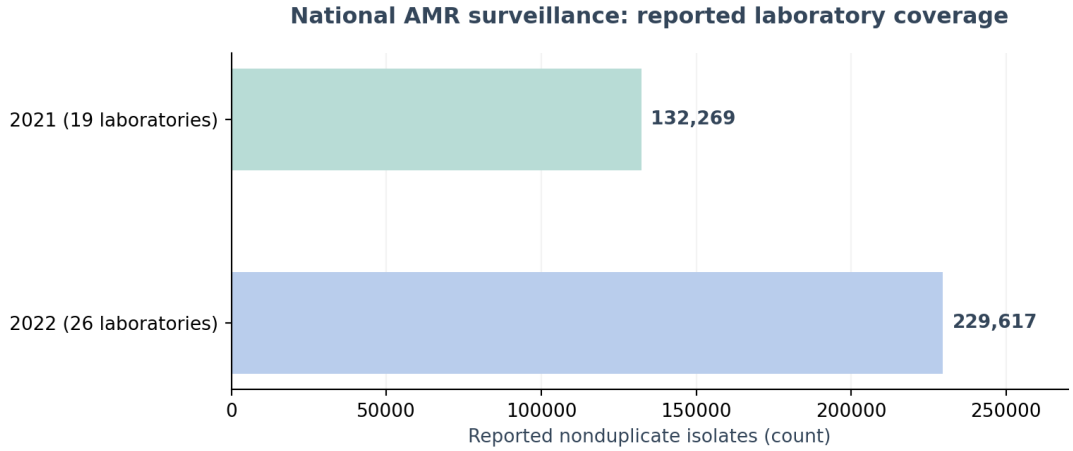


Figure 1. NIH Pakistan surveillance laboratory coverage and nonduplicate isolate counts, 2021–2022. Source: NIH national AMR surveillance report. Counts are not population incidence rates; the number of reporting laboratories differed by year.

4.2 Organism distribution

Table 2. Reported organism share of submitted isolates

Organism	2021 (%; source-reported)	2022 (%; source-reported)
E. coli	35	36
K. pneumoniae	9	12
S. aureus	13	10
P. aeruginosa	3	7

Table 2 shows the reported mix of laboratory isolates, not population incidence. Differences may reflect changes in source composition and culture practice. All percentages in Table 2 are source-reported, and the annual laboratory totals aren't organism-specific susceptibility-testing denominators.

4.3 E. coli susceptibility

Table 3. E. coli susceptibility testing, NIH 2022

Antibiotic	Isolates tested for this drug (n)	Resistance (%; source-reported)
Ceftriaxone	77,998	74.6
Cefotaxime	19,654	76.5
Ceftazidime	11,719	73.5
Meropenem	53,022	13.5

Imipenem	42,035	14.4
Ciprofloxacin	68,406	69.5
Amikacin	57,325	8.8
Gentamicin	46,429	27.9
Piperacillin–tazobactam	60,483	20.2
Nitrofurantoin (urine)	49,651	9.2
Fosfomycin (urine)	46,737	7.1

Table 3 reproduces the source-reported NIH 2022 resistance percentages next to the tested-isolate counts for each organism–antibiotic pair. Those counts, not the national isolate total, are the denominators. Nitrofurantoin and fosfomycin testing is urine-specific. Percentages rounded to one decimal place don't uniquely identify exact resistant counts, so we didn't calculate confidence intervals. Comparisons across agents are descriptive, because the tested populations can differ. Figure 2 shows the same data.

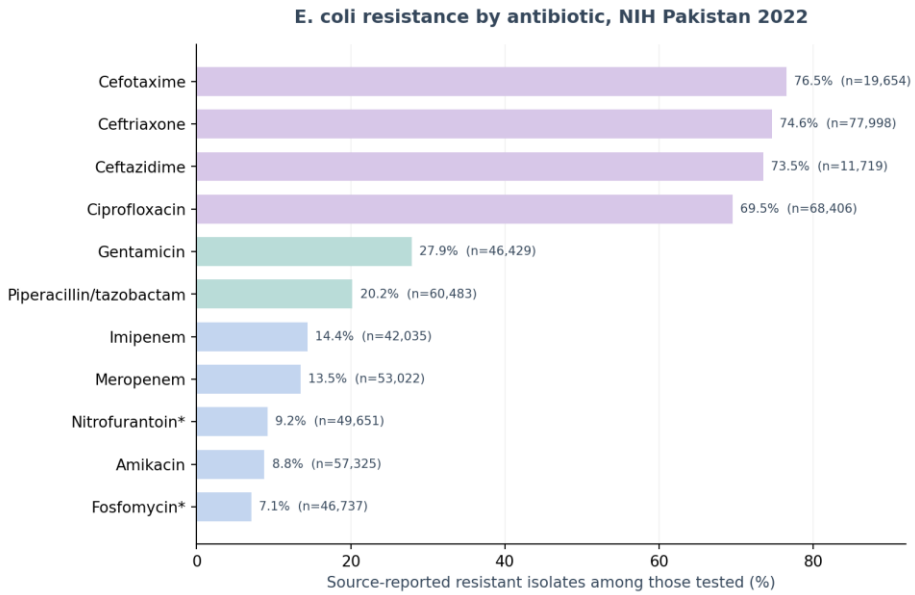


Figure 2. Source-reported E. coli resistance percentages by antibiotic in 2022, with antibiotic-specific tested-isolate denominators (n). Source: NIH Pakistan national AMR surveillance report. *Nitrofurantoin and fosfomycin are urine-isolate results. These percentages are not patient-level risks.

4.4 Other priority pathogens

Table 4. Other organism–antibiotic pairs, NIH 2022

Organism	Antibiotic	Isolates tested for this drug (n)	Resistance (%; source-reported)
K. pneumoniae	Ceftriaxone	26,087	66.4
K. pneumoniae	Meropenem	19,502	30.7
K. pneumoniae	Ciprofloxacin	21,126	54
P. aeruginosa	Piperacillin/tazobactam	15,339	21

P. aeruginosa	Meropenem	10,899	27.4
P. aeruginosa	Ciprofloxacin	13,526	36.5
S. Typhi	Ceftriaxone	16,121	72.4
S. Typhi	Azithromycin	14,702	1.9
Acinetobacter spp.	Imipenem	7,336	74
Acinetobacter spp.	Meropenem	7,455	73
Acinetobacter spp.	Minocycline	3,262	9

Table 4 shows how much the results vary across pathogens. Ceftriaxone resistance was reported for 66.4% of tested K. pneumoniae isolates, and meropenem resistance among Acinetobacter species was 73.0%. These percentages shouldn't be pooled across organisms or clinical syndromes. Each resistance percentage is source-reported, and the tested-isolate denominator for that antibiotic is shown in the same row. None of them is a proportion of all national isolates.

4.5 Antibiotic prescribing and uncertainty

Table 5. Punjab prescribing indicators

Measure	Value and provenance
Patients surveyed	1,954 (source-reported)
Patients receiving antimicrobials	1,516 (77.6%) (source-reported)
Wilson 95% CI	75.7–79.4% (independently calculated from 1,516/1,954)
Ceftriaxone share of reported prescribing	35.0% (source-reported)
Metronidazole share	16.0% (source-reported)
Ciprofloxacin share	6.0% (source-reported)
Surgical prophylaxis >1 day	97.4% (source-reported)

Table 5 separates published prescribing percentages from the Wilson interval we calculated for 1,516 antibiotic-exposed patients among 1,954 surveyed inpatients. Drug-specific shares refer to the published prescribing distribution, not to the total inpatient denominator. The 97.4% figure for prolonged surgical prophylaxis refers to prophylaxis courses as defined in the original survey. It isn't a proportion of all 1,954 patients. Figure 3 shows the same data.

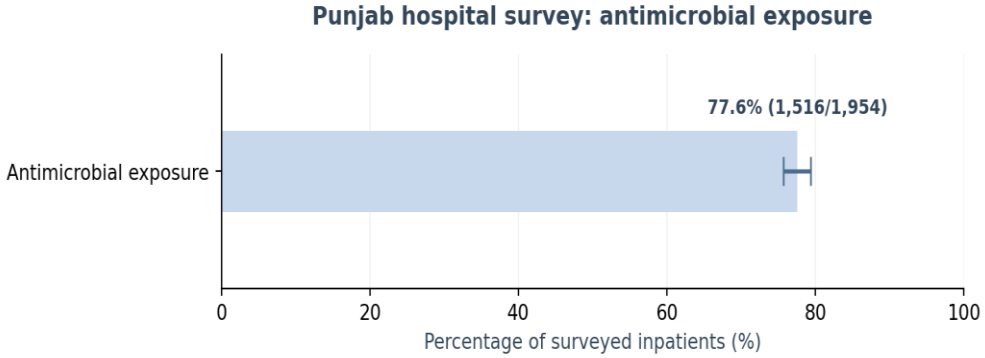


Figure 3. Antimicrobial exposure in the Punjab 13-hospital point-prevalence survey. The percentage (77.6%) is source-reported; the 95% Wilson confidence interval (75.7–79.4%) is independently calculated from 1,516/1,954. This is antimicrobial exposure, not specifically systemic-antibiotic exposure.

4.6 Statistical estimability

Table 6. Descriptive outcomes supported by the available data

Reported measure	Result and provenance	Source / interpretation
Inpatient antibiotic exposure	1,516/1,954; 77.6% source-reported; Wilson 95% CI 75.7–79.4% independently calculated	Punjab point-prevalence survey
Organism–antibiotic resistance	Source-reported resistance percentage and antibiotic-specific tested-isolate count (Tables 3–4)	NIH surveillance, 2022; rounded percentages

Table 6 summarizes selected descriptive measures and shows where each came from. The available sources don't allow patient-level estimation of prescribing–resistance associations.

4.7 Provincial hospital evidence and limits of geographical comparison

Table 7. Additional provincial hospital evidence (distinct study populations; no pooled estimates)

Area / study	Setting and denominator	Published finding	Comparability restriction
Sindh: Indus Karachi [14]	Adult inpatient PPS; n=300	67% received ≥1 antimicrobial	Single-center PPS, September 2021
Sindh: Dow Karachi [44]	Eligible inpatients n=186 (224 surveyed)	83.3% antibiotic use; 80.8% Watch share	Different exclusions and time window
KP: six-hospital survey [13]	Six public hospitals incl. Peshawar; n=837	78.5% antibiotic use overall	No verified KP-specific prevalence
KP: Peshawar typhoid [45]	Two tertiary hospitals; blood-culture Salmonella	Organism-specific susceptibility evidence	Not general inpatient prescribing
Balochistan: Quetta meningitis [46]	Two hospitals; n=894 suspected meningitis	CSF-based pathogen and resistance assessment	Disease-selected admissions
Balochistan: Quetta Pseudomonas [47]	Surgical/burn units; 23 isolates	Carbapenem-resistance gene findings	Small, selected isolate series
Islamabad: teaching hospital [18]	Retrospective; 1,012 selected records	Antibiotic prescribing review	Stay ≥4 days; selection bias
National: 14 hospitals [12]	National multicenter PPS	75% antibiotic use average	Cannot infer province-specific rates

Our targeted provincial update found direct hospital-level evidence from Sindh (Karachi), Khyber Pakhtunkhwa (Peshawar), Balochistan (Quetta) and Islamabad, along with national multicenter studies. Table 7 lists the distinct populations and outcomes. It's an evidence map, not a pooled provincial prevalence analysis.

In Karachi, the Indus Hospital adult point-prevalence survey recorded 67% antimicrobial exposure among 300 admitted patients [14]. The later Dow University Hospital study reported 83.3% among 186 eligible inpatients (95% CI 77.5–88.2%), with 80.8% of antibiotic prescriptions in the Watch category [44]. Sampling windows, eligibility and definitions differ, so these values can't be read as a within-city time trend.

The six-public-hospital prescribing study (837 inpatients, 78.5% receiving antibiotics) included a Peshawar facility but didn't give an independently extracted Peshawar-specific numerator and denominator [13]. Two Peshawar tertiary hospitals contributed typhoid blood-culture susceptibility data [45]. The Quetta studies covered meningitis admissions (894 suspected cases) and resistance-gene findings in a small series of P. aeruginosa from surgical and burn units. Neither describes prescribing prevalence across all wards [46,47]. The Islamabad review covered 1,012 selected records with stays of at least four days [18].

We calculated no province-specific pooled estimate, cross-province significance test or adjusted provincial effect. Several studies share health systems or facilities with other national surveys, so patient-level overlap can't be excluded. The geographic coverage helps place the findings in context but doesn't make any province's evidence representative.

5. DISCUSSION

The surveillance and prescribing data point to different aspects of antimicrobial stewardship in Pakistan. Surveillance identifies resistance among selected cultured isolates. The prescribing surveys identify substantial antimicrobial exposure among inpatients at the surveyed hospitals. Neither source alone establishes the timing, indication or individual consequence of antibiotic exposure. Turning their percentages into a correlation would give an ecological comparison across different years, populations and data collection systems.

The E. coli findings matter for empirical prescribing, because resistance to third-generation cephalosporins was high among tested isolates. Even so, urine-only susceptibility patterns and mixed-specimen profiles should be read alongside site-specific antibiograms and the infection syndrome. The high carbapenem resistance reported in Acinetobacter spp. likewise can't be extrapolated to the prevalence of resistant infection among all hospitalized patients. Global estimates name these organisms as important AMR burdens, but they don't justify extrapolating Pakistani sentinel percentages to national incidence [7,8].

Antibiotic use in the Punjab survey was frequent, and the reported prolonged surgical prophylaxis offers a concrete target for stewardship audit [3]. The WHO AWaRe framework can help organize prescribing reviews, but drug-class proportions would need to be recalculated from the underlying antibiotic lists before anyone claims an AWaRe distribution [10,11]. The survey doesn't support the claim that any specific prescription caused the resistance patterns seen in national surveillance.

A useful next step would link hospital pharmacy orders or administrations, indication, ward, dates of antibiotic exposure, cultures, susceptibility results and patient outcomes. A design like that could examine prior exposure while adjusting for age, comorbidity, infection syndrome, ICU status and hospital clustering. Until such records exist, what we offer is a transparent, denominator-aware description of the available Pakistani evidence, not an independent risk-factor model.

The high antibiotic exposure percentages across Pakistani studies look similar, but they shouldn't be read as a pooled national estimate. The 13-hospital Punjab survey, the 14-hospital WHO-method survey, the six-public-hospital survey, the single-hospital Karachi sample and the Islamabad studies differ in geography, study year, case mix and sampling unit [3,12–14,18,24]. A formal pooled prevalence would need prespecified eligibility, full denominator extraction, an overlap assessment and study-level bias evaluation.

Intervention evidence helps turn descriptive findings into testable actions. Pakistani studies have looked at carbapenem stewardship, pharmacist-led prescription review, staff education and institutional stewardship infrastructure [17,19–22,25]. They support audits of indication, culture timing, de-escalation, surgical prophylaxis duration and AWaRe distribution. They don't show that the resistance patterns in the NIH laboratory network were caused by prescribing in these other samples.

International hospital point-prevalence surveys are useful methodological comparators, not interchangeable national benchmarks [27–29]. WHO guidance recommends combining surveillance, stewardship capacity and improvements in diagnostic quality [30–34]. The next analysis should use a logged search and explicit study-level risk-of-bias assessment, and should keep inpatient prescribing studies, laboratory surveillance and stewardship interventions apart.

Provincial evidence adds nuance, not a single geographic ranking. The Karachi point-prevalence surveys document high antibiotic exposure but differ in eligibility and study period [14,44]. The Peshawar and Quetta studies, by contrast, mostly address disease-specific susceptibility or resistance mechanisms [45–47]. Comparing these figures as provincial antibiotic-use rates would mix up patients, isolates, prescriptions and selected syndromes.

Coverage is still uneven. The published studies we found are concentrated in urban tertiary centers, and rural and secondary-care populations are poorly characterized. The multi-hospital surveys improve coverage but don't consistently publish province-by-province denominators that can be extracted [12,13]. Future surveillance should report province, hospital type, ward, specimen, infection indication and tested-isolate denominators, with explicit deduplication rules.

6. LIMITATIONS

This analysis has several limits: nonrepresentative sentinel laboratory sampling, changing reporting sites, uncertain overlap of tested isolates across antibiotic panels, possible variation in susceptibility testing methods, no exact resistant counts, and no patient-level records. Our targeted evidence review wasn't exhaustive, and it had no registered protocol or completed formal study-level risk-of-bias assessment. We didn't include other provincial studies quantitatively without verified source details. The analysis can't establish a nationwide resistance prevalence among hospitalized patients, a longitudinal association between prescribing and resistance, or clinical determinants.

First, the laboratory component relies on sentinel surveillance, not a probability sample of all infections or admissions in Pakistan. Illness severity, access to diagnostic services, prior treatment, referral patterns and institutional practices all influence culture requests. The reported susceptibility proportions may therefore over-represent particular clinical settings or patients with hard-to-treat infections. The rise in contributing laboratories between reporting years also means changes in isolate totals can't be read as national temporal trends [1].

Second, susceptibility estimates depend on the organism–drug combinations that were actually tested. Different antibiotic panels, specimen distributions, laboratory procedures and reporting rules can produce unequal denominators, even within the same organism. Published percentages are often rounded and don't always come with exact resistant-isolate counts, so we couldn't reliably calculate additional confidence intervals from them. We kept the published tested-isolate denominators where available, but we can't independently confirm isolate deduplication, testing completeness or uniform use of susceptibility breakpoints across all contributing sites.

Third, the prescribing evidence comes from hospital studies done in different places, years and patient populations. Point-prevalence surveys measure use on a survey day, while other studies may report prescriptions, courses or particular clinical indications. These measures aren't interchangeable. Study-specific percentages shouldn't be pooled into a national estimate without harmonized eligibility criteria, compatible denominators, an assessment of overlapping samples and a formal synthesis plan. Evidence from urban tertiary hospitals may not represent secondary-care facilities, rural populations or hospitals with different diagnostic and stewardship resources.

Fourth, the laboratory and prescribing datasets aren't linked by patient, hospital or time period. That prevents us from assessing whether a patient's prior antibiotic exposure came before a resistant isolate, whether resistance affected prescribing decisions, or whether either factor independently predicted mortality, length of stay or other clinical outcomes. We therefore report no adjusted odds ratios, causal associations or patient-level determinants. Any parallel patterns in prescribing and resistance should be read as separate descriptive observations, not as evidence of an exposure–outcome relationship.

Fifth, our literature identification was targeted and not an exhaustive, reproducible systematic search across all major databases. We developed a preliminary search log and source appraisal separately, but comprehensive database coverage, independent duplicate screening, full-text eligibility adjudication and completed formal risk-of-bias ratings aren't available for all potentially relevant studies. Publication and reporting biases may therefore affect the balance of evidence we present, and we may have missed findings from underrepresented provinces or institutions. The work is best described as a secondary-data evidence synthesis, not a completed systematic review or meta-analysis.

Finally, relying on published aggregate reports limits our ability to check source data, reclassify antibiotic indications, reconstruct WHO AWaRe categories consistently, investigate missing observations, or run robust subgroup and sensitivity analyses. These limits don't erase the descriptive value of the findings, but they narrow how far the findings can be generalized. Future studies should prospectively harmonize patient identifiers, dates of antimicrobial exposure, specimen and culture information, infection indications, ward characteristics and clinical outcomes, and should document laboratory quality control and complete denominator definitions.

7. CONCLUSION

This secondary analysis brings together two complementary sources of evidence on antimicrobial resistance and antibiotic prescribing in Pakistan: national sentinel-laboratory surveillance and published hospital-based studies. The surveillance findings show substantial resistance among selected, clinically important bacterial pathogens, particularly to several commonly used antibiotics. Multicenter inpatient surveys, in turn, document frequent antimicrobial exposure and point to prescribing practices, including prolonged surgical prophylaxis, that deserve closer review. Resistance and antibiotic use should be examined together, but each measure has to keep the distinct population and denominator it's based on. The organism–antibiotic-specific results also show why a single national percentage can't describe resistance adequately. Susceptibility estimates depend on the organism, drug, specimen selection, testing practices and reporting laboratory. The tested-isolate denominators add descriptive value, but they don't remove selection bias or establish trends in a stable patient population. Hospital prescribing estimates from different provinces and clinical settings likewise can't be combined into a representative national prevalence without harmonized definitions, complete study-level information and an appropriate assessment of study quality.

The most immediate implications concern stewardship and surveillance quality. Hospitals should prioritize routinely updated, locally relevant antibiograms; documentation of prescribing indications and treatment duration; timely microbiological testing where clinically appropriate; and regular review of empirical treatment and surgical prophylaxis. Integrating microbiology, pharmacy and clinical records would make it possible to evaluate prescribing quality alongside patient outcomes instead of comparing unrelated aggregate datasets. Wider participation from secondary-care facilities and underserved regions would also make future evidence easier to interpret and more geographically complete.

This study doesn't show that the observed prescribing patterns caused the resistance reported by national laboratories, and it doesn't identify independent patient-level determinants of resistant infection. Its contribution is a transparent synthesis of the available evidence, including the limits set by differing sampling frames and tested denominators. Future multicenter studies should use linked, de-identified patient records, standardized susceptibility reporting, prespecified isolate-deduplication rules and appropriate adjustment for clinical and hospital-level factors. That work is needed to determine how antibiotic exposure, patient characteristics and care settings relate to resistance, and whether stewardship interventions improve clinical outcomes in Pakistan.

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