**Original research**

**A repeated point prevalence survey of antimicrobial use in specialized cancer care hospital of Pakistan: findings and implications**

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(Accepted for publication Hospital Practice – please keep Confidential)

**Abstract**

**Background:** The extensive use of broad-spectrum antimicrobials in immunocompromised patients is inevitable in situations where culture and sensitivity testing is challenging. However, their overuse leads to an increase in antimicrobial resistance (AMR), which is a growing concern.

**Method:** A repeated point prevalence survey (PPS) was conducted to assess the pattern of antimicrobial prescribing in a specialized cancer care hospital in Pakistan using the methodology employed by the European Centre of Disease Prevention and Control.

**Results:** Out of 313 hospitalized patients, 156 (49.8%) were prescribed one or more antimicrobials, 82 (50.9) in 2017 and 74 (48.7) in 2018. The average bed occupancy in the hospital was 80.3%. Fever in neutropenic patients (20.2%), lower respiratory tract infections (17.8%), and sepsis (14.9%) were the three most common clinical indications. The total number of prescribed antimicrobials was 242, of whom, 41 (16.9%) were given orally and 201 (83.1%) were given parenterally. The most commonly used antimicrobials were piperacillin plus enzyme inhibitor (31.8%), meropenem (7.9%), ceftriaxone (6.2%) and vancomycin (6.2%). Of the total prescribed antimicrobials, 42 (17.3%) antimicrobials were used in surgical departments, 89 (36.8) in adult medical departments, 73 (30.1%) in pediatric medical departments and 38 (15.7) in the intensive care unit (ICU). In addition to these antibacterials, there was relatively high use of antivirals (acyclovir; 4.1%) and antifungals (fluconazole; 3.7%, amphotericin B; 2.9%).

**Conclusion:** The study concluded that broad-spectrum antimicrobial usage in cancer hospitals in Pakistan is high, which can be a risk factor for the emergence of AMR. Repeated PPS is a fruitful way to maintain a focus on inappropriate antimicrobial use and develop pertinent intervention programs targeteing specific issues to improve future use.

**Keywords:** Point Prevalence Survey; Cancer; Antimicrobial Use; Pakistan; Antimicrobial Resistance

**Introduction**

The extensive use of broad-spectrum antimicrobials for immunocompromised patients is common. Unfortunately, the overuse of antimicrobials leads to the emergence of resistance which is growing exponentially worldwide, potentially rendering antimicrobials ineffective ([1](#_ENREF_1)). Antimicrobial resistance (AMR) is a major hurdle in health care service provision along with increasing economic implications ([2-5](#_ENREF_2)). The prescribing of colistin, which was discovered a century ago, is growing despite side-effect problems as physicians are forced to prescribe it again due to the emergence of carbapenem-resistant gram-negative bacteria ([6](#_ENREF_6), [7](#_ENREF_7)). Irrational antimicrobial use can increase direct and indirect treatment cost, including additional visits to the emergency department for surplus examinations or procedures, extra prescription load for adjuvant therapies or prolong hospital stay ([8](#_ENREF_8), [9](#_ENREF_9)). Antimicrobial stewardship programs (ASP) positively influence the use of antimicrobials, reducing total consumption and associated costs ([10-14](#_ENREF_10)). ASPs need to be implemented in hospitals for the optimal use of antimicrobials; however, we know this practice can be very variable in lower and middle-income countries (LMICs) due to a number of challenges. These include manpower issues, training as well as the ready availability of laboratory services ([4](#_ENREF_4), [15](#_ENREF_15), [16](#_ENREF_16)). The World Health Organization (WHO), Infectious Disease Society of America (IDSA), Joint Commission International (JCI) and Society of Healthcare Epidemiology of America (SHEA) are all involved in the implementation of ASP in different institutions to improve future antibiotic use.

The rise in AMR is particularly an issue in patients who are immunocompromised from chemotherapy, who may experience life-threatening complications from organisms that have become resistant to antibiotics and the safety of surgical procedures may be threatened due to the increasing AMR. Inappropriate antimicrobial use is common in Pakistan ([17-21](#_ENREF_17)). However, nationwide surveillance to capture data on antimicrobial use and resistance is currently not in place. Point prevalence surveys have been conducted across countries to determine patterns of antimicrobial use, particularly in acute hospitals, as a basis for developing pertinent strategies to improve future use ([22-26](#_ENREF_22)). As mentioned, this is particularly important in cancer patients given their compromised health. In addition, regular surveillance of antimicrobial use is particularly important in LMICs with their growing number of cancer patients and concerns generally about their care with limited resources in countries with existing high rates of infectious diseases ([25](#_ENREF_25), [27-30](#_ENREF_27)). To the best of our knowledge, we believe this is the first study to assess the pattern of antimicrobial prescribing in a specialized cancer care hospital of Punjab, Pakistan, using a Point Prevalence Survey (PPS) approach. We believe the findings will be of use not only in this hospital to develop pertinent interventions but also other leading hospitals in Pakistan treating cancer patients.

**Methodology**

***Study design and settings***

The repeated PPS Data was collected using the methodology employed by the European Centre of Disease Prevention and Control (ECDC) ([31-33](#_ENREF_31)). This structured survey method was used to observe and document hospital, ward and patient level data. The survey included all inpatients receiving an antimicrobial on the day of the PPS in the hospital. The data collected included details on the antimicrobials prescribed, their regimens, and indications. Data was collected from a 195 beds specialized cancer care hospital, Punjab, Pakistan. The hospital has recently been accredited by Joint Commission International (JCI). JCI continually strives to identify trends in health care to ensure standards help organizations provide safer patient care. One of several new standards developed for the JCI addresses the issue associated with AMR. This new standard requires organizations to develop and implement an antimicrobial stewardship program (ASP). The JCI recommends that hospitals develop and implemented different programs to enhance the appropriate use of antibiotics including Pharmacy and Therapeutic Committees (P & TC) for approving restricted antimicrobials listed on the formulary, regular audit on the prescribing and use of antimicrobials by physicians, pharmacists and nurses, installation of computerized clinical decision support systems integrated into the health record and routine access to an infectious disease specialist.

Application for Ethics clearance prior to the conduct of the study was sought from the Human Ethics Division of University College of Pharmacy, University of Punjab, Lahore (HEC/1000/PUCP/1925RPPS). Subsequent approval to conduct the study in the hospital was obtained from the hospital management. All collected data were anonymized during the time of data collection.

***Data collection***

The data were collected using a structured data collection tool used in previous studies ([31-33](#_ENREF_31)). All the patients admitted to the ward at 0800 hrs on the day of the survey were included. All the prescribed antimicrobials at the time of the survey were included. Data were collected from the patients who were receiving at least one antimicrobial for at least one clinical condition or prophylaxis at the time of the survey. All antibacterial, antifungal and antiviral were cataloged as antimicrobials. Infections in more than one site in the same patient were reported as separate infections. All patients admitted to the ward after 0800 hr were not included. The details of clinical history taken from the patient’s medical case notes and prescribing charts were recorded. Data from all wards of this hospital were collected within one day. One day data was collected in March 2017 and March 2018.The Anatomical Therapeutic Chemical (ATC) classification of the WHO was used to classify the different antimicrobials used ([34](#_ENREF_34)).We did not break the various cancers down into the various types including haematological cancers and solid tumours as our main goal was to gain an understanding of key issues including the extent of broad spectrum antibiotic use, the extent of IV versus oral use as well as issues of extended prophylaxis. Similarly we did not check current antimicrobial use against current antibiograms. Data were analyzed using the latest versions of Microsoft Excel and SPSS (version 22 IBM, California, USA).

**Results**

Overall antimicrobial use prevalence is presented in Table 1.

During this PPS, 313 patients were hospitalized on the day of study. The average bed occupancy in the hospital was 80.3%. Out of these, 156 (49.8%) patients were using one or more antimicrobials, 82 (50.9) in 2017 and 74 (48.7) in 2018.

**Table 1:** Overall antimicrobial use prevalence

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics** N (%) | **2017** | **2018** | **% change** | **Total** |
| **Hospitalized patients (Bed Occupancy)** | 161 (82.6) | 152 (77.9) | -5.59 | 313 (80.3) |
| **Number of treated patients** | 82 (50.9) | 74 (48.7) | -9.76 | 156 (49.8) |
| **Prescribed antibiotics** | 140 | 102 | -27.14 | 242 |
| **Prescribed antibiotics by departments** |  |  |  |  |
| Adult Intensive Care Unit | 16 (11.4) | 22 (26.6) | 37.50 | 38 (15.7) |
| Adult Surgical Ward | 19 (13.6) | 23 (27.5) | 21.05 | 42 (17.3) |
| Adult Haematology-Oncology Ward | 54 (38.6) | 35 (34.4) | -35.19 | 89 (36.8) |
| Pediatric Haematology-Oncology Ward | 51 (36.4) | 22 (11.8) | -56.86 | 73 (30.1) |
| **Route of administration** |  |  |  |  |
| Oral | 25 (17.9) | 16 (15.7) | -36.00 | 41 (16.9) |
| Parenteral | 115 (82.1) | 86 (84.3) | -25.22 | 201 (83.1) |
| **Indication** |  |  |  |  |
| Therapeutic use | 106 (75.7) | 64 (62.7) | -39.62 | 170 (70.2) |
| Prophylaxic use | 34 (25.3) | 38 (37.3) | 11.76 | 72 (15.7) |
| **Indication for prophylaxis** |  |  |  |  |
| Medical | 18 (52.9) | 13 (34.2) | -27.78 | 31 (43.1) |
| Surgical | 16 (47.1) | 25 (65.8) | 56.25 | 41 (56.9) |
| **Indication for infection** |  |  |  |  |
| Community-acquired | 69 (65.1) | 48 (75.0) | -30.43 | 117 (68.8) |
| Hospital-acquired | 37 (34.9) | 16 (25.0) | -56.76 | 53 (31.2) |
| **Reason on Notes** |  |  |  |  |
| Yes | 78 (55.7) | 32 (31.4) | -58.97 | 110 (45.5) |
| No | 62 (44.3) | 70 (68.6) | 12.90 | 132 (54.5) |
| **Empirical Therapy** | 92 (65.7) | 95 (93.1) | 3.26 | 187 (77.2) |
| **Culture Reports** | 22 | 21 | -4.55 | 43 |

The total number of prescribed antimicrobials was 242, of whom, 41 (16.9%) were given orally and 201 (83.1%) were given parenterally. Of the total 242 antibiotics, 140 were given in 2017 and 102 in 2018 representing a 27.14% reduction. The average number of antimicrobials prescribed per patient was 1.56. Of the total prescribed antimicrobials, 42 (17.3%) antimicrobials were used in surgical departments, 89 (36.8%) in adult medical departments, 73 (30.1%) in pediatric medical departments and 38 (15.7%) in the ICU. The admitted patients were more likely to receive antimicrobials as per their therapeutic indication, 106 (75.7%) in 2017 and 64 (62.7%) in 2018. All antimicrobials for surgical prophylaxis were given for more than one day. For the management of infections, 117 (68.8%) antimicrobials were given for community-acquired infections whereas 53 (31.2%) were given for hospital-acquired infections. In half of the cases, the reasons for prescribing antimicrobials were not mentioned in the patient’s medical file.

Physicians in the hospital were currently prescribing 24 different types of antimicrobials. The details about their use for different clinical indications are given in Tables 2, 3 & 4. Fever in the neutropenic patient (20.2%), lower respiratory tract infection (17.8%), and sepsis (14.9%) were the three most common clinical indications for antimicrobial use. However, the number of patients with these conditions were less in 2018 as compared to 2017.

**Table 2:** Antimicrobial Use Prevalence in Different Indications

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indications** | **2017** | **2018** | **% change** | **Total** |
| Fever in the Neutropenic patient | 38 (27.1) | 11 (10.8) | -71.05 | 49 (20.2) |
| Lower Respiratory Tract Infection | 26 (18.6) | 17 (16.7) | -34.62 | 43 (17.8) |
| Sepsis | 19 (13.6) | 17 (16.7) | -10.53 | 36 (14.9) |
| Skin and Soft Tissues Infections | 15 (10.7) | 7 (6.9) | -53.33 | 22 (9.1) |
| Obstetric or Gynaecological Prophylaxis | 6 (4.3) | 12 (11.8) | 100.00 | 18 (7.4) |
| Gastro-Intestinal Tract Infections | 12 (8.6) | 4 (3.9) | -66.67 | 16 (6.6) |
| General Medical Prophylaxis | 4 (2.9) | 12 (11.9) | 200.00 | 16 (6.6) |
| Gastro-Intestinal Tract Prophylaxis | 2 (1.4) | 7 (6.9) | 250.00 | 9 (3.7) |
| Bone & Joint Prophylaxis | 3 (2.1) | 5 (4.9) | 66.67 | 8 (3.3) |
| Lower Urinary Tract Infection | 6 (4.3) | 1 (1.0) | -83.33 | 7 (2.9) |
| Upper Respiratory Tract Infection | 2 (1.4) | 2 (2.0) | 0.00 | 4 (1.7) |
| Other | 5 (3.5) | 7 (6.9) | 40.00 | 12 (5.0) |

The most commonly used antimicrobials were piperacillin, enzyme inhibitor (31.8%), meropenem (7.9%), ceftriaxone (6.2%) and vancomycin (6.2%). Interestingly, there was a significant reduction in the use of meropenem in 2018. In addition to these antibacterial, relatively high use of antiviral (acyclovir; 4.1%) and antifungal (fluconazole; 3.7%, amphotericin B; 2.9%) was observed.

**Table 3:** Use prevalence of main antimicrobials classes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Antibiotics**  | **2017** | **2018** | **% change** | **Total** |
| **ANTIBACTERIALS (J01)** | **119 (85)** | **86 (84.3)** | -27.73 | **205 (84.7)** |
| **Penicillins** (J01C) | 49 (35.0) | 40 (39.2) | -18.37 | 89 (36.8) |
| **Cephlosporins & Penams** (J01D) | 37 (26.4) | 15 (14.7) | -59.46 | 52 (21.2) |
| **Sulfonamides & trimethoprim** (J01E) | 4 (2.9) | 10 (9.8) | 150.00 | 14 (5.8) |
| **Macrolides & lincosamides** (J01F) | 7 (5.0) | 8 (7.8) | 14.29 | 15 (6.2) |
| **Aminoglycosides** (J01G) | 1 (0.7) | 1 (1.0) | 0.00 | 2 (0.8) |
| **Quinolones** (J01M) | 4 (2.9) | 4 (3.9) | 0.00 | 8 (3.3) |
| **Other antibacterials** (J01X) | 17 (12.1) | 8 (7.8) | -52.94 | 25 (10.3) |
| **Antimycotics (J02)** | **10 (7.1)** | **9 (8.8)** | -10.00 | **19 (7.9)** |
| **Antivirals  (J05)** | **5 (3.6)** | **6 (5.9)** | 20.00 | **11 (4.5)** |
| **Antiprotozoals (P01)** | **1 (0.7)** | **-** | -100.00 | **1 (0.4)** |
| **Antidiarrheals (A07)** | **5 (3.6)** | **-** | -100.00 | **5 (2.1)** |

**Table 4:** Antimicrobials use prevalence

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Antibiotics** | **2017** | **2018** | **% change** | **Total** |
| **Piperacillin, enzyme inhibitor** (J01CR05) | 40 (28.6) | 37 (36.3) | -7.50 | 77 (31.8) |
| **Meropenem** (J01DH02) | 14 (10.0) | 5 (4.9) | -64.29 | 19 (7.9) |
| **Ceftriaxone** (J01DD04) | 10 (7.1) | 5 (4.9) | -50.00 | 15 (6.2) |
| **Vancomycin** (J01XA01) | 9 (6.4) | 6 (5.9) | -33.33 | 15 (6.2) |
| **Co-trimoxazole** (J01EE01) | 4 (2.9) | 10 (9.8) | 150.00 | 14 (5.8) |
| **Azithromycin** (J01FA10) | 7 (5.0) | 7 (6.9) | 0.00 | 14 (5.8) |
| **Co-amoxiclav** (J01CR02) | 9 (6.4) | 3 (2.9) | -66.67 | 12 (5.0) |
| **Aciclovir** (J05AB01) | 5 (3.6) | 5 (4.9) | 0.00 | 10 (4.1) |
| **Fluconazole (J02AC01)** | 4 (2.9) | 5 (4.9) | 25.00 | 9 (3.7) |
| **Amphotericin B (J02AA01)** | 4 (2.9) | 3 (2.9) | -25.00 | 7 (2.9) |
| **Cefuroxime** (J01DC02) | 3 (2.1) | 3 (2.9) | 0.00 | 6 (2.5) |
| **Imipenem and enzyme inhibitor** (J01DH51) | 5 (3.6) | 1 (1.0) | -80.00 | 6 (2.5) |
| **Metronidazole** (J01XD01) | 6 (4.3) | - | -100.00 | 6 (2.5) |
| **Ciprofloxacin** (J01MA02) | 3 (2.1) | 2 (2.0) | -33.33 | 5 (2.1) |
| **Others** | 14 (10.0) | 10 (9.8) | -28.57 | 24 (9.9) |

**Discussion**

Antimicrobial surveillance is important to identify the targets for quality improvement and to control the emergence of AMR, especially among immunocompromised patients. In the present study, the prevalence of antimicrobial use appears high at 49.8%, which is higher than the prevalence reported in previous studies ([33](#_ENREF_33)), but less than China ([35](#_ENREF_35)). This may be because of the nature of the patients. The high proportion of broad-spectrum antimicrobial use in this present study is a concern as lower use of broad-spectrum antimicrobials indicates better prescribing practice ([36](#_ENREF_36)). The UK has effectively managed to decrease the use of the broad spectrum antimicrobial use by introducing ASPs ([13](#_ENREF_13), [14](#_ENREF_14)), providing guidance to others. This high use of broad-spectrum antimicrobials may be because of patient factors or the severity of diseases. The specialized cancer care hospitals have more immunocompromised patients as compared to small hospitals. This will be investigated further in future research projects.

Another concern is the very high use of parenteral antimicrobials in this study, which may be due to the high use of broad-spectrum antimicrobials for which no per-oral equivalent is available. In addition, a number of physicians consider parenteral therapy is better than oral administration and that ([37](#_ENREF_37)). Additionally, parenteral antimicrobial use is unavoidable in immunocompromised patients with life-threatening infections. Whenever possible though, hospitals should develop institutional guidelines to switch from IV to oral therapy ([38](#_ENREF_38), [39](#_ENREF_39)). The timely change to oral from parenteral therapy is a potential quality parameter, owing to its many benefits, such as reduced costs, reduced possibility of catheter-related infections and the likelihood of early discharge ([38](#_ENREF_38), [40](#_ENREF_40), [41](#_ENREF_41)). However, it is not fully recognized yet to what level different routes of antimicrobial administration have on AMR rates ([42](#_ENREF_42)).

Future strategies to rationalize antibiotic use can include looking at ways to reduce the extend of extended prophylaxis to prevent surgical site infections as this can enhance AMR rates as well as the extent of hospitalization ([43](#_ENREF_43)). This can be followed up as part of implementing ASPs in this hospital, acknowledging these are more difficult in LMICs ([4](#_ENREF_4), [12](#_ENREF_12)). We will be following this up in the future in this hospital to improve future antimicrobial use. ASPs can include prescribing guidance and categories of antimicrobial use, e.g. restriction of certain antibiotics. ASPs can also include greater use of culture and sensitivity reports with less reliance on the empiric use of antibiotics, as well as emphasizing the need to document the rationale for the antibiotic chosen in terms of potential organisms and the infection site. ASPs can also reduce the length of prescribing of antibiotics to reduce surgical site infections in cancer patients given concerns with longer lengths ([43](#_ENREF_43), [44](#_ENREF_44)) as well as enhance earlier switching from IV to oral antibiotics where appropriate. However, implementing an ASP takes resources and time. It may be useful to initiate small and grow, and we will be pursuing this in our hospital. We are aware that there are some limitations with our study. Firstly, it was not possible to evaluate the appropriateness of antimicrobial treatment due to the absence of institutional and national antimicrobial prescribing guidelines. This can be a critical part of any future ASP in the hospital. Secondly, we have not checked the type of cancer, type micro-organism and co-morbid conditions of each patients for some of the reasons stated. This will be followed up in future research as part of ASPs. Lastly, as this was the first PPS in this cancer care hospital, successive surveys must be conducted in other hospitals to know the exact pattern of use in cancer patients.

**Conclusion**

There is a concern regarding the high use of broad-spectrum antimicrobials in this cancer hospital, which can be a risk factor for the emergence of multidrug-resistant microbes. Repeated PPS is a fruitful way to maintain a focus on appropriate antimicrobial use leading to the development of pragmatic intervention programs targeted at specific issues.

**Funding**

This paper was not funded.

**Declaration of interest**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

**Acknowledgments**

This study would not have been possible without the contribution and involvement of administration and staff of the hospital.Their cooperation is thankfully appreciated.

**Contributions of authors**

Z Saleem and M A Hassali were involved in the conception and design of the study. M A Hassali, O A Bhutta and F K Hashmi helped in analysis and interpretation of the data. M A Hassali, B Godman and Z Saleem were involved in the drafting of the paper. Z Saleem and B Godman revised it critically for intellectual content. M A Hassali gave the final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

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