ORIGINAL ARTICLE

Point prevalence survey on antibiotics usage at a tertiary care public sector hospital employing WHO methodology

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ABSTRACT

Background: Antimicrobial resistance (AMR) kills 7 million people annually. WHO recognized AMR as a global threat in 2017 and launched the Point Prevalence Survey (PPS) methodology in 2018. The situation in Pakistan is even worse with an overall prevalence of antibiotic usage of 75 per 100 population.

Material and Methods: This cross-sectional survey was conducted on a single day, 25th May 2024, at the Pakistan Institution of Medical Sciences (PIMS), with a sample size of 271 of 822 eligible patients. The PPS team collected the data using a questionnaire based on the WHO PPS methodology. All acute care and ward patients hospitalized at or before 8:00 A.m. were included.

Results: A total of 271 patients were included in the survey, 110 (40.60%) were females, and 161 (59.40%) were males. The patients aged> 2 months were 248 (91.50%) and < 2 months were 23 (8.5%). The prevalence of antibiotic use in PIMS was 210 (77.6%). The culture sample sent before the first dose of antibiotic was only in 57 (27.1%) patients. The largest indication was community-acquired infections 40 (55.56%). Blood was the most common form of sample sent 45 (47.36%). The culture positivity rate was 21.05%. Klebsiella Pneumoniae was the most detected organism at 25% followed by Pseudomonas aeruginosa at 15%. The target antibiotic prescriptions were only 13.3%. Ninety percent of the antibiotics were given via parenteral route. Ceftriaxone was the most popular antibiotic used 62(20%).

Conclusion: Antibiotics are widely used in our hospital, with the majority being empirical. Most antibiotics are used to treat community-acquired illnesses. Patients whose cultures were sent before their initial antibiotic treatment make up a minor proportion.

Keywords: Community-acquired infections, Indication, Culture, Antibiotic consumption, Point prevalence survey, MDROs

BACKGROUND

The emergence of antibiotic resistance has increased morbidity and mortality rates among patients across the globe. Antimicrobial resistance results in the death of 7 million people annually, reducing 2.5% of the world's GDP.[1] Antimicrobial resistance (AMR) is usually a consequence of multiple factors like injudicious use of antibiotics owing to incorrect dosage, duration, and indication; knowledge gap in prescribing antibiotics; over-the-counter (OTC) availability; and limitations in diagnostics due to cost and unavailability.[2] The Centers for Disease Control and Prevention (CDC) endorses improvement in diagnostics and treatment. Infection prevention control and monitoring of prescribing practices.[3]

WHO recognized AMR as a global threat in 2017 and published guidelines for global antimicrobial resistance and the use of surveillance systems[2]. WHO launched the Point Prevalence Survey (PPS) methodology of hospital antibiotic use in 2018. The PPS was already in use at multiple centers in Europe and the USA, The WHO decided to develop a method that reflects both resource limitations of low and middle-income countries (LMIC)and is also comparable to data collected in high-income countries.[4] Global PPS launched in 2015 in Belgium is used by more than 700 hospitals worldwide including LMIC. It provides a detailed method of antimicrobial stewardship programs and support to participating hospitals for electronic data entry and analysis.[5]

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During the COVID-19 pandemic, there was a massive increase in injudicious use of antibiotics. The antibiotic stewardship programs were affected due to the diversion of resources to harness the COVID-19 Pandemic.[6 7]The increase in hospital-acquired infections during the pandemic in resource-limited countries like Pakistan had a drastic impact on antimicrobial utilization in hospitals.[7]

A multicenter survey conducted in Punjab the largest province of Pakistan reported 77.6% use of antibiotics at different centers throughout the province.[8] The same team endorsed their finding in another article through a longitudinal survey of three weeks in Lahore. The AMR network and 20 healthcare facilities all over Pakistan are establishing the Pakistan AMR Surveillance System (PASS).[2] The AMR team from the National Institute of Health Pakistan recently published a PPS showing a prevalence of 75 per 100 population in collaboration with WHO across 14 tertiary care hospitals designated as GLASS sentinel sites as a step towards establishing PASS.[1]

This Point Prevalence survey was conducted at the Pakistan Institute of Medical Sciences (PIMS), the largest public sector hospital in the northern region of Pakistan. PIMS caters to thousands of patients daily. The findings of this survey will generate a step toward the launch of the Antimicrobial Stewardship Program, and it will impact overall cost reduction and diversion of resources toward improving diagnostic facilities at PIMS and other healthcare facilities.

MATERIAL AND METHODS

This cross-sectional survey was conducted on a single day on 25th May 2024 at the Pakistan Institute of Medical Sciences (PIMS) after taking the approval from Institutional Ethical Review Board (vide reference number F.1-1/2015/ERB/SZABMU/1274). The sample size was 268, calculated by the WHO calculator within a 95% confidence interval. The anticipated population proportion of antibiotic usage was 77.6% from a reference study. The absolute precision was 0.05. The study setting is the inpatient departments of the Pakistan Institute of Medical Sciences

The inclusion and exclusion criteria were according to the WHO methodology document and stratification given in that, except for a few changes.

1. **Hospital:** This survey is primarily designed for tertiary acute care hospitals with an inpatient psychiatric department excluding all nursing homes: rehabilitation and psychiatric centers.
2. **Ward:** Acute care inpatient wards and the emergency departments linked to the ward. The long-term care and daycare medical and surgical wards were excluded from the survey.
3. **Patients:** Patients hospitalized as an inpatient at or before 08:00 am with a special note.
   a) All neonates born before 08:00 on the day of the survey are included and counted separately from their mother, that is mother and baby count as two different patients.
   b) All patients meeting the eligibility criteria were included in the survey regardless of whether they received antibiotic treatment.
   c) All eligible patients underwent the consent approval process.
   d) The patients of outpatient clinics, day surgery/ day treatment, outpatient dialysis, discharged patients waiting for transportation, outpatient parenteral antibiotic therapy (OPAT), and parents/relatives of admitted children were excluded.
4. **Antibiotics:** All Listed antibiotics (Annex XI of WHO document)[4] and ongoing treatment at 08:00 am were included in the survey. The treatment initiated after 08:00, and treatment discontinued before 08:00 was excluded. There were some special situations as follows.
   i. Those antibiotics that were not administered daily, but the patient was on therapy before 08:00 am, were still reported. i.e. patients with renal impairment with reduced dosing frequency or long-acting antibiotics which are administered at prolonged intervals, such as every 48 hours or more.
   ii. Single-dose regimes, such as gentamycin in combination with other antibiotics, were included if the dose was given within 24 hours before 08:00 am on the survey day.
   iii. If the patient was on treatment of antibiotic A at 08:00 on the day of the survey, but the treatment was changed to antibiotic B at 10:00, then only antibiotic A was reported.

iv. The antibiotics administered through oral, parenteral, rectal, or inhalation routes were included in the survey. The topical applications, eye drops, ear drops, and vaginal suppositories were excluded.

The survey team included doctors from the ID department, the IPC unit, medicine, surgery, Gynae, Federal Medical and Dental College community medicine department, and data entry personnel. The team was given proper training on the survey and questionnaire a week before the survey in a day workshop. The training on all the codes mentioned in WHO methodology (ANNEX I- ANNEX XI) was offered for the team[4]. The handouts were also provided for ready reference.

After ethical approval by the board, the survey was conducted in the whole hospital including Emergency Departments of different specialties and the inpatient facilities linked to those like Medicine & Allied, Surgery & Allied, Pediatrics, Gynae & Obstetrics, Cardiac ER, and burn center. The survey was also done in the Intensive Care Areas linked to medical, Surgical, Pediatrics& Neonates, Burn, Gynae & Obstetrics, and cardiology units (MICU, SICU, PICU, NICU, BICU, OBS HDU, and CCU). The information about the date, procedure, and time of PPS was disseminated through prior notification to all departments by the hospital administration. The informed consent was also attached to the notification.

The list of all admitted patients was obtained one night before the survey. After informed consent, every first and third patient from each site was included in the study. The WHO questionnaire (ANNEX XV) was converted into Google Forms for easy data collection.

The data collected was segregated further into ward and patient levels because this survey was for the in-hospital use of antibiotics in a tertiary care hospital in Pakistan.[4]

1. **Ward-level data:** The ward-level data included information on the type of ward, number of eligible and included patients, and ward characteristics.
2. **Patient-level data:** The patient-level data was categorized into three distinct groups:
   i. **Patient Information:** This included patient characteristics and was gathered for all surveyed individuals, regardless of antibiotic treatment. Collected data encompassed sociodemographic factors (e.g., age and gender) and risk factors influencing antibiotic administration during the current hospitalization. These details aided in adjusting for the variation in patient populations across different hospitals.
   ii. **Indication Information:** This section entailed data concerning the rationale behind antibiotic prescription, encompassing factors like diagnosis, indication type (therapeutic or prophylactic), and infection type (hospital-acquired, community-acquired), among others. Multiple indications may necessitate antibiotic treatment, or the specific indication might be unknown.
   iii. **Antibiotic Therapy Information**: This category comprised details on prescribed antibiotics including total count administered since admission, type, administration route, dosage strength, frequency, and adherence to clinical protocols. Antibiotics were documented for all included patients using the clinical name mentioned in notes and the International Nonproprietary Names (INN) of the substance(s). Each antibiotic substance was tallied only once, irrespective of whether different formulations were prescribed or if the same substance was administered multiple times with intermittent interruptions in treatment.

The data was analyzed by IBM SPSS (Statistical Package for Social Sciences) version 29. The variables were categorized as core and optional: core variables collect information necessary to achieve the survey objectives, including estimating the prevalence of antibiotic use and assessing the treatment indication. For ease of data management and analysis, responses to the survey were entered uniformly between the wards.

RESULTS

Out of 822 eligible patients in different wards 271 patients (every 1 in 3) were included in the survey. Both core and optional variables were recorded according to WHO methodology but only core variables are reported in results. The data was recorded at the hospital, ward, and patient levels. The prevalence of antibiotic usage in PIMS was 210 (77%). A total of 61 (23%) patients were not on antibiotics. The culture samples were taken only

from 57 (27.1%) patients before antibiotic administration. In 153 (72.8%) patients, culture samples were not sent.

The data was analyzed and presented at the hospital, ward, and patient levels. The core variables were documented and presented in results although optional variables were also recorded during the survey. Table I shows key variables recorded about the hospital and wards on the survey day.

The patient-level data is further segregated into patient demographics, indication data, and antibiotics data. The demographics of all 271 patients were mentioned regardless of whether they were on antibiotics. There were 110 (40.60%) females, and 161 (59.40%) males. The patients of age > 2 months were 248 (91.50%) and < 2 months were 23 (8.50%). The indications mentioned for all the 210 patients were numbered up to 4 for each patient according to WHO methodology[4]. The indications were reported overall of which most were Community-acquired infections 45 (55.56%) followed by Hospital-acquired infections, 25 (28.08%), and Surgical Prophylaxis 10 (11.23%). The surgical prophylaxis usually comprises multiple doses (SP2, SP3), rather than a single dose (SP1). It was given mostly for Gastrointestinal, skin, soft tissue, bone, joint, and Otolaryngologic surgeries.

The indication data also contained information about microbiology. Multiple specimens were sent for each patient in a total of 95, out of which 73 (76.84%) were specimen 1, 18 (18.94%) specimen 2, and 4 (4.21%) were specimen 3. Blood was the most sample type 45 (47.36%) followed by Urine 21 (22.10%). Positive results were about 20 (21.05%) of all specimens. Klebsiella pneumoniae was the most detected microorganism 5 (25%) followed by Pseudomonas aeruginosa 3 (15%) and Acinetobacter spp. 2 (10%). All the detected Acinetobacter spp., half of the Pseudomonas aeruginosa, one-fourth of Staphylococcus aureus, and 20 % of the Klebsiella pneumoniae were of the resistant phenotype. A total of 310 antibiotics listed in the treatment list of patients were included. Mostly these were parenteral 279 (90%), and only 31 (10%) were oral. No antibiotics were via inhalational and rectal routes of administration. The number of antibiotics per patient was mostly one or two. Most of these were empirical, Figure 1. Maximum (up to 4) antibiotics per patient were prescribed in ICUs. None of the patients were on antibiotics 5 and 6, Table II.

Ceftriaxone was the most favorite antibiotic 62 (20%) followed by cefoperazone-sulbactum 42 (13.5%). Piperacillin-tazobactam 35 (11.29%) and Meropenem 25 (8.08%) were also widely used, Figure II.

Table-I: Core variables at hospital and ward levels.

Hospital		
Hospital Type	Tertiary care	
Hospital Ownership	Public	
Hospital total beds	1260	
Hospital acute beds	105	
Hospital ICU beds	115	
Hospital high-risk bed	41	
Hospital bed occupancy rate	70%	
Hospital Eligible Patients	822	
Hospital included patients	271	
Ward		
Wards Type	**Eligible Patients**	**Included Patients**
Burn Care Centre	14	6
Acute Care Area	21	11
Medicine and Allied	204	94
Surgery and Allied	196	89
Critical Care Area	67	38
Gynae & Obs	20	12
Pediatrics	40	21

Table-II: Patient-level data (Demographics, Indication data, antibiotic data).

Patient Demographics		
Gender	Females	110 (40.6%)
	Males	161 (59.4%)
Age	<2years	23 (8.5%)
	>2years	248 (91.5%)
Preterm birth		4 (1.5%)
Central Venous Catheter		14 (5.2%)
Peripheral Vascular Catheter		194 (71.6%)
Urinary Catheter		82 (30.3%)
Intubation		31 (11.4%)
Surgery since admission		24 (6.4%)
Indication data		
Indication	Yes	89 (42.4%)
	No	121 (57.6%)
Indication Type	Community Associated Infections (CAI)	45 (50.6%)
	Hospital Associated Infections (HAI)	25 (28.1%)
	Medical Prophylaxis (MP)	9 (10.1%)
	Surgical Prophylaxis (SP)	10 (11.2%)
Surgical Prophylaxis duration	SP2: multiple doses within 24 hours	2 (20%)
	SP3: multiple doses for a duration extending 24 hours	8 (80%
The reason mentioned in the notes		134 (49.4%)
Total Specimens sent		n=95
Specimen Type	Blood	45 (47.4%)
	Urine	21 (22.1%)
	BAL/Sputum	11 (11.6%)
	Sterile Fluids	13 (13.7%)
	Shunt tip	1 (1.1%)
	Pus	1 (1.1%)
	Tissue	1 (1.1%)
	Wound	2 (2.1%)
Culture Results (Positive)		20 (21.1%)
Microorganism Detected	Acinetobacter spp.	2 (10%)
	Klebsiella Pneumoniae	5 (25%)
	Pseudomonas Aeruginosa	3 (15%)
	Staphylococcus Aureus	4 (20%)
	Klebsiella and Pseudomonas	1 (5%)
	Mycobacterium kansasii	1 (5%)
	MTB	2 (10%)
	Candida spp.	1 (5%)
	Aspergillus flavus	1 (5%)
	Cryptococcus neoformans	1 (5%)
Resistant Phenotype	Acinetobacter spp. (CAR, COL, Unknown)	2 (100%)
	Pseudomonas aeruginosa (CAR, Unknown)	2 (50%)
	Staphylococcus aureus (MSSA, MRSA, VRSA, VISA, Unknown)	1 (25%)
	Enterobacteriaceae (C3G, CAR, ESBL, Unknown)	1 (20%)
Antibiotics data		
Antibiotics prescribed		n=310
Route of administration	Parenteral	279 (90%)
	Oral	31 (10%)
	Inhalational	0
	Rectal	0

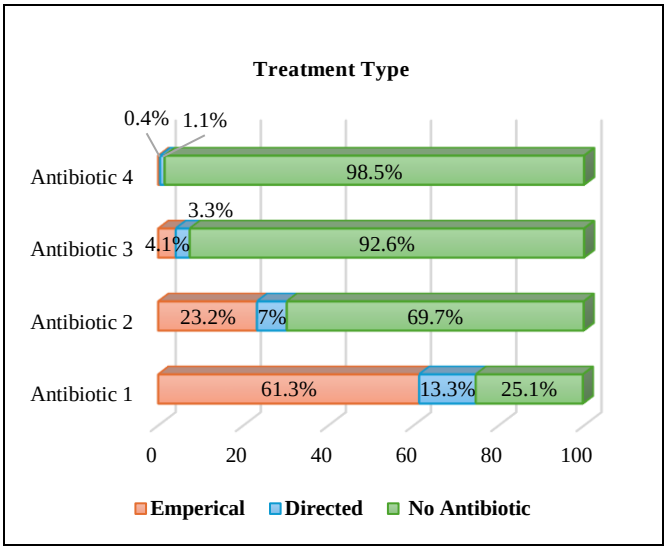

Figure I: Number of antibiotics and treatment type.

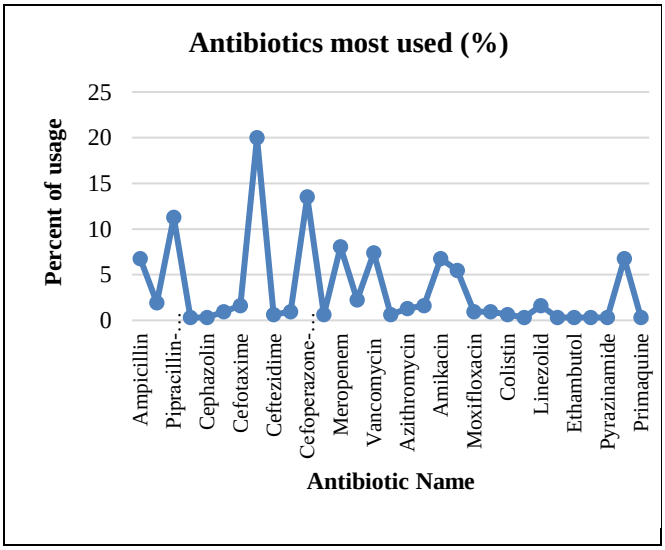

Figure II: Antibiotics names and their usage.

DISCUSSION

This Point Prevalence Survey (PPS) was conducted in Pakistan's largest tertiary care hospital as a pre-study for the launch of the Antimicrobial Stewardship Program. Global-PPS recommends first baseline PPS to initiate AMS activities to drive changes in antimicrobial prescribing practices in the institution. The repeated Global-PPS can be used to measure the impact of tailor-made AMS interventions.[9] The AMS is a dire need for a large public hospital like this to reduce the burden on both pharmacy and microbiology laboratories keeping improvement in patient care as a prime goal. Unfortunately, in this survey, 77% of the patients were on antibiotics, and only 26.9% of specimens were sent for cultures. The Global-PPS was conducted in 248 hospitals worldwide, with a high antimicrobial use prevalence (60.4%) reported. This percentage varies between 50-95% in different studies published in various areas of Pakistan[2,3,8,10] The National Institute of Health (NIH) and the World Health Organization (WHO) conducted a national PPS at fourteen acute tertiary care hospitals from the public and private sectors designated as GLASS sentinel sites. This study reported a 70% prevalence in public hospitals and 68% in private Hospitals.[1]

A national PPS in 41 hospitals in Thailand reported that the tertiary care hospitals had the highest percentage of antibiotic use about 55%, again highlighting the importance of this survey at our facility. Antibiotic use was highest in the critical care area, 76.7%. This is comparable to our survey, in which critical care was the largest antibiotic-using site about 56.71%.[11] Another study shows that the medicine department was the largest antibiotic-utilizing site instead of ICUs (medicine 41%, ICUs 35%).[14] Our study showed trends in the use of invasive devices like those all over the world, i.e., Peripheral venous catheter (71.6% versus 84%), central venous catheter (5.2% versus 4%), Urinary Catheter (30.30% versus 15%), and Intubation (11.40% versus 3%).[12] Another study indicates that community-acquired infections (CAI) were the main cause of antibiotic prescription (30.17%), like our study in which the CAIs were 58.56% and HAIs 28.08%.[6] In contrast, another study reported HAI (40.3%) and CAI (33.8%).[13] As shown in our study's results, surgical prophylaxis was multiple doses (SP3 80%, SP2 20%). This is consistent with the results from a Global-PPS survey conducted in four African Hospitals (SP2 17.9%, SP3 75.5%).[14]

The microbiology section of ANNEX XV of the WHO questionnaire contains important variables about the microbiology lab. The recording and analysis of these can profoundly impact the implementation of interventions to improve microbiology lab.[4] This will ultimately result in overall cost reduction through decreased utilization of antimicrobials due to targeted therapy. Sadly, only 26.9% of culture specimens were sent to our facility. This is consistent with data from other facilities in Pakistan i.e. in one study only 18.87% of the sample sent of all patients on antibiotic therapy. The percentage of positive results was 19.23% of all retrieved reports as of similar percent (21.05%) in our study.[15] The blood sample is the first most favorite sample for culture and sensitivity at most hospitals

(53.44%), and the Urine sample is the second one (21.9%). The samples sent to our hospital were also mostly blood (47.36%) followed by Urine (22.10%). The organisms detected from these samples were mostly Klebsiella pneumoniae (KP, 25%), Staphylococcus aureus (20%), and Pseudomonas aeruginosa (15%). These results were slightly different from many other published studies i.e. one of these studies showed E. coli at 20.08%, Acinetobacter at 16.0%, KP at 15.4%, and Staphylococcus aureus at 8.2% of the samples.[13] The percentages of Multidrug-resistant organisms (MDROs) calculated during our survey were Acinetobacter and Pseudomonas aeruginosa both 10%, and MRSA and Enterobacteriaceae (All were KP) 5% each. A study from India showed MRSA 18.4%, Enterobacteriaceae (ESBL and CRE, 9.1%), Acinetobacter (2.6%), and Pseudomonas (2.6%).[16]

The last part of the WHO questionnaire is information about antibiotics. A large amount of data was recorded about dose, frequency, and missed doses of each antibiotic but could not be presented due to the limitations of this script. The antibiotic therapy was mostly empirical at our hospital with only 13.3% of one antibiotic, 7% of the second antibiotic, and 3.3% of the third antibiotic targeted. This percentage is quite improved in the west i.e. 39.4% from a Global PPS in 47 Canadian hospitals.[17] Most of the antibiotics administered were parenteral rather than of other routes (Parenteral 90%, Oral 10%). This finding was like other public tertiary care hospitals (Parenteral 95.5%, Oral 5.5%).[12] The data on the type of antibiotic used in our hospital is heavily influenced by antibiotic availability in the hospital formulary, as many patients admitted are non-affording and have no other option but to be prescribed antibiotics from the hospital formulary. Ceftriaxone was found to be of the highest percentage (13%), of all "Watch" antibiotics utilized worldwide according to the global-PPS 2023 report. The use of meropenem is 4.3% across the world and highest in Asia at 5.2%.[18] In our survey, ceftriaxone was also the most favorite antibiotic used in the hospital (20%) followed by cefoperazone-sulbactam (13.54%), and piperacillin-tazobactam (11.29%). The meropenem has also been the choice of prescribing pen although it's not frequently available in hospital formulary (8.06%).

The WHO PPS is oversimplified to facilitate adoption, but this has compromised the reliability and comparability of estimates. It does not guide many issues that have been identified in various studies. The documentation is often deficient and clinical information is fragmented at large public hospitals. Public hospitals like ours have only limited implementation of EMR and the data is scattered among patient files and EMR. The PPS team must be well acquainted with local EMR. The lack of supervision and quality control can generate inconsistencies in data recording. The patients are sometimes relocated to different wards due to the unavailability of beds. The clinical characteristics of patients will then not correspond to their wards leading to misclassification of patients. Antibiotics prescribed for different indications can sometimes lead to false interpretations of PPS estimates. The classification of HAI is sometimes misleading if the diagnostic tests are not done and the exact date of onset of infection is not known. It is also influenced by the concerns relating to the consequences of higher authorities.[19]

There should be proper training in PPS and the type and timing of training should be clarified. Formal and quantitative assessment of inter-observer agreement should be done before data collection. The team must be familiar with and have access to hospital EMR. The discordances in the data must be discussed with care providers and inconsistencies should be recorded. The team should formalize a method of recording antibiotics used for more than one indication beforehand. The HAI should be classified carefully, the problems should be discussed with healthcare personnel otherwise data should be classified as missing.[19]

CONCLUSION

There is a high prevalence of antibiotic use at our hospital, most of which are empirical. Most antibiotics are prescribed for community-acquired infections. The patients whose cultures were sent before the first dose of antibiotics constitute only a fraction of the total number of patients whose cultures were sent. The percentage of MDROs is on the rise globally and in our hospitals but many infections are never recorded due to many factors, especially at public sector hospitals. There is a need to strengthen microbiology services to implement interventions for AMS. Proper training of the PPS team and their knowledge of local challenges can improve the reliability of oversimplified WHO PPS.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Sana Tahir Virk: Conceptualization, data analysis, data interpretation, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Nasim Akhtar: Critical review for intellectual content, revisions, final approval, agreement to be accountable for all aspects of the work

Kazim Abbas Virk: Study design, literature search, final approval, agreement to be accountable for all aspects of the work

Abeer Zafar: Data collection, data interpretation, final approval, agreement to be accountable for all aspects of the work

Syed Zawwar Zia: Data collection, data interpretation, questionnaire design, final approval, agreement to be accountable for all aspects of the work

Wajeh Haider: Substantial contribution in data collection, final approval, agreement to be accountable for all aspects of the work

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