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Evaluation of the antimicrobial prescribing pattern and the stewardship programs among COVID-19 hospitals in the capital city of Kurdistan-Northern Iraq: A multicenter point prevalence study

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ABSTRACT

Antimicrobial resistance (AMR) is a significant threat to healthcare system as making infections difficult to be cured and enhances disease transmission and death. Thus, prudent antimicrobial use is crucial to combat AMR, particularly in Erbil City/Northern Iraq because of the high rate of multidrug-resistance microorganisms. There is limited data on the extent and quality of antimicrobial use in Kurdistan, including COVID-19 hospitals. This study aimed to assess the prevalence and quality indicators of antimicrobial use, the status of antimicrobial stewardship program (ASP), and hospital capacity infrastructures. From September 30th 2021 to February 8th 2022, all COVID-19 hospitals in Erbil/Northern Iraq were surveyed using the Global point prevalence survey methodology. Prevalence of antimicrobial use was at the top (100%, n = 71/71), and carbapenem was the most used antimicrobial class (44.0%, n = 55/125). The majority of the prescribed antimicrobials were in WHO Watch class (88.4%, n = 76/86), high use of parenteral therapy (99.2%, n = 124/125), low targeted therapy (2.4%, n = 3/125) and neither stop/review dates documented, nor local guidelines were available. ASP was not implemented while most of the hospitals had a priority for the medium or long term to implement ASP (66.7%, n = 2/3) out of 11 hospital capacity infrastructures, only four of them were present adequately. The findings demonstrated a high and sub-optimal quality of antimicrobial prescriptions, lack of ASP, and inadequate hospital capacity infrastructures. Quick action is necessary to establish ASP to combat antimicrobial resistance, and the critical target areas include development of the local guidelines and documenting stop/review date.

Keywords: Antimicrobial use, COVID-19, Point prevalence survey, Antimicrobial stewardship program.

1. Introduction

Wuhan, China, became the epicenter of unexplained pneumonia cases in December 2019. Chinese scientists identified it as a new coronavirus in January 2020, temporarily dubbed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As the disease spread worldwide, the WHO changed its name to coronavirus disease 2019 (COVID-19) in February 2020[1].

Despite the viral origin of COVID-19 and the absence of evidence of bacterial superinfection in a vast majority of cases, physicians are compelled to prescribe a multitude of antimicrobials due to the lack of a specific antiviral treatment and vaccine against it, inability to distinguish between bacterial pneumonia and COVID-19, and unreliability about secondary bacterial infection[2]. Antibiotics were prescribed for 72% out of "2010" of COVID-19 patients, these drugs tended to be broad-spectrum and empirical[3] which affect the long-term care of COVID-19 patients and control the antimicrobial resistance (AMR)[4]. Point prevalence surveys (PPS) offers a quick way to determine the quantity and quality of antibiotic prescription, hence facilitating the development of antimicrobial stewardship initiatives[5].

Iraq has a significant prevalence of multidrug-resistant (MDR) microorganisms, including *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella*, and *Staphylococcus aureus*. The leading cause of their resistance is the misuse of antibacterial drugs[6]. In Iraq including the Kurdistan Regional Governorates, despite of the presence of high rates of AMR, the data on antimicrobial consumption patterns in secondary healthcare settings especially among COVID-19 patients are very limited, aside from one study being conducted in Sulaymaniyah governorate prior to the COVID-19 pandemic period, which included three public hospitals, and was solely focused on antibiotics rather than antimicrobials drugs, and did not examine the status of ASP and hospital capacity infrastructures[7]. Consequently, this study aims

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to assess the prevalence and quality of antimicrobial prescribing patterns, ASP status and hospital capacity infrastructures in all COVID-19 hospitals in Erbil City, Northern Iraq.

2. Patients and Methods

2.1. Study design and setting

This study was a multicenter, cross-sectional PPS of antimicrobial prescribing practices using a methodology being validated for use in the Global PPS[8]. Data were collected between September 30th 2021 and February 8th 2022 from all three COVID-19 hospitals in Erbil City (capital of the Kurdistan Region) in North Iraq. Hospital characteristics are available as Supplementary data at Passer online (Table S1).

2.2 Inclusion and exclusion criteria

All male and female adult inpatients aged ≥18 staying overnight, present on the ward at 8 a.m., and receiving “at least one antimicrobial drug” on the day(s) of the survey. For the status of ASP and assessing the capacity of hospital, the participants were hospital managers or key personnel involved in and/or knowledgeable about the management, administration, and performance of significant hospital policies and initiatives. The study excluded patients who were admitted to outpatient or emergency departments, as well as day hospitalizations such as endoscopy or renal dialysis and patients who were hospitalized before 8 a.m. or after 8 a.m. on the day of the survey.

2.3 Data collection

The approved standard PPS tools were used to gather data, as described in depth in the Global PPS protocol[9]. All wards were surveyed on any weekday except weekends and public holidays, and surgical wards were surveyed 24 hrs after surgery. For prevalence and quality of antimicrobial prescription, brief data were obtained using the two PPS forms for each hospital see Supplementary data at Passer online (Figures S1 and S2): Ward form was used to collect ward-level data for each ward, including the total of inpatients (the denominator), and the patient form was used to record the number of patients on antimicrobials (the numerator), data collection of each ward completed in a single day. The diagnosis was changed to either confirmed or suspected COVID-19 if on invasive or non-invasive mechanical ventilation or on oxygen mask only in the patient form.

For the status of ASP and assessing hospital capacity, participants were directly visited at their offices and were initially informed about the study aims, objectives, and a piece of a detailed information about the questionnaire; then, they were invited to participate. Those who agreed to participate were provided with the study questionnaire. The status of ASP was assessed using a questionnaire, see Supplementary data at Passer online (Figure S3), which was designed by the CDC and the WHO[10,11]; both tools contain questions that are related and mapped to the seven core elements of ASP. Moreover, the capacity of each hospital was assessed using a validated questionnaire, see Supplementary data at Passer online (Figure S4).

2.4 Study outcome and output measures

The estimation of the prevalence and quality of antimicrobial usage and assessing the status of ASP and hospital capacity were the primary study outcome measures. Prevalence of antimicrobial use was calculated by dividing the number of patients receiving antimicrobials (the numerator) by the total number of admitted patients (the denominator), then stratifying the results according to individual hospitals and ward types (medical, surgical, ICU). According to the WHO Anatomical Therapeutic Chemical (ATC) classification, antimicrobial agents were categorized to include all antimicrobial agents listed in the Global PPS protocol, then stratifying the results according to the ward types and COVID-19 severity.

Quality indicators being used in this study depend on the previous PPS studies, including the frequency of parenteral therapy and targeted therapy, availability of local treatment guidelines, documentation of the antibiotic indication, diagnosis and dose, along with documentation of a stop/review date[12]. In addition, antibiotics were categorized according to the most recent Access, Watch and Reserve (AWaRe) categorization developed by the WHO[13], and the results were stratified according to the hospitals and the ward types (medical, surgical, ICU). The hospital capacity infrastructures and status of ASP were summarized as percentages and proportions overall and for each individual core element of the ASP.

2.6 Ethics

The study data is recorded anonymously, and no patient identifiers are collected. The study does not entail direct contact with patient; hence, patient consent is unnecessary. For the status of ASP and assessing hospital capacity, formal consent is given to those who accept to enlist in the study questionnaire. The study protocol is approved by the Research and Ethics Committee of Hawler Medical University/College of Pharmacy and General Health Directorate of Erbil.

3. Results and Discussion

There are no studies concerning patterns of antimicrobial use in COVID-19 patients in Iraq and its neighbors. Therefore, our findings are being compared to those of other nations being studied. Prevalence of antimicrobial use was 100% (n = 71/71) regardless of ward types (Tables 1 and 2), which is higher that of a systematic review and meta-analysis including 24 countries (71.9%)[14], and a systematic review and meta-analysis including 22 countries (61.77%), from Asia (40.81%)[15].

Table 1: Prevalence of antimicrobial use in COVID-19 hospitals.

Hospitals		**Prevalence of antimicrobial use**		
	N*	**No.**	**(%)**	**P-value**
West Erbil Emergency Hospital	44	44	(100.0)	
RCU Lalav Hospital	10	10	(100.0)	
Central Emergency Hospital	17	17	(100.0)	NA**
Total	71	71	(100.0)	

*N: Number of admitted patient. **NA: Not applicable.

Table 2: Prevalence of antimicrobial use in COVID-19 hospitals stratified by ward types.

	Hospital 1		**Hospital 2**		**Hospital 3**		**Total**
Ward**	**N***	**No. (%)**	**N***	**No. (%)**	**N***	**No. (%)**	**No. (%)**
AMW	33	33 (100.0)	-	-	17	17 (100.0)	50 (100.0)
ASW	-	-	-	-	-	-	
AICU	11	11 (100.0)	10	10 (100.0)	-	-	21 (100.0)
P-value		NA†		NA †		NA†	

*N: Number of admitted patient. **Ward type: AMW: Adult medical ward. ASW: Adult surgical ward. AICU: Adult intensive care unit. †NA: Not Applicable.

Variation in the prevalence of antimicrobial prescription between our study and compared studies is primarily due to the lack of ASP (Figure 1), lack of local treatment guidelines, lack of stop/review date, high empirical therapy, shortage in hospital capacity infrastructures (Figure 2), and possibly due to several other factors; such as prescriber's uncertainty about the diagnosis, knowledge, attitudes, and perception regarding antimicrobial prescribing, local epidemiology, patterns of microbial resistance as well as lack of well-trained clinical pharmacist[16]. Also, could be due to the novel feature of the infection and pandemic fear due to the advanced awareness of mass media in our country[17] as well as the confirmation of suspected co-infection in hospitalized patients[18].

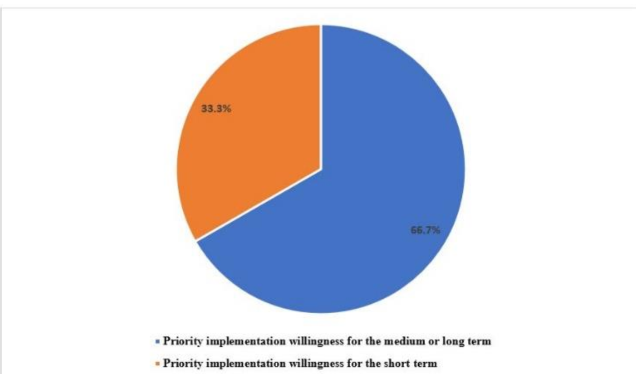

Figure 1: Prevalence of implementing antimicrobial stewardship program in short, intermediate, and long term in COVID-19 hospitals.

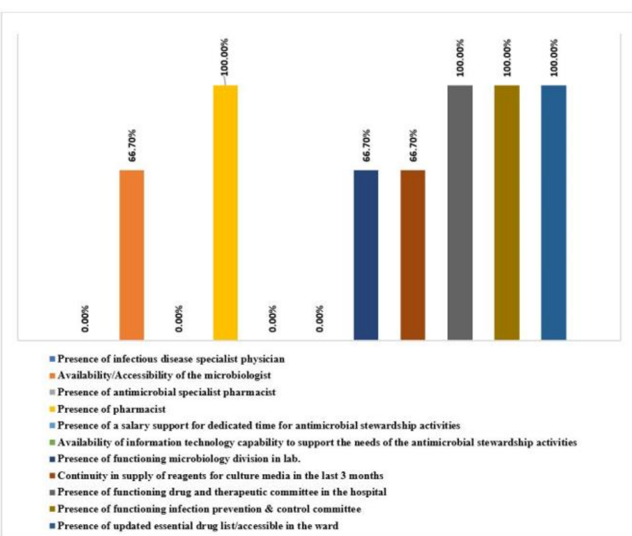

Figure 2: Prevalence of hospital capacity infrastructures in COVID-19 hospitals.

Our study was comparable to a Bangladesh PPS, including 193 patients (100%)[19] and a systematic review and meta-analysis including 43 articles involving low and middle-income countries (89%). This high rate might be attributed to the lack or poor ASP in low and-middle income countries but good ASP status in high-income countries[20]. Additionally, comparable to the studies of the same region involving non-COVID-19 patients in Sulaymaniyah/Northern Iraq which included three major public hospitals in 2019 (93.7%), possibly reflecting lack of ASP, inadequate hospital capacity infrastructures and poor quality of antimicrobial prescription in Iraqi cities[7].

The most prescribed antimicrobial class was carbapenems (mainly meropenem) (J01DH) (44.0%, n = 55/125), followed by the RNA polymerase inhibitor (J05XX) (26.4%, n = 33/125) (Table S2). While the most prescribed class in Pakistan were azithromycin (35.6%), ceftriaxone (32.9%), and meropenem (7.6%)[21].

In our study, the higher prescribed carbapenem than above mentioned compared studies owing to the perception of a high prevalence of extended-spectrum β-lactamase (ESBL) producing Gram-negative bacteria. The Absence of infectious disease physician specialists (Figure 2), Lack of ASP, a fundamental lack of guidance and stop/review date, and probably underutilization of existing microbiological diagnostic facilities are leading the possible cataeuses of unregulated empirical prescribing[22]. The underutilization of the available microbiology laboratory facilities may be attributable to several factors, such as costly laboratory tests and the delays in the culture and sensitivity process (C/S) testing from the point of ordering until the result (7-10 days)[7]. Therefore, it is possible that prescribers, especially those doubtful about the diagnosis, tend to prescribe empirical broad-spectrum antibiotics such as carbapenems. The results are consistent with earlier studies conducted in Iraq and suggest that C/S testing is being saved for patients who have not responded to many regimens of antibiotics[23]. The high prescription of RNA polymerase inhibitor reflects a lower mortality rate in COVID-19 patients (56% vs. 92%)[24], reduce hospital stay and progression to the need of mechanical ventilation[25].

Among the wards, carbapenems (J01DH) were prescribed at a comparable rate in AMW (47.6%, n = 40/84) and AICU (36.6%, n = 15/41), in comparison, RNA polymerase inhibitor (J05XX) mainly was prescribed in AMW (32.1%, n = 27/84), ($p = 0.037$) (Table S2), because RNA polymerase inhibitor (remdesivir) prescribed as a five-day course only so rarely prescribed in ICU (where patients stay for a longer time) in the studied COVID-19 hospitals. There is no significant variation the five-day course versus the ten-day course of remdesivir[26]. Another study found out carbapenem consumption is high in ICU[27]. Carbapenems remained the cornerstone of antibiotic treatment in AICU for severe infections, such as infections caused by ESBL-producing bacteria[28].

The most common type of COVID-19 severity was patients not on mechanical ventilation/on oxygen (in AMW), followed by patients on continuous positive airway pressure (CPAP) (in AICU), with statistically significant variation among the antimicrobial classes prescribed for each different COVID-19 severity ($p < 0.001$). For the first patient type, the most prescribed antimicrobial class was carbapenems (J01DH) (47.7%, n = 42/88) followed by RNA polymerase inhibitor (J05XX) (31.8%, n = 28/88), while for the second patient type was other antimicrobials (45.8%, n = 11/24) followed by carbapenems (J01DH) (37.5%, n = 9/24) and RNA polymerase inhibitor (16.7%, n = 4/24) (Table S3), the results were in agreement with Goldman *et al.*, who claimed that RNA polymerase inhibitor indicated for patients not requiring mechanical ventilation[29].

High consumption of carbapenems in both AMW and AICU has been shown to generate carbapenemase-producing Gram-negative bacteria, which might lead to secondary bacterial infections in COVID-19 inpatients and be associated with a high risk of mortality rate[30]. More surveillance and investigations are required regarding the use of carbapenems in COVID-19 patients. Other antimicrobial agents that frequently prescribed in AICU are; fluoroquinolones, glycopeptide antibacterials, tetracyclines, polymyxins and triazole derivatives possibly reflecting the resistant pattern to first-line antimicrobials and multiple secondary bacterial and fungal infections, and most of the bacterial isolates recognized were MDR implying that empirical treatment could not be beneficial in such cases[31]. Consequently, establishing ASP and increasing trends toward C/S testing can reduce the spread of such resistant bacteria in healthcare settings, as they were lacking in this study.

Overall, the documented antimicrobial dose was at 100% (n = 125/125) (Table S4). Most of the antimicrobials were administered parenterally (99.2%, n = 124/125) without significant difference among wards (Tables S4 and S5). In the current study, the high use of parenteral therapy reflects high prescription of intravenous (IV) carbapenem (mainly meropenem). Appropriate selection of the route of administration ideally depends on the infection severity, lesion type, oral tolerance, age, the sensitivity of the infecting pathogen and presence of dosage form. However, most prescribers consider the parenteral route as more effective route[32]. The IV-to-oral switch program is considered to be a wise program and a key area for antimicrobial stewardship intervention to decrease the length of hospital stay, cost and nosocomial infections such as catheter-associated infections even with similar efficacy[33]. The IV to oral switch is recommended when patient's health stabilizes after 48hrs of IV therapy (body temperature of <38°C), causative pathogen/diagnosis is identified, and oral therapy is tolerable or not contraindicated[34].

Most of the prescribed antibiotics were in the 'Watch' class (88.4%, n = 76/86), mainly driven by meropenem, varied non-significantly among wards (Tables S4 and S5), identically was the highest class in Russia (73.3%)[35]. The second standard class was the 'Reserve' class (9.3%, n = 8/86) which was only prescribed in hospital 1 (14.8%, n = 8/54), indicating that imipenem/ cilastatin, colistin and tigecycline prescriptions, particularly in critical COVID-19 wards are used when the bacteria are resistant, this will favor the prescription of broad-spectrum antimicrobial agents. The 'Access' class was the most minoe prescribed class (2.3%, n = 2/86) (Table S4), while in Russia 'Reserve' class was the last class (4.3%)[35]. The high prescription of 'Watch' and 'Reserve' class antibiotics reflects a lack of ASP, inadequate hospital capacity infrastructures, and lack of local guidelines, targeted therapy and review date. Moreover, 'Watch' and 'Reserve' class antibiotics possess the high risk of bacterial resistance, thus they require further surveillance to provide appropriate antibiotic use.

Recording indication and diagnosis in patient's notes is a crucial quality indicator as it ensures communication of diagnosis and subsequent therapy plans among prescribers. In this study indication, and diagnosis were recorded in patient's note at 100% (n = 125/125) of prescribed antimicrobials (Tables S4), comparable to Singapore (97%)[36]. This high rate is owing to the novel, pandemic, and communicable nature of COVID-19.

Documenting stop/review dates for antimicrobials was utterly lacking in all hospitals (Table S4). However international standard of national adaptation plans for documenting stop dates is > 95%[37]. Opposite to Russia, which recorded 85.2%. It is recommended to review patients 48-72 hr after initiation of therapy to re-evaluate antibiotic use as diagnostic information becomes more apparent. De-escalation of antibiotic, IV to oral switch and discontinuation of therapy might be required to improve judicious antibiotic use[38]. Stop/review dates are especially important when antibiotics are started empirically, as it is seen in Iraq, with a restricted antibiotics list for empiric use and suggested replacements of antibiotics[39]. Antibiotic time-out or review date was a very new or unrecognized practice for health care providers in Erbil City, and it is a critical prioritized area for ASP intervention.

The global antibiotic policy recommended that 90% of antimicrobial prescriptions should be compliant with guidelines,[40] unfortunately compliance to local treatment guidelines was utterly lacking in all hospitals (Table S4), in contrast with Singapore, where guideline compliance was at 73%[36]. The lack of compliance with local guidelines in this study reflects the lack of local antimicrobial guidelines at hospitals, even at the country level[41]. Ideally, it is critical to improve compliance in prescribing, firstly by applying then updating comprehensive local evidence-based guidelines periodically, and an ASP that offers guidance in each hospital.

Additionally, targeted therapy according to culture and sensitivity testing was almost lacking (2.4%, n = 3/125), which was only performed in hospital 1 (4.2%, n = 3/71) (Table S4), which could be considered as the main COVID-19 hospital. Likewise, targeted therapy accounts for 12% of a Pakistani study included in the systemic review[20]. The lack of targeted therapy is a severe concern and contributes to the lack of ASP, inadequate hospital capacity infrastructure, the lack of review date, and probably multifactorial in this study; for instance, most patients receiving initial treatment were likely to depend on clinical judgments and experience while underutilization of microbiological facilities due to delayed C/S results because of limited resources and technology advancement[42].

Targeted therapy according to bacterial culture and sensitivity testing was highest in AICU (4.9%, n = 2/41) non-significantly (Table S5). Similarly, was highest in ICU (47%) in another PPS[43]. Based on our results, targeted therapy is deficient if it exists primarily prescribed in AICU where more resistant pathogens available needs a C/S test[44].

ASP was neither implemented in the studied hospitals nor in any other hospitals in Iraq[25]. Thus, we could not do the evaluation for each core elements of ASP but duration of willingness to implement ASP had been analysed. Majority of hospitals (66.7%, n = 2/3) had a priority for the medium or the long term to implement ASP (Figure 1). Nonetheless, ASP was employed in nearby countries such as Iranian pediatric hospital[45], and hospitals of Turkey[46]. Based on this study, despite the high prevalence and low quality of antimicrobial use, most of the hospitals had a priority for the medium or the long term to implement ASP, which is a serious issue. Thus, the government should take the initiative for the proper use of antimicrobials by putting in place a solid program, for instance, ASP. Lack of finance, staff, medical equipment[47], and inadequate hospital capacity infrastructures are possibly regarded as primary barriers to implement ASP.

Regarding ASP, the following hospital infrastructures in Erbil City to encourage prudent antimicrobial use looks inadequate (Figure 2). Out of 3 involved hospitals, the most prevalent infrastructures (100%, n =3/3) were pharmacists, whose interventions play a crucial role in providing judicious antimicrobial use, lowering toxicity and decreasing cost[48], available drugs and therapeutics committee, available infection prevention and control committee and updated essential drug list in the ward. While they were available at a lower rate (50%, 90%, 100%, and 40% respectively) in Botswana PPS hospitals, potentially leading to the prevalence of HIV (40%) and TB (25%)[49].

Infectious disease specialist physicians are essential competent resources for developing and directing ASP in all healthcare settings[50], but the infectious disease physician, antimicrobial specialist pharmacists, salary support for dedicated time for antimicrobial stewardship activities and information technology to support the needs of the antimicrobial stewardship activities were not available in any of these hospitals. In this study, the latter two infrastructures were not present because the ASP was not in place in any hospital. Close to a Botswana PPS as they were present at 0% and 40% only respectively[49].

Availability of the microbiologist was at 66.7% (n = 2/3) only. In contrast, microbiologists significantly contribute to enhancing C/S reports and rapid diagnostic test availability[51], Functional microbiology division in laboratory and continuity in the supply of reagents for culture media in the last 3 months were present at 66.7% (n = 2/3). On the other hand, the three mentioned infrastructures were accessible at 50%, 100%, and 90%, respectively in Botswana PPS[49]. The above existing capabilities could be utilized as a basis for developing relevant ASP across hospitals in Erbil City, identical to those observed in Africa[52].

Conclusion

The prevalence of antimicrobial use was high (particularly carbapenem), which is against guidelines and an area of high concern. The quality of antimicrobial use was poor; the majority of the prescribed antimicrobials were in the 'Watch' class, administered parenterally and empirically with the lack of review date and local treatment guidelines. ASP was not implemented across the studied COVID-19 hospitals. Unfortunately, majority of the hospitals indicated a priority and willingness to implement ASP in the medium or the long-term period. Hospital capacity infrastructures in the context of ASP implementation were inadequate among hospitals except for four infrastructures. Quick action is necessary to establish ASP in hospitals to combat AMR, and the critical target areas include the development of the local guidelines and documenting

Recommendations

There is an urgent need to establish a National Action Plan for combating AMR in Kurdistan, as recommended by the WHO as the first step to tackle the threat of AMR. Urgent action is also required to establish ASP in hospitals to improve the use and quality of antimicrobial use based on the seven ASP core elements as recommended by the CDC. Conducting a PPS nationally to assess antimicrobial prescribing practices, status of ASP and hospital capacity infrastructures. Prevalence of antimicrobial use to be controlled for the difference in resistance patterns and hospital factors among the studied hospitals. Other quality indicators can be examined to evaluate antimicrobial prescribing patterns; for instance, the type of biomarkers on which the therapy is based (WBC, procalcitonin, C-reactive protein, etc.) and the type of biological fluid cultures (blood, urine, cerebrospinal fluid, etc.). Further investigation on hospital capacity infrastructures is needed to determine the influence of each unique infrastructure on antimicrobial usage.

Authors contribution

Authors attest that the submitted manuscript is original and that neither the submitted manuscript nor a manuscript with substantially comparable material under their authorship has been published or is under consideration for publication elsewhere.

Conflict of interests

None

References

1. Kermali, M., Khalsa, R. K., Pillai, K., Ismail, Z., Harky, A. The role of biomarkers in diagnosis of COVID-19: A systematic review. *Life Sci*. **254**, 1: e117788, doi: 10.1016/j.lfs.2020.117788 (2020).
2. Clancy, C. J., Nguyen, M. H. Coronavirus disease 2019, superinfections, and antimicrobial development: What can we expect?. *Clin Infect Dis* **71**, 2736-2743, doi: 10.1093/cid/ciaa524 (2020).
3. Rawson, T. M., Moore, L. S. P., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., et al. Bacterial and fungal coinfection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis* **71**, 2459-2468, doi: 10.1093/cid/ciaa530 (2020).
4. Wu, J., Liu, J., Zhao, X., Liu, C., Wang, W., Wang, D., et al. Clinical characteristics of imported cases of coronavirus disease 2019 (COVID-19) in Jiangsu province: A multicenter descriptive study. *Clin Infect Dis* **71**, 706-12, doi: 10.1093/cid/ciaa199 (2020).
5. Versporten, A., Zarb, P., Caniaux, I., Gros, M. F., Drapier, N., Miller, M., et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: Results of an internet-based global point prevalence survey. *The Lancet Global Health* **6**, e619-29, doi: 10.1016/S2214-109X(18)30186-4 (2018).
6. Hussein, N. H. Emergence of NDM-1 among carbapenem-resistant Klebsiella pneumoniae in Iraqi hospitals. *Acta Microbiologica et Immunologica Hungarica* **65**, 211-27 (2018).
7. Kurdi, A., Hasan, A. J., Baker, K. I., Seaton, R. A., Ramzi, Z. S., Sneddon, J., et al. A multicentre point prevalence survey of hospital antibiotic prescribing and quality indices in the Kurdistan regional government of Northern Iraq: The need for urgent action. *Expert Rev Anti Infect Ther* **19**, 805-814, doi: 10.1080/14787210 (2020)
8. Singh, S. K., Sengupta, S., Antony, R., Bhattacharya, S., Mukhopadhyay, C., Ramasubramanian, V., et al. Variations in antibiotic use across India: multi-centre study through global point prevalence survey. *Journal of Hospital Infection* **103**, 280-83, doi: 10.1016/j.jhin.2019.05.014 (2019).
9. Goossens, H., Versporten, A., Pauwels, I. Global point prevalence survey of antimicrobial consumption and resistance. https://docslib.org/doc/7916745/global-pps-protocol-with-optional-hai-module-jan-2021 (2021).
10. Centers for Disease Control and Prevention. The core elements of hospital antibiotic stewardship programs: Antibiotic stewardship program assessment tool. Available from: https://www.cdc.gov/antibiotic-use/healthcare/pdfs/assessment-tool-P.pdf (2021).
11. World Health Organization. Antimicrobial stewardship program in health-care facilities in low- and middle-income countries: a WHO practical toolkit. www.who.int/publications/i/item/9789241515481 (2019).
12. Al Matar, M., Enani, M., Binsaleh, G., Roushdy, H., Alokaili, D., Al Bannai, A,. et al. Point prevalence survey of antibiotic use in 26 Saudi hospitals in 2016. *J Infect Public Health* **12**, 77-82 (2019).
13. Sharland M, Pulcini C, Harbarth S, Zeng M, Gandra S, Mathur S, *et al*. Classifying antibiotics in the WHO Essential Medicines List for optimal use-be AWaRe. *Lancet Infect Dis* **18**, 18-20, doi: 10.1016/S1473-3099(17)30724-7 (2018).
14. Langford, B., J., So, M., Raybardhan, S., Leung, V., Westwood, D., MacFadden, D. R., et al. Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. *Clin Microbiol Infect* **26**, 1622-1629, doi: 10.1016/j.cmi.2020.07.016 (2020).
15. Alshaikh, F. S., Godman, B., Sindi, O. N., Seaton, R. A., Kurdi. Prevalence of bacterial coinfection and patterns of antibiotics prescribing in patients with COVID-19: A systematic review and meta-analysis. *PLoS One* **17**, e0272375 (2022).
16. Abdulah, D. M., Perot, K. A. Factors influencing prescribing perceived utility of drugs: Experiences from Iraqi Kurdistan. *Innov Pharm* **10**, e24926 (2019).
17. Ahmad AR, Murad HR. The impact of social media on panic during the COVID-19 pandemic in Iraqi Kurdistan: Online questionnaire study. *J Med Internet Res* **22**, e19556, doi: 10.2196/19556 (2020).
18. Ramzan, K., Shafiq, S., Raees, I., Mustafa, Z. U., Salman, M., Khan, A. H., et al. Co-infections, secondary infections, and antimicrobial use in patients hospitalized with COVID-19 during the first five waves of the pandemic in Pakistan: Findings and implications. *Antibiotics* **11**, 789, doi: 10.3390/antibiotics11060789 (2022).
19. Molla, M. M. A., Yeasmin, M., Islam, M. K., Sharif, M., M., Amin, M. R., Nafisa, T., et al. Antibiotic prescribing patterns at COVID-19 dedicated wards in Bangladesh: Findings from a single center study. *Infect Prev Pract* **3**, 100-134. doi: 10.1016/j.infpip.2021.100134 (2021).
20. Khan, S., Hasan, S. S., Bond, S. E., Conway, B. R., Aldeyab, M. A. Antimicrobial consumption in patients with COVID-19: A systematic review and meta-analysis. Expert Rev Anti Infect Ther **20**, 749-72, doi: 10.1080/14787210.2022.2011719 (2022).
21. Mustafa, Z. U., Saleem, M. S., Ikram, M. N., Salman, M., Butt, S. A., Khan, S., et al. Co-infections and antimicrobial use among hospitalized COVID-19 patients in Punjab, Pakistan: Findings from a multicenter, point prevalence survey. *Pathog Glob Health* **116**, 421-7, doi: 10.1080/20477724.2021.1999716 (2022).
22. Chem, E. D., Anong, D. N., Akoachere JKT. Prescribing patterns and associated factors of antibiotic prescription in primary health care facilities of Kumbo East and Kumbo West Health Districts, North West Cameroon. *PLoS One* **13**, e0193353, doi: 10.1371/journal.pone.0193353 (2018).
23. Nassr, O. A., Alridha, A. M. A., Naser, R. A., Abas, R. S. Antibiotic prescribing in the acute care in Iraq. *Hernia* **13**, 485-489, doi.org/10.5281/zenodo.1474831 (2018).
24. Pasquini, Z., Montalti, R., Barchiesi, F. Effectiveness of remdesivir in patients with COVID-19 under mechanical ventilation in an Italian ICU-authors' response. *J Antimicrob Chemother* **76**, 1651-1652 (2021).
25. Beigel, J. H. What is the role of remdesivir in patients with COVID-19?. *Curr Opin Crit Care* **27**, 487-492 (2021).
26. Ippolito M, Cortegiani A. Length of remdesivir treatment in patients with severe COVID-19. *Breathe Sheff* **17**, e200276, doi: 10.1183/20734735.0276-2020 (2020).
27. AlBahrani, S., Almogbel, F., Alanazi, W., Almutairi, S. H., Alanazi, M., Maximos, S., et al. Carbapenem use correlates with percentage of patients with COVID-19 in intensive care units. *Infection* **3**, 1–6, doi: 10.1007/s15010-022-01867-y (2022).
28. Patrier, J., Timsit, J. F. Carbapenem use in critically ill patients. *Curr Opin Infect Dis* **33**, 86-91 (2020).
29. Goldman, J. D., Lye, D. C. B., Hui, D. S., Marks, K. M., Bruno, R., Montejano, R., et al. Remdesivir for 5 or 10 days in patients with severe Covid-19. *N Engl J Med* **383**, 1827-1837, doi: 10.1056/NEJMoa2015301 (2020).
30. Pintado, V., Ruiz-Garbajosa, P., Escudero-Sanchez, R., Gioia, F., Herrera, S., Vizcarra, P., et al. Carbapenemase-producing Enterobacterales infections in COVID-19 patients. *Infect Dis Lond*. **54**, 36-45, doi: 10.1080/23744235.2021.1963471 (2021).
31. Boorgula, S. Y., Yelamanchili, S., Kottapalli, P., Naga, M. D. An update on secondary bacterial and fungal infections and their antimicrobial resistance pattern (AMR) in COVID-19 confirmed patients. *J Lab Physicians* **14**, 260-264, doi: 10.1055/s-0041-1741438 (2022).
32. Saleem, Z., Hassali, M. A., Godman, B., Versporten, A., Hashmi, F. K., Saeed, H., et al. Point prevalence surveys of antimicrobial use: A systematic review and the implications. *Expert Review of Anti-Infective Therapy* **18**, 897-910, doi: 10.1080/14787210.2020.1767593 (2020).
33. Umeokonkwo, C. D., Madubueze, U. C., Onah, C. K., Okedo-Alex, I. N., Adeke, A. S., Versporten, A., Point prevalence survey of antimicrobial prescription in a tertiary hospital in South East Nigeria: a call for improved antibiotic stewardship. *J. Glob. Antimicrob. Resist* **17**, 291–295, doi: 10.1016/j.jgar.2019.01.013 (2019).
34. Akhloufi, H., Streefkerk, R. H., Melles, D. C., de Steenwinkel, J. E., Schurink, C. A., Verkooijen, R. P., et al. Point prevalence of appropriate antimicrobial therapy in a Dutch university hospital. *Eur J Clin Microbiol Infect Dis* **34**, 1631-1637, doi: 10.1007/s10096-015-2398-6 (2015).
35. Avdeev, S., Rachina, S., Belkova, Y., Kozlov, R., Versporten, A., Pauwels, I., et al. Antimicrobial prescribing patterns in patients with COVID-19 in

Russian multi-field hospitals in 2021: Results of the Global-PPS project. *Trop Med Infect Dis* **7**, 75 (2022).

36. Ng, T. M., Tan, S. H., Heng, S. T., Tay, H. L., Yap, M. Y., Chua, B. H., et al. Effects of coronavirus disease 2019 (COVID-19) pandemic on antimicrobial prevalence and prescribing in a tertiary hospital in Singapore. Antimicrobial Resistance & Infection Control **10**, 1-8, doi.org/10.1186/s13756-021-00898-8 (2021).

37. James, R., Upjohn, L., Cotta, M., Luu, S., Marshall, C., Buising, K., et al. Measuring antimicrobial prescribing quality in Australian hospitals: Development and evaluation of a national antimicrobial prescribing survey tool. *J. Antimicrob. Chemother* **70**, 1912–1918, doi: 10.1093/jac/dkv047 (2014).

38. Afriyie, D. K., Sefah, I. A., Sneddon, J., Malcolm, W., McKinney, R., Cooper, L., et al. Antimicrobial point prevalence surveys in two Ghanaian hospitals: Opportunities for antimicrobial stewardship. *JAC Antimicrob Resist* **2**, dlaa001, doi: 10.1093/jacamr/dlaa001 (2020).

39. Chigome, A. K., Matlala, M., Godman, B., Meyer, J. C. Availability and use of therapeutic interchange policies in managing antimicrobial shortages among south African public sector hospitals; findings and implications. *Antibiotics* **9**, 4, doi: 10.3390/antibiotics9010004 (2019).

40. Vandael, E., Latour, K., Goossens, H., Magerman, K., Drapier, N., Catry, B., et al. Point prevalence survey of antimicrobial use and healthcare-associated infections in Belgian acute care hospitals: Results of the Global-PPS and ECDC-PPS 2017. *Antimicrob Resist Infect Control* **9**, 13, doi: 10.1186/s13756-019-0663-7 (2020).

41. Kurmanji, JM., Hassali, A., Versporten, A., Younus, M., Pauwels, I., Goossens, H., et al. Global point prevalence survey in five teaching hospitals in Baghdad, Iraq. *DOAJ* **10**, 4274 (2021).

42. Oduyebo, O. O,. Olayinka, A. T., Iregbu, K. C., Versporten, A., Goossens, H., Nwajiobi-Princewill, P. I., et al. A point prevalence survey of antimicrobial prescribing in four Nigerian tertiary hospitals. *Annals of Tropical Pathology* **8**, 42-46 (2017).

43. Papst, L., Luzzati, R., Carević, B., Tascini, C., Gorišek Miksić, N., Vlahović Palčevski, V., et al. Antimicrobial use in hospitalised patients with COVID-19: An International multicentre point-prevalence study. *Antibiotics* **11**, 176, doi.org/10.3390/antibiotics11020176 (2022).

44. Ibrahim, M. E. High antimicrobial resistant rates among Gram-negative pathogens in intensive care units: A retrospective study at a tertiary care hospital in Southwest Saudi Arabia. *Saudi Med J* **39**, 1035-1043 (2018).

45. Rahbarimanesh, A., Mojtahedi, S. Y., Sadeghi, P., Ghodsi, M., Kianfar, S., Khedmat, L., et al. Antimicrobial stewardship program (ASP): An effective implementing technique for the therapy efficiency of meropenem and vancomycin antibiotics in Iranian pediatric patients. *Ann Clin Microbiol Antimicrob* **18**, 6, doi: 10.1186/s12941-019-0305-1 (2019).

46. Alp, E. E., Oncul, A., Dalgic, N., Akgun, C., Aktas, E., & Bayraktar, B. Antibiotic stewardship program experience in a training and research hospital. *Sisli Etfal Hastan Tip Bul* 55, 253-261, doi: 10.14744/SEMB.2020.96337 (2021).

47. Anthony, C. R., Moore, M., Hilborne, L. H., Rooney, A., Hickey, S., Ryu, Y., et al. Health sector reform in the Kurdistan Region-Iraq: primary care management information system, physician dual practice finance reform, and quality of care training. *Rand Health Quarterly* **8,** 1 (2018).

48. Mas-Morey, P., Ballesteros-Fernández, A., Sanmartin-Mestre, E., & Valle, M. Impact of clinical pharmacist intervention on antimicrobial use in a small 164-bed hospital. *Eur J Hosp Pharm* **25**, 46-51, doi: 10.1136/ejhpharm-2017-001307 (2018).

49. Anand Paramadhas, B. D., Tiroyakgosi, C., Mpinda-Joseph, P., Morokotso, M., Matome, M., Sinkala, F., et al. Point prevalence study of antimicrobial use among hospitals across Botswana; findings and implications. *Expert Rev Anti Infect Ther* **17**, 535-546, doi: 10.1080/14787210.2019.1629288 (2019).

50. Ostrowsky, B., Banerjee, R., Bonomo, R. A., Cosgrove, S. E., Davidson, L., Doron, S., et al. Infectious diseases physicians: leading the way in antimicrobial stewardship. *Clinical Infectious Diseases* **66**, 995-1003, doi: 10.1093/cid/cix1093 (2018).

51. Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial stewardship: How the microbiology laboratory can right the ship. *Clin Microbiol Rev* **30**, 381-407 (2016).

52. Schellack, N., Bronkhorst, E., Coetzee, R., Godman, B., Gous, A. G. S., Kolman, S. Q. et al. SASOCP position statement on the pharmacist's role in antibiotic stewardship 2018. *S Afr J Infect Dis* **33**, 28–35, doi: 10.4102/sajid.v33i1.24 (2018).