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Impact of COVID-19 on antimicrobial stewardship program: Study protocol ☆

Duaa Salem Jawhar[a,b,*], Amer Hayat Khan[a], Usman Abubakar[c]

[a] School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia
[b] Saqr Hospital, Pharmacy Department, Emirates Health Service, Ras Al Khaimah, United Arab Emirates
[c] Department of Clinical Pharmacy and Practice, College of Pharmacy, QU Health, Qatar University, Doha, Qatar

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Retrospective observational study

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ABSTRACT

The coronavirus disease (COVID-19) pandemic affects the healthcare system worldwide and challenges many governments and institutions. Antimicrobial stewardship program advocating the wise use of antimicrobial agents. Its metrics include antimicrobial use measures, process, and outcome performance indications. We will conduct a retrospective observational study with the main hypothesis that the COVID-19 pandemic does not affect the antimicrobial stewardship program and its metrics. We will compare antimicrobial stewardship metrics (process, outcome, utilization) and antibiotic resistance two years before (2018–2019) (Group A) & two years with the COVID-19 pandemic (2020–2021) (Group B). The study will be conducted in Saqr Hospital, a secondary care hospital in the emirate of Ras Al Khaimah in the United Arab Emirates. Data will be analyzed using SPSS version 22. Numerical data will be presented as mean (SD) or median (IQR). Chi-square or Fisher's exact test will be used to analyze categorical data. The *t*-test or Mann–Whitney U test will be used to compare the difference of numerical variables. $p < 0.05$ will be considered statistically significant. Multivariate logistic regression will be used to investigate the relation between different variables with (1) cost and (2) antibiotic resistance.

Specifications table

Subject area:	Pharmacology, Toxicology and Pharmaceutical Science
More specific subject area:	Antibiotic stewardship
Name of your protocol:	Impact of COVID-19 on antimicrobial stewardship program: study protocol
Reagents/tools:	G*Power version (3.1) Data collection tool (Supplementary 1) Statistical package for the social sciences (SPSS) version (22)
Experimental design:	Retrospective observational
Trial registration:	Not-applicable
Ethics:	The Authors followed MethodsX ethical guidelines, this work does not involve direct contact with human subjects, animal experiments, or data collected from social media; thus, informed consent is not required. The Emirates health service research section in data and statistical department reviewed and approve the study protocol reference number EHS/DSD/Form/002/013/04–2024. Ethical approval has been obtained from Ministry of health and prevention Ras Al Khaimah's ethics committee reference number MOHAP/REC/2024/36–2024-F-P.

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☆ **Related research article:** Not applicable.

* Corresponding author at: School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia.
E-mail address: duaa.jawhar@ehs.gov.ae (D.S. Jawhar).
Social media: @its_duaasalem (D.S. Jawhar)

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Value of the Protocol:

- This is a protocol for a high-quality retrospective observational study, assessing the effect of COVID-19 on the antibiotic stewardship program (ASP)
- We describe the detailed process from the rationale of the study, research question, and operational definitions to the statistical analysis plan
- By publishing this protocol in a peer-reviewed journal, we aim to make our research plan directly accessible and discussable; which might help other researchers to use it in re-testing the hypothesis in a wider scope of nations

Description of protocol

Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus and led to a global pandemic in 2020 [1]. Meta-analysis on COVID-19 patients highlights the high rate of antibiotic use, reaching up to 75%, despite the viral source of infection [1]. Center of disease control and prevention (CDC) alarm about concerns related to the emergence of antibiotic resistance due to COVID-19 and advises monitoring the effect of COVID-19 on resistance trends and antibiotic use [2].

An antimicrobial stewardship program (ASP) is an inter-professional effort that involves optimal antimicrobial use for patients across a continuum of care, including acute, inpatient, outpatient, and long-term settings [3]. The Society for healthcare epidemiology of America (SHEA), center for disease control and prevention (CDC), and infectious disease society of America (IDSA) strongly recommend toward implementation of an antimicrobial stewardship program to decrease the prevalence of antimicrobial resistance [4]. Different metrics can be used to assess and monitor the antimicrobial stewardship program; it's classified into process metrics, outcome metrics, and antibiotic use measures. Process metrics include adherence to local ASP guidelines, acceptance rate to feedback intervention, and performing antibiotic time-out. An example of outcome metrics is the rate of clostridioides difficile infection, antimicrobial cost, and consumption. Antibiotic use measures include days of therapy (DOTs) and defined daily doses (DDDs) [5].

Limited data highlight the effect of the COVID-19 pandemic on antimicrobial stewardship programs in the Gulf Cooperation Council (GCC), in general, and in the United Arab Emirates (UAE), specifically. Our study may help better understand the COVID-19 effect on antimicrobial stewardship program performance, metrics, and resistance trends. Knowing the impact of COVID-19 on ASP might help increase future preparedness to stand over any future pandemic or healthcare crisis.

Methods and analysis

Study design and objectives

This is a retrospective observational study, with the main aim to compare antimicrobial stewardship metrics (process, outcome, utilization) and antimicrobial resistance trends two years before (2018–2019) (Group A) & two years with the COVID-19 pandemic (2020–2021) (Group B). The null hypothesis of this study is that the COVID-19 pandemic has no impact on antimicrobial stewardship program metrics and the prevalence of antibiotic resistance. Meanwhile, the alternative hypothesis is that the COVID-19 pandemic impacts antimicrobial stewardship program metrics and the prevalence of antibiotic resistance.

Outcome measures include the prevalence of antibiotic resistance and the cost of administered antibiotics. Process metrics involve documented prospective audit-feedback interventions. Antimicrobial utilization measures include the type of antibiotic agent and days of therapy. Pharmacoeconomic evaluation of the COVID-19 pandemic on antimicrobial stewardship program will be assessed using the cost of illness analysis focusing on the cost of administered antibiotics.

Research questions

1. What's the effect of the COVID-19 pandemic on the prescribing practice of access, watch, and reserve antimicrobials?
2. What's the influence of the COVID-19 pandemic on the process metrics of the antimicrobial stewardship program?
3. Does the COVID-19 pandemic impress the prevalence of antibiotic resistance?
4. How far does the COVID-19 pandemic impact the cost of administered antibiotic agents?

Study setting and population

The study will be conducted in Saqr Hospital, a secondary care hospital in the emirate of Ras Al Khaimah in the United Arab Emirates. The hospital is considered a governmental hospital under the Emirates Health Service Establishment's (EHS) administration. It provides health care services in a variety of specialties, including general surgery, pediatrics, critical care, urology, orthopedics, ophthalmology, ear-nose-throat (ENT) surgery, neurosurgery, vascular surgery, thoracic surgery, maxillofacial surgery, plastic surgery, breast surgery, accident & emergency, and out-patient services. Inclusion criteria: pediatric (1 year up to 16 years) and adult (16 years and above) inpatients who receive systemic antibiotic agents from all hospital wards of either gender. Exclusion criteria: outpatient and emergency department patients with orders of antibiotic agents. In addition, patients with antibiotic orders are limited to antiretroviral or antituberculosis agents.

Sampling method and sample size calculation

The hospital electronic statistical system (SAP®), linked with hospital electronic medical records, will be used to extract data about patients on antibiotic agents during the study period. The data will be classified into Group A (2018–2019) before COVID-19, and Group B (2020–2021), during COVID-19. Then, G*Power (3.1) [6] will be used in the calculation of sample size using a power of 0.99, confidence level of 95% (Z value: 1.96), effect size of 0.5, allocation ratio of 1, and two mean formulae will be used. A minimum sample size of 479 per arm will be required for the analysis, making a minimum total of 958 patients. Then, a simple random sampling method using the random number function (RAND) in Microsoft Excel will be used after assigning individual numbers to each patient in each study group [7,6].

Data collection

The hospital statistical system (SAP®), linked with the hospital's electronic medical records, will be used to extract data about patients on systemic antibiotic agents during the study period. After applying inclusion and exclusion criteria, patients will be classified into group A (2018–2019); before COVID-19 and group B (2020–2021); during COVID-19. Each patient will be assigned a unique number, which will be used to extract a random sample through the (RAND) function in Microsoft Excel by using a simple random sampling method to the required sample size. Demographic and clinical data will be obtained from patients' electronic medical records (Cerner®). Information related to the price of antibiotic agents will be gained from the facility medication price list. Then, the antibiotic cost will be calculated by multiplying the number of administered systemic antibiotics by their price. Prospective audit-feedback intervention data will be acquired by calculating the number of documented antimicrobial stewardship recommendations in electronic records. Prevalence of antimicrobial resistance will be obtained by comparing rate of (1) extended-spectrum-beta-lactamases (ESBL) Enterobacterales, (2) carbapenem-resistant Enterobacterales, (3) carbapenem-resistant Pseudomonas aeruginosa, (4) Carbapenem-resistant Acinetobacter, (5) Methicillin resistant staphylococcus aureus, (6) Vancomycin resistant enterococcus Pre- and during COVID-19 pandemic. For patients with multiple admissions to the hospital, data points will be counted once per patient. Data will be collected as per requirement in the research data sheet (Appendix 1)

Operational definitions

- Antimicrobial resistance trends: prevalence of antimicrobial resistance over the studied period.
- Audit-feedback intervention: documented feedback intervention by the antimicrobial stewardship team in the patient's electronic medical record based on the prospective audit.
- Length of hospital stay: the duration the patient is hospitalized in the studied hospital.
- Days of Therapy (DOT): the number of days that a patient is on an antimicrobial
- Days of Therapy/ 1000 patient days: number of days a patient is on an antimicrobial adjusted per hospitalization days.

Statistical analysis

Data will be entered and analyzed using a statistical package for the social sciences (SPSS) version 22. Descriptive statistics will be used to summarize the socio-demographic characteristics of subjects. Kolmogorov-Smirnov test will be used to examine the normality of distributions. A value of $p < 0.05$ is considered statistically significant. Numerical data will be presented as mean with standard deviation (SD) for normal distributions or median with interquartile range (IQR) for non-normal distributions. Categorical data will be presented as frequency (percentage) and analyzed using Chi-square or Fisher's exact test. Parametric (independent *t*-test) or non-parametric (Mann–Whitney U test) will be used to compare the difference of continuous data. Spearman rank correlation coefficient will be used to assess the correlation between different variables with (1) antimicrobial resistance, and (4) cost. Significant correlations will be further analyzed using multivariate logistic regression.

Ethics and dissemination

The patient's name will be coded as initials while entering the datasheet. Only the researcher will have access to the patient's data. The patient's details will be kept on a password-protected computer to protect the patient's identity. Only the researcher knows the password; therefore, the researcher is the only person who can access the computer. Data analysis will also be performed on the same computer. Once the study has been completed, the data in the computer will be copied into USP first before being deleted from the computer. The USP will be stored in a locked storage cabinet with the principal investigator for at least three years, after which it will be destroyed. Any data relating to the identification of the patient will not be published or presented. The Emirates health service research section in data and statistical department reviewed and approve the study protocol reference number EHS/DSD/Form/002/013/04–2024. Ethical approval has been obtained from the Ministry of Health and Prevention Ras Al Khaimah's ethics committee reference number MOHAP/REC/2024/36–2024-F-P. The study findings will be submitted to a peer-reviewed journal and relevant conferences to disseminate results. The Authors followed MethodsX ethical guidelines; this work does not involve direct contact with human subjects, animal experiments, or data collected from social media; thus, informed consent is not required.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Duaa Salem Jawhar: Writing – review & editing, Methodology, Writing – original draft. **Amer Hayat Khan:** Investigation, Methodology, Writing – review & editing, Supervision. **Usman Abubakar:** Investigation, Methodology, Writing – review & editing, Supervision.

Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.mex.2024.102767.

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