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Predictors of antibiogram performance and antibiotic resistance patterns in the northern Syrian region: A cross-sectional investigation

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ABSTRACT

Introduction: Antibiogram use is crucial in the fight against antibiotic resistance in Syria, helping to guide treatment decisions, monitor resistance trends, and implement measures to mitigate this global health threat. This study explores the predictors of antibiogram performance and antibiotic resistance patterns in hospital settings in the Northern Syrian region.
Methods: An observational cross-sectional study was performed over six months, from the beginning of September 2022 to February 2023, targeting patients admitted to two hospitals in Syria with susceptibility to infection. The study excluded patients who did not consent or were unwilling to participate, while all individuals admitted due to infectious diseases, regardless of age, sex, or race, were included in the research. Data were collected prospectively, and antimicrobial susceptibility evaluations were performed using the disc diffusion method (the Kirby-Bauer test). Statistical analyses, including the analysis of the results, were conducted utilizing the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois) Version 29.
Results: Of 300 hospitalized patients taking antibiotics, an antibiogram was performed for 200 individuals (cases), while 100 patients (controls) received direct treatment. One-hundred eighty-five cases had a positive culture (69.7% Gram-negative and 30.3% Gram-positive) and subsequently underwent assessment for antibiotic resistance. Cases comprised more females (56.0%) than controls (48.0%), with no statistically significant differences ($p > 0.05$). Significantly more patients between 25 and 63 were cases (63.8%) than controls (51.0%), while older ages were notably higher among controls (31.7%; $p = 0.044$), history of cardiovascular diseases was higher among controls (59.0%) than cases (47.0%; $p = 0.050$). *Escherichia coli* ($N = 60$; 30%), *Klebsiella* ($N = 37$; 18.5%), and *Streptococcus* ($N = 32$; 16%) were the most common bacteria. The study explored antibiotic resistance patterns among identified germs, emphasizing the high sensitivity of all identified germs for broad-spectrum antibiotics, including meropenem, amikacin, gentamicin, and fluoroquinolones (levofloxacin, ciprofloxacin). High resistance (%Sensitivity below 60%) was noted for Sulfamethoxazole, nalidixic acid, amoxiclav, lincomycin cefotaxime, ceftriaxone, and cefixime. Specifically, *Escherichia coli* exhibited robust sensitivity to meropenem (100%), amikacin (93.2%), and ciprofloxacin (92.7%). However, notable resistance was observed against sulfamethoxazole (68.8%), amoxicillin-clavulanate (78.3%), and cefotaxime (88.3%). For Klebsiella, resistance rates were prominent, particularly against sulfamethoxazole (69.4%), amoxicillin (83.8%), and nalidixic acid (100%). Among Gram-positive bacteria, Staphylococcus demonstrated significant resistance to sulfamethoxazole (95.2%) and ceftriaxone (78.3%) while maintaining high sensitivity to meropenem (100%) and vancomycin (100%). Streptococcus exhibited notable resistance against sulfamethoxazole (87.5%) and cefotaxime (90.6%).
Conclusion: The increase in resistance to penicillins, sulfonamides, and cephalosporins, along with continued sensitivity to broad-spectrum antibiotics, including aminoglycosides, carbapenems, and fluoroquinolones, emphasizes the importance of promoting antibiogram use and antibiotic stewardship programs. The limited availability of new antibiotics reinforces the need for urgent efforts to optimize antibiotic use and improve clinical outcomes in Northern Syria.

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1. Introduction

Antibiotic resistance, often called antimicrobial resistance (AMR), and the persistence of resistant strains pose a heightened risk of treatment ineffectiveness and recurring infections.[1] AMR plays a significant role in elevating morbidity and mortality rates and escalating healthcare expenses.[2] Infections caused by antibiotic-resistant bacteria currently lead to approximately 700,000 deaths annually globally. By 2050, this number is projected to surpass 10 million deaths yearly.[3,4] In 2019, antibiotic-resistant illnesses were responsible for 1.27 million deaths, contributing to 4.95 million deaths due to associated complications.[5] The accessibility of antibiotic treatment has markedly reduced mortality rates, contributing to an overall increase in life expectancy.[6] Nevertheless, the misuse of antibiotics induced the emergence of multidrug-resistant (MDR) bacteria.[7] A significant correlation between AMR and various socioeconomic variables was reported,[8] with a bidirectional relationship between the intake of antibiotics and the development of resistance between animals and humans, namely in Low- and Low-Middle-Income Countries (LMICs). This underscores the imperative for integrated control strategies that target the prevention of transmission across multiple domains within the One Health framework[9] and the necessity for improved surveillance and control efforts to combat AMR in LMICs.[10,11]

In clinical settings, obtaining an antibiogram before administering antibiotics can enable healthcare providers to select the most suitable antibiotic by identifying the specific bacteria causing the infection and their susceptibility to different antibiotics, ensuring optimal treatment outcomes.[12] Moreover, it aids in combating antibiotic resistance,[13] as tailoring treatment based on antibiogram results minimizes the risk of fostering antibiotic-resistant bacterial strains, which can mitigate the occurrence of associated adverse reactions and shorten hospital stays.[14] The Middle East faces a serious challenge with antibiotic resistance due to the high frequency of multidrug-resistant (MDR) infections, especially among Gram-negative bacteria.[15] In addition, an alarming rise in antimicrobial resistance has been observed in Middle Eastern Arab countries, which poses a significant challenge to medical professionals treating infectious diseases.[16] Antibiotic-resistant nosocomial infections (NIs) are also becoming an issue in the Middle East; the most commonly reported types are surgical site infections (SSIs) and bloodstream infections (BSIs).[17]

In Syria, antibiotic resistance holds significant importance due to the collapse of healthcare and mass displacement, exacerbating the spread of infections and the improper use of antibiotics and inducing the emergence of antibiotic-resistant strains.[18] Numerous investigations carried out in Damascus Hospital and Al-Razi Hospital have shown that the incidence of antibiotic resistance in Syria is a serious concern. This research shows numerous samples, including blood, sputum, urine, and others, have shown a significant prevalence of antibiotic resistance.[19] In the intricate web of the Syrian conflict and subsequent mass displacement, the emergence of antimicrobial resistance (AMR) poses a significant threat to public health. The protracted nine-year armed conflict in Syria, compounded by dire living conditions and the collapse of healthcare infrastructure, has created ideal conditions for the development and spread of AMR. Overcrowded living spaces, damaged healthcare facilities, medication shortages, and a scarcity of resources have fueled the rise of public health challenges, amplifying the rates of AMR. The connection between AMR and socioeconomic variables becomes glaringly evident in this crisis. This linkage is further supported by emerging evidence from conflict-affected regions, emphasizing the need for targeted interventions and strategies. The exploration delves into the current situation of AMR among the Syrian displaced population and refugees, proposing a roadmap for essential interventions to address the escalating threat of AMR within the complex landscape of the Syrian crisis.[20]

Access to healthcare services has been severely constrained, prompting self-medication and unsupervised antibiotic use.[21] The disruption in the supply chain for essential medicines, including antibiotics, further exacerbates the situation by promoting broad-spectrum antibiotics over more targeted options.[20] This complex challenge necessitates a holistic approach encompassing healthcare infrastructure rehabilitation, improved healthcare access, enhanced infection control practices, and the promotion of responsible antibiotic usage. This study aims to assess the predictors of antibiogram performance in hospital settings and antibiotic resistance among hospitalized patients in two hospitals in the Northern Syrian region.

2. Methods

2.1. Study design

An observational prospective cross-sectional study was performed over six months (from the beginning of September 2022 to February 2023), targeting patients admitted to two hospitals in Syria, Dar Al-Shifaa and Wassem Maaz, with susceptibility to infection.

2.2. Study sample

Patients were included in the study if they were taking an antibiotic during their hospital stay. And any types of infections, including urinary infection, diabetic foot infection, respiratory infection, cerebrospinal infection. No selection criteria were based on age, sex, race, or nationality. They were excluded only if they refused to sign the informed consent. Fig. 1 displays the flowchart of the sample. In total, 300 patients met the criteria for inclusion. Among them, an antibiogram was performed for 200 individuals, while 100 received direct treatment without undergoing an antibiogram. Of the 200 patients, 185 had a positive culture and subsequently underwent assessment for antibiotic resistance. The remaining 15 patients exhibited a negative culture.

2.3. Data collection

Data were gathered prospectively through a meticulous data collection form designed for individual cases (patients). Two pharmacists and the responsible doctor undertook rigorous validation and reliability assessments of the survey instrument in each hospital. This encompassing survey captured patients' characteristics, medical history, comorbidities diagnosed through medical records, and other information throughout their hospitalization.

The 200 samples originated from diverse sources, including blood, urine, sputum, catheters, skin, pleural fluid, cerebrospinal fluid (CSF), seminal fluid, and vaginal swabs. These samples were obtained from hospitalized patients who exhibited a range of infections. All specimens obtained from these patients were subsequently sent to a centralized microbiology facility to identify bacteria and conduct antibiotic sensitivity assessments. At the microbiology center, antimicrobial susceptibility evaluations were performed using the disc diffusion method, specifically the Kirby-Bauer test.[22] This analysis was executed on Mueller Hinton agar under the Clinical and Laboratory Standards Institute guidelines.

2.4. Patients' characteristics and microbiology data

A record was maintained for each patient, documenting demographic details like age, sex, height, and weight. To calculate the Body Mass Index (BMI), the weight (in kilograms) was divided by the square of height (in meters).[23] The patient's lifestyle habits, such as smoking and coffee consumption, and any food or drug allergies were also documented. Vaccination histories were recorded, including COVID-19, H1N1, and tetanus and history of surgical procedures. Existing comorbidities, like cardiovascular disease, hypertension, diabetes mellitus, and chronic pulmonary or kidney diseases, were collected. Patients' signs (dysuria, body pain, shortness of breath, infected wound, cough, fever, and post-surgery inflammation) were assessed during the admission, and symptoms (fever, pain, dysuria, vomiting, cough, expectoration, and diarrhea) were reported before admission and prior antibiotic use were documented**.** The identified microbiological pathogens were noted, specifying the exact type of bacterium found in the culture.

2.5. Ethical considerations

Data was collected through a survey, avoiding invasive procedures or interventions. The study protocol, survey instrument, and consent form underwent a thorough review and received approval from the hospital's institutional review board (reference 811/B; July 25th, 2023) of Dar Al-Shifa. For Wassem Maaz Hospital, data collection was conducted under the explicit permission of the hospital director.

The collected data were maintained in an anonymous and non-identifiable manner, in compliance with the guidelines of the General Data Protection Regulation. Written informed consent was obtained from each participant, with full transparency regarding their option to withdraw from the study at any stage. Findings were exclusively used for research purposes, and the participants were not provided financial incentives.

2.6. Statistical analysis

Statistical analyses used Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois) Version 29. Frequencies and percentages represented categorical variables, while patients' age and BMI were presented as means and standard deviations. Age was categorized into ≤25, 25–63, and > 63 years. Bivariate analyses examined differences in baseline characteristics and signs and symptoms between individuals who underwent an antibiogram (cases) and those who did not (controls). Subsequently, a multivariate analysis was conducted using a logistic regression model to investigate the combined impact of predictors, specifically patients' characteristics, on the likelihood of undergoing an antibiogram. Covariates were considered if they exhibited a p-value<0.3 in the bivariate analyses. A significance level of $p < 0.05$ was used to determine statistical significance. Using the Clinical and Laboratory Standards Institute guidance (the updated CLSI M39),[24] A color scheme was implemented to indicate varying levels of sensitivity (%S): green (often associated with safety or suitability) is used to depict %S values >80%, red (commonly associated with danger or caution) is assigned to %S values less than or equal to 60%, and yellow (often used to signify caution or an intermediate state) is applied to %S values falling between these two thresholds.

3. Results

3.1. Differences in the baseline characteristics of the study sample

Overall, 300 patients were included in the study. Table 1 compares the baseline characteristics of the participants based on performing or not an antibiogram. Cases comprised more females (56.0%) than controls (48.0%), with no statistically significant differences ($p > 0.05$). Significantly more patients between 25 and 63 were cases (63.8%) than controls (51.0%), while older ages were notably higher among controls (31.7%; $p = 0.044$). Regarding lifestyle habits (coffee consumption and smoking status) and the existence of food or drug allergies, comparable distribution was found among the two groups with insignificant differences. Concerning vaccination, significantly more patients vaccinated against Covid-19 performed an antibiogram (68.5%) compared to controls (54.0%; $p = 0.014$). In contrast, those with a history of cardiovascular diseases were higher among controls (59.0%) than cases (47.0%; $p = 0.050$). A similar pattern was observed for patients with hypertension ($p = 0.041$). Patients with other comorbidities (diabetes, chronic pulmonary disease, and chronic kidney disease) and those having a previous surgery were comparably distributed among cases and controls (no significant difference). More patients starting an antibiotic before hospital admission were among cases (84.0%) than controls (76.0%), with no statistically significant differences.

3.2. Signs and symptom

Fig. 2 compares cases and controls regarding their (A) symptoms and (B) signs. When asked about their symptoms, fever was reported comparably in both groups (100% of the control group vs 98.2% of cases; $p = 0.155$). Pain was reported in both groups, with higher frequency among controls (67%) than cases (61%) without statistically significant differences. Similar patterns were observed for cough, dysuria, expectoration, and diarrhea. Nevertheless, significant differences in reporting vomiting as a symptom between the two groups were noted (36% in controls vs 19% for cases; $p = 0.001$). As regards the signs

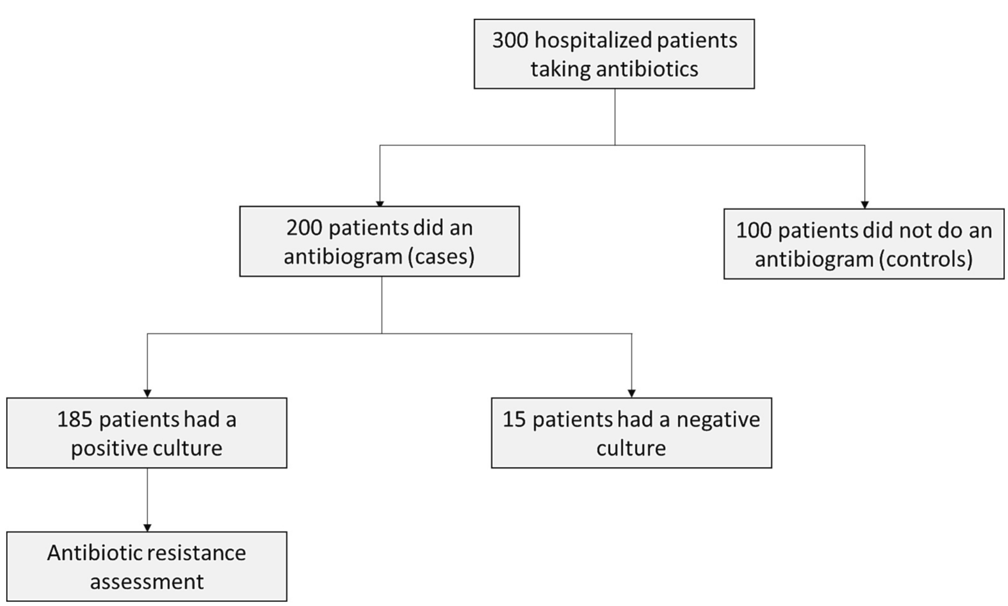

Fig. 1. Flowchart of the study design.

Table 1
Differences in the baseline characteristics of patients doing an antibiogram (cases) and those who did not (controls).

		Cases ($N = 200$) Frequency (%)	Controls ($N = 100$) Frequency (%)	*p*-value
Sex	Male	88 (44.0%)	52 (52.0%)	0.190
	Female	112 (56.0%)	48 (48.0%)	
Age (years)	**Mean ± SD**	48.2 ± 38.8	51.2 ± 27.1	0.495
	≤25 years	34 (17.1%)	17 (17.3%)	
	25–63 years	127 (63.8%)	50 (51.0%)	**0.044**
	>63 years	38 (19.1%)	31 (31.7%)	
BMI (years)	**Mean ± SD**	26.6 ± 4.8	26.9 ± 5.1	0.577
	Normal (<25 Kg/m^2)	76 (38.6%)	33 (33.0%)	
	Overweight (25–30 Kg/m^2)	91 (46.2%)	45 (45.0%)	0.313
	Obese (>30 Kg/m^2)	30 (15.2%)	22 (22.0%)	
Smoking status	Smoker	96 (48.0%)	41 (41.0%)	0.251
	Non-smoker	104 (52.0%)	59 (59.0%)	
Coffee consumption	Yes	113 (56.5%)	51 (51.0%)	0.367
	No	87 (43.5%)	49 (49.0%)	
Food allergy	Yes	8 (4.0%)	2 (2.0%)	0.505
	No	192 (96.0%)	98 (98.0%)	
Drug allergy	Yes	9 (4.5%)	2 (2.0%)	0.347
	No	191 (95.5%)	98 (98.0%)	
COVID-19 Vaccination	Yes	137 (68.5%)	54 (54.0%)	**0.014**
	No	63 (31.5%)	46 (46.0%)	
H1N1 Vaccination	Yes	66 (33.0%)	36 (36.0%)	0.605
	No	134 (67.0%)	64 (64.0%)	
Tetanus Vaccination	Yes	101 (50.5%)	42 (42.0%)	0.165
	No	99 (49.5%)	58 (58.0%)	
Cardiovascular diseases	Yes	94 (47.0%)	59 (59.0%)	**0.050**
	No	106 (53.0%)	41 (41.0%)	
Hypertension	Yes	93 (46.5%)	59 (59.0%)	**0.041**
	No	107 (53.5%)	41 (41.0%)	
Diabetes Mellitus	Yes	68 (34.0%)	43 (43.0%)	0.128
	No	132 (66.0%)	57 (57.0%)	
Chronic pulmonary diseases	Yes	5 (2.5%)	3 (3.0%)	0.805
	No	194 (97.5%)	97 (97.0%)	
Chronic kidney disease	Yes	8 (4.0%)	9 (9.0%)	0.077
	No	192 (96.0%)	91 (91.0%)	
History of surgery	Yes	36 (18.0%)	21 (21.0%)	0.532
	No	164 (82.0%)	79 (79.0%)	
Antibiotic use before hospital admission	Yes	168 (84.0%)	76 (76.0%)	0.094
	No	32 (16.0%)	24 (24.0%)	

Results are given in frequency (percentage) or mean ± standard deviation. *p*-values<0.05 are presented in bold and represent statistical significance.

reported by healthcare providers, dysuria was the most prominent sign, with a comparable incidence between cases (44.5%) and controls (37%; $p = 0.215$). Body pain was significantly more reported among controls than cases (23% vs 12.5%; $p = 0.019$). No significant differences were noted for the other signs (shortness of breath, infected wound, cough, fever, and post-surgery inflammation).

The predictors of performing an antibiogram among hospitalized patients are presented in Table 2. In cases and after adjusting for covariates, patients aged 63 years or older had 67% lower odds of performing an antibiogram than those aged 25 years or less (OR 0.33, 95% CI 0.11–0.95; $p = 0.041$). Patients vaccinated against COVID-19 had 2.21 higher odds of performing an antibiogram than others (OR 2.21, 95% CI 1.24–3.95; $p = 0.007$). Despite being significant predictors for antibiogram tests in the crude model, cardiovascular diseases and hypertension were not among the predictors in the adjusted model. Patients who reported vomiting as a symptom had 56% lower odds of performing an antibiogram than others (OR 0.44, 95% CI 0.24–0.79; $p = 0.006$).

3.3. Antibiotic resistance assessment

In total, 200 samples were collected from the patients for microbiological analysis (antibiogram). An analysis of the sample type reveals that urine samples accounted for the highest proportion ($N = 105$; 52.5%), followed by sputum ($N = 55$; 27.5%), skin ($N = 23$; 11.5%), seminal fluid (N = 5; 2.5%), and the rest from blood, and pleural and cerebrospinal fluids. One hundred eighty-five cases (92.5%) exhibited bacterial growth after 48 h, of which 129 cases (69.7%) were classified as Gram-negative and 56 (30.3%) as Gram-positive. Among Gram-negative bacteria, the prevalent types and their respective percentages included *Escherichia coli* ($N = 60$; 30%), Klebsiella ($N = 37$; 18.5%), Enterobacter ($N = 26$; 13%), and Pseudomonas ($N = 7$; 3.5%). Streptococcus ($N = 32$; 16%) and *Staphylococcus aureus* ($N = 23$; 11.5%) were prominent on the Gram-positive spectrum. Fig. 3 presents the resistance profile of the different isolated germs. High sensitivity of *Escherichia Coli* was noted for meropenem (100%), linezolid (86.7%), amikacin (93.2%), nitrofurantoin (88.5%), ciprofloxacin (92.7%) and gentamycin (86.0%). In contrast, most *Escherichia Coli* germs were resistant to sulfamethoxazole (68.8%), amoxicillin-clavulanate (78.3%), amoxicillin (91.2%), cefotaxime (88.3%), cefaclor (80.0%) and lincomycin (100%) among others. Regarding *Klebsiella* germs, 69.4% were resistant to sulfamethoxazole, 83.8% and 72.9% to amoxicillin and amoxicillin-clavulanate, respectively, 85.7% to nitrofurantoin, and 100% to nalidixic acid and norfloxacin. Concerning the Gram-positive bacteria, the sensitivity of *Staphylococcus* was highly conserved to meropenem (100%), vancomycin (100%), and amikacin (90%). Significant resistance of *Staphylococcus* to sulfamethoxazole (95.2%), amoxicillin-clavulanate (82.6%), cefotaxime (91.3%), ceftriaxone (78.3%), cefixime (100%), cefdinir (100%), and nalidixic acid (83.3%) was noted. *Streptococcus* germs exhibited comparable resistance and sensitivity profiles, namely to sulfamethoxazole (87.5%), amoxicillin-clavulanate (77.4%), cefotaxime (90.6%), and nalidixic acid (88.6%). The analysis of the susceptibility of *Enterobacter* to antibiotics underscores a high sensitivity toward meropenem (100%), amikacin (100%), levofloxacin (100%), ciprofloxacin (92.3%), and vancomycin (100%). The seven cases of Pseudomonas infection were sensitive to Meropenem, Amikacin, levofloxacin, and vancomycin, while they were resistant to sulfamethoxazole, amoxicillin-clavulanate, linezolid, nitrofurantoin, and vancomycin.

Fig. 4 illustrates the sensitivity of the germs to antibiotics using color coding. All the identified germs had a high resistance level, below 60% sensitivity to sulfamethoxazole, amoxicillin, amoxicillin-clavulanate, cefotaxime, and ceftriaxone. Notably, *Pseudomonas* and *Enterobacter* showed intermediate sensitivity to ceftriaxone, ranging from 60% to 80%. Levofloxacin emerged as a highly effective antibiotic, with an 80% or higher efficacy against all detected germs, except for *Staphylococcus*, which displayed sensitivity between 60% and 80%. Regarding vancomycin, it maintained a high potency (80% or more) when tested against Gram-positive bacteria (*Staphylococcus aureus, Streptococcus, Enterobacter*) but exhibited lower activity (below 60%) against Gram-negative bacteria (*Escherichia coli, Klebsiella*) and *Pseudomonas*. Meropenem and amikacin remained vigorous (80% or more) against all detected germs. This comprehensive assessment highlights a high prevalence of antibiotic resistance, especially evident in the low sensitivity percentages

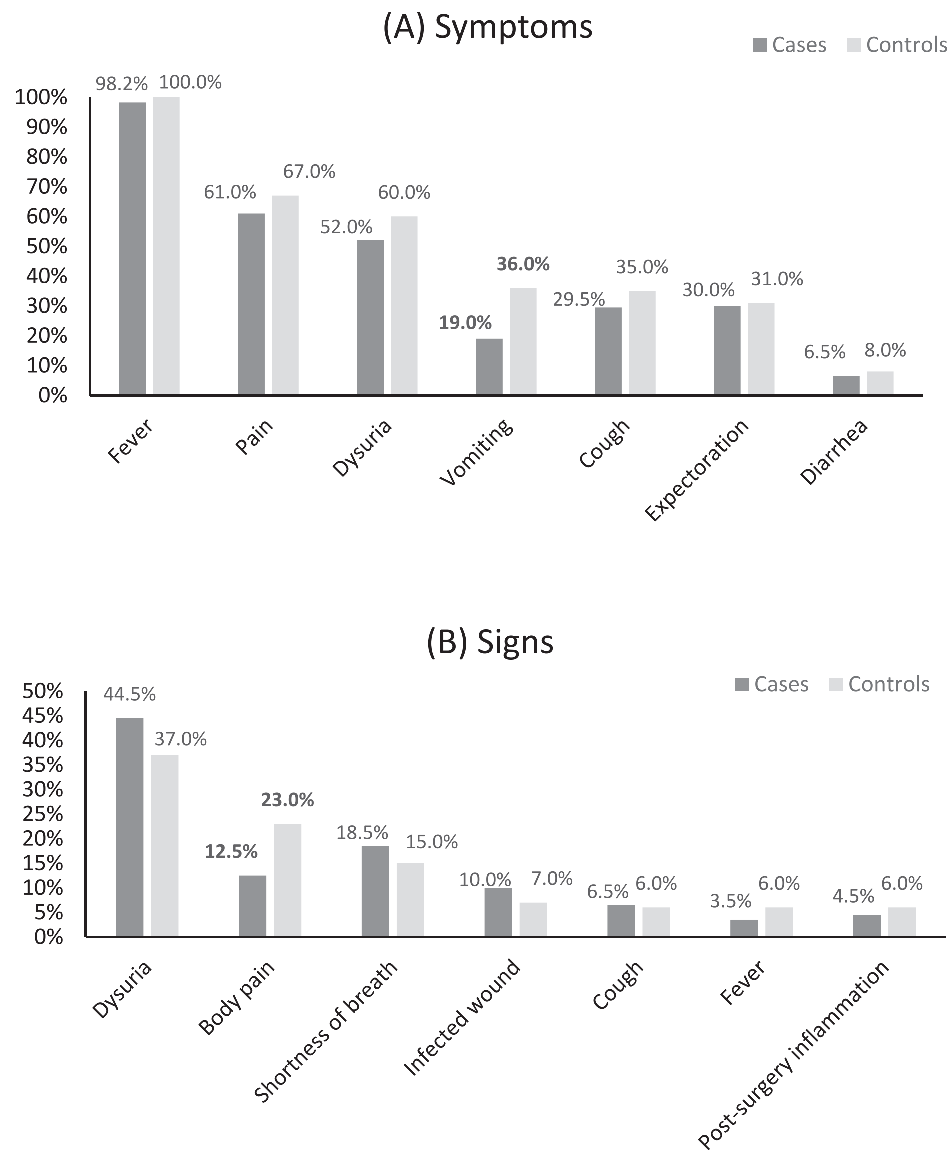

Fig. 2. Comparison between cases and controls in terms of the registered (A) symptoms and (B) signs.

observed for key antibiotics.

4. Discussion

To control infectious diseases and thoroughly understand the distribution of microbial pathogens and the infections they cause, the current study determined the predictors of antibiogram use, the prevalence of common pathogenic microorganisms, and the potential antibiotic susceptibility. In highlighting the strengths of our study, it is noteworthy that no similar research has been conducted in the northern region of Syria. This originality adds significant value as our study contributes to the understanding of antibiotic resistance in this specific geographical context and pioneers in examining the predictors influencing antibiogram creation. The novel approach of investigating the factors associated with making antibiograms distinguishes our study from previous works on assessing antibiotic resistance prevalence. This dual focus not only broadens the scope of our research but also provides a more comprehensive insight into the intricacies of antibiotic resistance management in the region. Despite its significant importance mainly due to the high infection rate among children (64%)[25] and the ongoing outbreaks in this area.[26] The choice to conduct antibiogram testing can help doctors at the facility level and antimicrobial stewardship programs (ASPs) to address challenges from evolving antimicrobial resistance.[24] Age-related trends were noted in the use of antibiotics among the population, with older patients in the control group. This finding suggests the systematic use of empiric antibiotics without undergoing an antibiogram among older, possibly limiting hospital stay and the corresponding risk of nosocomial infections (more common among older patients).[27] Patients aged 63 years or older had significantly lower odds of getting an antibiogram than younger patients. In Syria, it is commonly the cut-off age for retirement and can limit healthcare access and out-of-pocket payment after the multifaceted crises.[28] Individuals who received the COVID-19 immunization had 2.21 times higher odds of getting an antibiogram. This might be related to their perceived better defense and the possibility of waiting for the antibiogram results before starting the treatment. Hypertension and cardiovascular diseases were significant predictors of receiving an antibiogram in the crude model but did not affect the odds of antibiogram use when adjusted for other variables. This might suggest that comorbidities, particularly controlled chronic diseases, had no impact on doctors' decisions. Nevertheless, this decision was significantly influenced by the patient's clinical presentation taking into account the symptoms, such as vomiting, since it can

Table 2
Predictors of the odds of antibiogram test among hospitalized patients.

	Crude model		Adjusted model	
	OR [95% CI]	P-value	aOR [95% CI]	p-value
Age group (≤25 years as a reference)				
25–63 years	1.27 [0.65–2.48]	0.483	0.61 [0.25–1.52]	0.289
>63 years	0.61 [0.29–1.30]	0.201	0.33 [0.11–0.95]	**0.041**
Female sex (male as a reference)	1.38 [0.85–2.23]	0.292	–	–
Smoking (non-smoker as a reference)	1.33 [0.82–2.16]	0.252	–	–
COVID-19 vaccination (No as a reference)	1.85 [1.13–3.04]	**0.014**	2.21 [1.24–3.95]	**0.007**
Tetanus vaccination (No as a reference)	1.41 [0.87–2.29]	0.165	–	–
Cardiovascular diseases (No as a reference)	0.62 [0.38–0.99]	**0.050**	0.77 [0.42–1.42]	0.398
Hypertension (No as a reference)	0.60 [0.37–0.98]	**0.042**	–	–
Diabetes Mellitus (No as a reference)	0.68 [0.42–1.12]	0.129	–	–
Chronic Kidney disease (No as a reference)	0.42 [0.16–1.13]	0.085	–	–
Antibiotic use before hospital admission	1.66 [0.92–3.01]	0.096	–	–
Vomiting as a symptom	0.42 [0.24–0.72]	**0.001**	0.44 [0.24–0.79]	**0.006**
Dysuria as a symptom	0.72 [0.44–1.18]	0.190	–	–
Body pain as a sign	0.48 [0.26–0.89]	**0.021**	1.54 [0.77–3.10]	0.225

*OR: Odds Ratio; CI: Confidence interval. *p*-values<0.05 are presented in bold and represent statistical significance.

indicate gastrointestinal infections with known common germs. Other factors might have impacted the performance of an antibiogram but were not studied, including the local prevalence of antibiotic resistance in the neighborhood or healthcare facility, the cost and resources, such as laboratory capacities and testing expenses.

Regarding the microbiology results and in agreement with previous findings, gram-negative bacteria (GNB) were more prevalent than gram-positive isolates, with higher resistance patterns in GNB.[29] In clinical settings, research also reported a higher prevalence of GNB among hospitalized patients.[30,31] The predominant bacterium is *E. coli*, constituting 30% of the cases found in our study, making it the most common type of germ. This is an important observation, especially in light of the noted regional differences in antibiotic resistance patterns. The frequency of *E. coli* in Syria's north may indicate particular healthcare customs, patient demographics, or environmental variables affecting microbiological dynamics. Subsequent investigations could focus on certain risk factors, treatments, or medical procedures that could provide insight into the unique microbiological environment seen in the context of northern Syria. In similar settings in Nigeria (a low-income country), *E. coli* constitutes up to 74.2% of the clinical isolates from urine, blood, and wound samples.[32] The profile of *E. coli* sensitivity and resistance varied between research. The study showed high resistance of *Escherichia coli* to amoxicillin, amoxiclav, sulfamethoxazole, cefotaxime, cefaclor, cefixime, and nalidixic acid, which express high resistance to *E. coli* on penicillin, and cephalosporins in addition to sulfamethoxazole. In a study on bloodstream infection isolates, 35% of the isolates were amoxicillin-clavulanate resistant.[33] In a separate study conducted in a hospital setting, antibiotic sensitivity was monitored, and antibiotic resistance was evaluated. The research indicated a correlation between patient age and increased resistance, noting a diminished clinical effectiveness of cephalosporin drugs against *E. coli.*[34] In addition, research concerning uropathogenics reported a connection between biofilm development and resistance to third-generation cephalosporins.[35] *Escherichia coli* exhibited high sensitivity to meropenem, amikacin, nitrofurantoin, levofloxacin, and gentamicin, in agreement with a previous study showing significant resistance to fluoroquinolones, despite their high susceptibility to imipenem, meropenem, tazobactam, cefoperazone + sulbactam, and amikacin.[36] In the present study, all identified pathogens exhibited significant resistance to third-generation cephalosporins, including ceftriaxone, cefotaxime, and cefixime. Previous research revealed that resistance to third-generation cephalosporins in low- and middle-income countries is linked to higher mortality rates and prolonged hospitalization among patients with bloodstream

	Escherichia Coli (N=60)		Klebsiella (N=37)		Pseudomonas (N=7)		Staphylococcus aureus (N=23)		Streptococcus (N=32)		Enterobacter (N=26)	
	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive
Meropenem (N=147)		100%		100%		100%		100%		100%		100%
Sulfamethoxazole (N=156)	68.8%	31.2%	69.4%	30.6%	100%		95.2%	4.8%	87.5%	12.5%	90.0%	10.0%
Amoxicillin+Clavulanate (N=184)	78.3%	21.7%	72.9%	27.1%	100%		82.6%	17.4%	77.4%	22.6%	88.5%	11.5%
Linezolid (N=68)	13.3%	86.7%	66.7%	33.3%	100%		58.3%	41.7%	27.3%	72.7%	40.0%	60.0%
Amoxicillin (N=173)	91.2%	8.8%	83.8%	16.2%	100%		94.7%	5.3%	82.1%	17.9%	100%	
Cefotaxime (N=185)	88.3%	11.7%	59.5%	40.5%	71.4%	28.6%	91.3%	8.7%	90.6%	9.4%	88.5%	11.5%
Cefaclor (N=116)	80.0%	20.0%	45.5%	54.5%	100%		86.7%	13.3%	95.5%	4.5%	81.8%	18.2%
Ceftriaxone (N=174)	61.7%	38.3%	43.2%	56.8%	28.6%	71.4%	78.3%	21.7%	48.4%	51.6%	37.5%	62.5%
Lincomycin (N=76)	100%		50.0%	50.0%	100%		50.0%	50.0%	70.6%	29.4%	50.0%	50.0%
Amikacin (N=164)	6.8%	93.2%	5.7%	94.3%		100%	10.0%	90.0%	14.3%	85.7%		100%
Nitrofurantoin (N=103)	11.5%	88.5%	85.7%	14.3%	100%		40.0%	60.0%	36.4%	63.6%	75.0%	25.0%
Ciprofloxacin (N=176)	7.3%	92.7%	27.0%	73.0%	66.7%	33.3%	38.1%	61.9%	19.4%	80.6%	7.7%	92.3%
Cefixime (N=154)	68.6%	31.4%	67.6%	32.4%	85.7%	14.3%	100%		74.2%	25.8%	77.8%	22.2%
Levofloxacin (N=149)	17.0%	83.0%	13.9%	86.1%		100%	38.9%	61.1%	13.8%	86.2%		100%
Vancomycin (N=70)	47.1%	52.9%	56.3%	43.8%	100%			100%	5.6%	94.4%		100%
Gentamycin (N=139)	14.0%	86.0%	24.2%	75.8%		100%	37.5%	62.5%		100%	22.7%	77.3%
Nalidixic acid (N=66)	74.4%	25.6%	100%				83.3%	16.7%	88.9%	11.1%	100%	
Norfloxacin (N=75)	19.1%	80.9%	100%				66.7%	33.3%	18.2%	81.8%	37.5%	62.5%
Cefdinir (N=43)	78.9%	21.1%	75.0%	25.0%			100%		40.0%	60.0%	50.0%	50.0%
Azithromycin (N=36)	66.7%	33.3%	100%				53.8%	46.2%	87.5%	12.5%	25.0%	75.0%
Clarithromycin (N=34)	50.0%	50.0%	66.7%	33.3%			11.1%	88.9%	25.0%	75.0%		100%

Fig. 3. Distribution of the resistance profile of the different isolated germs.

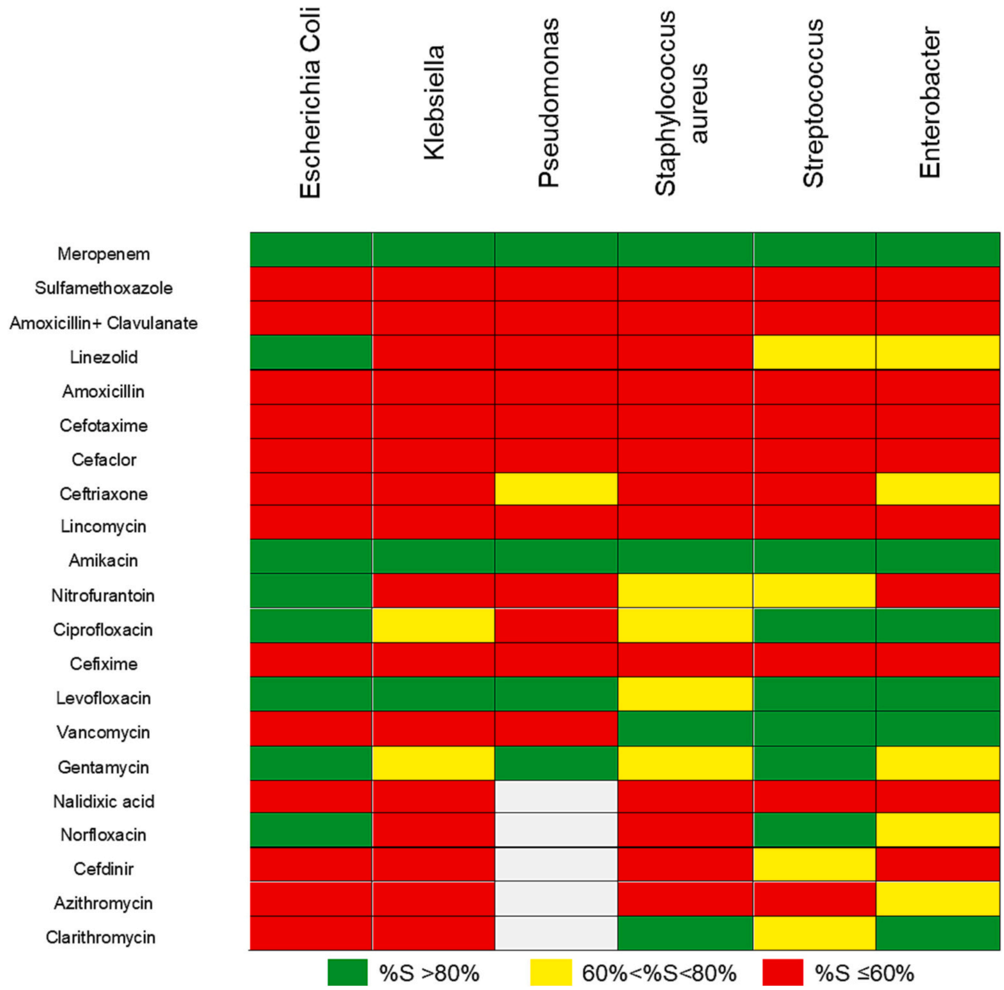

Fig. 4. Color coding reflecting the sensitivity percentage.

infections.[37] In contrast, it's noteworthy that all identified pathogens continue to exhibit susceptibility to the broad-spectrum antibiotics meropenem, amikacin, and levofloxacin. It is crucial to consider the potential implications and hazards linked to broad-spectrum antibiotics, as they may not consistently represent the most suitable choice for treatment.

In the Syrian context, the previous findings align with an expanding body of evidence highlighting elevated rates of antimicrobial resistance (AMR) among Syrian refugees. This encompasses AMR colonization as well as infections attributed to resistant bacteria. Notably, drug-resistant bacteria were frequently isolated from displaced patients, particularly those injured during the armed conflict. The circumstances surrounding the conflict, including medical evacuation flights and compromised healthcare infrastructure, create an environment conducive to colonization. Factors such as low hygiene levels and poorly controlled antimicrobial use further contribute to the prevalence of AMR.[20]

Antibiogram use can be a valuable tool to help doctors make informed decisions and reduce potentially inappropriate medication use.[38] It can also control antibiotic resistance, particularly in low-income areas like Syria. This study is subject to several limitations that should be carefully considered. Firstly, including hospitalized patients may introduce selection bias, as individuals with more severe illnesses might be overrepresented in the sample, potentially impacting the generalizability of findings. Moreover, the recruitment was limited to two hospitals, raising concerns about extrapolating results to diverse healthcare settings in Syria. Another noteworthy limitation pertains to potential information bias stemming from data collection or measurement errors, which could lead to inaccurate or imprecise results. Despite efforts to mitigate this bias, such as analyzing all samples in the same laboratory using standardized methods, residual bias cannot be eliminated. In addition, the study is dependent on the accuracy of sample collection. Although rigorous measures were implemented to ensure precise sampling procedures, variations in sample quality might have influenced the results. Specific details about the microbiology center's capabilities and quality control measures during the disc diffusion method, especially in the context of the Kirby-Bauer test, were not fully disclosed. This lack of detailed information raises concerns about the reliability of bacterial identification and sensitivity assessments, compromising the robustness of the study's microbiological findings.

Furthermore, efforts were made to minimize interviewer bias by instructing data collectors not to interfere with patient results. However, despite these precautions, the potential for interviewer bias cannot be entirely ruled out. Lastly, the overrepresentation of urine samples in the dataset may introduce a bias toward urinary tract infections, limiting the broader applicability of the study's findings to other infection types. It is essential to acknowledge these limitations when interpreting the study's outcomes, and future research should aim to address these constraints for a more comprehensive understanding of antibiotic resistance in diverse clinical settings across Syria. It is advisable to conduct a nationwide longitudinal study in Syria to enhance the external validity and representativeness of the findings. In light of our study's findings, healthcare practitioners in Syria should be attentive to the high prevalence of AMR when prescribing antibiotics. It becomes essential to put strong antimicrobial stewardship programs in place to encourage the prudent use of antibiotics. Public health campaigns should also prioritize informing the public about the dangers of antibiotic abuse.

5. Conclusion

The findings of this investigation highlight the critical need for accurate pathogen identification before initiating antibiotic treatment. There is a call to action, highlighting the need for all-encompassing approaches to tackle the growing problem of antibiotic resistance. The increasing prevalence of antibiotic resistance presents a significant risk to the effectiveness of current treatment approaches, which could impact patient outcomes. It is necessary to take immediate action, which includes putting strong antimicrobial stewardship policies in place in healthcare facilities. Such programs are essential for encouraging the prudent use of antibiotics, reducing the pace of resistance, and preserving the long-term effectiveness of the antibiotics that are now in use.

Ethics approval and consent to participate

The hospital institutional review board approved this study after reviewing the study protocol, questionnaire, and consent form (reference 811/B; July 25th, 2023). Written informed consent was obtained from each participant.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Nour Bourgi: Writing – original draft, Project administration, Investigation, Data curation, Conceptualization. **Abd Alrahman Olaby:** Writing – original draft, Validation, Investigation, Formal analysis, Data curation. **Ali Najdi:** Writing – review & editing, Supervision, Conceptualization. **Georges Hatem:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation, Formal analysis, Conceptualization.

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.

Data availability

Not applicable.

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Not applicable.

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