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ORIGINAL ARTICLE

Prevalence and Antimicrobial Susceptibility Profile of Gram-negative and Gram-positive Bacteria in a Tertiary Hospital: A Retrospective Study

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ABSTRACT

Background: *To address the growing threat of drug-resistant organisms, it's crucial to establish effective stewardship programs. However, before doing so, it's vital to ensure access to evidence-based information on the local emergence of antibiotic resistance.* ***Objective:*** *The current study aims to determine the frequency of pathogens at one of Cairo University Hospitals and detect the antibiotic resistance profile of bacterial pathogens recovered from various sites of infections.* ***Methodology:*** *A three-year retrospective study was conducted (January 2020 and December 2022). We examined the information from the microbiology laboratory's Laboratory Data Manager, including the antimicrobial resistance profiles of pathogens isolated and identified from microbiological samples sent for routine culture.* ***Results:*** *Gram-negative isolates were more prevalent than Gram-positive ones. The most prevalent isolated pathogens were Klebsiella spp., Escherichia coli, Pseudomonas spp., and Coagulase-negative Staphylococci. Among Gram-negative organisms, more than 80% resistance was towards ceftriaxone, cefotaxime, ceftazidime, amoxicillin/clavulanic acid, and cefepime, while tigecycline showed the least resistance (19.15%). While, among Gram-positive organisms, vancomycin showed the least resistance (2.12%), and linezolid displayed minimal resistance (5.2%).* ***Conclusions****: Most of the investigated bacteria have become resistant to most antibiotics. This indicates an impending disaster that might threaten the future medical profession and needs extreme caution and continuous monitoring. Supporting local and national surveillance programs with ongoing monitoring of antimicrobial resistance patterns at the national and regional levels is a crucial step in the fight against emerging antimicrobial resistance. These findings imply that hospital resources should be the primary focus of efforts to reduce antibiotic resistance.*

INTRODUCTION

Antimicrobial resistance is the capacity of microorganisms to survive in the presence of antimicrobial compounds at concentrations usually suitable to inhibit or kill them[1, 2]. It is quickly gaining attention on a global scale, particularly in light of the growing number of organisms resistant to current antimicrobials. Gram-positive (Gm +ve) and Gram-negative (Gm -ve) bacteria are included, and their global prevalence rates are at least 60% [3]. An additional challenge in delivering contemporary hospital care is the emergence of antimicrobial-resistant bacteria as a public health concern[4, 5]. The main resistant pathogens of concern are *Staphylococcus aureus (S. aureus), Pseudomonas aeruginosa (P. aeruginosa), Klebsiella spp., Enterococci* spp., and *Enterobacter spp*[4,6]. In hospitalized patients, methicillin-resistant *S. aureus* (*MRSA*) in particular is known for significantly increasing rates of morbidity and mortality[7, 8]. The result of an infection brought on by resistant bacteria is that they can not only change the outcome of critically ill patients but also lower the likelihood that they will receive treatment, lengthen hospital stays, raise the expense of medical care, and facilitate the spread of infection while making prevention more challenging [4]. To optimize management and lower the rate of nosocomial infections, it is imperative to understand the appropriate antimicrobial prescription policy in a given setting. Nonetheless, identifying the causing agents and their antimicrobial susceptibility profile is an essential first step[6,7]. In general, it is challenging to locate information regarding endemic antibiotic resistance, especially in nations where antibiotics are widely

available over the counter. Many reports show the prevalence and resistance patterns of various pathogens, but there aren't many published studies about the profile of endemic antibiotic resistance in developing nations [3, 7]. Therefore, it is essential to have evidence-based knowledge about the local pattern of antibiotic resistance in order to guide the use of antibiotics as well as empirical therapy for particular pathogens [3]. This manual is also crucial for designing regional and global research initiatives, as well as for efficient antimicrobial stewardship [3]. Since Cairo University tertiary Hospital Patients are more susceptible to nosocomial infections brought on by powerful microorganisms, therefore, the present study aimed to detect the prevalence of pathogens at New Kasr Alainy Teaching Hospital (NKATH) one of Cairo University hospitals and detect the Antibiotic resistance profile of pathogens (Gram-positive, Gram-negative) recovered from various sites of infections along with determining the prevalence of multiple drug resistance using 3-years retrospective study

METHODOLOGY

The study design:

A three-year retrospective study was conducted at the adult tertiary NKATH, between January 2020 and December 2022. We examined the information gathered from the hospital's microbiology laboratory's Laboratory Data Manager (LDM).

The retrieved information included the antimicrobial resistance profiles of pathogens isolated and identified from various microbiological samples that were sent to the microbiology lab for routine culture, including blood, urine, respiratory, pus, wound, CSF, and pleural fluid. These samples were collected either during routine diagnosis of inpatients in various Surgical and Medical wards and ICUs of the hospital or from outpatients. The age group of the inpatients was 16 years and older, while the outpatients ranged from neonates and infants to toddlers, children, adolescents, and adults.

Microbiological specimens processing and identification

The microorganisms were identified, and the samples were processed following the laboratory's standard operating procedures [9]. All culture media used were purchased from Oxoid, UK. The samples were cultured on commonly used microbiological media and then incubated for 24-48 hours at 35°C.

To perform blood cultures, an automated Bact/ALERT microbial detection system from BioMerieux Inc., Durham, USA, was employed. The blood cultures were then incubated for five days. Initially, positive blood culture bottles were cultivated using blood agar, chocolate agar, and MacConkey agar for 24-48 hours at 35-37 °C [10].

The identification of isolated microorganisms involved Gram staining, standard confirmatory biochemical tests, and examination of colony morphology. Hemolytic activity on blood agar was utilized for identifying gram-positive bacteria, followed by further characterization using various biochemical tests such as the catalase reaction, slide and tube coagulase tests, DNase agar culture, Mannitol salt agar, and bile esculin.

For Gram-negative bacteria, detection was carried out through biochemical tests including oxidase, motility indole ornithine, citrate, lysine iron arginine, triple sugar iron, and urease tests.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing for bacterial isolates was carried out using the Kirby-Bauer disc diffusion method. A standard inoculum, adjusted to 0.5 McFarland standard turbidity, was evenly spread across the surface of Mueller Hinton agar (Oxoid, Ltd., UK). Antimicrobial discs were then applied to the Mueller Hinton agar plates using an automatic disc dispenser. After overnight incubation at 35°C, the zone of inhibition was measured and interpreted following the guidelines of the Clinical Laboratory Standard Institute (CLSI 2020), except for tigecycline, which was interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines [9, 11, 12]. The antibiotic discs used in the testing were regularly provided by Oxoid. Methicillin resistance in *Staphylococcus* was identified through the use of a cefoxitin disc (30 µg). The screening for Vancomycin-resistant Enterococci (VRE) and vancomycin-resistant S*taphylococcus* began with the use of Vancomycin screening agar (brain heart infusion agar (BHI) with 6 µg/ml vancomycin). Any suspected colonies underwent further confirmation through Minimum Inhibitory Concentration (MIC) testing using the Vitek2 compact system (Biomerieux, France).

Quality control:

The sterility of the recently opened medium was verified before its use. To assess the performance of each medium and antimicrobial disks, recommended reference strains, including *E. coli* (ATCC®25922), *S. aureus* (ATCC®25923), *K. pneumoniae* (ATCC®700603), *S. pneumoniae* (ATCC®49619), and *P. aeruginosa* (ATCC®27853), were employed.

Data Collection and Analysis:

The data retrieved from the LDM included only final verified results of isolates ≥30 isolates tested against routinely used antimicrobial agents during the routine diagnosis and not for surveillance purposes. The data were further stratified into inpatients and outpatients for further analysis and comparison [13].

Statistical methods:

The data were entered and coded using IBM Corp.'s statistical software for the social sciences, SPSS version 28 (Armonk, NY, USA). Percentages were used to

summarize the data, including frequencies (number of cases) and relative frequencies. The Chi-square test was utilized for comparing categorical data, and in cases where the expected frequency was below 5, an exact test was applied. Statistical significance was defined as a P-value equal to or less than 0.05.

RESULTS

A total of 15108 microbiological culture tests were performed over the period of three years (6076 outpatient tests and 9032 inpatient tests). From various clinical samples, a total of 5591 pathogens have been retrieved from our hospital's LDM (laboratory data manager) system.

Prevalence of pathogens in all hospital

Urine cultures showed the highest number of pathogens isolated 2345 (41.94%), the urine cultures included 1291 pathogens isolated from outpatients and 1054 from inpatients. The number of pathogens which were isolated from blood cultures was 1194 (21.36%), the blood cultures included 108 pathogens isolated from outpatients and 1086 from inpatients. The number of pus and wound pathogens was 1064 (19.03%), the samples included 407 pathogens isolated from outpatients and 657 from inpatients. Regarding respiratory pathogens, 670 (11.98%) pathogens were isolated; the cultures included 75 pathogens from outpatient and 595 from inpatient. Strains isolated from CSF was 282 (5.04%), the cultures included 275 pathogens from outpatient and 7 from inpatient. However, the pleural sample cultures contained the fewest pathogens that were isolated 36 (0.64%), the cultures included 27 pathogens from outpatients and 9 from inpatients.

The greatest number of pathogens were separated from urine cultures 2345 (41.94%), after that blood cultures 1194 (21.35%). While the least isolated pathogens were isolated from pleural samples 36 (0.64%).

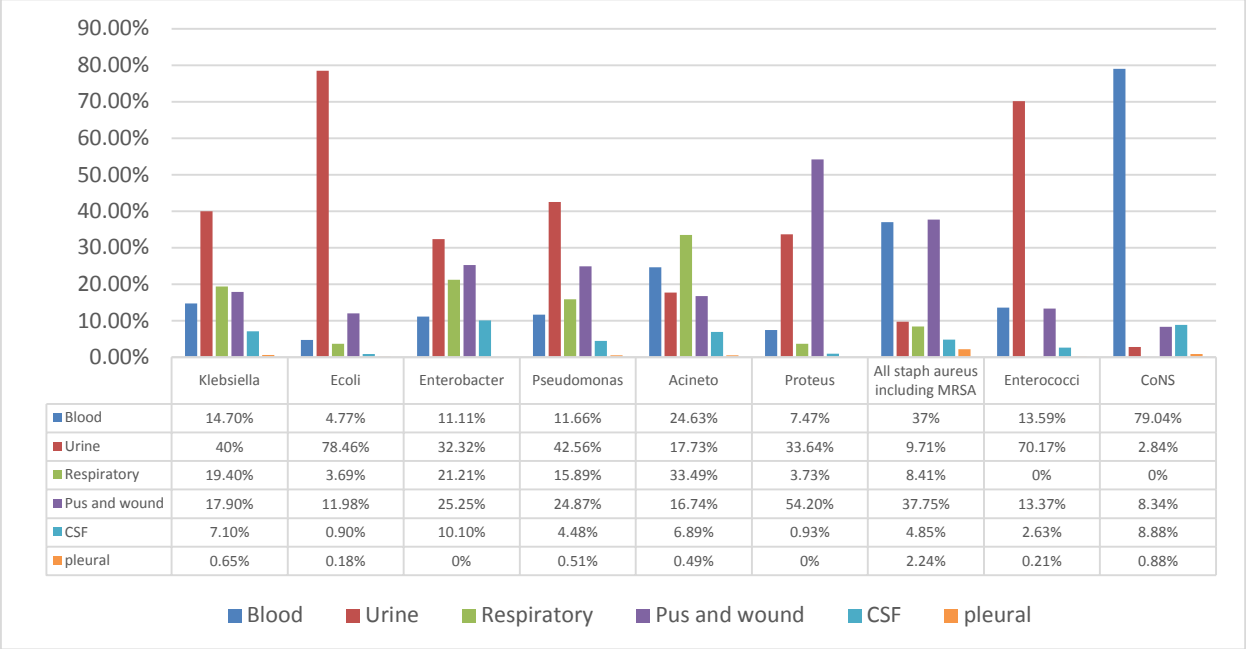
The most prevalent isolated pathogens were *Klebsiella spp.* (1535/5591), after that *E. coli* (1110/5591), *Pseudomonas spp.* (780/5591), and Coagulase-Negative Staphylococci *CoNS* (563/5591), while *Proteus spp*., and *Enterobacter spp.*, constituted the smallest set among the studied isolates.

Bloodstream infections were mainly caused by *CoNS* (445/ 563) and *Acinetobacter spp.* (100/406). The two main pathogens linked to urinary tract infections were *E. coli* (871/1110), and *Enterococci* (320/456). The respiratory infections were mainly caused by *Acinetobacter spp.* (136/ 406) and *Enterobacter spp.* (21/ 99). The commonly isolated pathogens from wounds and Pus were *Proteus spp.* (58/107). The CSF infections are mostly due to *Enterobacter spp.* The pleural infections were mainly due to *S. aureus* (including *MRSA*).

The prevalence of all pathogens in the hospital is shown in Table S1 & Figure 1.

Table S1. The prevalence of pathogens in all hospital

Organism	Total from 5591	Blood	Urine	Respiratory	Pus and wound	CSF	pleural
Klebsiella	1535 (100%)	226/1535 (14.7%)	614/1535 (40%)	299/1535 (19.4%)	276/1535 (17.9%)	110/1535 (7.1%)	10/1535 (0.65%)
Ecoli	1110 (100%)	53/1110 (4.77%)	871/1110 (78.46 %)	41/1110 (3.69%)	133/1110 (11.98%)	10/1110 (0.9%)	2/1110 (0.18%)
Enterobacter	99 (100%)	11/99 (11.11%)	32/99 (32.32%)	21/99 (21.21%)	25/ 99 (25.25%)	10/99 (10.1%)	0/ 99 (0%)
Pseudomonas	780 (100%)	91/780 (11.66%)	332/780 (42.56%)	124/780 (15.89%)	194/780 (24.87%)	35/780 (4.48%)	4/780 (0.51%)
Acinetobacter	406 (100%)	100/406 (24.63%)	72/406 (17.73%)	136/406 (33.49%)	68/406 (16.74%)	28/406 (6.89%)	2/406 (0.49%)
Proteus	107 (100%)	8/107 (7.47%)	36/107 (33.64%)	4/107 (3.73%)	58/107 (54.2%)	1/107 (0.93%)	0/107 (0%)
All *Staph aureus* including *MRSA*	535 (100%)	198/535 (37%)	52/535 (9.71%)	45/535 (8.41%)	202/535 (37.75%)	26/535 (4.85%)	12/535 (2.24%)
Enterococci	456 (100%)	62/456 (13.59%)	320/456 (70.17%)	0/456 (0%)	61/456 (13.37%)	12/456 (2.63%)	1/456 (0.21%)
CoNS	563 (100%)	445/563 (79.04%)	16/563 (2.84%)	0/563 (0%)	47/563 (8.34%)	50/563 (8.88%)	5/563 (0.88%)
Total	5591 (100%)	1194/5591 (21.35%)	2345/5591 (41.94%)	670/5591 (11.98%)	1064/5591 (19.03%)	282/5591 (5.04%)	36/5591 (0.64%)



	Klebsiella	Ecoli	Enterobacter	Pseudomonas	Acineto	Proteus	All staph aureus including MRSA	Enterococci	CoNS
Blood	14.70%	4.77%	11.11%	11.66%	24.63%	7.47%	37%	13.59%	79.04%
Urine	40%	78.46%	32.32%	42.56%	17.73%	33.64%	9.71%	70.17%	2.84%
Respiratory	19.40%	3.69%	21.21%	15.89%	33.49%	3.73%	8.41%	0%	0%
Pus and wound	17.90%	11.98%	25.25%	24.87%	16.74%	54.20%	37.75%	13.37%	8.34%
CSF	7.10%	0.90%	10.10%	4.48%	6.89%	0.93%	4.85%	2.63%	8.88%
pleural	0.65%	0.18%	0%	0.51%	0.49%	0%	2.24%	0.21%	0.88%

Fig. 1: The prevalence of all pathogens in the hospital.

Antibiotic resistance profile of pathogens recovered from various sites of infections of the Hospital.

Gram-positive Bacteria (resistance %)

The study of the antibiotic resistance profiles of various Gram-positive organisms was conducted. The results indicated that cefoxitin had the highest percentage of resistance (87.34%), followed by erythromycin (63.38%) and ciprofloxacin (56.25%). On the other hand, vancomycin showed the least resistance (2.12%) and linezolid displayed minimal resistance (5.2%) among Gram-positive organisms. In terms of the most common resistance phenotypes among the various isolates, *S. aureus* showed high rates of resistance to a variety of antibiotics; 87.1% of the isolates showed resistance to cefoxitin (MRSA), and 61.2% showed resistance to low concentrations of gentamicin. Conversely, isolates of *S. aureus* showed 100% susceptibility to vancomycin. *Enterococci* showed highest resistance for erythromycin (81.54%) and for ciprofloxacin with a percentage (71.71%).

CoNS showed the highest resistance for cefoxitin (*MRCoNS*) (87.34%) and for ciprofloxacin with a percentage (55.79%). *CoNS* showed 100% susceptibility to vancomycin. Additionally, a statistically significant variation in the antimicrobial potentials of various isolates was found in this data.

Antimicrobial resistance profile in various Gram-positive organisms is illustrated in Table S2.

Table S2. Antimicrobial resistance profile in various Gram-positive organisms

Antibiotic	All *Staph aureus* including *MRSA*	*Enterococci*	*CoNS*	Total Gentamycin positive	P Value for each antibiotic between the 3 organisms
Amikacin	88/278 (31.65 %)	NA*	75/279 (26.88%)	163/557 (29.26%)	0.216
Gentamycin Low	254/415 (61.2%)	NA*	165/365 (45.2%)	419/780 (53.71%)	< 0.0001
Gentamycin High	NA*	31/157 (19.74%)	NA*	31/157 (19.74%)	-
Trimethoprim/ Sulfamethoxazole	118/365 (32.32%)	NA*	206/375 (54.93%)	324/740 (43.78%)	< 0.0001
Erythromycin	236/457 (51.64%)	137/168 (81.54 %)	207/290 (71.37%)	580/915 (63.38%)	< 0.0001
Clindamycin	203/471 (43%)	NA*	218/414 (52.65%)	421/885 (47.57%)	< 0.0001
Doxycycline	182/441 (41.26%)	110/164 (67.07%)	163/428 (38.08%)	455/1033 (44.04%)	< 0.0001
Vancomycin	0 /535 (0%)	*33/456 (7.23%)	0/563 (0%)	33/1554 (2.12%)	-
Teicoplanin	19/391 (4.85%)	22/300 (7.33%)	22/380 (5.78%)	63/1071 (5.88%)	0.389
Linezolid	22/459 (4.79%)	16/368 (4.34%)	27/423 (6.38%)	65/1250 (5.2%)	0.387
Cefoxitin	**466/535 (87.1%)	NA*	493/563 (87.57%)	***959/1098 (87.34%)	0.817
Ampicillin	NA*	158/366 (43.16%)	NA*	158/366 (43.16%)	-
Ciprofloxacin	168/365 (46.02%)	180/251 (71.71%)	178/319 (55.79%)	526/935 (56.25%)	< 0.0001
Levofloxacin	137/384 (35.67%)	144/258 (55.81%)	166/337 (49.25%)	447/979 (45.65%)	< 0.0001
Ofloxacin	145/354 (40.96%)	167/261 (63.98%)	190/350 (54.28%)	502/965 (52.02%)	< 0.0001

*NA = not applicable

** The resistance for Ampicillin was deduced from Cefoxitin; ***P value*** < 0.05 is considered significant

Gram-negative Bacteria (resistance %)

It was discovered that over 80% of the Gram-negative organisms analyzed had antibiotic resistance profiles that were resistant to ceftriaxone, cefotaxime, ceftazidime, amoxicillin/clavulanic acid, and cefepime (Beta lactamases).

Conversely, among Gram-negative organisms, tigecycline exhibited the least resistance (19.15%). Regarding the predominant resistance phenotypes between the different isolates, *Klebsiella spp.* exhibited high resistance rates to several antibiotics where more than 90% of the isolates revealed resistance to ceftriaxone, ceftazidime, and cefotaxime. Conversely, the least resistance rate of *Klebsiella spp.* was exhibited towards tigecycline. *E. coli* showed the highest resistance for ceftazidime (80.58%) and for cefotaxime with a percentage (80.22%). Moreover, *E. coli* showed 88.11% susceptibility to tigecycline and 86.8% susceptibility to meropenem.

Enterobacter spp. displayed high resistance rates to several antibiotics where more than 90% of the isolates showed resistance to ceftriaxone, amoxicillin/clavulanic acid, ceftazidime, and cefotaxime. On the other hand, the least resistance rate of *Enterobacter spp.* was exhibited towards tigecycline by a percentage (15.62%).

Similarly, *Pseudomonas spp.* showed the highest resistance for meropenem (carbapenemase) (85.94%) and for ceftazidime with a percentage (83.51%). *Pseudomonas spp.* least resistance rate was exhibited towards amikacin by a percentage (54.82%). *Acinetobacter* spp. showed high resistance rates to several antibiotics where more than 90% of the isolates revealed resistance to piperacillin/tazobactam, ceftriaxone, cefepime, ceftazidime, cefotaxime, and ciprofloxacin. While *Acinetobacter spp.* Showed the least resistance towards tigecycline by a percentage (32.97%). Similarly, *Proteus spp.* showed the highest resistance for trimethoprim/sulfamethoxazole (83.11%) and for amoxicillin-clavulanic acid with a percentage (75.96%). *Proteus spp.* showed the least resistance rate towards meropenem. Additionally, a statistically significant variation in the antimicrobial potentials of various isolates was found in the data.

The results of the resistance profile of pathogens recovered from various sites of infections of the Hospital are summarized in Tables S2 and S3.

Table S3. Antimicrobial resistance profile in various Gram-negative organisms

Antibiotic	*Klebsiella*	*Ecoli*	*Enterobacter*	*Pseudomonas*	*Acinetobacter*	*Proteus*	Total Gentamycin negative	P Value for each antibiotic between the 6 organisms
Cefoxitin	1014/1366 (74.23%)	318/971 (32.74%)	77/99 (77.78%)	NA*	NA*	49/105 (46.66%)	1458/2541 (57.38%)	< 0.0001
Amoxicillin +clavulanate	1226/1363 (89.94%)	711/952 (74.68%)	86/93 (92.47%)	NA*	NA*	79/104 (75.96%)	2102/ 2512 (83.67%)	< 0.0001
Piperacillin +tazobactam	821/1081 (75.94%)	262/751 (34.88%)	67/81 (82.71%)	336/492 (68.29%)	356/380 (93.68%)	26/80 (32.5%)	1868/2865 (65.2%)	< 0.0001
Ceftazidime	1238/1356 (91.29%)	772/958 (80.58%)	91/99 (91.91%)	603/722 (83.51%)	330/338 (97.63%)	75/105 (71.42%)	3109/3578 (86.89%)	< 0.0001
Cefotaxime	1272/1409 (90.27%)	791/986 (80.22%)	91/99 (91.91%)	NA*	346/355 (97.46%)	78/107 (72.9%)	2578/2956 (87.21%)	< 0.0001
Ceftriaxone	1355/1474 (91.92%)	762/969 (78.63%)	91/98 (92.85%)	NA*	346/352 (98.29%)	78/107 (72.9%)	2632/3000 (87.73%)	< 0.0001
Cefepime	1075/1209 (88.91%)	636/861 (73.86%)	67/89 (75.28%)	460/611 (75.28%)	283/296 (95.6%)	57/92 (61.95%)	2578/3158 (81.63%)	< 0.0001
Imipenem	791/1312 (60.28%)	143/930 (15.37%)	39/88 (44.31%)	417/638 (65.36%)	268/330 (81.21%)	22/100 (22%)	1680/3398 (49.44%)	< 0.0001
Meropenem	726/1189 (61.05%)	110/832 (13.22%)	38/81 (46.91%)	369/626 (85.94%)	249/298 (83.55%)	16/107 (14.95%)	1508/3133 (48.13%)	< 0.0001
Ciprofloxacin	730/949 (76.92%)	420/667 (62.96%)	42/70 (60%)	273/390 (70%)	220/240 (91.66%)	48/82 (58.53%)	1733/2398 (72.26%)	< 0.0001
Ofloxacin	704/956 (73.64%)	419/718 (58.35%)	38/73 (52.05%)	365/513 (71.15%)	217/242 (89.66%)	47/76 (61.84%)	1790/2578 (69.43%)	< 0.0001
Levofloxacin	756/1054 (71.72%)	389/729 (53.36%)	39/77 (50.64%)	301/456 (65.57%)	226/262 (86.25%)	50/96 (52.08%)	1761/2674 (65.85%)	< 0.0001
Amikacin	632/1016 (62.2%)	163/718 (22.7%)	47/83 (56.62%)	307/560 (54.82%)	209/259 (80.69%)	19/82 (23.17%)	1377/2718 (50.66%)	< 0.0001
Gentamycin	670/1131 (59.23%)	211/898 (23.49%)	44/86 (51.16%)	371/547 (67.82%)	204/260 (78.46%)	43/78 (55.12%)	1543/3000 (51.43%)	< 0.0001
Trimethoprim/Sulfamethoxazole	788/964 (81.74%)	430/719 (59.8%)	40/64 (62.5%)	NA*	205/244 (84.01%)	64/77 (83.11%)	1527/2068 (73.83%)	< 0.0001
Tigecycline	76/486 (15.63%)	12/101 (11.88%)	5/32 (15.62%)	NA*	61/185 (32.97%)	NA*	154/804 (19.15%)	< 0.0001

NA = not applicable; ***P value*** < 0.05 is considered significant

Inpatient versus Outpatient Analysis:

Distribution of different types of Cultures and bacteria among inpatient and outpatient

Within the inpatient department, about 93.6% of blood culture tests, 49.2% of urine culture tests, 87.2% of respiratory culture tests, 59.9% of pus and wound culture tests, 6% of CSF culture tests, and 51.8% of pleural culture tests were performed. In contrast, the outpatient department performed 48.2% of pleural culture tests, 40.1% of pus and wound culture tests, 50.8% of urine culture tests, 12.8% of respiratory culture tests, 94% of CSF culture tests, and 6.4% of blood culture tests.

In inpatients, 28.55% of the bacteria isolated were Gram-positive bacteria and 71.45% were Gram-negative. While 26.61% of the bacteria isolated in outpatient were Gram-positive bacteria and 73.39% were Gram-negative.

Distribution of different types of cultures and bacteria among inpatients and outpatients are shown in Table S4 and Figure 2.

Table S4. Distribution of different types of cultures

Test	Inpatient Count	Inpatient %	Outpatient Count	Outpatient %	All Hospital (Inpatient & Outpatient) Count & %
Blood Culture Tests	3168	93.56	218	6.43	3386 (100%)
Urine Culture Tests	3822	49.22	3943	50.78	7765 (100%)
Respiratory Culture Tests	1119	87.22	164	12.78	1283 (100%)
Pus & Wound Culture Tests	721	59.93	482	40.07	1203 (100%)
CSF Culture Tests	74	6.05	1150	93.95	1224 (100%)
Pleural Culture Tests	128	51.82	119	48.18	247 (100%)

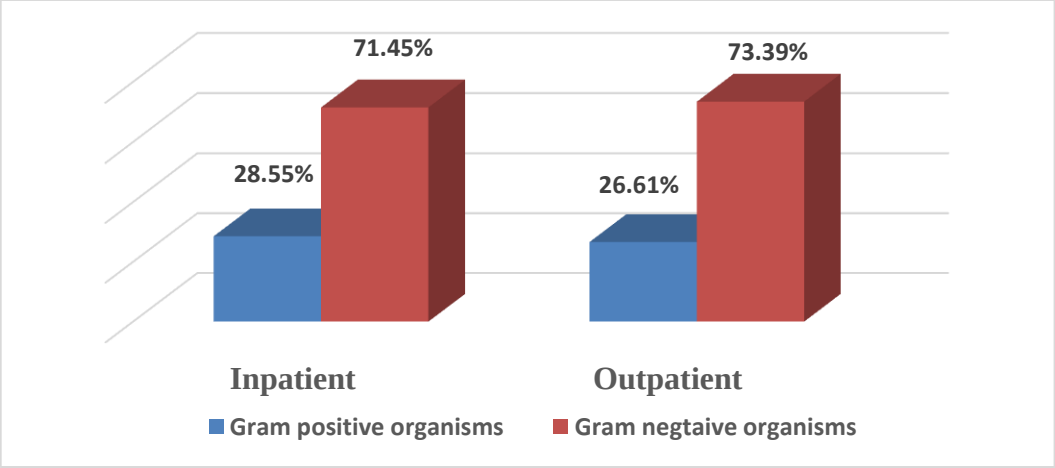


Fig. 2: Distribution of Gm-positive and Gm-negative pathogens among inpatient versus outpatient

Antibiotic resistance profile of pathogens recovered from various sites of infections (Inpatient versus Outpatient)

Regarding Gram-positive Bacteria (resistance %)

The greatest resistance percentage in the inpatient department was exhibited by *CoNS* and *S. aureus* towards cefoxitin (89.52%) followed by *Enterococcus* towards erythromycin (83.9%) and ciprofloxacin (76.15%). On the other hand, vancomycin showed the least resistance (1.44%) (all vancomycin resistance in Gram-positive bacteria were *Enterococci* vancomycin resistance *Enterococci* (*VRE*) and linezolid displayed low resistance (6.14%) among Gram-positive organisms.

The highest percentage of resistance in the outpatient department was exhibited by *CoNS* and *S. aureus* towards cefoxitin (85.32%) followed by *Enterococcus* towards erythromycin (79.1%) and ciprofloxacin (76.15%). On the other hand, vancomycin showed the least resistance (3%) (all vancomycin resistance in Gram-positive bacteria were *Enterococci* vancomycin resistance *Enterococci* (*VRE*) and linezolid displayed low resistance (3.8%) among gram-positive organisms.

Regarding Gram-negative Bacteria (resistance %)

The greatest resistance percentage in the inpatient department was displayed by *Acinetobacter spp.* towards most of the antibiotics by more than 90%. On the other hand, tigecycline showed the least resistance among Gram-negative organisms.

The greatest resistance percentage in the outpatient department was shown by *Acinetobacter* spp. and *Enterobacter spp.* towards most of the antibiotics. The Gram-negative organisms that exhibited the least resistance to tigecycline were found. Antibiotic resistance characteristics of pathogens isolated from different infection sites.

(Inpatient versus Outpatient) are shown in Tables S5 and S6.

Table S5. Gram-positive (resistance number and %)

Antibiotic	Bacteria Gram-positive	Inpatient resistance n	Inpatient resistance %	Outpatient resistance number	Outpatient resistance %	P value for each
Amikacin	*Staph aureus*	63/150	42	52/128	40.62	0.817
	Enterococci	NA*	NA*	NA*	NA*	NA*
	CoNS	57/204	27.94	18/75	24	0 .510
Total Amikacin		120/354	33.89	70/203	34.48	0 .888
Ampicilin	*Staph aureus*	NA*	NA*	NA*	NA*	NA*
	Enterococcus	94/178	52.81	64/188	34.04	< 0.0001
	CoNS	NA*	NA*	NA*	NA*	NA*
Total Ampicilin		94/178	52.81	64/188	34.04	< 0.0001
Ciprofloxacin	*Staph aureus*	112/200	56	56/165	33.93	< 0.0001
	Enterococcus	99/130	76.15	81/121	66.94	0.105
	CoNS	141/233	60.51	37/86	43.02	0.005
Total Ciprofloxacin		352/563	62.52	174/372	46.77	< 0.0001
Clindamycin	*Staph aureus*	127/257	49.42	76/214	35.51	0.002
	Enterococcus	NA*	NA*	NA*	NA*	NA*
	CoNS	169/296	57.09	49/118	41.52	0.0004
Total Clindamycin		296/553	53.52	125/332	37.65	< 0.0001
Doxycycline	*Staph aureus*	117/251	46.61	65/190	34.21	0.008
	Enterococcus	59/84	70.24	51/80	63.75	0.376
	CoNS	123/310	39.68	40/118	33.89	0.271
Total Doxycycline		299/645	46.35	156/388	40.2	0.0538
Erythromycin	*Staph aureus*	152/253	60.08	84/204	41.17	0.00005
	Enterococcus	73/87	83.91	64/81	79.01	0.413
	CoNS	133/182	73.08	74/108	68.51	0.406
Total Erythromycin		358/522	68.58	222/393	56.48	0.0002
Cefoxitin	*Staph aureus*	254/290	87.59	212/245	86.53	0.716
	Enterococcus	NA*	NA*	NA*	NA*	NA*
	CoNS	333/372	89.52	160/191	83.77	0.050
Total Cefoxitin		587/662	88.67	372/436	85.32	0.102
Gentamycin High	*Staph aureus*	NA*	NA*	NA*	NA*	NA*
	Enterococcus	17/82	20.73	14/75	18.66	0.745
	CoNS	NA*	NA*	NA*	NA*	NA*
Total Gentamycin High		17/82	20.73	14/75	18.66	0.745
Gentamycin Low	*Staph aureus*	143/227	63	111/188	59.04	0.411
	Enterococcus	NA*	NA*	NA*	NA*	NA*
	CoNS	117/259	45.17	48/106	45.28	0.984
Total Gentamycin Low		260/486	53.49	159/294	54.08	0.874
Levofloxacin	*Staph aureus*	92/208	44.23	45/176	25.56	0.0001
	Enterococcus	88/137	64.23	56/121	46.28	0.003
	CoNS	134/251	53.39	32/86	37.2	.010
Total Levofloxacin		314/596	52.68	133/383	34.72	< 0.0001
Linezolid	*Staph aureus*	16/257	6.23	6/202	2.97	0.105
	Enterococcus	6/178	3.37	10/190	5.26	0.373
	CoNS	24/314	7.64	3/109	2.75	0.071
Total Linezolid		46/749	6.14	19/501	3.79	0.066
Ofloxacin	*Staph aureus*	101/198	51.01	44/156	28.2	0.00001
	Enterococcus	100/139	71.94	67/122	54.91	0.0042
	CoNS	147/252	58.33	43/98	43.87	0.014
Total Ofloxacin		348/589	59.08	154/376	40.95	< 0.0001
Trimethoprim/Sulfamethoxazole	*staph aureus*	77/212	36.32	41/153	26.79	0.054
	enterococcus	NA*	NA*	NA*	NA*	NA*
	CoNS	159/280	56.79	47/95	49.47	0.215
Total Trimethoprim/ Sulfamethoxazole		236/492	47.96	88/248	35.48	0.001
Vancomycin	*Staph aureus*	0/310	0	0/225	0	-
	Enterococcus	14/240	5.83	17/216	7.87	0.388
	CoNS	0/423	0	0/140	0	-
Total Vancomycin		14/973	1.44	17/581	2.99	0.042
Teicoplanin	*Staph aureus*	12/227	5.29	7/164	4.26	0.644
	Enterococcus	15/161	9.32	7/139	5.03	0.156
	CoNS	17/288	5.9	5/92	5.43	0.867
Total Teicoplanin		44/676	6.5	19/395	4.81	0.254

***NA* = not applicable;P value** < 0.05 is considered significant

Table S6. Gram negative (resistance number and %)

Antibiotic	Bacteria Gram negative	Inpatient resistance n	Inpatient resistance %	Outpatient resistance number	Outpatient resistance%	P value each
Amikacin	*Klebsiella*	436/652	66.87	196/364	53.84	<0.0001
	Ecoli	89/330	26.97	74/388	19.07	0.011
	Enterobacter	23/36	63.89	24/47	51.06	0.243
	Pseudomonas	230/373	61.67	77/187	41.17	<0.0001
	Acinetobacter	170/198	85.86	39/61	63.93	0.001
	Proteus	10/52	19.23	9/30	30	0.266
Total Amikacin		958/1641	58.37	419/1077	38.9	<0.0001
Amoxicillin +Clavulanate	*Klebsiella*	773/844	91.59	453/519	87.28	0.010
	Ecoli	333/423	78.72	378/529	71.45	0.010
	Enterobacter	51/55	92.72	35/38	92.1	0.911
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	NA*	NA*	NA*	NA*	NA*
	Proteus	51/66	77.27	28/38	73.68	*0.*680
Total Amoxicillin + Clavulanate		1208/1388	87.03	894/1124	79.53	<0.0001
Ceftazidime	*Klebsiella*	791/847	93.39	447/509	87.81	0.0004
	Ecoli	367/427	85.95	405/531	76.27	0.0002
	Enterobacter	50/54	92.59	41/45	91.11	0.788
	Pseudomonas	424/481	88.15	179/241	74.27	<0.0001
	Acinetobacter	251/256	98.05	79/82	96.34	0.377
	Proteus	51/69	73.91	24/36	66.66	0.435
Total Ceftazidime		1934/2134	90.62	1175/1444	81.37	<0.0001
Ciprofloxacin	*Klebsiella*	487/594	81.99	243/355	68.45	<0.0001
	Ecoli	208/288	72.22	212/379	55.93	<0.0001
	Enterobacter	25/38	65.79	17/32	53.12	0.281
	Pseudomonas	192/252	76.19	81/138	58.69	0.0003
	Acinetobacter	177/184	96.2	43/56	76.78	<0.0001
	Proteus	37/57	64.91	11/25	44	0.077
Total Ciprofloxacin		1126/1413	79.68	607/985	61.62	<0.0001
Ceftriaxone	*Klebsiella*	898/955	94.03	457/519	88.05	<0.0001
	Ecoli	366/430	85.11	396/539	73.46	<0.0001
	Enterobacter	50/52	96.15	41/46	89.13	0.178
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	267/270	98.89	79/82	96.34	0.119
	Proteus	55/75	73.33	23/32	71.88	0.877
Total Ceftriaxone		1636/1782	91.8	996/1218	81.77	<0.0001
Cefotaxime	*Klebsiella*	808/883	91.51	464/526	88.21	0.0444
	Ecoli	378/438	86.3	413/548	75.36	<0.0001
	Enterobacter	50/52	96.15	41/47	87.23	0.104
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	266/271	98.15	80/84	95.23	0.137
	Proteus	59/80	73.75	19/27	70.37	0.733
Total Cefotaxime		1561/1724	90.54	1017/1232	82.55	<0.0001
Cefepime	*Klebsiella*	716/781	91.68	359/428	83.87	<0.0001
	Ecoli	311/390	79.74	325/471	69	0.0004
	Enterobacter	40/49	81.63	27/40	67.5	0.124
	Pseudomonas	333/416	80.05	127/195	65.12	<0.0001
	Acinetobacter	231/238	97.06	52/58	89.65	0.014
	Proteus	39/62	62.9	18/30	60	0.788
Total Cefepime		1670/1936	86.26	908/1222	74.3	<0.0001
Cefoxitin	*Klebsiella*	662/859	77.07	352/507	69.42	0.002
	Ecoli	173/432	40.05	145/539	26.9	<0.0001
	Enterobacter	47/55	85.45	30/44	68.18	0.040
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	NA*	NA*	NA*	NA*	NA*
	Proteus	32/65	49.23	17/40	42.5	0.502
Total Cefoxitin		914/1411	64.77	544/1130	48.14	<0.0001
Gentamycin	*Klebsiella*	430/691	62.23	240/440	54.54	0.010
	Ecoli	115/326	35.28	96/572	16.78	<0.0001
	Enterobacter	26/41	63.41	18/45	40	0.030
	Pseudomonas	270/377	71.62	101/170	59.41	0.005
	Acinetobacter	166/197	84.26	38/63	60.31	<0.0001
	Proteus	31/50	62	12/28	42.85	0.103
Total Gentamycin		1038/1682	61.71	505/1318	38.31	<0.0001
Imipenem	*Klebsiella*	547/842	64.96	244/470	51.91	<0.0001
	Ecoli	83/421	19.71	60/509	11.78	<0.0001

Antibiotic	Bacteria Gram negative	Inpatient resistance n	Inpatient resistance %	Outpatient resistance number	Outpatient resistance%	P value each
	Enterobacter	29/48	60.42	10/40	25	0.0008
	Pseudomonas	315/396	79.55	102/242	42.14	<0.0001
	Acinetobacter	223/253	88.14	45/77	58.44	<0.0001
	Proteus	17/70	24.29	5/30	16.66	0.399
Total Imipenem		1214/2030	59.8	466/1368	34.06	<0.0001
Levofloxacin	*Klebsiella*	505/649	77.81	251/405	61.97	<0.0001
	Ecoli	200/308	64.94	189/421	44.89	<0.0001
	Enterobacter	23/41	56.1	16/36	44.44	0.307
	Pseudomonas	210/299	70.23	91/160	56.87	0.004
	Acinetobacter	185/204	90.69	41/58	70.68	<0.0001
	Proteus	33/63	52.38	17/33	51.51	0.936
Total Levofloxacin		1156/1564	73.91	605/1113	54.35	<0.0001
Meropenem	*Klebsiella*	492/742	66.3	234/447	52.34	<0.0001
	Ecoli	66/360	18.33	44/472	9.322	0.0001
	Enterobacter	25/44	56.82	13/37	35.13	0.051
	Pseudomonas	274/412	66.5	95/214	44.39	<0.0001
	Acinetobacter	201/224	89.73	48/74	64.86	<0.0001
	Proteus	11/71	15.49	5/36	13.89	0.826
Total Meropenem		1069/1483	72.08	439/1280	34.3	<0.0001
Ofloxacin	*Klebsiella*	490/624	78.53	214/332	64.45	<0.0001
	Ecoli	212/315	67.3	207/403	51.36	<0.0001
	Enterobacter	25/40	62.5	13/33	39.39	0.049
	Pseudomonas	273/358	76.26	92/155	59.35	<0.0001
	Acinetobacter	175/186	94.09	42/56	75	<0.0001
	Proteus	33/51	64.71	14/25	56	0.463
Total Ofloxacin		1208/1574	76.74	609/1004	60.65	<0.0001
Trimethoprim/ Sulfamethoxazole	*Klebsiella*	523/606	86.3	265/358	74.02	<0.0001
	Ecoli	209/312	66.99	221/407	54.29	0.0005
	Enterobacter	29/38	76.32	11/26	42.3	0.006
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	169/197	85.79	36/47	76.59	0.122
	Proteus	45/53	84.91	19/24	79.16	0.533
Total Trimethoprim/ Sulfamethoxazole		975/1206	80.84	552/862	64.03	<0.0001
Tigecycline	*Klebsiella*	55/355	15.49	21/131	16.03	0.885
	Ecoli	6/73	8.22	6/28	21.42	0.066
	Enterobacter	4/25	16	1/7	14.28	0.912
	Pseudomonas	NA*	NA*	NA*	NA*	NA*
	Acinetobacter	55/158	34.81	6/27	22.22	0.199
	Proteus	NA*	NA*	NA*	NA*	NA*
Total Tigecycline		120/611	19.63	34/193	17.61	0.533
Piperacillin +Tazobactam	*Klebsiella*	562/709	79.27	259/372	69.62	0.0004
	Ecoli	141/335	42.09	121/416	29.08	<0.0001
	Enterobacter	38/43	88.37	29/38	76.31	0.152
	Pseudomonas	247/335	73.73	89/157	56.68	0.0001
	Acinetobacter	303/317	95.58	53/63	84.12	0.0006
	Proteus	16/52	30.77	10/28	35.71	0.652
Total Piperacillin +Tazobactam		1307/1791	72.97	561/1074	52.23	<0.0001

NA* = *not applicable;P value < 0.05 is considered significant

DISCUSSION

Overuse of antibiotics has resulted in a high incidence of antimicrobial resistance [14]. Bacterial pathogens will get harder to control over time because they will develop resistance to all antibacterial therapies[15]. Consequently, it was designated as a major global health threat by the World Health Organization [4]. To stop this spiraling out of control, comprehensive oversight of antibiotic use in developing countries is necessary. However, information on antibiotic resistance is not enough to precisely assess the problem's extent. Hospitals are thought to be breeding grounds for recently emerging high-level resistance based on previous research. More research in other countries and medical facilities is therefore encouraged[3]. Gram-negative isolates outnumbered Gram-positive ones in this study. Gram-negative bacteria are becoming increasingly resistant to many different medications as well as the majority of antibiotics currently in use. These bacteria have the innate capacity to create novel resistance mechanisms and the capacity to transfer genetic materials that allow other bacteria to acquire drug resistance [16]. A study by Halim et al. reported

similar findings, with Gram-negative bacteria constituting the majority of nosocomial pathogens at 53%, while Gram-positive organisms accounted for 37.9% [17]. In the study of Sawhney and colleagues, most of cases were also caused by Gram-negative organisms[18].

In our study the urine cultures represented the majority of the isolates (41.94%), followed by blood cultures (21.36%). That was also reported by a previous study [19]. In contrast, the majority of isolates were found in blood cultures, then urine cultures, according to Fahim, N.A.E.'s research [3].

Among Gram-negative organisms in our study, *Klebsiella spp*. constituted the majority (27.5%), followed by *E. coli* (19.9%), and then *Pseudomonas spp.* (13.9%). Conversely, *CoNS* (10.1%) emerged as the most common Gram-positive pathogen. Similar results were reported in previous studies [17, 18]. In contrast to our findings, Shebl et al.'s study indicated that *S. aureus* was much more prevalent than *CoNS* [19].

According to previous reports, the high prevalence of *CoNS* is caused by insufficient infection control procedures and high usage of invasive devices that healthcare workers repeatedly use [20]. In this study, *CoNS* and *Klebsiella spp.* emerged as the most frequently isolated pathogens from blood cultures, in line with the distribution of pathogens across various clinical specimens. A previous study also affirmed that *CoNS* were the predominant pathogens isolated from blood cultures, whereas *E. coli* took precedence over *Klebsiella spp.* as a cause of bacteremia[21].

The primary causative agents of Urinary Tract Infections (UTI) are *E. coli, Candida albicans, Enterococcus faecalis, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Proteus mirabilis* [22]. In this study, *E. coli, Pseudomonas spp.,* and *Klebsiella spp.* were the predominant pathogens recovered from urine, a finding also supported by a prior Egyptian study[19].

Major microorganisms contributing to Lower Respiratory Tract infections include *Acinetobacter baumannii, Pseudomonas aeruginosa, S. aureus,* and *K. pneumonia* [23]. The major isolates from respiratory specimens in this study are *Acinetobacter spp., Enterobacter spp.,* and *K. pneumonia* A previous study reported that the most common isolates were *P. aeruginosa, Acinetobacter spp.,* and *K. pneumonia* [24]. This slight difference could be due to different geographic region and different empirical antimicrobial treatment [23].

As one of the major repeated nosocomial infections, wound infections are thought to be responsible for 70–80% of mortality as well as a significant cause of morbidity. Numerous pathogenic microorganisms, including bacteria, fungi, parasites, and viruses, are responsible for wound infections [25]. *Proteus spp.* and *S. aureus* were the most repetitively isolated organisms for the prevalent pathogens in pus and wound samples in this study. According to a previous Saudi study, *K. pneumoniae* and *Proteus mirabilis* were the two most prevalent wound pathogens [26]. *S. aureus* was found to be the most prevalent, followed by *Pseudomonas aeruginosa, K. pneumoniae,* and *E. coli,* according to another study from Egypt [27]. Numerous causes, such as environmental fears, healthcare performance, patient situations, personal hygiene, the number of participants in each study, and laboratory procedures, may account for the variations in the types and frequencies of pathogens between this study and the other studies [19].

A medical emergency with a high death rate is bacterial meningitis. The "golden standard" for diagnosing meningitis is cerebrospinal fluid (CSF) culture, and to rationalize treatment, it's critical to determine the causative microorganism's susceptibility. *Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis, S. aureus,* and *E.coli* were the commonest organisms separated from CSF [28]. The most common microorganism isolated from cerebrospinal fluids (CSF) in this study, is *Enterobacter spp.* (10%). A previous Saudian study reported the same result with the same percentage [29].

Following an examination of the antibiotic resistance profiles of various Gram-positive organisms in this study, it was found that cefoxitin (87.34%) had the highest percentage of resistance, followed by erythromycin (63.38%) and ciprofloxacin (56.25%). While vancomycin and linezolid demonstrated the least resistance (2.12 and 5.2%) respectively among Gram-positive bacteria. A previous Egyptian study showed nearly similar results [3].

The highly resistance towards cefoxitin among Staphylococcal isolates was reported in an another Egyptian study which is similar to the findings of this study [27]. *Enterococci* showed high resistance against erythromycin followed by ciprofloxacin.

A recent Saudi study found that *Enterococci* exhibited high sensitivity to linezolid, ciprofloxacin, moxifloxacin, teicoplanin, nitrofurantoin, and vancomycin (100%), but demonstrated significant resistance to tetracycline (100%), followed by erythromycin (66.67%), cefoxitin and gentamicin (50%), and ampicillin (42.86%) [30].

In this study, *CoNS* displayed the highest resistance to cefoxitin (87.34%) and ciprofloxacin (55.79%). However, *CoNS* showed 100% susceptibility to vancomycin. In contrast, a study by Taher Azimi et al. reported that *CoNS* strains exhibited high resistance to oxacillin (85.8%) and ampicillin (80.4%), while vancomycin (3.6%) and linezolid (4.7%) were the most effective antimicrobial agents against *CoNS* [31]. The same study by Taher Azimi et al. also noted that *CoNS* isolates displayed the highest and lowest resistance to vancomycin in 2013 and 2018, respectively [31].

CoNS isolated from clinical specimens may be often considered a common contaminant. Therefore,

implementing more effective measures such as hand hygiene for healthcare workers, regular disinfection of medical devices, and disinfection of sampling sites during specimen collection is essential. However, it should be noted that *CoNS* can cause various infections, including skin and soft tissue infections, and should not always be dismissed as contaminants [32]. A persistent *CoNS* infection is likely associated with a number of serious side effects, including septic thrombophlebitis, embolic complications, and metastatic seeding [33]. As such, assessing *CoNS* medical correlation is a difficult task. The primary diagnostic challenge in medical laboratories lies in discerning whether an anticipated *CoNS* isolate signifies routine colonization of the skin, soft tissue, or mucous membranes, contamination during specimen collection, handling, and processing, or clinically significant infection [34]. In cases of *CoNS* co-infection with other bacterial infections, resulting in polymicrobial infections, different isolates of the bacteria showcase diverse patterns of susceptibility and resistance, adding further complexity to the diagnostic scenario [34]. This medical and diagnostic issue can be resolved through tight cooperation between physicians and diagnostic laboratory experts. When patients with false-positive *CoNS* cases receive multiple antibiotic treatments, it is anticipated that this will result in not only extra expenses but also overuse of antibiotics, which may promote the antibiotic resistance emergency [35]. Therefore, it's critical to determine whether *CoNS* that was separated from a clinical specimen represents a true infection or is just a usual skin colonization or contamination. Several key indicators that can help predict a true infection include: 1) the repeated isolation of similar strains during the course of an infection following the isolation of a strain in pure culture from the infected site; 2) the requirement that patients with bloodstream infections show clinical signs of the infection with one positive blood culture or only two positive *CoNS* blood cultures through five days; and 3) the recommendation that, if *CoNS* is separated from a skin or soft tissue bacterial culture of a suspected infectious lesion, the isolated organism should be designated as a pathogen and appropriate treatment should be started [36].

Nearly 80% of bloodstream infections were caused by *CoNS*, which is a significant concern. This high rate may be attributed to the frequent use of medical devices, such as central venous lines, urinary catheters, and cannulas, in our hospital's various medical and surgical ICUs. These devices often serve as entry points for *CoNS* into patients' bodies.

Inconvenient use of antibiotics, geographic and socioeconomic variations, sampling biases, and patients with different characteristics could all be contributing factors to the higher antibiotic resistance rates reported by the aforementioned studies compared to the current results [37].

Compared to Gram-positive bacteria, and Gram-negative pathogens are 2.3 times more likely to result in hospital acquired infections (HAIs) [38].

The analysis of the antibiotic resistance profile of different Gram-negative organisms showed that more than 80% resistance was exhibited towards ceftriaxone, cefotaxime, ceftazidime, amoxicillin/clavulanic acid, and cefepime. A previous Saudian study reported 50% Gram-negative resistance [38]. This higher percentage in this research may be due to the inconvenient use of antibiotics in Egypt.

Several studies reported UTI as most common infections frequently caused by *E.coli* and *K. pneumoniae* with high resistance to broad spectrum antibiotics, that remains a major clinical problem in health care system [39, 40].

In current study, *Klebsiella spp.* exhibited high resistance rates to many antibiotics where more than 90% of the isolates displayed resistance to ceftriaxone, ceftazidime, and cefotaxime. The same findings were shown in a previous study, which reported that *Klebsiella* strains were resistant to a greater number of antibiotics [41]. *E.coli* showed in this study, highest resistance for ceftazidime and cefotaxime. Moreover, *E. coli* showed 88.11% susceptibility to tigecycline and 86.8% susceptibility to meropenem. A previous study reported high multidrug resistant *E.coli*, *K. pneumoniae* and *P. aeruginosa* implicated in the infections, during the period of the study [42].

In this study, *Pseudomonas spp*. showed the highest resistance for meropenem and for ceftazidime with a percentage (of 85.94% and 83.51%) respectively. *Pseudomonas spp*. Showed the least resistance for amikacin with a percentage (54.82%). In disagreement with our study, the study of Saad Alhumaid reported, *that Pseudomonas* species were sensitive to ciprofloxacin, piperacillin-tazobactam, imipenem, meropenem, and ceftazidime [38].

In this study, the most processed samples in inpatient departments were blood, respiratory, and pus & wound Culture. While, in outpatient departments, they were urine and CSF samples. The study of Faisal Ismail et al., reported that urine samples were mostly conducted in outpatient departments [43].

In this study, the highest percentage of resistance in inpatients and outpatients' departments was exhibited by *CoNS* and *S. aureus* towards cefoxitin followed by *Enterococcus* towards erythromycin and ciprofloxacin. On the other hand, vancomycin showed the least resistance and linezolid displayed low resistance among Gram-positive organisms.

The high isolation of *CoNS* and *S. aureus* may be as a result of skin contaminants; hence caution must be observed to avoid over diagnosis. As this may lead to increased resistance rates among bacterial isolates in clinical settings [44].

Regarding Gram-negative Bacteria, in this study, the highest percentage of resistance in inpatient department was exhibited by *Acinetobacter spp.* towards most of the antibiotics by more than 90%. On the other hand, tigecycline showed the least resistance among Gram-negative organisms.

The highest percentage of resistance in the outpatient department was exhibited by *Acinetobacter spp.* and *Enterobacter spp.* towards most of the antibiotics. On the other hand, tigecycline showed the least resistance among Gram-negative organisms.

Our findings imply that hospital resources should be the primary focus of efforts to reduce antibiotic resistance [45].

The increased incidence of drug resistance found in this study can be attributed to various factors. The main cause could be the widespread practice in Egypt, where nearly all patients take a variety of antibiotics before being admitted to the hospital, either on a doctor's prescription or as a form of self-medication because over-the-counter antibiotics are typically taken in incorrect dosages and for insufficient lengths of time [46, 47]. Geographical separation and genetic differences between pathogens from various studies are additional possible causes [48]. It is essential to keep in mind that the information provided in this study only offers an extensive overview of the horrifying circumstances that exist in the hospital that is the subject of the investigation. This suggests that to avoid this catastrophe, a successful containment action plan must be initiated.

The COVID-19 pandemic has had a significant impact on the trend of antimicrobial resistance (AMR) in various ways, including increased antibiotic use, disrupted healthcare services, delayed diagnosis and treatment, effects on surveillance and research, heightened use of broad-spectrum antibiotics, changes in infection patterns, and the relationship between public health measures and AMR. Overall, the pandemic has created conditions that could worsen the AMR crisis, highlighting the need for robust antimicrobial stewardship programs, enhanced infection control practices, and continued investment in AMR surveillance and research [49].

Although the study was conducted at a single center, it reflects the antimicrobial susceptibility patterns for all of Egypt. This is because Cairo University Hospital, the oldest and largest educational and medical institution in Egypt and the Middle East, serves as a central hub for medical care in the Arab region. It has played a significant role in the history of Cairo and Egypt, continues to do so today. Patients from all over Egypt and the Middle East come to Cairo University Hospital for treatment.

Limitations

1- Further multi-center studies across all regions of the country are needed to address the varying resistance rates in our hospitals.
2- There were no previous antibiogram studies conducted in our hospitals for a comprehensive year-to-year comparison of resistance rates.

CONCLUSIONS

The majority of the bacteria that are being investigated in the hospital have become resistant to most antibiotics. This indicates an impending disaster that might threaten the future medical profession and needs extreme caution and continuous monitoring. Supporting local and national surveillance programs with ongoing monitoring of antimicrobial resistance patterns at the national and local levels is a crucial step in the fight against emerging antimicrobial resistance. These findings imply that hospital resources should be the primary focus of efforts to reduce antibiotic resistance. Also, antibiotic stewardship program implementation and infection control measures adherence are mandatory.

Declarations

- **Ethics approval and consent to participate:** The Research Ethical Committee, Faculty of Medicine, Cairo University, approved this study under the code number (N-159-2023). **Consent to participate:** Not applicable**.**
- **Consent for publication:** Not applicable.
- **Competing interests:** The authors report no conflicts of interest.
- **Authors' contributions:**

All authors have made substantial contributions to the conception and design of the study, acquisition of data, analysis, and interpretation of data, drafting of the article, and final approval of the version to be submitted.

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