Journal of the
Bahrain Medical Society

Ardati et al., J Bahrain Med Soc. 2019;31(2):5-16

ORIGINAL ARTICLE

Prevalence of Bacterial Pathogens and Antimicrobial Susceptibility Pattern in Bahrain Tertiary Care Hospital

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Received date: March 06, 2019; **Accepted date:** May 16, 2019; **Published date:** June 30, 2019

Abstract

Background: Breach of human cell integrity triggers the development of infection by pathogenic bacteria. Although, antibiotics are competent in containment of bacteria, the emergence of antibiotic resistance has led to aggravated diseases and mortality rate, significantly. Hence, current study considered evaluating the frequently encountered bacterial species isolated from the clinical samples, and to examine their antimicrobial susceptibility pattern.

Methods: Current retrospective study was conducted during January–December 2017, in a tertiary care hospital. A total of 1931 isolates were included for microbiological analysis. Organisms isolated from the same site with similar sensitivity patterns for one month were excluded. Clinical samples were cultured on appropriate nutrient medium and characterized by microbiological techniques as well as automated system—Vitex analyzer. Antimicrobial susceptibility of few isolates was evaluated by Kirby-Bauer procedure and the rest by Vitex analyzer. Data were analyzed using R-3.4.1.

Results: Majority of the clinical samples were urine (29.7%) and wound swabs (10.5%). *Escherichia coli* (31.3%) and *Klebsiella pneumoniae* (14.4%) were predominant among the Gram-negative isolates, whereas, *Staphylococcus aureus* (70.6%) was prevalent among the Gram-positive isolates. Higher resistance pattern was observed towards β–lactams and cephalosporins, and greater susceptibility pattern was observed towards carbapenems. Bahraini patients showed higher predominance of extended-spectrum β–lactamase producers.

Conclusion: Urine and wound samples were the prominent sources and *S. aureus*, *E. coli*, and *K. pneumoniae* were the predominant organisms. Isolates were highly resistant to β–lactams as well as cephalosporins and were susceptible to carbapenems. Sensible utilization of antibiotics and reporting the susceptibility and resistance pattern of common organisms, periodically, assist in controlling antimicrobial resistance.

Keywords: Antibacterial; β–lactams; Carbapenems; Infection; Pathogens; Resistance.

Introduction

The human body harbors distinct bacterial forms as normal flora, without harming the host. Bacterial count across the human body reaches up to 38 trillion,[1] which interestingly exceeds the total human cell count in the body accounting for approximately 30 trillion.[1] Based on the requirement, bacterial communities restructure themselves to reside in different tissues or organs of the host such as the skin, gastrointestinal tract, rectum, mouth, and stomach. However, breach of the tissue integrity in any manner by either wound, cut, injury, or burn, furnishes an opportunity for the bacteria to colonize and cause disease.[2] Common opportunistic bacterial species include *Staphylococcus aureus* among the Gram-positive forms and *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella pneumoniae*, among the Gram-negative forms.[3, 4]

The bacterial population has the potentiality to interact within and between the species corresponding to their physiological and metabolic requirements.[5] To sustain themselves, they can also adapt themselves to the changing ecological conditions by genetic alterations.[3,5] These characteristics along with alteration of outer membrane proteins, efflux mechanisms, and production of hydrolyzing enzymes, such as extended-spectrum β–lactamases enable the bacteria to withstand against the antimicrobials used.[3] Although, antimicrobials are competent in eradicating bacteria, with the emergence of resistance, eradicating bacteria has become a substantial concern.[3] Bacteria acquire antimicrobial resistance (AMR) via gene level mutations, which are transferred *via* interaction with other bacterial species through plasmids.[6] Eventually, it aids in the development of multiple drug resistance in the bacteria.

Extended-spectrum β–lactamases are hydrolyzing enzymes synthesized within the organism that mediate the development of resistance to broad-spectrum antimicrobials, such as monobactams.[7] Over the past two decades, the extended-spectrum β–lactamases represented the onset of significant health constraints. The resistance is, predominantly, acquired through chromosomal DNA alteration and the acquired resistance mechanism might be encoded within the transferable genes of the bacterium, which is passed on to the neighboring bacterial species.[3]

The prevalence of AMR in the Arabian Gulf region is fairly large, especially, with the producers of extended-spectrum β–lactamases .[8] There is scarcity of studies regarding the evaluation of AMR in the Kingdom of Bahrain.[3, 9-11] Further, higher predominance of extended-spectrum β–lactamases-producing bacterial isolates were observed in the region of Bahrain[11]; however, researchers are emphasizing specifically on AMR without differentiating extended-spectrum β–lactamases-producing isolates. Therefore, the present study was performed to determine the frequently isolated bacterial species from various clinical samples. The antimicrobial susceptibility profile of the isolates was also derived, to determine the impact of exposure of common antibiotics on the isolates.

Materials & Methods

Study design and data collection

The present retrospective study was conducted from January-December 2017 and was approved by the Institutional Ethical Committee. During the study period, all the clinical samples received at a tertiary care hospital, for microbiological examination, were considered for the study.

The sociodemographic data such as age, gender, nationality, and presence of any comorbidities were recorded for evaluation on predesigned forms, by accessing the medical records of the patients. Clinical samples collected from multiple sites for the diagnosis included nasal swabs, ear swabs, sputum, stool, throat, abscess, eye swab, pharynx swab, urine, blood, wound, colonic tissue culture, bronchoalveolar lavage, pleural fluid, amnicator swabs, oral swabs, bile, peritoneal fluid, tissue/ surgical culture, drain fluid, semen, catheter tip, tracheal secretion, and vaginal and urethral swabs.

Identification

The standard microbial maintenance norms and procedures were followed; organisms isolated from the clinical samples were cultured appropriately using the following media formulations, which includes MacConkey agar, Sheep blood agar,

Campylobacter charcoal agar, Selenite broth, *Gardnerella vaginalis* agar, Sabouraud dextrose agar, Thayer Martin agar, Neomycin anaerobic agar, Fluid thioglycollate broth, *Salmonella Shigella* agar, and Chocolate bacitracin agar (Saudi Prepared Media Laboratory Company Ltd, Saudi Arabia). Incubation temperature was maintained at 35 °C for MacConkey agar, Sabouraud dextrose agar, *Salmonella Shigella* agar, and Mueller Hinton agar whereas, 43 °C with 5% CO_2 for *Campylobacter* charcoal agar, 35 °C with 5% CO_2 for Sheep blood agar, Chocolate agar, Chocolate bacitracin agar, *Gardnerella vaginalis* agar, and Thayer Martin agar, and 35 °C with 5% CO_2 in anaerobic agar with anaerobic gas pack for Neomycin anaerobic agar and Sheep blood agar for throat swabs.

Subsequently, majority of the cultured isolates were identified using Vitex automated analyzer (Vitex® bioMerieux, USA), whereas, few isolates were identified manually based on the routine microbiological techniques, such as morphological characteristics on culture plate, Gram staining, motility test, and biochemical characteristics analysis. [4, 12]

Antimicrobial susceptibility analysis

Antimicrobial susceptibility profile of each isolate was assessed using disk diffusion method (6-mm disc, OXOID, UK) by Kirby-Bauer procedure and Vitex automated analyzer (Vitex® bioMerieux, USA).[13] The various antibiotics specific for Gram-positive and Gram-negative organisms were tested, which included amikacin (30 µg), gentamicin (10 µg), amoxicillin/clavulanate (30 µg), piperacillin-tazobactam (110 µg), imipenem (10 µg), meropenem (10 µg), cefixime (5 µg), cefuroxime (30 µg), cefazolin (30 µg), linezolid (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), cefepime (30 µg), levofloxacin (5 µg), ciprofloxacin (5 µg), clindamycin (2 µg), erythromycin (15 µg), vancomycin (30 µg), and trimethoprim-sulfamethoxazole (25 µg). The inoculated plates (0.5 Mcfarland) were incubated under standard conditions for 24 h at 37 °C. Each plate was evaluated for the zone of clearance and the diameter (mm) of the zone, if present, was measured and compared with the standard Kirby-Bauer chart for characterizing the susceptibility of the isolates.[12, 14]

Statistical analysis

Data were recorded in Microsoft excel 2013 and analyzed using R-3.4.1. Chi-square test was used to determine the association between the commonly isolated groups of bacteria, absence or presence of common comorbidities, and association between the Bahraini and non-Bahraini culture-positive patients.

Results

Demographic characteristics

A total of 16,500 cultures were isolated from all the clinical samples received for microbiological analysis. Organisms cultured from the same site with similar sensitivity patterns of one month were excluded. After applying exclusion criteria, 1931 isolates were obtained from 1931 clinical samples and were considered for analysis.

Out of 1931 patients, four patients were excluded due to lack of demographic information. Among the 1927 patients considered for demographical analysis, 53.5% were females and the majority (38%) of the patients were aged between 21 and 40 years (Table 1).

Table 1: Socio-demographics of the culture positive patients (n=1927)

Variables	n (%)
Age (yrs)	
02–20	370 (19.21)
21–40	733 (38.04)
41–60	390 (20.24)
61–100	434 (22.53)
Gender	
Male	897 (46.5)
Female	1030 (53.5)
Nationality (Continent)	
Bahrain[‡]	731(37.8)
Non-Baharaini Asian	580 (30)
America	377 (19.53)
Africa	89 (4.6)
Australia	9 (0.46)
Europe	141 (7.3)

Based on the patients' geographical region, 37.8% were from Bahrain, whereas, 62% were non-Bahraini patients, including the Asian continent. Most (68.1%) of the study population were inhabitants of Asia, while the remaining non-Bahraini patients include Americans (19.5%), Europeans (7.3%), Africans (4.6%), and Australians (0.4%; Table 1).

Table 2: List of the specimens and the organisms isolated from the culture-positive patients

	Specimens N (%)																								
Isolates	**TS**	**TIS**	**PF**	**HVS**	**US**	**SE**	**PTF**	**OS**	**FD**	**CT**	**BAL**	**BI**	**CTC**	**AM**	**BF**	**NS**	**ES**	**SP**	**ST**	**TH**	**AB**	**EYS**	**PH**	**UR**	**BL**	**WO**	**Total isolates**
Achromobacter Group	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2 (1.15)	-	-	-	-	-	-	-	-	**2 (0.1)**
Acinetobacter baumannii	2 (9.52)	-	-	-	1 (2.4)	-	-	-	-	2 (14.28)	-	-	-	-	-	-	-	6 (3.45)	-	-	1 (0.85)	-	-	7 (1.22)	2 (4)	4 (1.97)	**25 (1.29)**
Aeromonas hydrophila	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2 (3.85)	-	-	-	-	-	-	-	**2 (0.1)**
Burkholderia cepacia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.58)	-	-	-	-	-	1 (0.18)	-	-	**2 (0.1)**
*Citrobacter spp**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.62)	-	-	5 (2.88)	-	-	-	-	-	4 (0.7)	1 (2)	-	**11 (0.56)**
Coagulase Negative *Staphylococci*	-	-	1 (100)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.85)	-	-	4 (0.7)	1 (2)	1 (0.5)	**8 (0.41)**
Enterobacter spp	2 (9.52)	-	-	-	-	-	-	-	1 (14.28)	-	-	-	-	-	2 (3.23)	4 (2.04)	1 (1.24)	3 (1.73)	-	-	3 (2.53)	-	2 (2.13)	20 (3.49)	1 (2)	4 (1.97)	**43 (2.22)**
Enterococcus faecalis	-	-	-	-	2 (4.8)	2 (14.3)	-	-	-	1 (7.14)	-	-	-	-	10 (16.13)	-	-	-	-	-	9 (7.57)	-	-	54 (9.41)	-	16 (7.85)	**94 (4.86)**
Escherichia coli	-	2 (28.58)	-	2 (8)	5 (11.2)	4 (28.6)	-	-	1 (14.28)	1 (7.14)	-	2 (100)	-	-	19 (30.65)	5 (2.54)	1 (1.24)	10 (5.75)	-	-	23 (19.33)	-	-	321 (55.93)	7 (14)	41 (20.1)	**444 (23)**
Haemophilus influenzae	-	-	-	3 (12)	6 (14.3)	1 (7.14)	-	-	-	-	-	-	-	-	-	50 (25.39)	1 (1.24)	22 (12.65)	-	1 (0.76)	1 (0.85)	28 (54.91)	24 (25.54)	-	1 (2)	4 (1.97)	**142 (7.35)**
Klebsiella spp	5 (23.8)	1 (14.3)	-	2 (8)	1 (2.34)	3 (21.4)	-	-	2 (28.57)	-	-	-	-	1 (100)	8 (12.91)	17 (8.63)	6 (7.41)	39 (22.42)	-	2 (1.51)	6 (5.05)	1 (1.97)	13 (13.83)	76 (13.25)	-	22 (10.79)	**205 (10.61)**
MRSA	-	-	-	2 (8)	-	-	-	-	-	-	1(100)	-	-	-	3 (4.84)	23 (11.68)	4 (4.94)	6 (3.45)	1 (1.93)	-	10 (8.41)	-	1 (1.07)	-	-	13 (6.38)	**64 (3.31)**
MRSE	3 (14.3)	-	-	-	-	-	1 (50)	-	-	4 (28.57)	-	-	-	-	2 (3.23)	1 (0.51)	-	12 (6.9)	-	-	-	-	-	11 (1.92)	24 (48)	5 (2.46)	**63(3.26)**
Morganella morganii	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3 (0.53)	-	2 (0.99)	**5 (0.25)**
Neisseria gonorrhoeae	-	-	-	-	23 (54.8)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**23 (1.19)**
Pantoea agglomerans	-	-	-	-	-	-	1 (50)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.18)	-	-	**2 (0.1)**
Proteus spp	-	-	-	1 (4)	-	1 (7.14)	-	-	-	-	-	-	-	-	3 (4.84)	2 (1.02)	1 (1.24)	1 (0.58)	-	-	4 (3.37)	-	-	31 (5.41)	-	12 (5.89)	**56 (2.9)**
Pseudomonas spp	4 (19.04)	-	-	1 (4)	1 (2.4)	-	-	-	-	4 (28.57)	-	-	-	-	1 (1.62)	2 (1.02)	38 (46.92)	36 (20.69)	-	-	3 (2.53)	1 (1.97)	-	16 (2.79)	5 (10)	21 (10.3)	**133 (6.88)**
Salmonella spp	-	-	-	-	-	-	-	-	-	-	-	-	1 (100)		1 (1.62)	-	-	-	47 (90.39)	-	-	-	-	-	-	-	**49 (2.53)**
Serratia marcescens	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.24)	3 (1.73)	-	-	-	2 (3.93)	-	1 (0.18)	-	1 (0.5)	**8 (0.41)**
Shigella boydii	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.93)	-	-	-	-	-	-	-	**1 (0.05)**
Sphingomonas paucimobilis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.5)	**1 (0.05)**
Staphylococcus spp	3 (14.3)	2 (28.58)	-	11 (44)	2 (4.8)	1 (7.14)		1 (50)	-	2 (14.28)	-	-	-	-	9 (14.52)	86 (43.66)	16 (19.76)	20 (11.5)	-	3 (2.26)	52 (43.7)	9 (17.65)	16 (17.03)	12 (2.1)	7 (14)	40 (19.61)	**292 (15.12)**
Stenotrophomonas maltophilia	2 (9.52)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2 (1.15)	-	-	-	-	-	2 (0.35)	-	6 (2.95)	**12 (0.62)**
Streptococcus spp		2 (28.58)		3 (12)	1 (2.4)	2 (14.3)		1 (50)	3 (42.85)	-	-	-	-	-	3 (4.84)	7 (3.56)	12 (14.8)	6 (3.45)	-	127 (95.5)	6 (5.05)	10 (19.6)	38 (40.4)	10(1.75)	1 (2)	11 (5.4)	**243 (12.58)**
Vibrio cholerae	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.93)	-	-	-	-	-	-	-	**1 (0.05)**
Total specimens	**21 (100)**	**7 (100)**	**1 (100)**	**25 (100)**	**42 (100)**	**14 (100)**	**2 (100)**	**2 (100)**	**7 (100)**	**14 (100)**	**1 (100)**	**2 (100)**	**1 (100)**	**1 (100)**	**62 (100)**	**197 (100)**	**81 (100)**	**174 (100)**	**52 (100)**	**133 (100)**	**119 (100)**	**51 (100)**	**94 (100)**	**574 (100)**	**50 (100)**	**204 (100)**	**1931 (100)**

More than one type was grouped as species (spp) of that genus to accommodate most of the bacteria in a single table; total number of isolates:* 1931; TS, Tracheal secretion; TIS, Tissue/surgical; PF, Pleural fluid; HVS, High vaginal swab; US, Urethral swab; SE, Semen; PTF, Peritonial fluid; OS, Oral swab; FD, Fluid (drains); CT, Catheter tip; BAL, Broncho-aleveolar lavage; BI, Bile; CTC, Colonic tissue culture; AM, Aminacator; BF, Body fluid; NS, Nasal swab; ES, Ear swab; SP, Sputum; ST, Stool; TH, throat; AB, Abscess; EYS, Eye swab; PH, Pharynx; UR, Urine; BL, Blood; WO, Wound; *MRSA,* Methicillin-resistant *Staphylococcus aureus; MRSE,* Methicillin-Resistant *Staphylococcus epidermidis*

Culture characteristics of isolates

Among the clinical samples cultured, majority of them were urine samples (29.7%) followed by wound (10.5%), and nasal swabs (10.2%; Table 2). A wide range of bacterial flora were isolated, accounting to 26 different bacterial species. Among the total isolates, 61.6% belonged to Gram-negative group dominated by *E. coli* and *K. pneumoniae* and 38.4% were Gram-positive organisms with *S. aureus* being the predominant organism. Interestingly, *Campylobacter* (21%) was observed to be the second predominant organism isolated in the stool samples and *Aspergillus* as the third most common isolate in the ear cultures. Out of 64 patients with methicillin-resistant *Staphylococcus aureus* (MRSA), 32% were from Bahrain followed by 26.5% from America. Majority (50%) of the *Campylobacter*-isolated-patients belonged to America. Most common organisms isolated from the clinical samples are represented in Table 3.

Table 3: Most common organisms isolated from clinical samples

Samples	Common organisms
AB	*Staphylococcus spp,* MRSA, *Enterococcus faecalis*
AM	*Klebsiella spp*
BAL	MRSA
BF	*Escherichia coli, Enterococcus faecalis, Staphylococcus spp*
BI	*Escherichia coli*
BL	MRSE, *Escherichia coli, Staphylococcus spp.*
CT	MRSE, *Pseudomonas spp., Acinetobacter baumannii*
CTC	*Salmonella spp.*
ES	*Pseudomonas spp, Staphylococcus spp,*
EYS	*Haemophilus influenzae, Streptococcus spp., Staphylococcus spp*
FD	*Streptococcus spp., Klebsiella spp., Escherichia coli, Enterobacter spp.*
HVS	*Staphylococcus spp., Haemophilus influenzae, Streptococcus spp*
NS	*Staphylococcus spp Haemophilus influenzae,* MRSA,
OS	*Staphylococcus spp., Streptococcus spp*
PF	Coagulase Negative *Staphylococci*
PH	*Streptococcus spp., Haemophilus influenzae., Staphylococcus spp.*
PTF	MRSE, *Pantoea agglomerans*
SE	*Escherichia coli, Klebsiella spp., Streptococcus spp.,Enterococcus faecalis*
SP	*Klebsiella spp, Pseudomonas spp, Haemophilus influenzae*
ST	*Salmonella spp., Camplylobacter, Aeromonas hydrophila, Shigella boydii.* TH
	Streptococcus spp, Staphylococcus spp, Klebsiella spp
TIS	*Escherichia coli, Staphylococcus spp, Streptococcus spp*
TS	*Klebsiella spp , Pseudomonas spp, Staphylococcus spp,* MRSE
UR	*Escherichia coli, Klebsiella spp., Enterococcus faecalis*
US	*Neisseria gonorrhoeae, Staphylococcus spp., Haemophilus influenzae*
WO	*Staphylococcus spp., Escherichia coli, Klebsiella spp.*

*More than one type was grouped as species (spp.) of that genus to accommodate most of the bacteria in a single table; TS, Tracheal secretion; TIS, Tissue/surgical; PF, Pleural fluid; HVS, High vaginal swab; US, Urethral swab; SE, Semen; PTF, Peritonial fluid; OS, Oral swab; FD, Fluid (drains); CT, Catheter tip; BAL, Broncho-aleveolar lavage; BI, Bile; CTC, Colonic tissue culture; AM, Aminacator; BF, Body fluid; NS, Nasal swab; ES, Ear swab; SP, Sputum; ST, Stool; TH, throat; AB, Abscess; EYS, Eye swab; PH, Pharynx; UR, Urine; BL, Blood; WO, Wound; *MRSA,* Methicillin-resistant *Staphylococcus aureus; MRSE,* Methicillin-Resistant *Staphylococcus epidermidis*

Antibiotic susceptibility profile of the isolates

Majority of the isolates showed high resistance pattern against the antimicrobial agents. Gram-negative isolates, such as extended-spectrum β–lactamases *E. coli*, extended-spectrum β–lactamases *K. pneumoniae*, *Acinetobacter baumannii*, and *Citrobacter freundii* exhibited comparatively high resistance, especially to β–lactams and cephalosporins.

Extended-spectrum β–lactamases *E. coli* showed greater resistance pattern to cefuroxime (98.6%) whereas, extended-spectrum β–lactamases *K. pneumoniae* showed prominent resistance pattern to ceftriaxone and amoxicillin/clavulanate (89.5%, each), followed by *Enterobacter aerogenes* (96.3%; Table 4). Extended spectrum β–lactamases *E. coli* and *K. pneumoniae* isolates were relatively resistant to amoxicillin/clavulanate and all six classes of cephalosporins were tested. However, greater susceptibility to all classes of carbapenems was observed in both extended-spectrum β–lactamases isolates—*E. coli* and *K. pneumoniae*. Among non-

Table 4: Details of resistant gram-negative bacteria (GNB) isolated from patients admitted at the hospital

GNB	ANTIBIOTICS n (%)															
	Aminoglycoside		β–lactam		Carbapenem			Cephalosporin						Fluoroquinolone		Sulfonamide
	AMK	GEN	AUC	TZP	IMP	MRP	ETP	CFX	CXM	CFZ	CTX	CAZ	CPM	LEV	CIP	SXT
AB (25)	13	16	15	13	16	13	9	7	4	1	17	16	14	15	15	4
	52.0%	64.0%	60.0%	52.0%	64.0%	52.0%	36.0%	28.0%	16.0%	4.0%	68.0%	64.0%	56.0%	60.0%	60.0%	16.0%
CF (2)	0	2	2	0	0	0	0	2	2	2	2	2	1	2	2	0
	0.0%	100%	100%	0.0%	0.0%	0.0%	0.0%	100%	100%	100%	100%	100%	50%	100%	100%	0.00%
CK (9)	0	0	4	1	0	0	0	3	4	4	0	0	0	4	4	3
	0.0%	0.0%	44.4%	11.1%	0.00%	0.00%	0.00%	33.3%	44.4%	44.4%	0.00%	0.00%	0.00%	44.4%	44.4%	33.3%
EA (27)	0	0	26	2	1	1	1	25	26	25	7	3	2	5	5	2
	0.0%	0.0%	96.3%	7.4%	3.7%	3.7%	3.7%	92.6%	96.3%	92.6%	25.9%	11.1%	7.4%	18.5%	18.5%	7.4%
EbC (15)	0	0	15	4	0	0	0	15	15	14	2	2	0	0	0	0
	0.0%	0.0%	100%	26.7%	0.0%	0.0%	0.0%	100%	100%	93.3%	13.3%	13.3%	0.00%	0.00%	0.00%	0.00%
EC (298)	0	10	56	1	0	0	0	4	5	6	2	3	3	49	52	84
	0.00%	3.40%	18.8%	0.30%	0.00%	0.00%	0.00%	1.30%	1.70%	2.00%	0.70%	1.00%	1.00%	16.4%	17.4%	28.2%
EC-ESBL (146)	2	40	142	16	2	2	3	142	144	138	143	141	123	74	76	76
	1.40%	27.4%	97.3%	11.0%	1.40%	1.40%	2.10%	97.3%	98.6%	94.5%	97.9%	96.6%	84.2%	50.7%	52.1%	52.1%
HI (142)	0	0	4	0	0	0	0	0	0	0	1	0	0	2	3	68
	0.00%	0.00%	2.80%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.70%	0.00%	0.00%	1.40%	2.10%	47.9%
KP (158)	0	9	30	8	8	8	8	10	13	14	10	10	10	8	8	6
	0.00%	5.70%	19.0%	5.10%	5.10%	5.10%	5.10%	6.30%	8.20%	8.90%	6.30%	6.30%	6.30%	5.10%	5.10%	3.80%
KP-ESBL (39)	5	18	35	9	3	3	4	34	35	32	35	34	33	16	19	15
	12.8%	46.2%	89.7%	23.1%	7.70%	7.70%	10.3%	87.2%	89.7%	82.1%	89.7%	87.2%	84.6%	41.0%	48.7%	38.5%
PM (55)	3	9	13	1	1	0	0	8	8	7	8	8	5	10	11	17
	5.50%	16.4%	23.6%	1.80%	0.00%	0.00%	0.00%	14.5%	14.5%	12.7%	14.5%	14.5%	9.10%	18.2%	20.0%	30.9%
PA (132)	7	19	-	15	30	15	1	-	-	-	-	18	-	22	19	-
	5.30%	14.4%	-	11.4%	22.7%	11.4%	0.80%	-	-	-	-	13.6%	-	16.7%	14.4%	-

GNB, Gram-negative bacteria*; AB*, *Acinetobacter baumannii; CF*, *Citrobacter freundii; CK*, *Citrobacter koseri; EA*, *Enterobacter aerogenes; EbC*, *Enterobacter cloacae; EC*, *Escherichia coli; EC-ESBL*, *Escherichia coli* ESBL*; HI*, *Haemophilus influenzae; KP*, *Klebsiella pneumoniae; KP*-ESBL, *Klebsiella pneumoniae* ESBL*; PM*, *Proteus mirabilis; PA*, *Pseudomonas aeruginosa;* AMK, Amikacin; ETP, *Ertapenem*; GEN, Gentamicin; AUC, Augmentin; TZP, Piperacillin-Tazobactum; IMP, Imipenem; MRP, Meropenem; CFX, Cefixime; CXM, Cefuroxime; CFZ, Cefazolin; CTX, Ceftriaxone; CAZ, Ceftazidime; CPM, Cefipime; LEV, Levofloxacin; CIP, Ciprofloxacin; SXT, Trimethoprim-Sulphamethoxazole

extended spectrum β–lactamases *E. coli,* only 1.2% of resistance pattern was observed towards cephalosporin antibiotics.

Among Gram-positive isolates, *Enterococcus faecalis* exhibited relatively greater resistance against most of the antimicrobial agents (Table 5). Ciprofloxacin resistance was prevalent among MRSA (53.1%), methicillin-resistant *Staphylococcus epidermidis* (MRSE) (82.5%), *S. aureus* (19.9%), and *Enterococcus faecalis* (19.9%).

Association of bacterial isolates with co-morbidities present among culture-positive patients

Among the study population, data regarding co-morbidities were available only for 657 culture-positive patients. Association between isolated groups of bacteria and presence of comorbidities, such as diabetes and hypertension showed that *A. baumannii*, non-extended and extended-spectrum β–lactamases *E. coli*, and *Haemophilus influenzae* in the Gram-negative group and *S. aureus*, *Streptococcus* Group A (*β*–hemolytic), and *Streptococcus pneumoniae* in the Gram-positive group were significantly present in patients with diabetes ($P<0.001$). Predominant isolates observed in hypertensive patients included *A. baumannii*, non-extended-spectrum β–lactamases *E. coli*, *H. influenzae*, MRSE, *S. aureus*, *Stenotrophomonas maltophilia*, *Streptococcus* Group A (*β*–hemolytic), and *S. pneumoniae* ($P<0.001$; Table 6).

Association of bacterial isolates with Bahraini and non-Bahraini culture-positive patients

Organisms such as *E. coli*, *A. baumannii, Enterococcus faecium*, extended spectrum β–lactamases *K. pneumoniae*, and *S. maltophilia* were significant and predominantly isolated from the samples of the Bahraini patients ($P=0.05$). Significantly observed isolates in non-Bahraini patients included non-extended and extended-spectrum β–lactamases *E. coli*, *H. influenzae*, *Klebsiella oxytoca*, *K. pneumoniae*, and MRSA ($P<0.001$; Table 7).

Table 5: Details of resistant Gram-positive bacteria (GPB) isolated from patients admitted at hospital

GPB	Antibiotics n(%)														
	Aminoglyco-sides		β–lactum		Carbapenems		Cephalospo-rin		Fluroquinolones		Glyco-peptides	Macrolides		Oxazo-lidinones	Sulfon-amides
	AMK	GEN	AUC	TZP	ETP	IMP	CTX	CXM	LEV	CIP	VAN	CLI	ERY	LNZ	SXT
En. Fl (90)	0	0	6	7	0	78	0	0	15	19	0	39	36	1	-
	0.0%	0.0%	6.7%	7.8%	0.0%	86.7%	0.0%	0.0%	16.7%	21.1%	0.0%	43.3%	40.0%	1.1%	-
En. Fm (4)	0	0	4	0	0	0	0	0	1	2	1	1	1	0	0
	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	25.0%	50.0%	25.0%	25.0%	25.0%	0.0%	0.0%
MRSA (64)	1	13	-	0	0	0	-	-	30	34	0	19	31	2	21
	1.6%	20.3%	-	0.0%	0.0%	0.0%	-	-	46.9%	53.1%	0.0%	29.7%	48.4%	3.1%	32.8%
MRSE (63)	9	28	-	0	0	1	-	-	45	52	0	29	50	0	32
	14.3%	44.4%	-	0.0%	0.0%	1.6%	-	-	71.4%	82.5%	0.0%	46.0%	79.4%	0.0%	50.8%
SA (266)	1	9	-	0	0	2	-	-	49	53	0	16	61	0	19
	0.4%	3.4%	-	0.0%	0.0%	0.8%	-	-	18.4%	19.9%	0.0%	6.0%	22.9%	0.0%	7.1%

En.Fl, *Enterococcus faecalis*; *En. Fm*, *Enterococcus faecium*; *MRSA*, Methicillin-Resistant *Staphylococcus aureus*; *MRSE*, Methicillin-Resistant *Staphylococcus epidermidis*; *SA*, *Staphylococcus aureus*; *IMP*, Imipenem; *LNZ*, Linezolid; *LEV*, Levofloxacin; *AUC*, Augmentin; *CXM*, Cefuroxime; *GPB, Gram-positive bacteria; CIP*, Ciprofloxacin; *SXT*, Trimethoprim-Sulphamethoxazole; *CLI*, Clindamycin; *ERY*, Erythromycin; *VAN*, Vancomycin; *TZP*, Piperacillin-Tazobactum; *CTX*, Ceftriaxone; *AMK*, Amikacin; *GEN*, Gentamicin

Table 6: Association between isolates and comorbidities in culture positive patients.

Organism	Diabetes			Hypertension		
	Present	Absent	P value	Present	Absent	P value
Acinetobacter baumannii	13	0	<0.001	13	0	<0.001
Aeromonas hydrophila	1	0	0.32	1	0	0.32
Citrobacter koseri	0	2	0.16	1	1	1.00
Coagulase Negative *Staphylococci*	2	0	0.16	2	0	0.16
Enterobacter aerogenes	10	5	0.20	10	5	0.20
Enterobacter cloacae	3	2	0.65	3	2	0.65
Enterococcus faecalis	10	16	0.24	10	16	0.24
Escherichia coli	15	68	<0.001	17	66	<0.001
Escherichia coli ESBL	7	40	<0.001	15	32	0.01
Haemophilus influenzae	1	61	<0.001	1	61	<0.001
Klebsiella oxytoca	0	7	0.01	7	0	0.01
Klebsiella pneumoniae	17	27	0.13	19	25	0.37
Klebsiella pneumoniae ESBL	11	3	0.03	13	1	0.00
Methicillin Resistant *Staphylococcus aureus (MRSA)*	8	13	0.28	8	13	0.28
Methicillin Resistant *Staphylococcus epidermidis (MRSE)*	18	5	0.01	20	3	<0.001
Morganella morganii	1	1	1.00	1	1	1.00
Neisseria gonorrhoeae	0	2	0.16	0	2	0.16
Proteus mirabilis	3	16	0.00	3	16	0.00
Pseudomonas aeruginosa	18	30	0.08	28	20	0.25
Salmonella Group A+E or G	0	2	0.16	0	2	0.16
Salmonella Group B	0	6	0.01	0	6	0.01
Salmonella Group C	0	4	0.05	0	4	0.05
Salmonella Group C+D	0	1	0.32	0	1	0.32
Salmonella Group D	0	5	0.03	0	5	0.03
Salmonella Group E or G	0	3	0.08	0	3	0.08
Serratia marcescens	0	3	0.08	1	2	0.56
Shigella boydii	0	1	0.32	0	1	0.32
Staphylococcus aureus	7	77	<0.001	6	78	<0.001
Staphylococcus epidermidis	2	0	0.16	1	1	1.00
Staphylococcus haemolyticus	3	0	0.08	3	0	0.08
Staphylococcus hominis	0	1	0.32	1	0	0.32
Staphylococcus saprophyticus	0	1	0.32	0	1	0.32
Stenotrophomonas maltophilia	10	0	0.00	10	0	<0.001
Streptococcus Group A (Beta Hemolytic)	1	65	<0.001	2	64	<0.001
Streptococcus Group B (Beta Hemolytic)	1	3	0.32	0	4	0.05
Streptococcus Group C (Beta Hemolytic)	0	6	0.01	0	6	0.01
Streptococcus Group G (Beta Hemolytic)	0	6	0.01	0	6	0.01
Streptococcus pneumoniae	0	13	<0.001	0	13	<0.001
Total	162	495		196	461	

ESBL, Extended-spectrum beta-lactamases*;* Significant, $P<0.005$

Table 7: Association between common bacterial isolates among Bahrain and Non-Bahrain culture positive patients

Organism (n)	Nationality		P value
	Bahrain n (%)	Non-Bahrain n (%)	
Achromobacter Group	2 (100)	0 (0)	0.16
Acinetobacter baumanii	19 (76)	6 (24)	0.01
Aeromonas hydrophila	1 (50)	1 (50)	1.00
Burkholderia cepacian	1 (50)	1 (50)	1.00
Citrobacter freundii	0 (0)	2 (100)	0.16
Citrobacter koseri	5 (55.6)	4 (44.4)	0.74
Coagulase Negative *Staphylococci*	3 (37.5)	5 (62.5)	0.48
Enterobacter aerogenes	17 (63)	10 (37)	0.18
Enterobacter cloacae	8 (53.3)	7 (46.7)	0.80
Enterobacter gergoviae	0 (0)	1 (100)	0.32
Enterococcus faecalis	44 (48.9)	46 (51.1)	0.83
Enterococcus faecium	4 (100)	0 (0)	0.05
Escherichia coli	110 (36.9)	188 (63.1)	<0.001
Escherichia coli ESBL	59 (40.4)	87 (59.6)	0.02
Haemophilus influenzae	43 (30.3)	99 (69.7)	<0.001
Klebsiella oxytoca	0 (0)	7 (100)	0.01
Klebsiella pneumoniae	51 (32.3)	107 (67.7)	<0.001
Klebsiella pneumoniae ESBL	28 (71.8)	11 (28.2)	0.01
MRSA	21 (32.8)	43 (67.2)	0.01
MRSE	39 (61.9)	24 (38.1)	0.06
Morganella morganii	2 (40)	3 (60)	0.65
Neisseria gonorrhoeae	6 (27.3)	16 (72.7)	0.03
Pantoea agglomerans	1 (50)	1 (50)	1.00
Proteus mirabilis	19 (34.5)	36 (65.5)	0.02
Proteus vulgaris	1 (100)	0 (0)	0.32
Pseudomonas aeruginosa	66 (50)	66 (50)	1.00
Pseudomonas putida	0 (0)	1 (100)	0.32
Salmonella Group A+E or G	2 (100)	0 (0)	0.16
Salmonella Group B	4 (23.5)	13 (76.5)	0.03
Salmonella Group C	3 (27.3)	8 (72.7)	0.13
Salmonella Group C+D	0 (0)	1 (100)	0.32
Salmonella Group D	3 (25)	9 (75)	0.08
Salmonella Group E or G	3 (50)	3 (50)	1.00
Serratia marcescens	3 (37.5)	5 (62.5)	0.48
Shigella boydii	1 (100)	0 (0)	0.32
Sphingomonas paucimobilis	0 (0)	1 (100)	0.32
Staphylococcus aureus	64 (24.1)	202 (75.9)	<0.001
Staphylococcus epidermidis	7 (53.8)	6 (46.2)	0.78
Staphylococcus haemolyticus (4)	3 (75)	1 (25)	0.32
Staphylococcus hominis (1)	0 (0)	1 (100)	0.32
Staphylococcus saprophyticus (6)	3 (50)	3 (50)	1.00
Stenotrophomonas maltophilia (12)	12 (100)	0 (0)	0.00
Streptococcus Group A (Beta Hemolytic) (144)	47 (32.6)	97 (67.4)	<0.001
Streptococcus Group B (Beta Hemolytic) (13)	4 (30.8)	9 (69.2)	0.17
Streptococcus Group C (Beta Hemolytic) (32)	6 (18.8)	26 (81.3)	<0.001
Streptococcus Group G (Beta Hemolytic) (24)	7 (29.2)	17 (70.8)	0.04
Streptococcus pneumoniae (30)	9 (30)	21 (70)	0.03
Vibrio cholera (1)	0 (0)	1 (100)	0.32

ESBL, Extended-spectrum beta-lactamases; *MRSE,* Methicillin Resistant *Staphylococcus epidermidis; MRSA,* Methicillin Resistant *Staphylococcus aureus; Significant, P < 0.005*

Discussion

The present retrospective study encountered female preponderance, with majority of the patients belonging to the younger age group. Clinical samples collected from Bahraini patients were significantly more compared to non-Bahraini patients belonging to the Asian continent as well as to other foreign continents.

Among the total isolates in the present study, majority belonged to the Gram-negative group with the prevalence of *E. coli* (31.3%) and *K. pneumoniae* (14.4%) and among Gram-positive group *S. aureus* (70.6%) was prevalent. Similarly, a study by Ali et al.[3] on AMR prevalence in and around the Gulf countries reported prevalence of *E. coli* (14%), *K. pneumoniae* (13.9%), *Enterococcus* spp. (76.5%), and MRSA (8.5%).

In the present study, majority of the clinical samples were urine and wound swab samples. The prevalent organisms isolated from the urine samples included *E. coli* and *K. pneumoniae*, whereas, *E. coli, S. aureus,* and MRSA were observed to be predominant in the wound samples. Similar observations were reported in the urine samples, globally.[15-20] Urinary tract infections are believed to be the second most predominant community-based and nosocomial infections, worldwide.[21, 22] These findings represent that urine and urinary tract environment demonstrate a higher prevalence of uropathogens due to the longer hospital stay, sexual activity, diabetes, hormonal imbalance, and genetic susceptibility.[23]

The breakthrough of infection management was the discovery of antimicrobials, which led the treating physicians to significantly manage the patients with infections. Alarming increase in antimicrobial commercialization, drug resistance development among organisms, and indiscriminate use without knowledge jeopardized the antimicrobial era into an economic burden era.[24] Although, many antibiotic discoveries are in place, the sensible use of antibiotics is the only means for controlling the development of AMR. In the current study, higher resistance pattern was observed to most of the antibiotics used, especially to *β–lactams and cephalosporins*. *Probable reason* might be the ease availability of antibiotics without a prescription in pharmacies and wrong psychological perception among people about antibiotics as the first-aid response to any health complications.

In the current study, amoxicillin/clavulanate and ciprofloxacin resistance were relatively high among the Gram-negative and Gram-positive groups, respectively Susceptibility profile of carbapenems was common among both Gram-positive and Gram-negative organisms. In a Gulf-centered study by Al et al.,[25] oral amoxicillin/clavulanate was reported to be the most unsuccessful antibiotic among the 54 patients. In another study conducted in the Kingdom of Bahrain,[10] carbapenems were the most susceptible class of antibiotics. In the present study, among the Gram-positive group, *Enterococcus* spp. represented relatively higher resistance pattern to antimicrobial agents. This is in accordance to a study conducted by Aly et al.,[3] wherein, resistance pattern was observed with *Enterococcus* spp. in the Bahrain region. Current study observed *Enterococcus* spp. and *S. aureus* isolates with 1.1% and 3.1% of resistance towards linezolid antibiotic, respectively which was uncommon in most of the institutions. Alteration of the antimicrobial's target sites, such as efflux pumps and porin channels on the bacterium prevent the binding of antibiotic molecules resulting in the development of resistance.[26]

Extended-spectrum β–lactamases enzymes are the class of *β*–lactams with a unique ability of resistance to penicillin, cephalosporins of first-, second-, and third-generation, and aztreonam with higher susceptibility profile to carbapenems. In most of the cases, extended-spectrum β–lactamases production was observed prevalent in Gram-negative organisms, especially in *E. coli* and *K. pneumoniae* isolates.[10] Presence of resistance profile towards extended-spectrum antibiotics, such as cephalosporins was first reported in Bahrain during 1980's.[10] In the late 1990's, the resistance was observed towards cephalosporins and aminoglycosides in majority of the *Klebsiella* isolates.[9] The extended spectrum β–lactamases-producing *K. pneumoniae* was first reported in 1995 in Bahrain.[9, 10] A study conducted by Bindayna[11] reported that among 2695 isolates analyzed, the majority of the isolates were *E. coli*

(52.4%) followed by *K. pneumoniae* (24.2%) and both were extended spectrum β–lactamases producers. Taking into consideration the higher prevalence of extended spectrum β–lactamases-producing *E. coli* and *K. pneumoniae* organisms, the current study considered distinguishing the *E. coli* and *K. pneumoniae* isolates for extended spectrum β–lactamases production. In present study, 32.9% and 18.27% of the *E. coli* and *K. pneumoniae* isolates, respectively, were extended spectrum β–lactamases producers; majority were susceptible to carbapenems and relatively resistant to all classes of cephalosporins. In 2011, another study by Bindayna et al.[27] reported that among the extended-spectrum β–lactamases producing isolates, such as *E. coli* and *K. pneumoniae,* greater AMR patterns was observed towards cephalosporins and higher susceptibility patterns towards carbapenems. Indiscriminate use, overuse, and reuse of antibiotics for broad spectrum infections have led to the development of extended-spectrum β–lactamases production.[28]

The present study reported the association between isolates and the presence of comorbid conditions—diabetes and hypertension in the patients. Organisms such as non-extended spectrum β–lactamases *E. coli*, *H. influenzae*, and *A. baumannii* among Gram-negative group and *S. aureus*, *Streptococcus* Group A, and *S. pneumoniae* among the Gram-positive group were significantly associated with the presence of co-morbidities. The probable reason behind the relationship between the prevalence of isolates and comorbidity is difficult to derive due to the complexity and heterogeneous nature of the co-morbidities. Although, studies have attempted to derive the association, it still remains unclear.[29, 30]

E. coli was prevalent among both the Bahraini and non-Bahraini patients. Among the extended spectrum β–lactamases producers, *E. coli* was predominant among the Bahraini patients, whereas, the non-extended spectrum β–lactamases *E. coli* was prevalent among the non-Bahraini patients. Similar findings were not found in the literature. These data represent that higher prevalence of *β*–lactam-producing isolates are emerging significantly in the Bahrain region. Studies considering similar parameters necessary in Bahrain region.

Conclusion

The urine and wound samples are the highest source of bacterial isolates among the various clinical samples predominantly with *S. aureus*, *E. coli,* and *K. pneumoniae* organisms. Isolates were highly resistant to *β*–lactams and cephalosporins and were susceptible to carbapenems. The prevalence of extended-spectrum β–lactamases was more among the Bahraini patients compared to the non-Bahraini patients. Further, studies are required to substantiate these findings with longer follow-ups and wider range of antibiotics.

Conflict of interest

Authors have no conflict of interest to declare.

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