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Current Antibiotic Sensitivity Pattern of Clinically Isolated *Klebsiella pneumonia*

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Original Research Article

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Abstract: An increasing antimicrobial resistance among *Klebsiella pneumoniae* (*K. pneumoniae*) has been rapidly growing. The cross-sectional, analytical and descriptive study was conducted to investigate the current in vitro susceptibility pattern of clinically isolated *K. pneumoniae*. Patient data for 700 different clinical specimens were collected from the case records during October 2016 to March 2017. Following isolation and identification of 113 isolates of *K. pneumoniae* to the species level, antibiotic susceptibility pattern for all isolates was examined using standard Kirby-Bauer disk diffusion method. Among113 *K. pneumoniae* isolates, 25 (12.6%) and 88 (39.5%) were isolated from outpatients and inpatients respectively were considered for the study. The isolates showed high levels of resistance to Penicillin (100.0%), Ampicillin (96.5), first-generation cephalosporins (>92.0%), Nalidixic acid (93.8%), Erythromycin (96.5), Roxithromycin (99.1%). The isolates were less resistant to Amikacin (27.4%), Imipenem (29.2%). Good antibiotics activity against community-acquired (CA) compared to hospital-acquired (HA) isolates and the difference in resistant rate between them was found statistically significant for several antibiotics. A general increase in the resistance pattern of *K. pneumoniae* was detected to all the antibiotics that confirm the greatest and frightening problem in our country. Mechanisms for HA infection control measures must be evaluated to reduce pathogenic resistant bacterial strains spreading. Also, strike regulation of the antibiotics buying and intake by the public need to be applied.

Keywords: *K. pneumoniae*, Antibiotic resistance, Hospital-acquired, Community-acquired.

INTRODUCTION

Klebsiella pneumoniae (*K. pneumoniae*) is an important pathogen associated with serious nosocomial and community-acquired (CA) infections. *K. pneumoniae* known as an urgent threat to human health due to the emergence of multidrug-resistant strains that are hard to eradicate by using available antibiotics. Infections involving resistant bacteria are responsible for an increased morbidity and mortality [1]. The emergence and spread of antibiotic-resistant bacteria have been rapidly growing like a snow ball and is being commonly reported from all over the world [2, 3], due to that the microorganisms are becoming resistant to both older and newer antibiotics [4].

K. pneumoniae have the genetic ability to transmit and acquire resistance to drugs which are utilized as therapeutic agents and transferring the resistance from one strain to other. While, the overuse, underuse, and misuse of antibiotics have become major causes of the development of antibiotic-resistance in bacteria. In addition, extensive use of broad-spectrum antibiotics in hospitalized patients has led to both increased carriage and the development of multidrug-resistant strains [5, 6]. Moreover, the resistance mechanisms of *K. pneumoniae* against different classes of antibiotics could be related to several factors such as the release of antibiotic-inactivating enzymes, change in membrane permeability, modification of antibiotic

target sites, activation of efflux pump systems, and alteration of metabolic pathways [7-10].

Multidrug-resistant *K. pneumoniae* strains can cause treatment failure with current antibiotic therapy [8, 9]. The inevitable consequence of the widespread use of antimicrobial agents has been the emergence of antibiotic resistant pathogens, fueling an ever-increasing need for new drugs. However, reducing the inappropriate antibiotic use is thought to be the best way to control resistance among pathogenic organisms [9].

In Yemen, few studies have been done regarding antibiotic resistant and its consequences among bacterial pathogens in general and among *K. pneumoniae*, in particular. It is still unclear and need several studies to understand the problem. Therefore, the aim of our study is to determine the current antibiotic sensitivity pattern of clinically isolated *K. pneumonia*.

MATERIALS AND METHODS

Study design

Cross-sectional, analytical and descriptive study.

Location, target population and study period

This study was carried out on bacterial isolates obtained from sub-culturing of different clinical specimen isolates that were sent for routine laboratory investigation according to physician orders in the hospitals or clinics at Sana'a city, Yemen from October 2016 to March 2017. Relevant information about age, sex, type of specimen and ward of admission for all selected isolates was gathered from request form and medical records.

Included & excluded criteria

All cases with complete demographic data were included in this study. Duplicate and missed data specimens were excluded.

Target pathogenic bacteria

All common pathogens isolated from clinical specimens were subjected to microbial investigation during the period of the study. Only aerobe and/or facultative anaerobe Gram-negative *K. pneumoniae* was involved in this study.

METHODS

Laboratory Identification of Isolates

A total of 421 microorganisms were prospectively isolated and identified from different clinical specimens like urine, pus, sputum, aspirate, vaginal swabs, etc.., during the period of October 2016 to March 2017, where the isolates were submitted for routine microbiological analysis from both out and inpatients. Organisms, which were daily isolated from clinical specimens, are identified by culture using standard microbiological techniques. Confirmation to the species level was done by using API 20 E diagnostic system (bioMerieux, France).

Antimicrobial susceptibility test

Antimicrobial susceptibility was evaluated by the disk diffusion method according to the Kirby–Bauer method on Muller Hinton agar (Oxoid Ltd. Hampshire, United Kingdom). Thirty antimicrobial agents were tested and standardized according to the MIC breakpoints recommended by the National Committee for Clinical Laboratory Standards (NCCLS) with Clinical & Laboratory Standards Institute (CLSI) guidelines. Using the following antimicrobial drugs; Penicillin 10µg, Ampicillin 10µg, Piperacillin 100µg, Ticarcillin 75µg, Amoxiclav 20/10µg, Piperacillin-tazobactum 100+10µg, Aztreonam 30µg, Imipenem 10µg, Cefradine 30µg, Cephadroxil 30µg, Cephalothin 30µg, Cefuroxime 30µg, Ceftizoxime 10µg, Cefotaxime 30µg, Cefepime 30µg, Nalidixic acid 30µg, Nitrofurantoin 300µg, Ciprofloxacin 5µg, Lomefloxacin 10µg, Levofloxacin 5µg, Moxifloxacin 5µg, Erythromycin 15µg, Azithromycin 15µg, Roxithromycin 15µg, Amikacin 10µg, Tobramycin 10µg, Tetracycline 30µg, Minocycline 30µg , Co-trimoxazole 25µg, Chloramphenicol 30µg. All of the antibiotic discs were manufactured by Oxoid Ltd. Hampshire, United Kingdom. The isolated microorganisms and their antimicrobial resistance patterns were analyzed with consideration of the admission, age, and sex of the patients. Only a single positive culture per patient was included in the study.

Statistical analysis

The bacterial resistance of all isolates was determined and was expressed as a percentage. Descriptive statistics of antibiotics activity and other characteristics of the isolated bacterial population were computed. A *p*-value less than 0.05 was calculated to be statistically significant. The statistical difference was also evaluated by applying the Chi-square test. All the statistical analysis was done using the Statistical Package for Social Sciences (SPSS) software package version 20. (SPSS Inc. Chicago, Illnois, USAT).

RESULTS

Seven hundred clinical specimens were received for culture and sensitivity assay during the study period. Among these, 421 samples (60.1%) yielded significant bacterial growth; 279 samples (39.9%) showed no growth. Out of total 421 isolated bacteria, 113 (26.8%) were confirmed as *K. pneumoniae* which are subjected to antibiotics susceptibility study and hence included in the analysis. The prevalence of isolated *K. pneumoniae* among males and females was 76 / 264 (28.8%) and 37 / 157 (23.6%) respectively. The result of these study showed that the difference in the prevalence of isolated organisms in relation to gender was statistically insignificance.

K. pneumoniae was found significantly (p < 0.05 and OR=2.3) among those >51 years old age group as compared to other isolates (Table-1).

The recent study revealed that, 198 (47.0%) were outpatients and 223 (53.0%) were inpatients, where, the frequency of CA and HA *K. pneumoniae* among them was 25⁄198 (12.6%) and 88⁄223 (39.5%) respectively, and the difference in prevalence of CA and HA isolated *K. pneumoniae* among inpatients as compared to outpatients was statistically significant (p < 0.000 and OR=4.5).

Regarding hospital words, it was found that 31 (36.5%), 22 (30.6%) and 35 (53.0%) of *K. pneumoniae* was isolated from Medical Words (MW), Surgical Words (SW) and Intensive Care units (ICU) respectively. The difference in the prevalence of *K. pneumoniae* was found statistically significant in MW (p < 0.025 and OR=1.8) and ICU (p < 0.000 and OR=4.0). However, *K. pneumoniae* was found significantly more frequent isolates (p < 0.05, and OR=4.3) from sputum (62.8).

Antibiotic susceptibility pattern

The recent study revealed high resistant rates of *K. pneumoniae* among inpatients compared to outpatients. The difference in the resistance rates between CA and HA isolates showed significant concerning Ampicillin, Ticarcillin, Piperacillin, Piperacillin-tazobactam, Amoxiclav, Cefepime, Tetracyclines, and Sulphonamide (P < 0.0005) and all Quinolones except for Nalidixic acid

Penicillins

The result of this study showed that 100.0% *K. pneumoniae* was resistant to limited spectrum penicillin, and 96.5% to Ampicillin. While the difference in the resistant rate among inpatient (98.9%) as compared to outpatient (88.0%) was found statistically significant (p < 0.05 and OR=11.8) for Ampicillin. In the other hand, the isolated *K. pneumoniae* yielded moderate (59.3%) resistant to aztreonam and the difference in the prevalence among HA (65.9%) and CA (36.0%) isolates was statistically insignificant (p >0.005 and OR=2.4).

Cephalosporins

K. pneumoniae exhibited insignificant (p > 0.005) high (>90%) resistant rate to first-generation cephalosporins (Cefradine and Cephadroxil) and second-generation Cephalothin compared marked resistant to second-generation Cefuroxime(78.8%) and third-generation Ceftizoxime (78.8%) and Cefotaxime (77.0%). In contrast to previously mentioned cephalosporins, the result of recent study revealed that 66.4% of isolated *K. pneumoniae* was resistant to fourth-generation cephalosporin Cefepime, while, the difference in resistant rates between of inpatients (70.5%) and outpatient (48.0%) was found statistically insignificant (p > 0.05)

Beta-lactamase inhibitors

Piperacillin-tazobactam and Amoxiclav are used as beta-lactam inhibitor. Where 47.8% and 68.1% of isolated *K. pneumoniae* was resistance to Piperacillin-tazobactam and Amoxiclav respectively. Statistically significant was found in the difference of resistant among inpatients (55.6% and 72.7%) and outpatients isolates (20.0% and 52.2%), to Amoxiclav (p < 0.05 and OR=2.5) and Piperacillin-tazobactam (p < 0.05 and OR=5.0) respectively.

Quinolones

The difference in the prevalence of *K. pneumoniae* resistant rates to all Quinolones were found statistically significant except for Nalidixic acid. The resistant rates was found higher to Nalidixic acid (93.8%) followed by Ciprofloxacin (80.5%), Lomefloxacin (70.8%), Levofloxacin (63.7%) Moxifloxacin (52.2%) and Nitrofurantoin (44.2%). Regarding resistant rates among HA and CA isolates, the resistant rates of *K. pneumoniae* to Quinolones ranged from72percentage to 80% and from 32% to 64% among HA and CA isolates respectively. While more than 92.0% of the HA and CA isolates were resistant to Nalidixic acid.

Aminoglycosides

Marked resistant rate of *K. pneumoniae* against Tobramycin was (71.1%) compared to mild resistant to Amikacin (27.4%) and no statistical significance was observed in the resistance difference among HA and CA isolates toward Amikacin and Tobramycin, where, 27.3% and 75% of HA isolate were resistant to Amikacin and Tobramycin.

Macrolides, Tetracyclines, and others

Generally, *K. pneumoniae* exhibited high resistant rate (>90.0%) to Erythromycin and Roxithromycin. HA *K. pneumoniae* was 100.0% of resistant to each compared to CA isolates. While 65.9% and 35.0% of HA and CA isolates were found resistant to Azithromycin respectively. The present study revealed high resistant to Tetracycline (83.2%) while moderate resistant (45.1%) to Minocycline activity toward isolated *K. pneumoniae*. In addition, the difference in resistance rates of CA and HA isolates against Tetracycline (84.0% and 83.0%) and Minocycline (50.0% and 28.0%) was found statically insignificance. On the other hand, marked (from 64%to 77.3%) and moderate (from 40.0% to 52.7%) *K. pneumoniae* resistant against Cotrimoxazole and Chloramphenicol without statistical significance was found in the resistance difference among of each CA and HA isolates.

Table-1: Frequency of *K. Pneumoniae* isolates in relation to gender, age, admission and site of infections

Gender	***Kleb* N(113)**		***Others* N(308)**		**Total isolates N(421)**		χ^2	**OR**	**CI**	***P***
	N	**%**	**N**	**%**	**N**	**%**				
Male	76	28.8	188	71.2	264	37.3	1.4	1.3	0.8-3.1	0.242
Female	37	23.6	120	76.4	157	62.7	1.4	0.8	0.5-1.2	0.242
Age groups										
0-10	9	28.1	23	71.9	32	7.6	0.03	1.1	0.5-2.4	0.865
11-20	7	23.3	23	76.7	30	7.1	0.2	0.8	0.3-2.0	0.653
21-30	24	25.0	72	75.0	96	22.8	0.2	0.8	0.5-1.5	0.643
31-40	23	21.7	83	78.3	106	25.2	1.9	0.7	0.4-1.2	0.167
41-50	14	20.3	55	79.7	69	16.4	1.8	0.7	0.3-1.2	0.179
>51	36	40.9	52	59.1	88	20.9	11.2	2.3	1.4-3.8	0.001
Admission										
Outpatients	25	12.6	173	87.4	198	47.0	38.5	0.2	0.1-0.4	0.000
Inpatients	88	39.5	135	60.5	223	53.0	38.5	4.5	2.3-7.4	0.000
MW	31	36.5	54	63.5	85	20.2	5.0	1.8	1.1-3.0	0.025
SW	22	30.6	50	69.4	72	17.1	0.6	1.3	0.7-2.2	0.435
ICU	35	50.0	31	47	66	15.7	27.3	4.0	2.3-6.9	0.000
Specimens										
Urine	42	24.7	128	75.3	170	40.4	0.7	0.8	0.5-1.3	0.416
Pus	32	22.2	112	77.8	144	34.2	2.4	0.7	0.4-1.2	0.123
Sputum	27	62.8	16	37.2	43	10.2	31.5	5.7	3.0-11.1	0.000
Vaginal swab	3	23.1	10	76.9	13	3.1	0.1	0.8	0.2-3.0	0.756
Body fluid	7	35.0	13	65.0	20	4.8	0.7	1.5	0.6-3.9	0.399
Aspirate	2	25.0	6	75.0	8	1.9	0.01	0.9	0.1-4.6	0.906

* Statistically significant, χ^2: Chi-square, OR: Odd ratio, N: number, CI: Confidence interval, p: probability. ($\chi^2 \geq 3.84$, $p < 0.05$: significant).MW: medical ward, SW: surgical ward, ICU: intensive care unit.

Table-2: Pattern of *K. Pneumoniae* resistant in general and among CA (OP) and HA (IP) isolates

Antibiotics	Antibiotic	Total (N=113)		HA (N=88)		CA (N=25)		χ^2	*OR*	*CI*	*P*
		N	%	N	%	N	%				
Penicillin	Penicillin	113	100	88	100	25	100	-	-	--	--
	Ampicillin	109	96.5	87	98.9	22	88.0	6.7	11.8	1.2-119	0.009
	Aztreonam	67	59.3	58	65.9	9	36.0	3.5	2.4	1.0-6.2	0.059
	Ticarcillin	106	93.8	85	96.6	21	84	5.3	5.4	1.1-26	0.021
	Piperacillin	100	88.5	81	92.0	19	76	4.9	3.7	1.1-12.1	0.026
Betalactam inhibitors	piperacillin-tazobactam	54	47.8	49	55.6	5	20.0	9.9	5.0	1.7-14.6	0.002
	Amoxiclav	77	68.1	64	72.7	13	52.2	3.9	2.5	0.1-5.1	0.050
Carbapenems	Imipenem	33	29.2	28	31.8	5	20.0	1.3	1.8	0.6-5.5	0.251
Cephalosporins	Cefradine	109	96.5	86	87.7	23	92.0	1.9	3.7	0.5-28.0	0.171
	Cephadroxil	105	92.9	83	94.3	22	88.0	1.2	2.3	0.5-10.2	0.277
	Cephalothin	105	92.9	81	91.0	24	96.0	0.5	0.5	0.1-4.1	0.496
	Cefuroxime	89	78.8	72	81.8	17	68.0	2.2	2.1	0.8-5.8	0.130
	Ceftizoxime	89	78.8	68	77.3	21	84.0	0.5	0.6	0.2-2.1	0.468
	Cefotaxime	87	77.0	69	78.4	18	72.0	0.5	1.4	0.5-3.9	0.502
	Cefepime	75	66.4	62	70.5	12	48.0	4.3	2.6	1.0-8.4	0.037
Quinolones	Nalidixic acid	108	93.8	83	94.3	23	92.0	0.2	1.4	0.3-7.9	0.671
	Nitrofurantoin	50	44.2	44	50.0	8	24.0	5.3	3.2	1.2-8.7	0.021
	Ciprofloxacin	91	80.5	75	80.2	16	64.0	5.6	3.2	1.2-8.9	0.018
	Lomefloxacin	80	70.8	70	79.5	10	40.0	14.7	5.8	2.2-15.1	0.000
	Levofloxacin	72	63.7	64	72.7	8	32.0	14.0	5.7	2.2-14.8	0.000
	Moxifloxacin	59	52.2	52	59.1	7	28.0	7.5	3.7	1.4-9.8	0.006
Macrolides	Erythromycin	109	96.5	88	100.0	21	84.0	14.6	-	--	0.000
	Azithromycin	67	59.3	59	65.9	8	35.0	7.2	3.4	1.4-8.7	0.007
	Roxithromycin	112	99.1	88	100.0	24	96.0	3.6	0.9	0.1-6.8	0.059
Aminoglycosides	Amikacin	31	27.4	24	27.3	7	28.0	0.01	1.0	0.4-2.6	0.943
	Tobramycin	81	71.7	66	75.0	15	60.0	2.2	2.0	0.8-5.1	0.142
Tetracycline	Tetracycline	94	83.2	73	83.0	21	84.0	0.02	0.9	0.3-3.1	0.902
	Minocycline	51	45.1	44	50.0	7	28.0	3.8	2.6	1.0-6.8	0.051
Others	Cotrimoxazole	84	74.3	68	77.3	16	64.0	1.8	1.9	1.1-7.4	0.180
	Chloramphenicol	59	52.2	59	55.7	10	40.0	1.9	1.9	0.8-4.7	0.166
	* Statistically significant, χ^2: Chi-square, OR: Odd ratio, N: number, CI: Confidence interval, *p*: probability. ($\chi^2 \geq 3.84$, $p < 0.05$: significant).MW: medical ward, SW: surgical ward, ICU: intensive care unit, CA: Community-acquired, HA:: hospital-acquired.										

DISCUSSION

Frequency of *K. pneumoniae*

The predominance of *K. pneumoniae* among males in this study is inconsistent with other studies, which showed that, *K pneumoniae* more frequent isolates among females than males [11–14]. In addition, *K. pneumoniae* was found more frequent isolates among inpatients and in sputum which was found in agreement with that reported by Minami *et al.* [15]. Similar frequent isolates *K. pneumoniae* from pus was reported by Kumar *et al.*, [4]. The present study revealed similar, high prevalence rates of *Klebsiella* species among the following age groups (0-10 and those of more than 51 years old), to that reported by Meatherall *et al.*, [16]. It is suggested to decrease immunity in the extremes of age groups.

The high rate nosocomial *K pneumoniae* infections in this study can be explained by the ability of *Klebsiellae* adaptation to the hospital environment and can survive longer than other bacteria, facilitating cross-infection within hospitals [17, 18]. Furthermore, *Badura et al.*, [19] found the prevalence rate of CA (52.3%) *Klebsiella* species isolates were higher than HA (47.7%). While Babakhani *et al.*, [20] reported a similar high (57.5%) prevalence *Klebsiella* among ICU admitted patients and less (17.5%) prevalence among SW admitted patients.

Antibiotics resistant

The result of the recent study revealed high resistance rates among inpatients as compared to outpatient isolates toward most antibiotics tested which was found inconsistent with that reported by Tasy *et al.*, [21]. Where, high (100.0%) *K. pneumoniae* resistance rates to Ampicillin has been reported in Saudi Arabia [22] and elsewhere [23–25]. On the other hand, Kumar *et al.*, [4] found that 89.5% of *K. pneumoniae* was

resistant to Ampicillin. Less Ampicillin (16.7%) resistance has been reported Chikwendu *et al.*, [14]. However, as compared to similar study conducted by Alzubiry *et al.*, [26], the result of present study showed that the *K. pneumoniae* isolates exhibited high resistance to Penicillin, Ampicillin, which could be related to bacterial isolates which were collected from different governorates (Sana'a, Taiz, and Aden) of Yemen, where the resistant profiles were taken.

Similar studies have been found less Piperacillin resistance (38.7%) [27] and (43.6%) [28] and others have found high resistance to Piperacillin (95.0%) [18] and (100.0%) [4]. Similar statistics which are significant in the difference of Piperacillin resistant between CA (17%) and HA (44.0%) *K. pneumoniae* has been reported by Tasy *et al.*, [21]. In another aspect, high Ticarcillin resistant (100.0%) reported by Aljanaby and Alhasani [29]. While Babakhani *et al.*, [20] showed that, 66.2% *K. pneumoniae* was resistant to Ticarcillin.

The present study revealed that 59.3% of isolates were resistant to Aztreonam. This finding differs from the result obtained by Lee *et al.*, [30] (7.1%) and Bahadin *et al.*, [31] (82.8% susceptible). Related to the resistant difference between CA and HA *K. pneumoniae*, the result of the present study revealed similar significance to that reported by Tasy *et al.*, [21], who found less resistance of CA (5.0%) and HA (25.0%) *K. pneumoniae* toward Aztreonam as compared to present study. While *Dehghan et al.*, [32], found 75.0% and 38.2% of CA and HA *K. pneumoniae* isolates were resistant to Aztreonam.

Our study showed high Amoxiclav resistance than that reported by While Kumar *et al.*, [4] (50%) and Shalini *et al.*, [33] (34.5%), likewise other studies [20, 31] and that conducted in Saudi Arabia[34] have found higher *K. pneumoniae* resistance to Amoxiclav (60-90.0%) than the result of recent study. Furthermore, very bad Amoxiclav activity have documented elsewhere (>90%) by several studies [23, 26, 33]. In addition, the present study occurred quite similar resistant rate against piperacillin-tazobactam to that reported by *Kersh et al.*, [22] (54.0% susceptible) and higher than that reported by Susethira *et al.*, [25] (25.0%), Mohsen *et al.*, (26.4%) [28] and Lee *et al.*, (4.4%**)** [30]. From another aspect the resistance rates of HA and CA *K. pneumoniae* isolates against beta-lactam inhibitors Amoxiclav and Piperacillin tazobactam, fewer resistance rates (from 3 to <18.0%) than our findings has been reported in other studies [20, 31].

Carbapenems such as Imipenem exhibited marked activity against *K. pneumoniae*. Less Imipenem resistance (15) % was reported by Khan in Saudi Arabia [34]. While Mohsen *et al.*, [28] and Lee *et al.*, [30] reported that 3.6% and 0.5% of *K. pneumoniae* isolates were resistant to Imipenem respectively. However, There was a significant increase in resistance of *K. pneumoniae* to carbapenems over the years are particularly problem worldwide [35]. For example, studies by the European Antimicrobial Resistance Surveillance (EARS-Net) showed that the prevalence of carbapenem-resistant *K. pneumoniae* has increased from one to 2% to 15% in Italy in-between 2006-2009 [36] to reach 35% in 2013 [37]**.** While higher Imipenem-resistant (67.5%) have reported by Babakhani *et al.*, [20].

High *K. pneumoniae* resistance to first-generation Cephadroxil (88.8%) which is in compliance with another study reported by *Kumar et al.*, [4]. While others found 100.0% of *K. pneumoniae* isolates were resistant to Cephradine [26, 28]. Similar *K. pneumoniae* resistance rate to second-generation Cefuroxime (77.4%) reported by *Kumar et al.*, [4] and higher Cefuroxime resistance (85.7%) was reported by Shatalov [23]. On other hands, less Cefuroxime (>95% susceptible) and Cephalothin (28%) resistant reported by Vasquez *et al.*, [38] and Cunha [39]. Related to resistance rate of CA *K. pneumoniae*, Bahadin *et al.*, [31] (34.5%) and Vasquez *et al.*, [38] (17.1%) found less CA *K. pneumoniae* resistance rates to Cephalothin.

Similar resistance rates to third-generation cephalosporins reported by Amin *et al.*, [40]. Whereas a strikingly high prevalence *K. pneumoniae* resistant to Ceftizoxime (90.0%-100.0%) reported by several studies [1, 23, 26, 29]. Baig *et al.*, [41], found high (98.0%) compared to marked (50.0%) *K. pneumoniae* resistant isolates of Cefotaxime has been reported by Alsohaili *et al*., [42]. Less resistant among CA 2.7% and HA 9.2% *K. pneumoniae* to Cefotaxime was reported by Badura [19] whereas Vasquez *et al.*, [38] reported the best cefotaxime activity against CA *K. pneumoniae* (100% susceptible).

Relative studies, on the other hand, which are a quite similar showing Cefepime resistance (66.6%) that reported by *Susethira et al.*, [25]. Relative *K. pneumoniae* resistance toward Cefepime (31.2%) was reported by Babakhani *et al.*, [20] and Chowdhury and Parial [43], whereas Lee *et al.*, [30] reported excellent Cefepime activity against *K. pneumoniae* (2.2%). While *Baig et al.*, [41] found 98.2% of nosocomial *Klebsiella* isolates were resistant to Cefepime.

The overall rates of resistance to Fluoroquinolones in *K. pneumoniae* were found high in Nalidixic acid and Ciprofloxacin, marked to Levofloxacin and Moxifloxacin to moderate resistance against Nitrofurantoin. Whereas the resistance rates were found higher among CA as compared HA *K. pneumoniae* isolates, this difference was found statistically significant to all Fluoroquinolones except for Nalidixic acid which revealed low activity against isolated *K. pneumoniae* in general and as well as against CA and HA isolates. Furthermore, high (100.0%) and less Fluoroquinolones resistance (3.3%) was reported in

a study conducted by Varughese *et al.*, [12] and Minami *et al.*, [15] respectively.

Aljanaby and Alhasani [29] found 100.0% of isolated *K. pneumoniae* was resistant to Nitrofurantoin, while, excellent Nitrofurantoin activity against *K. pneumoniae* (93.2% susceptible) reported by Chowdhury and Parial [43]. Regarding susceptibility pattern of CA and HA isolates. Others studies [19, 38] revealed less CA (12-21%) and HA (< 32.0%) *K. pneumoniae* resistance than the result of present study rates against Nitrofurantoin. Furthermore, high nosocomial resistance (80%) toward Nitrofurantoin was reported by Babakhani *et al.*, [20].

The observed resistance in *Klebsiella* to Ciprofloxacin (80.5%) and Levofloxacin (63.7%) was higher than studies conducted by Shalini *et al.*, [33] who found that 31.04% and 27.59% of *K. pneumoniae* isolates were resistant to Ciprofloxacin and Levofloxacin respectively, While, high Ciprofloxacin and Levofloxacin resistant (100.0%) was reported by Varughes *et al.*, [12].

Related to Ciprofloxacin activity among HA and CA isolates. Similar (82.5%) HA *K. pneumoniae* resistance against Ciprofloxacin was reported by Babakhani *et al.*, [20], whereas, Very good Ciprofloxacin activity toward CA (5.6%) and HA (7.4%) *K. pneumoniae* reported by Badura *et al.*, [19]. Less resistant rates of HA (49.2%) and CA (51.9%) *K. pneumoniae* against Ciprofloxacin has been reported by Somily *et al.*, [44].

The result of Amikacin resistance is in agreement with other studies [23, 31]. Less Amikacin (2.2%) and Tobramycin (4.4% **)** resistance than the result of present study has been reported by Lee *et al.*, [30] and Vasquez *et al.*, [38]. Other studies [18, 43] revealed Excellent (98.6% susceptible) and very good (85.0% susceptible) Amikacin activity against *K. pneumoniae* respectively. Furthermore, the best performance of Amikacin, particularly against CA and HA *K. pneumoniae*, (< 10%resistant) was reported in several studies [19, 20, 38, 44].

High resistant (89.7%), moderate(54.3%) and excellent Cotrimoxazole activity (3.3% resistant) against *K. pneumoniae* has been reported by Shalini *et al.*, [33] Alsohaili *et al.*, [42] and Lee *et al.*, [30] respectively. Similar statistically significant in the resistant difference of CA and HA *K. pneumoniae* reported by Tsay *et al.*, [21], while, Badura *et al.*, [19] found 9.5 % and 12.3% of CA and HA *K. pneumoniae* resistant to Cotrimoxazole. Vasquez *et al.*, [38] was reported high susceptibility rate of CA *K. pneumoniae* to Cotrimoxazole (93.8%).

Resistance rates of CA and HA *K. pneumoniae* to Tetracycline in our study found quite similar to a number of studies [18]. Less CA *K. pneumoniae* Tetracycline resistance rate (21.9%) is reported by Vasquez *et al.*, [38] and Aljanaby and Alhasani [29] (34.4%). Sarathbabu *et al.*, [45] found that 51-60% of *K. pneumoniae* resistant to Tetracycline. While, highly resistant (89.7%) to Minocycline was reported by Shalini *et al.*, [33].

It was found that, 52.2% of *K. pneumoniae* isolates were resistant to Chloramphenicol, compared to relative (31.3%) reported by Aljanaby and Alhasani [29] and Chikwendu *et al.* [14] (27.2%). Slightly higher Chloramphenicol resistance than the present study reported by Sikarwar and Batra [46] (40.0% susceptible). While, moderate Chloramphenicol activity has been reported by Chowdhury and Parial [43] (44.8%).

CONCLUSION

There was a general increase in the resistance pattern of *K. pneumoniae* to all the antibiotics tested. The current findings confirm that bacterial resistance would be the greatest and frightening problem in our country. Mechanisms for HA infections controlling must be evaluated to reduce pathogenic resistant bacterial strains spreading. Also, strike regulation of the antibiotics buying and intake by the public need to be applied.

RECOMMENDATION

Further comprehensive studies required with the usage of the phenotypic assay for ESBL confirmation as well as the genotypic method for resistance pattern investigation.

List of abbreviations

CA: Community-acquired
CDC: Centers for Disease Control and Prevention
CLSI: Clinical and Laboratory Standards Institute
HA: Hospital-acquired
ICU: intensive care unit
IP: Inpatient
MW: medical ward
NCCLS: National Committee for Clinical Laboratory Standards
OP: Outpatient
SPSS: Statistical Package for Social Sciences
SW: surgical ward
WHO: World Health Organization

Declarations

Ethical considerations

Ethical clearance was obtained from the Faculty Ethics Committee of Faculty of Medicine and Health Sciences, Taiz University, Taiz, Yemen. All obtained demographic data was treated confidently.

Consent for publication: Not applicable

Availability of data and materials

The data that support the findings of this study are available from the hospitals or clinics of Sana'a city but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the hospitals or clinics of Sana'a city.

Competing interests

The authors declare that they have no competing interests. All authors read and approved the final manuscript.

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Authors' contribution

TA contributed to study design, data collection and analysis, and manuscript review. TH and HA contributed to data interpretation and manuscript drafting and review. AA contributed to the manuscript review. LA data collection assistant.

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