Experimental Research

ANNALS OF MEDICINE & SURGERY

OPEN

Resistance patterns of bacterial pathogens causing lower respiratory tract infections: Aleppo-Syria

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Background: Globally, lower respiratory tract infections (LRTIs) are one of the lead causes of death. Bacterial and susceptibility profiles are not constant over time and geographically, and different patient factors can be correlated with those infections.
Objective: This study aimed to scan the bacterial spectrum causing LRTIs, their susceptibility profile and patient related risk factors.
Material and methods: Two hundred sixty-eight specimens from LRTIs suspected patients attending University Hospital were collected. Specimens included bronchial washings, transtracheal aspiration samples and sputum. After appropriate culture and identification tests, susceptibility test was done using minimum inhibitory concentration method. Data were collected from patients for further analysis.
Results: of total specimens, 150 showed positive culture results (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Citrobacter koseri*, *Escherichia coli*, *Klebsiella pneumonia, Staphylococcus aureus, Staphylococcus epidermidis*, *Staphylococcus haemolyticus, Streptococcus pneumonia* and *Candida spp.*). The antibiogram showed high resistance among all bacterial isolates against most antibiotics. Good susceptibility rates were shown to colistin in Gram-negative group and piperacillin\tazobactam in Gram-positive group. Trimethoprim\sulfamethoxazole showed good susceptibility results in both groups. Many factors showed correlation with LRTIs such as age ($P = 0.004$), smoking ($P = 0.049$), residency ($P = 0.043$), hypertension ($P = 0.012$), lung chronic disease ($P = 0.007$) and cancer ($P = 0.048$).
Conclusion: The leading cause of LRTIs in our study were *A. baumannii* and *P. aeruginosa* which both are very troublesome pathogens and multidrug resistant frequency was alarming. Random empirical antibiotic using can highly lead to increased resistance. Further care must be taken after patients with risk factors, and adjustments should be done to those modifiable factors.

Keywords: Antibiotic- Lower respiratory tract Infections– MIC – MDR – risk factor

Introduction

Worldwide speaking, lower respiratory tract infections (LRTIs) are a prime cause of death. In 2019, there were 488.9 million incidents of LRTIs and 2.4 million deaths[1]. LRTIs are often misdiagnosed, mistreated and undervalued due to their non-specific clinical presentation and most episodes of LRTIs are self-limiting and last between 1 and 3 weeks[2].

In developing countries, the situation is even worse, LRTIs are accounting for 20–40% of paediatric hospital visits, and are one of the most common causes of death in children less than five years old and adults older than 70 years[3]. In Middle East and North Africa region, LRITs incidence rate ranged from 761.1 to 1019.9 cases per 100 000 population[4].

LRTI is not a single disease but a group of specific infection with different epidemiology, pathogeneses, clinical presentations and outcomes[5]. In general, the infections recovery depends on the precise identification of a causative agent and proper antibiotics prescription. Unfortunately, bacterial culture and susceptibility tests often take multiple days to obtain results; which can lead to exposing patients to possibly ineffective therapies with significant safety repercussions[6]. Therefore, physician often follow empirical therapy with antimicrobial agents. The antimicrobial agent is often chosen based on the patient profile, local resistance pattern, availability on the market and cost[7]. However, proper choosing of antibiotics is becoming more

HIGHLIGHTS

- Lower respiratory tract infections are a prime cause of death.
- Aetiological agents of lower respiratory tract infections and their antibiotic susceptibility profiles are not constant over time and among geographical locations.
- *Acinetobacter baumannii*, *Pseudomonas aeruginosa* were the most predominant species among lower respiratory infection in our study.
- Antibiogram showed high resistance among all bacterial isolates against most of antibiotics with multidrug resistant rate (63.23%).
- The most important risk factor for lower respiratory infections were: age, smoking, residency and chronic disease.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2023) 85:2655–2661

Received 4 April 2023; Accepted 27 April 2023

Published online 8 May 2023

http://dx.doi.org/10.1097/MS9.0000000000000778

challenging along with the rising issue of antimicrobial resistance, which leads to probable failure of empirical therapy. Treatment failure due to antibiotic resistance is frequent with LRTIs patients[8]. As causative agents of LRTIs and their antibiotic susceptibility profiles are not constant over time and among geographical locations[9,10]. Monitoring the antimicrobial resistance patterns of the causative agents is required, not only to guide the clinician when prescribing antibiotic therapy but also to observe the trend of these infections.

Much like any other infections, lower respiratory tract infections can be related to many factors, such as age, gender, smoking and household conditions[11].

It has been always realized that viral respiratory infections put patients at risk of bacterial infections, and that these co-infections have worse outcome than either infection on its own[12]. Since this study was carried out during the pandemic, this thought was kept in mind.

Another important issue came along with COVID-19 was the extensive use of macrolides in the course of treatment, which could be a cause of raising macrolides resistance in bacteria[13].

This study is concerned of what bacterial trend is causing LRTIs in the mean time in our region and the recent susceptibility profiles with the focus on azithromycin, which can give practitioners better leads on how to choose proper therapy. In addition, our aimed to analyze possible social and clinical variables as possible risk factors for LRTIs in our society in Aleppo-Syria.

Material and methods

Study design

This study was a cross-sectional, laboratory-based study.

Study population

Patients of both genders and all ages, who attending out-patient clinics of University Hospital between (March 2021 and March 2022), complaining of one or more of various chronic and acute lower respiratory symptoms (productive\dry cough, fever, dyspnoea, chest pain, hemoptysis and weight loss) were enroled in this study. Suspected or confirmed Covid-19 patients and those who were taking antibiotics therapy during period of study were excluded

Data collection and sampling

Different types of samples were chosen for more thorough results, and due to different conditions such as inability to perform a valid sputum sample by some patients such as females, infants and teenagers. The respiratory specimens included, sputum, bronchial washings (BWs) and transtracheal aspirations (TTAs). BWs specimens were collected via bronchoscopy, by instilling about 10–20 ml of saline into the bronchoscope and aspiration to a sterile tube, while TTAs specimens were collected by inserting a sterile catheter into the trachea which induces secretions. Both procedures were performed by a specialist.

A structured interviewer administered questionnaire was used to collect data about sociodemographic characteristics, clinical information and other relevant variables. The questionnaire was prepared in Arabic language, and then it was translated to English during writing article.

Assessment of specimens and organisms identification

Soon after collection, the specimens were transported to the bacteriology laboratory using an ice box and processed within 30 min of collection. Reliable specimens were those containing fewer than 10 epithelial cells and 25 or more polymorphonuclear cells. Specimens were evaluated using Gram stain, and then cultured on blood agar, MacConkey agar and chocolate agar which was incubated using the candle jar method to provide CO_2.

Microbes isolated from specimens were identified using traditional selective media (e.g. Mannitol-Salt agar, Cetrimide agar, etc.) and biochemical test such as oxidase, catalase, etc[14].

Antibiotic susceptibility test

Minimum inhibitory concentration (MIC)

MIC was performed following the National Committee for Clinical Laboratory Standards (NCCLS)[15], using the broth microdilution method as described by Wiegand *et al.*[16] A 0.5 McFarland suspension of the tested isolate was prepared in cation adjusted MHB (CAMHB), 100 fold diluted with sterile broth and 100 µl of final suspension was inoculated in each well of 96-well sterile polystyrene microplate after adding 100 µl of the serial of antibiotic dilutions. Wells containing only sterile broth were negative control, whereas positive controls (growth controls) were in wells containing bacterial suspension + 100 µl of sterile broth. Microplate was incubated for 24 ± 2 h at 37°C. MIC result was read as the least antibiotic concentration with no visible growth. The antibiotics used for Gram-negative isolates were piperacillin\tazobactam, cefepime, ceftriaxone, ceftriaxone\sulbactam, meropenem, ciprofloxacin, levofloxacin, azithromycin, trimethoprim\sulfamethoxazole, colistin, ceftazidime and gentamicin. For Gram-positive isolates; cefpodoxime was used instead of colistin. However, the streptococci isolates were tested against cefepime, ceftriaxone, levofloxacin, azithromycin, meropenem and trimethoprim\sulfamethoxazole.

Multidrug resistant (MDR), extended drug resistant (XDR) and pandrug resistant (PDR) isolates were evaluated according to Magiorakos and colleagues; where an isolated was considered MDR if it was resistant to one or more antibiotics in three or more antibiotic categories, XDR isolates were those that showed non-susceptibility to at least one agent in all but two or less anti-

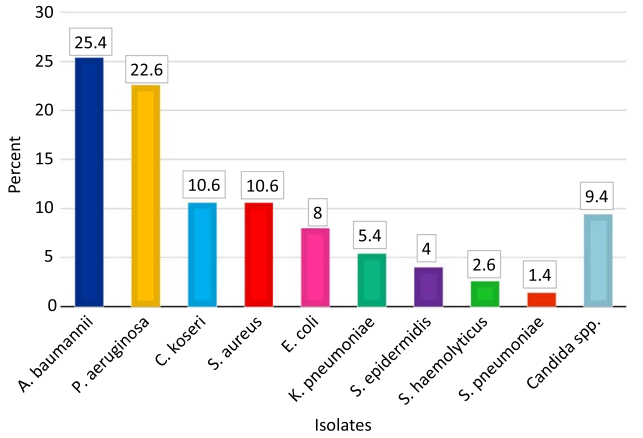

Figure 1. Identified isolates from positive culture specimens.

microbial categories and PDR isolates were resistant to all agents in all categories. Extended spectrum Beta-Lactamase producer isolates were detected according to results of ceftriaxone and ceftriaxone\sulbactam testing, when MIC in ceftriaxone\sulbactam is at least three twofold concentration steps lower than ceftriaxone alone (NCCLS)[15,17].

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences software (version 16, SPSS Inc.). The association of variable with the prevalence of bacterial species was assessed using χ^2 tests. *P* less than 0.05 was considered to be statistically significant.

Results

Distribution of bacterial isolates

A total of 268 specimens included in this study, 182 (65.98%) BWs, 68 (27.91%) sputum specimens and 18 (6.09%) TTAs. One hundred fifty (56.34%) samples showed positive growth; among them 14 were *Candida spp*. The distribution of positive cultures among different types of specimens was 47.25% % of BWs, 67.64% of sputum specimens and 100% of TTAs.

Table 1

Social demographic and clinical-related factors

Variable	LRTI + , *N* (%)	LRTI–, *N* (%)	ð 2	*P*
Age				
0–20	22 (61.1)	14 (38.9)	13.288	*0.004
21–40	32 (76.2)	10 (23.8)		
41–60	44 (44)	56 (56)		
> 60	52 (57.8)	38 (42.2)		
Sex				
Male	106 (57.6)	78 (42.4)	0.640	0.424
Female	40 (47.6)	44 (52.4)		
Smoking status				
Smoker	80 (48.8)	84 (51.2)	3.870	*0.049
Non-smoker	38 (36.5)	66 (63.5)		
Residency				
Countryside	48 (48)	52 (52)	4.112	*0.043
City	102 (60.7)	66 (39.3)		
Occupation				
Outdoor work	48 (61.5)	30 (38.5)	5.513	0.064
Indoor work	50 (47.2)	56 (52.8)		
No work	52 (61.9)	32 (38.1)		
LRCD				
Positive	34 (73.9)	12 (26.1)	7.255	*0.007
Negative	116 (52.3)	106 (47.7)		
Hypertension				
Positive	128 (59.8)	86 (40.2)	6.365	*0.012
Negative	22 (40.7)	32 (40.7)		
Diabetes				
Positive	14 (63.6)	8 (36.4)	0.572	0.450
Negative	136 (55.3)	110 (44.7)		
Cancer				
Positive	24 (70.6)	10 (29.4)	3.377	*0.048
Negative	126 (53.8)	108 (46.2)		

*Statistically significant.

LRCD, lung-related chronic diseases such as asthma, COPD and broniectasis; LRTI – , negative for bacterial lower respiratory infection; LRTI + , positive for bacterial lower respiratory infection.

Out of the isolated bacteria, (79.4%) were Gram-negative bacteria and (20.6%) Gram-positive bacteria. *Acinetobacter baumannii* was the predominant species (Fig. 1).

LRTIs risk factors

The median age of study population was 45 years with a range from infants to 80 years. Male patients were 184 (68.6%) while female patients were 61 (31.4%). Patients were categorized into two groups; those from the city and others from the countryside, based on environmental conditions and overcrowded population in order to have a more accurate evaluation. Occupations also were taken into account and similar types of jobs were included in groups (indoor or outdoor) and an additional group for unemployed patients (Table 1).

Antibiotic resistance patterns

The resistance patterns of the 136 bacterial isolates using MIC showed that at least 50% of Gram-negative isolates were resistant to all antibiotics except for colistin and piperacillin\tazobactem. More than 95% of isolates were resistant to ceftriaxone and ceftriaxone\sulbactam, 4 Isolates of *A. baumannii* were Extended spectrum Beta-Lactamase (Table 2).

In Gram-positive pathogens, the 2 isolates of *Streptococcus pneumoniae* pathogen showed sensitivity to all tested antibiotics (Tables 3). Among Staphylococci isolates, the highest resistance rate was also to ceftriaxone and ceftriaxone\sulbactam (84.61%), whereas, resistance rates to the rest of tested antibiotics were significantly lower (Table 4). On the other hand, frequencies of multi resistant isolates (MDR, XDR and PDR) were determined among both positive and negative Gram isolates as shown in (Fig. 2). The most multidrug resistant species was *A. baumannii* followed by *P. aeruginosa* (Table 4).

Discussion

Our research offers a vision of the most common bacteria responsible for infections in LRTs in Aleppo-Syria and their resistance profiles to the most common antibiotics available on the market. This study will inform and guide policy and practice in decision-making, and guide researchers in future investigations in the field of respiratory bacterial infections.

In this study, Gram-negative bacteria were the most common cause of LRTs bacterial infections (79.4%), with *A. baumannii* being the prominent species, followed by—with not much of a difference- *P. aeruginosa* (28% and 25%, respectively). In addition to bacterial species, 14 *Candida spp*. were isolated from our patients. *Candida* were historically considered a commensal organism with low virulence potential[18]. However, numerous studies have reported the isolation of *Candida* from pulmonary biopsies or bronchoalveolar lavage fluid in critically ill patients that may contribute to exacerbation of lung disease[19].

Our results correspond to a study in India by Summaiya *et al.*[20] and other studies in Nepal, where Shrestha *et al.*[21] also found out that Gram-negative bacteria were the primary cause with the leading of *A. baumannii* in ventilator associated pneumonia in neurosurgical patients (55.6%). However, the prominent pathogen in Mishra *et al.*[22] study was *K. pneumoniae* in nosocomial LRTIs patients (19.1%). Also, Baidya *et al.*[23] reported almost similar findings. Nevertheless, unlike our finding,

Table 2

Antibiotic susceptibility patterns in Gram-negative isolates

		Bacterial isolates susceptibility, *N* (%)				
Antibiotic	Pattern	Acinetobacter baumannii (*n* = 38)	Pseudomonas aeruginosa (*n* = 34)	Citrobacter koseri (*n* = 16)	Escherichia coli (*n* = 12)	Klebsiella pneumoniae (*n* = 8)
P\T	S	6 (15.8)	16 (47.1)	14 (87.5)	2 (16.7)	0
	I	10 (26.3)	6 (17.6)	2 (12.5)	10 (83.3)	0
	R	22 (57.9)	12 (35.3)	0	0	8 (100)
FEP	S	2 (5.3)	0	8 (50)	6 (50)	0
	I	4 (10.5)	8 (23.5)	4 (25)	2 (16.7)	2 (25)
	R	32 (84.2)	26 (76.5)	4 (25)	4 (33.3)	6 (75)
CAX	S	0	0	0	0	0
	I	0	0	0	4 (33.3)	0
	R	38 (100)	34 (100)	16 (100)	8 (66.7)	8 (100)
C\S	S	2 (5.3)	0	0	0	0
	I	2 (5.3)	0	0	4 (33.3)	0
	R	34 (89.5)	34 (100)	16 (100)	8 (66.7)	8 (100)
MER	S	12 (31.6)	12 (35.5)	0	10 (83.3)	0
	I	0	6 (17.6)	0	2 (16.7)	0
	R	26 (68.4)	16 (47.1)	16 (100)	0	8 (100)
CIP	S	2 (5.3)	4 (11.8)	8 (50)	0	0
	I	2 (5.3)	2 (5.9)	8 (50)	0	0
	R	34 (89.5)	28 (82.4)	0	12 (100)	8 (100)
LVX	S	4 (10.5)	12 (35.3)	16 (100)	0	2 (25)
	I	4 (10.5)	4 (11.8)	0	10 (83.3)	2 (25)
	R	30 (78.9)	18 (52.9)	0	2 (16.7)	4 (50)
AZ	S	0	0	4 (25)	6 (50)	2(25)
	I	0	8 (23.5)	4 (25)	0	2 (25)
	R	38 (100)	26 (76.5)	8 (50)	6 (50)	4 (50)
T\S	S	6 (15.8)	24 (70.6)	16 (100)	0	2 (25)
	I	N\A	N\A	N\A	N\A	N\A
	R	32 (84.2)	10 (29.4)	0	12 (100)	6 (75)
COL	S	18 (47.4)	14 (41.2)	14 (87.5)	8 (66.7)	8 (100)
	I	N\A	N\A	N\A	N\A	0
	R	20 (52.6)	20 (58.8)	2 (12.5)	4 (33.3)	0
CTZ	S	2 (5.3)	2 (5.9)	16 (100)	2 (16.7)	0
	I	2 (5.3)	0	0	0	0
	R	34 (89.5)	32 (94.1)	0	10 (83.3)	8 (100)
GEN	S	2 (5.3)	8 (23.5)	10 (62.5)	8 (66.7)	0
	I	4 (10.5)	6 (17.6)	2 (12.5)	0	2 (25)
	R	32 (84.2)	20 (58.8)	4 (25)	4 (33.3)	6 (75)

AZ, azithromycin; C\S, ceftriaxone\sulbactam; CAX, ceftriaxone; CIP, ciprofloxacin; COL, colistin; CTZ, ceftazidime; FEP, cefepime; GEN, gentamicin; I, intermediate; LVX, levofloxacin; MER, meropenem; N\A, not available; P\T, piperacillin\tazobactam; R, resistant; S, sensitive; T\S, trimethoprim\sulfamethoxazole.

in their study, *P. aeruginosa* was the predominant cause, followed by *A. baumannii* in Ventilator Associated Pneumonia patients. It has been reported that bacterial community acquired pneumonia is most commonly caused by *Streptococcus pneumonia* and *Haemophilus influenza*, which disagrees with our results. However, recent study has suggested that as consequences of the pandemic COVID-19 microbiological distribution of respiratory pathogens has been changed. and the rate of multidrug resistant microorganisms has been driven especially due to the overuse of antibiotics during this period[24]

In our research, LRTIs were relatable to age ($P = 0.004$) and the highest rate of infection was in age group (20–40) 76%, which can be explained by the high social activity in the young adults group, hence being more exposed to contagious diseases. That rate was followed by age group older than 60 (57%) that can be vulnerable due to weakened immunity.

Sex variations in community acquired pneumonia Community Acquired Pneumonia incidence have been reported in many epidemiological studies, all showing males with higher incidence[25]. Several studies have been conducted to understand sex differences in pathogenesis, immune response and epidemiology of Community Acquired Pneumonia and it is been hypothetically concluded that female's response to pneumonia is more targeted and less destructive than male's[26]. In this study, sex was not a risk factor for LRTIs ($P = 0.424$). However, male patients showed a higher infection rate 57.6% than female patients 47.6%. It should be mentioned that males in our study group have higher outdoor activity, and most of female patients in the group study were housewives.

About half of the smoker group had infections and that group showed significantly ($P = 0.049$) more vulnerability to infection compared to the non-smoker patients (48.8% and 36.5%, respectively). Smoking disrupts mucociliary clearance and increases mucus production in the airways[27].

Owing to higher population density and more human contact lifestyle, compared with rural regions, people who live in the city are

Table 3

Antibiotic susceptibility patterns in Gram-positive isolates

		Bacterial isolates susceptibility, *N* (%)			
Antibiotic	Pattern	Staphylococcus aureus (*n* = 16)	Staphylococcus epidermidis (*n* = 6)	Staphylococcus haemolyticus (*n* = 4)	Streptococcus pneumoniae (*n* = 2)
P\T	S	10 (62.5)	4 (66.7)	2 (50)	N\A
	I	N\A	N\A	N\A	N\A
	R	6 (37.5)	2 (33.3)	2 (50)	N\A
FEP	S	4 (25)	6 (100)	2 (50)	2 (100)
	I	10 (62.5)	0	0	0
	R	2 (12.5)	0	2 (50)	0
CAX	S	0	0	0	2 (100)
	I	0	4 (66.7)	0	0
	R	16 (100)	2 (33.3)	4 (100)	0
C\S	S	0	0	0	N\A
	I	0	4 (66.7)	0	N\A
	R	16 (100)	2 (33.3)	4 (100)	N\A
MER	S	8 (50)	2 (33.3)	2 (50)	2 (100)
	I	6 (37.5)	2 (33.3)	0	0
	R	2 (12.5)	2 (33.3)	2 (50)	0
CIP	S	8 (50)	6 (100)	0	N\A
	I	0	0	0	N\A
	R	8 (50)	0	4 (100)	N\A
LVX	S	12 (75)	2 (33.3)	0	2 (100)
	I	2 (12.5)	2 (33.3)	0	0
	R	2 (12.5)	2 (33.3)	4 (100)	0
AZ	S	4 (25)	6 (100)	0	2 (100)
	I	2 (12.5)	0	0	0
	R	10 (62.5)	0	4 (100)	0
T\S	S	16 (100)	6 (100)	2 (50)	2 (100)
	I	N\A	N\A	N\A	0
	R	0	0	2 (50)	0
CPD	S	0	6 (100)	0	N\A
	I	2 (12.5)	0	0	N\A
	R	14 (87.5)	0	4 (100)	N\A
CTZ	S	2 (12.5)	4 (66.7)	0	N\A
	I	8 (50)	2 (33.3)	2 (50)	N\A
	R	6 (37.5)	0	2 (50)	N\A
GEN	S	2 (12.5)	6 (100)	2 (50)	N\A
	I	6 (37.5)	0	0	N\A
	R	8 (50)	0	2 (50)	N\A

AZ, azithromycin; C\S, ceftriaxone\sulbactam; CAX, ceftriaxone; CIP, ciprofloxacin; CPD, cefpodoxime; CTZ, ceftazidime; FEP, cefepime; GEN, gentamicin; I, intermediate; LVX, levofloxacin; MER, meropenem; N\A, not available; P\T, piperacillin\tazobactam; R, resistant; S, sensitive; T\S, trimethoprim\sulfamethoxazole.

at greater risk of disease-transmission. Additionally, rural people can have better immune response due to their various pathogen exposure in early life[28]. Our results are consistent with previous and infection rate showed a significant relation to residency areas ($P = 0.043$). Patients who live in the city areas showed a higher rate of infections 60.7% than those living in the countryside 48%.

Table 4

Antibiotic multi-resistance frequencies among isolates

	MDR	XDR	PDR
Staphylococcus spp.	0	0	0
S.aureus	6	2	0
S.haemolyticus	4	0	2
P. aeruginosa	22	6	8
K. pneumoniae	6	4	0
A. baumannii	34	14	12
E. coli	10	2	0
Citrobacter spp.	4	0	0
Total No. (%)	86 (63.23)	28 (20.58)	22 (16.17)

MDR, multidrug resistant; PDR, pandrug resistant; XDR, extended drug resistant.

Transmission of infectious diseases in workplace is relative depending on workplace conditions, work practices and human contact[29]. In our study, unemployed patients showed a higher infections rate. However, when comparing work conditions, patients who work outdoors were more vulnerable than those who work indoors (61.5% > 47.2%).

Patients with a history of lung-related chronic disease such as asthma, Chronic Obstructive Pulmonary Disease and bronchiectasis showed more tendency to have LRTIs ($P = 0.007$), which can be related to ineffective mucus drainage in such disorders[30,31]. Same association was shown in hypertension patients ($P = 0.012$), perhaps due to high blood pressure which leads to pulmonary obstruction and heightens pneumonia risk[32]. Cancer patients also showed significantly more vulnerability to LRTIs ($P = 0.048$), knowing that cancer in general

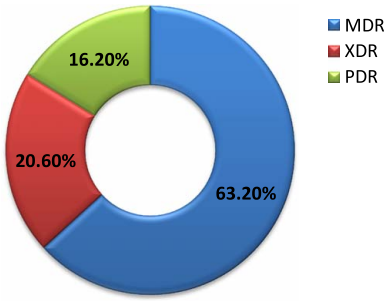

Figure 2. MDR, XDR and PDR rates among isolates. MDR, multidrug resistant; PDR, pandrug resistant; XDR, extended drug resistant.

jeopardizes humoral and cellular immunity function. Also, lung masses may block normal mucus clearance[33,34].

Despite of the higher percentage of LRTIs among diabetic patients (63%) due to reduced immunity in diabetic patients[35] but there was no significant correlation ($P = 0.450$). However, this may be related to the low number of diabetic patients in our study (22 of total 268 patients).

MDR pathogens were prominent in our study (63%). Out of total Gram-negative isolates, only four of *A. baumannii* were Extended spectrum Beta-Lactamase. The studies by Baidya and colleagues and Summaiya and colleagues also reported a high MDR rate (77.5% and 66.1%, repectively)[20,23]. The antibiogram of Gram-negative isolates showed best susceptibility to colistin (57.4%), followed by trimethoprim\sulfamethoxazole (46.3%) and piperacillin\tazobactam (35.2%). The most resistance rates were to ceftriaxone (96.3%), ceftriaxone\sulbactam (92.6%) and ceftazidime (77.7%). Regarding Gram-positive isolates, trimpethoprime\sulfamethoxazole showed the highest sensitivity rate (92.3%) followed by piperacillin\tazobactam (76.9%). As in the case of Gram-negative pathogens, the highest resistance rate of Gram-positive pathogens was to ceftriaxone and ceftriaxone\sulbactam (84.6%). The high rates of resistance to ceftriaxone and ceftriaxone\sulbactam among all isolates could be related to the random antibiotic abuse in our community[36]. Baidya *et al.*[23] reported that the highest susceptibility rate among Gram-negative isolates was to colistin (100%) followed by piperacillin\tazobactam (47.6%), trimethoprim\sulfamethoxazole was showed only 20% susceptibility against *staphylococcus spp*.

Both Gram-positive and Gram-negative isolates showed at least 50% resistance rate to azithromycin. However, Gram-positive pathogens showed more susceptibility rate than Gram-negative pathogens (38.4% > 11.11). The low or average susceptibility to azithromycin can be explained by the extensive use during the COVID-19 pandemic[13,24,36].

A. baumannii and *P. aeruginosa* have arisen as one of the most problematic pathogens for health care institutions[37,38]. In our study those species were the leading bacterial cause of LRTIs (28% and 25%). In fact, (89.47%) of *A. baumannii* isolates and (64.7%) of *P. aeruginosa* were MDR. On the other hand, 47.36% of *A. baumannii* isolates were susceptible to colistin, 26.3% to meropenem and all isolates were resistant to azithromycin. The results of both Summaiya and colleagues and Baidya and colleagues studies correlated with ours where colistin recorded the highest susceptibility (100%). Nonetheless, in the latter, meropenem showed lower susceptibility rate compared to piperacillin\tazobactam[20,23].

Best susceptibility rate for *P. aeruginosa* was to trimethoprim \sulfamethoxazole (70.6%), followed by a rate of (41.2%) for both colistin and piperacillin\tazobactam, and the same applies to meropenem along with levofloxacin (35.3%) and no isolates showed susceptibility to azithromycin. Colistin also showed 100% susceptibility rate in both of the mentioned studies where trimethoprim\sulfamethoxazole was not included. However, Summaiya and colleagues showed meropenem with a higher susceptibility rate than piperacillin\tazobactam. On the other hand, Baidya and colleagues agreed with our finding where piperacillin\tazobactam showed the second best susceptibility rate after colistin[20,23].

Finally, as with the majority of studies, there may be some potential limitations in ours. This study was conducted in one medical centre which patients from around the city and the countryside attend. Our results of bacterial sensitivity profiles were against only 12 antibiotics which the most common prescribed in the field. However, future studies of multicenter with more antibiotics sensitivity can give a more comprehensive vision. In addition, due to the random sample selection, there was a lack of focus on specific groups of patients, which may give confounding results analyzing of risk factors. Therefore, more focused studies can be conducted for more accurate analysis.

Conclusion

Out of 268 specimens, 150 showed positive growth, with the leading of *A. baumannii* and *P. aeruginosa* which both are very troublesome pathogens. MDR frequency among bacterial pathogens in our study population forces us to apprehend the threat of bacterial infections. Random empirical antibiotic using, such as azithromycin, ceftriaxone and ceftriaxone\sulbactam, can highly lead to increased resistance. As shown above, age, smoking, residency, hypertension, lung chronic diseases and cancer are all risk factors for LRTIs. Thus, further care must be taken after patients with such risk factors and adjustments should be done to those modifiable factors.

Ethical consideration

The study obtained ethical approval from Faculty of pharmacy NO (7/3:4-2-2021).

Patients consent

Informed consent from each patient was obtained after clear explanation about the purpose of the study. Confidentiality and privacy of data were maintained.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Author contribution

All authors have significantly contributed to the investigation, development and writing of this article.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

NA.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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