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ORIGINAL ARTICLE

Susceptibility and Resistance Pattern of Bacterial Isolates in Patients with Pleuro-Pulmonary Infections

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ABSTRACT

Background: One of the biggest threats to global health is the prevalence of antimicrobial resistance (AMR) in respiratory tract infections, which results in significant morbidity and mortality worldwide.This study aimed to decrease the prevalence of bacterial resistance in those suffering from pleuropulmonary infections. **Methods**: This Retrospective cross sectional study was conducted at the Chest Department and Chest ICU at Zagazig University Hospital on 120 patients with pleuropulmonary infections. During this study, Patients with pleuropulmonary infections were considered for analysis and identification of the clinical isolates. **Results:** The most common organisms isolated were gram-ve in 110 cases (79.7%), distributed as k. pneumoniae 58 (42.0%), E.coli 21 (15.2%), P.aeruginosa 20 (14.4%), acinetobacter baumannii 11 (7.9), while gram +ve organisms were isolated in 28 cases (20.2%), distributed as Staph Arouse 12 (8.6%) Coagulase -VE Staph 11 (7.9%), and Staph haemolyticus 5 (3.6%). K.Pneumonia, E. coli and P.aeruginosa were predominantly isolated from sputum 42.9%, 15.2%, 15.2% respectively, K.Pneumonia, Staph Aureus, P.aeruginosa, Acinetobacter baumannii and Staph haemolyticus were predominantly isolated from infected Pleural fluid with 36.0%, 20, 12.0%, 12.0%, respectively. **Conclusions:** the most common organisms that isolated from our cases were k. pneumoniae, E.coli and P.aeruginosa, Acinetobacter baumannii as a gram -ve were Susceptible for Carpenems, Colisten while resistance for Pipracillin, Ciprofloxacin, Levofloxacin and Ceftazidime, Cefipime. On the other hand, the gram + ve isolates were Coagulase negative staph, Staph.aureus and Staph haemolyticus found susceptible for Gentamycin, Vancomycin, Linezolid, while

resistance for Flouroqoinolones and, Erthromycine.

Keywords: Susceptibility; Resistance; Bacterial Isolates; Pleuropulmonary Infections

INTRODUCTION

One of the biggest threats to global health is the prevalence of antimicrobial resistance (AMR) in respiratory tract infections, which results in significant morbidity and mortality worldwide. Comprehending the molecular mechanisms underlying resistance will facilitate the development of innovative approaches to combat these infections, which are becoming more prevalent daily and posing a severe risk to human health **[1]**.These kinds of antibiotic-resistant bacterial strains were uncommon in the past and restricted to nosocomial infections, but they are now quite prevalent **[2]**.Bacteria have a variety of resistance mechanisms. Some are "intrinsic," meaning the cell may use its own genes to withstand antibiotic exposure, and others are "acquired," meaning the cell can acquire new genetic material that gives it new capacities that aid in survival**[3]**. Moreover, a number of variables, such as extensive development, excessive use of antibiotics, excessive reliance on broad-spectrum medications, and a lack of target-oriented antimicrobial treatments, may be contributing to the rise in multidrug-resistant bacteria (MDR) **[2]**. This study aimed to decrease the prevalence of bacterial resistance in those suffering from pleuropulmonary infections.

METHODS

This retrospective cross sectional study was conducted in the inpatient of Chest Department and Chest ICU at Zagazig University Hospital from January 2023 to June 2023.Assuming that all cases met the inclusion and exclusion criteria were included. During the study period (6 months), 20 cases/ month, 120 cases were included as a comprehensive sample.

***Study population*:** All patients with pleuropulmonary infections were admitted to Chest Department and Chest ICU during period of the study. Inclusion criteria were age ≥ 18 years and any patient with pleuropulmonary infections. Exclusion criteria were inappropriate or insufficient sample.

Methods: Data was collected from patient records regarding detailed Full history taking in the form of (Personal demographic data as name, age, occupation, sex, residence, occupation, special habits). Also history of the Present illnessn regarding history of associated co-morbidities, and Previous history of pulmonary TB or malignancy or Family history of any chest disease as pulmonary TB, malignancy, DM , HTN. Full clinical Examination**;** General examination of all other systems rather than chest and Local Examination for signs of all chest disease including that (Inspection, Percussion , Palpation, Auscultation) as well as Plain X ray chest , chest Computed tomography (CT) and chest ultrasound and routine hematological investigation (CBC , ESR and CRP , Renal and liver functions , bleeding and clotting time , Fasting and postprandial blood sugar , Serological analysis).Patients with pleuropulmonary infections were considered for analysis and identification of

the clinical isolates. All possible respiratory samples were collected, including sputum, broncho-alveolar lavage (BAL) fluid, endotracheal aspirate (ETA), a swab from endotracheal intubation, and pleural fluid. All the specimens were collected with mandatory aseptic precautions and sent to the microbiology lab for analysis and identification. The clinical samples were cultured on 5% blood agar and MacConkey agar and incubated overnight (16–18 h) at 37◦ C in an incubator. A direct gram-stained smear was made from all samples and examined under a bright field microscope for preliminary identification. The clinical isolates were identified by conventional microbiological methods.

The antimicrobial susceptibility testing kirby–bauer disk diffusion method: Antimicrobial Susceptibility testing was done by the Kirby–Bauer disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) recommendations 2020 **[4]**. Antibiotics were used, including Amikacin , Cefepime , Colistin , Gentamycin , Ciprofloxacin, Meropenem, Ceftazidime, Ceftriaxone, Imipenem, Cefoxitin, Tigecycline, Trimethoprim/ Sulfame-thoxazole, Piperacillin-Tazobactam, Piperacillin, Amoxicillin/clavulanic acid, Cefuroxime, Ampicillin , and Levofloxacin. The zones of inhibition diameter was noted and interpreted as sensitive or resistant, according to the CLSI guidelines 2020.

ETHICAL CONSIDERATION

After protocol approval by our Local Ethics Committee (IRB # 10863). All patients provided written informed consent to participate in the study. Study protocol conformed to the ethical guidelines of the Declaration of Helsinki (1975) for studies involving humans.

RESULTS

The mean age of the study group was 55.44±15.91years ranging from 18 to 92 years; percent of females were (54.2%) and males were (45.8%) as detailed in **table 1**.

The total number of bacterial isolates were 138 organisms, which is consistent with the number of samples that taken from the patients were some of them had performed more than one specemin .The most common organisms isolated were Gram-ve 110 (79.7%), distributed as Klebsiella Pneumoniae58 (42.0%), Escherichia Coli21(15.2%), Pseudomonas aeruginosa 20 (14.4%), Acinetobacter baumannii 11 (7.9), and Gram+veregardingorganismsisolatedwere28 (20.2%),distributedas Staph Aureus 12(8.6 %), Coagulase-VEStaph11(7.9 %), andStaphhaemolyticus5(3.6%) as shown in **Figure S1**.

The Klbesiella Peumonia, E. coli and Pseudomonas aeruginosa were predominantly isolated from Sputum with a percent 42.9%, 15.2%,15.2% respectively. Klbesiella Peumonia, Staph Aureus, Pseudomonas aeruginosa, Acinetobacter baumannii and Staphylococ haemolyticus were predominantly isolated from infected Pleural fluid with a percent 36.0% , 20 , 12.0% ,12.0 % , respectively. Klbesiella Peumonia, E. coli were predominantly isolated from Broncho alveolar lavage with a percent 60%, 40%, respectively as detailed in **table 2**.

The antibiotics tested against klebesillaPneumoni were found klebesilla Pneumonia organism mainly susceptible forMeroneum, Impenem, Amikacin,

Gentamycin,whilecompletelyresistanceforPipracillin,Ciprofloxacin,and Levofloxacin, Ceftazidime as detailed in **table 3**.While, the antibiotics that testedagainst E.coliwerefoundEcoliorganismmainlysusceptible for Gentamycin, Meroneum, Amikacin, Impenem while completely resistance forCiprofloxacin, Ceftazidime, Cefipime, Pipracillin .

Regarding antibiotics tested against Acinetobacter baumannii werefound Acinetobacter baumanniiorganism mainly susceptible for Colistin, whilemainly resistanceforCiprofloxacin,Meroneum,Impenem,Pipracillin, Pipracillin- tazobactam, Ceftazidime, Trimeth- SULF as shown in **table 4.**

AntibioticstestedagainstPseudomonasAeruginouswerefound mainly susceptible for Colistinwhile mainly resistance forCeftazidime, CefipimeandCiprofloxacin. As shown in **table 5**.

Antibioticstestedagainst Staph Aureus werefoundStaph Aureus organism mainly susceptible for Gentamycin, Trimeth- SULF**,** Linezolid,Cefipime, Nitrofurntine, while mainly resistance for Eyrthromcin, Clinidmycin, Ciprofloxacin**,** Moxifloxacine **,** Ticracyclinasshown in **table 6.**

The antibiotics tested against Coagulase -VE Staph were found Coagulase -VE StaphorganismmainlysusceptibleforGentamycin, Linezolid, Vancomycin,Nitrofurntine while mainly resistance for, Levofloxacin, Eyrthromcin, Ciprofloxacin as detailed in **table 7**.

AntibioticstestedagainstStaphylococcalhaemolyticuswerefoundStaphylococcal haemolyticus organism mainly susceptible for Vancomycin, Gentamycin, Linezolid, Nitrofurantoin, Clindamycinwhile mainly resistance for Ciprofloxacin, Levofloxacin, Moxifloxacine .

Table (1) Frequency and Percentage Distribution of the Studied Patients According to Demographic Data (n.120)

Variables		
Age per years Mean ±SD range	**55.44±15.91 18-92**	
	n.	**%**
Gender		
Males	**55**	**45.8**
Females	**65**	**54.2**

Table (2): DistributionofOrganismIsolateAccordingtoSpecimen(n=138)

Specimenn(%)			**Specimen(n=138)**	
			No.	**%**
Sputum 105(87.5%)	Gram– ve	KlbesiellaPeumonia	45	42.9
		E.coli	16	15.2
		PseudomonusAeruginous	16	15.2
		Acinetobacterbaumannii	8	7.6
	Gram	Coagulase-VEStaph	9	8.5

Specimenn(%)			Specimen(n=138)	
			No.	%
	+ve	StaphAureus	7	6.6
		Staphylococcushaemolyticus"	2	1.9
Infected Pleural Fluid 25(20.8%)	Gram ve	Klbesiella Peumonia	9	36.0
		PseudomonusAeruginous	4	16.0
		Acinetobacterbaumannii	3	12.0
		E.coli	2	8.0
	Gram +ve	Staph Aureus	5	20
		Staphylocochaemolyticus	3	12.0
		Coagulase-VEStaph	1	4.0
Broncho alveolar lavage 5(4.2%)	Gram- ve	KlbesiellaPeumonia	3	60.0
		E.coli	2	40.0
Endotracheal Aspiration 3(2.5%)	Gram- ve	KlbesiellaPeumonia	1	33.3
		E.coli	1	33.3
	Gram +ve	Coagulase-VEStaph	1	33.3

Table (3): ResponseProfileklebsilellaOrganismAgainstDifferentAntibiotics

	Antibioticsensitivityofklebesilla Pneumonian.58			
	Sensitive		Resistance	
	n	%	n	%
Gentamycin	19	32.7	28	48.2
Tobramycin	13	22.4	28	48.2
Amikacin	21	15.2	11	18.9
Vancomycin	3	5.1	2	3.4
Ceftrixon	5	8.6	10	17.2
Cefotaxime	4	6.8	16	27.5
Cefuraxime	3	5.1	14	24.1
Ceftazidime	13	22.4	33	56.8
Cefipime	10	17.2	30	51.7
Colistin	16	27.5	0	.0
Ciprofloxacin	10	17.2	36	62.0
Levofloxacin	9	15.5	33	56.8
Meroneum	25	43.1	25	43.1
Impenem	22	38.1	24	41.3
Minocycline	11	18.9	15	25.8
Ticracyclin	17	29.3	18	31.0
Amoxicillin/Clavlunic Acid	15	25.8	18	31.0
Pipracillin	8	13.7	37	63.7
Pipracillin TAZOBACTAM	14	24.1	32	55.1
AZITHROMYCIN	8	13.7	4	6.8
Trimeth- SULF	12	20.6	26	44.8

Table(4): Response Profile Acinetobacter Baumannii OrganismAgainst Different Antibiotics

	AntibioticsensitivityofAcinetobacterbaumanniin.11			
	Sensitive		Resistance	
	n	%	n	%
Gentamycin	3	27.2	5	45.4
Tobramycin	2	18.1	4	36.3
Amikacin	2	18.1	4	36.3
Cefotaxime	1	9.0	4	36.3
Ceftazidime	3	27.2	6	54.5
Cefipime	2	18.1	5	45.4
Colistin	5	45.4	0	.0
Ciprofloxacin	2	18.1	7	63.6
Levofloxacin	1	9.0	6	54.5
Meroneum	2	18.1	7	63.6
Impenem	2	18.1	7	63.6
Minocycline	2	18.1	4	36.3
Ticracyclin	2	18.1	4	36.3
Amoxicillin/Clavlunic Acid	2	18.1	2	18.1
Pipracillin	2	18.1	7	63.6
Pipracillin TAZOBACTAM	2	18.1	6	54.5
Trimeth- SULF	1	9.0	6	54.5

Table (5): ResponseprofilePseudomonasAeruginosaorganismagainst different antibiotics

	Antibiotic sensitivity of Pseudomonas Aeruginous n.20			
	Sensitive		Resistance	
	n	%	n	%
Gentamycin	5	25.0	8	40.0
Tobramycin	7	35.0	8	40.0
Amikacin	6	37.5	5	25.0
Vancomycin	2	30.0	3	15.0
Cefotaxime	1	5.0	2	12.5
Cefuraxime	2	10.0	3	15.0
Ceftazidime	6	37.5	10	50.0
Cefipime	5	25.0	10	50.0
Colistin	12	60	0	.0
Ciprofloxacin	5	25.0	10	50.0
Levofloxacin	5	25.0	8	40.0
Meroneum	7	35.0	8	40.0
Impenem	8	40.0	7	35.0
Minocycline	1	5.0	3	15.0
Ticracyclin	3	15.0	8	40.0
Amoxicillin/Clavlunic Acid	3	15.0	4	20.0
Pipracillin	6	37.5	9	45.0
pipracillin tazobactam	7	35.0	7	35.0
azithromycin	3	15.0	0	.0
Trimeth- SULF	5	25.0	7	35.0

Table (6): Response Profile Staph Aureus, Organism Against Different Antibiotics

	Antibiotic sensitivity of Staph Aureus n.12			
	Sensitive		Resistance	
	n	%	n	%
Gentamycin	7	58.3	2	16.6
Tobramycin	2	16.6	1	8.3
Amikacin	2	16.6	0	.0
Vancomycin	4	33.3	0	.0
Ceftazidime	4	33.3	1	8.3
Cefipime	5	41.6	1	8.3
Linezolid	5	41.6	0	.0
Ciprofloxacin	3	25.0	4	33.3
Levofloxacin	3	25.0	3	25.0
Moxifloxacine	3	25.0	4	33.3
Nitrofurntine	5	41.6	0	.0
Meroneum	4	33.3	1	8.3
Impenem	4	33.3	1	8.3
Ticracyclin	1	8.3	4	33.3
Amoxicillin/ClavlunicAcid	3	25.0	2	16.6
PipracillinTAZOBACTAM	1	8.3	2	16.6
AZITHROMYCIN	2	16.6	1	8.3
Eyrthromcin	2	16.6	5	41.6
Clinidmycin	3	25.0	5	41.6
Trimeth-SULF	6	50.0	0	0

Table (7): Response profile Coagulase-VES taph Organism Against Different Antibiotics

	Antibiotic sensitivity of Coagulase-VEStaphn.11			
	Sensitive		Resistance	
	n	%	n	%
Gentamycin	8	72.7	1	9.1
Tobramycin	2	18.2	0	.0
Amikacin	2	18.2	1	9.1
Vancomycin	6	54.5	2	18.2
Ceftazidime	1	9.1	3	27.3
Cefipime	2	18.2	3	27.3
Linozlide	7	63.6	0	.0
Ciprofloxacin	3	27.3	7	63.6
Levofloxacin	2	18.2	9	81.8
Moxifloxacine	4	36.4	3	27.3
Nitrofurntine	6	54.5	1	9.1
Meroneum	4	36.4	0	.0
Impenem	3	27.3	0	.0
Ticracyclin	3	27.3	4	36.4

	Antibiotic sensitivity of Coagulase-VEStaphn.11			
	Sensitive		Resistance	
	n	%	n	%
Amoxicillin/Clavlunic Acid	2	18.2	1	9.1
PipracillinTAZOBACTAM	1	9.1	2	18.2
Eyrthromcin	0	.0	8	72.7
Clinidmycin	3	27.3	5	45.5
Trimeth-SULF	4	36.4	3	27.3

DISCUSSION

The results of our study showed that the study group's mean age was 55.44±15.91 years, with a range of 18 to 92 years; 54.2 percent of the group were female and males were 45.8%. Pneumonia was the most common clinical diagnosis in our investigation, accounting for 34.2% of all study cases, or roughly one third, and infective exacerbation COPD in 17.5% of patients, Infective exacerbation bronchial asthma 10 % , Empyaema 20.8 %, lung abscess 8.3 %, Infective exacerbation Bronchetasis 7.5% and cystic fibrosis 1.7% as shown in F**igureS2** . The most common co-morbidity was underlying lung illnesses, which was recorded in 35% of recruited patients Furthermore, 62.5% of the patients reported having previously used antibiotics, and 85% of them were stable. A study by **Michal et al** , demonstrates how to analyze the risk factors for antibiotic resistance model by using prior antibiotic use as binary indicators and selecting cut-off dates that can be anywhere from a few days to a year prior to the bacterial sample under study. Antibiotic use cut-offs that are applied close to the result (such as 30 or 90 days) may cause patients who used antibiotics prior to the cut-offs to have their risk significantly underestimated. On the other hand, patients who have recently taken antibiotics may have their relationship between prior use and resistance underestimated if distant cut-offs, such as one year, are employed **[5]**.As regard frequency and percentage distribution of respiratory pathogens in studied samples , the most common organisms isolated were gram-ve in 110 cases (79.7%), distributed as klebsiella pneumoniae 58 (42.0%), Escherichia Coli 21 (15.2%), Pseudomonas aeruginosa 20 (14.4%), Klbesiella Peumonia, E. coli and Pseudomonas aeruginosa were predominantly isolated from sputum with a percent 42.9%,15.2%,15.2% respectively .

Klbesiella Peumonia, Staph Aureus, Pseudomonas aeruginosa, Acinetobacter baumannii and Staphylococ haemolyticus were predominantly isolated from infected Pleural fluid with a percent 36.0% , 20 , 12.0% ,12.0 % , respectively. Klbesiella Peumonia, E. coli were predominantly isolated from Broncho alveolar lavage with a percent 60%, 40%,respectively. Our results run parallel with study from **Debnath et al**. were klebsiella pneumoniae (52.16%) was the most common isolates in the sample **[6]** . On the other hand Gram + veregarding organisms isolatedwere28 (20.2%),distributedas Staph Aureus 12(8.6 %), Coagulase-VEStaph11(7.9 %),andStaphhaemolyticus5(3.6%).**Samad et al.** reported that the most frequent gram-negative isolate was P. aeruginosa (32.2%) followed by Klebsiella (16.5%) and E. coli (12.5%) **[7].** As regard response profile,

antibiotics tested against klebesilla Pneumoni found that it is mainly susceptible for Meroneum, Impenem, Amikacin, Gentamycin, while complete resistance was reported for Pipracillin, Ciprofloxacin, Levofloxacin and Ceftazidime.

A study from **Mączyńska et al.** investigation on klebsiella isolates reveals total resistance to cephalosporins, aminopenicillins, penicillins with β-lactamase inhibitors, quinolones, and most notably tigecycline and tobramycin. The tested Klebsiella isolates were more sensitive to the remaining aminoglycosides (strains sensitive to amikacin, 66%; strains sensitive to gentamycin, 33%). Variations in the absorption of carbapenems (imipenem, meropenem) were observed **[8]**. Antibiotics that tested against E.Coli found that it is susceptible for Gentamycin, Amikacin, Meroneum, Impenem while complete resistance was reported for Ciprofloxacin, Ceftazidime, Cefipime and Pipracillin. E. coli. Isolates in study according to **Guclu et al**. was mainly sensitive to Colistin, Tigecycline while resistance to Cefuroxime Ceftriaxone, Levofloxacin, Ciprofloxacin, and Imipenem and Meropenem resistance rates were 4.3% and 5.1% **[9].** Antibiotics tested against Acinetobacter baumannii found that it is susceptible for Colistin while complete resistance was reported for Ciprofloxacin, Meroneum, Impenem, Pipracillin, Pipracillin-tazobactam, Ceftazidime, Trimeth- SULF. A study by **Aylin et al** show Only 11.8%, 12.4%, 13.6%, and 37.9% from Acinetobacter baumannii were susceptible to Levofloxacin, Imipenem, Amikacin, and Doxycycline, respectively. All MDR isolates were entirely responsive to only last resort antibiotics, i.e., Colistin Sulfate and Polymyxin B **[10]**. Antibiotics tested against Pseudomonas Aeruginosa found susceptible for Colistin while complete resistance was reported for Ceftazidime, Cefipime and Ciprofloxacin. Our results regarding P.Aeruginosa was compatible with a study from **Santella et al.** were Colistin was the medicine with the lowest resistance rates. Ciprofloxacin had the highest resistance rates compared to the others. Ceftazidime exhibited higher resistance rates (44.4%) than Cefepime (34.3%). Colistin was found to be 92.5% effective against P. Aeruginosa. Intermediate. P. Aeruginosa isolates were susceptible to Piperacillin, Piperacillin/tazobactam, Cefepime, Ceftazidime, Imipenem, Meropenem, and Aztreonam at rates of 10.2%, 5.1%, 6.1%, 4.1%, 3.2%, 8.3%, and 42.2%, respectively **[11]**. Antibiotics tested against Staph Aureus found that it is susceptible for Gentamycin, Trimeth- sulf, Linezolid,Cefipime, Nitrofurntine while complete resistance was reported for Eyrthromcin, Clinidmycin, Ciprofloxacin, Moxifloxacine and Ticracyclin. Our findings regarding staph aureus susceptibility run in line with **Rossato et al.** the highest resistance rates among SA isolates were found for Erythromycin (74.2%), Ciprofloxacin (64.5%), and Clindamycin (46.1%). Furthermore, 2.3% of the isolates displayed intermediate resistance to Erythromycin and 1.4% to Clindamycin, while lower resistance rates were detected against Gentamicin (28.6%), Tetracycline (14.3%), and Trimethoprim-Sulfamethoxazole (13.8%) **[12]**. Antibiotics tested against Coagulase -VE Staph (CoNS) found that it is susceptible for Gentamycin, Vancomycin, Linezolid, Nitrofurntine while complete resistance was reported for Ciprofloxacin, Levofloxacin and Eyrthromcin.

Susceptibility patterns of CoNS by according to **Al Tayyar et al.** shown sensitivity to Vancomycin (100%), Linozolid (98.2%), Rifampin (95.5%), and Nitrofurantoin (92.8%). The lowest sensitivity rates were seen with Ampicillin (1.8%), Penicillin (2.7%), Ceftriaxon (22%), Cefazolin (22.4%), Amoxicillin-clavulanic acid (24.2%), and Erythromycin (24.2%) **[13]**. Antibiotics tested against Staphylocochaemolyticus found that it is susceptible for Vancomycin, Gentamycin, Linezolid, Nitrofurntine and Clindamycin while complete resistance was reported for Ciprofloxacin, Levofloxacin and Moxifloxacine.

CONCLUSIONS

In our study the most common organisms that isolated from our cases were klebsiella pneumoniae, escherichia coli and Pseudomonas aeruginosa, Acinetobacter baumannii as a gram negative were susceptible mainly for Carpenems, Colisten while resistance for Pipracillin, Ciprofloxacin, Levofloxacin and Ceftazidime, Cefipime. On the other hand, the gram + ve isolates were Coagulase negative Staph , Staph Aureus and Staph haemolyticus found susceptible for Gentamycin, Vancomycin, Linezolid, while resistance for Flouroqoinolones and , Erthromycine.

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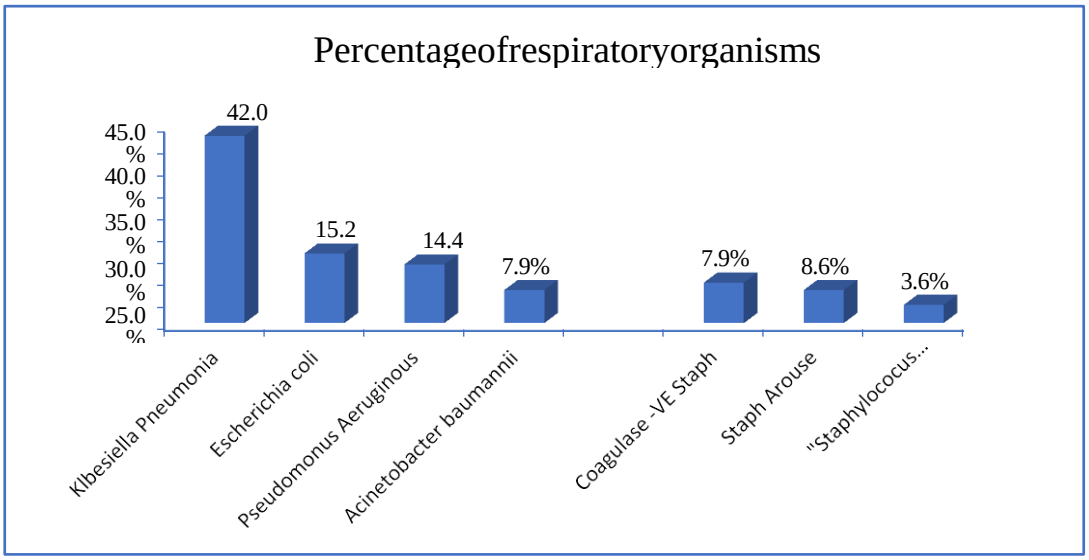

Figure (S1):Percentageofrespiratorypathogensinstudiedsamples

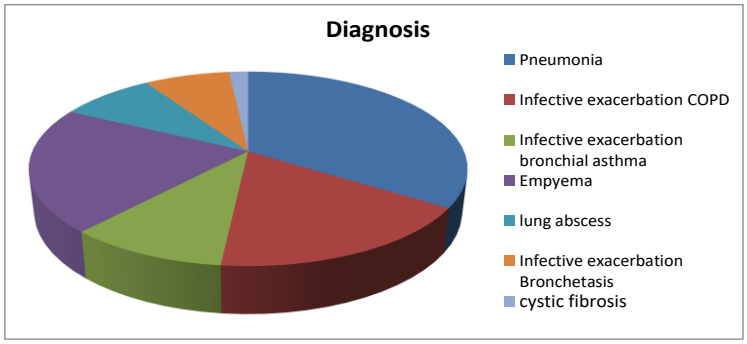

Figure (S2): Pie chart showing distribution of studied cases regarding to diagnosis

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