Indian Journal of Microbiology Research 2020;7(3):293–298

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Indian Journal of Microbiology Research

Journal homepage: www.ipinnovative.com

Original Research Article

Aerobic bacteriological profile of acute exacerbations of chronic obstructive pulmonary disease in a tertiary care hospital

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ARTICLE INFO

Article history:
Received 30-04-2020
Accepted 08-08-2020
Available online 28-10-2020

Keywords:
AECOPD
Bacteriological
Gram positive bacteria
Gram negative bacteria

ABSTRACT

COPD is a major cause of morbidity and one of the predominant causes of the death across the world, characterised by a worsening in the patient's respiratory symptoms which is beyond normal day-to-day variations and eventually leads to a change in the medication. Causative agents for the exacerbation includes factors such as viruses, bacteria and common pollutants.

Materials and Methods: This was a retrospective study conducted from sputum samples received from 551 diagnosed cases of AECOPD to the department of microbiology KIMS Hubli.

Result: Out of 551 patient's sputum samples, 335(60.79%) were Males and 216 (39.20%) were females. The total number of culture positive isolates were 51.17%. Among the 282 culture positive isolates, 280 were Mono-microbial (99.3%) and 2 were Polymicrobial (0.7%). Among 282 isolates, Gram Negative Bacilli were 263 (93.26%) and Gram Positive Cocci were 19 (6.74%) Among the total isolates *Klebsiella pneumoniae* 116 (41.13%) was the predominant isolate followed by *Escherichia coli* 63 (22.34%), *Pseudomonas aeruginosa* 28(9.93%), *Citrobacter species* 26 (9.22%), NFGNB 25 (8.87%), *Enterobacter species* 5 (1.79%), *Staphylococcus aureus* 16 (5.67%), CONS 2(0.7%) and *Streptococcus pneumoniae* 1(0.35%). 51(43.96%) of the *Klebsiella pneumoniae* isolates were found to be ESBL producers. In case of gram positive organisms, 2(12.5%) were methicillin resistant.

Conclusion: This study shows that *Klebsiella pneumoniae* and *Escherichia coli* are the commonest organisms associated with acute exacerbation of COPD. A high rate of ESBL producers was observed.

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disease state characterised by airflow limitation and is irreversible, this includes chronic bronchitis and emphysema. [1]

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is characterised by a worsening in the patient's respiratory symptoms which is beyond normal day-to-day variations and eventually leads to a change in the medication. [1]

COPD is a major cause of morbidity and one of the predominant causes of the death across the world. [2] According to the World Health Organisation (WHO) estimates in 2004, currently 64 million people have this disease and a whopping 3 million people have died of COPD. [3] By 2030 COPD will become the third leading cause of death worldwide as predicted by WHO. [3] A significant percentage of COPD mortality is contributed by India with about 556,000 out of a world total of 2,748,000 annually accounting to >20%, which is estimated to be amongst the highest in the world. [4] Majority of the information available pertaining to COPD prevalence, morbidity and mortality is mainly from high-income countries. [3]

The principal cause of COPD is tobacco smoke which includes second-hand or passive exposure, other risk factors include indoor air pollution like solid fuel used for cooking and heating; outdoor air pollution, occupational dusts and chemicals like vapours, irritants, fumes and also frequent

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https://doi.org/10.18231/j.ijmr.2020.053

lower respiratory tract infections during childhood.[5]

Major pathogenic factor in exacerbations are infectious agents, other contributing factors include air pollution, low temperature and interruption of regular treatment.[6] As per estimations bacterial infections are deemed to be responsible for more than 40% of all exacerbations in India.[7] In AECOPD cases due to infection, three classes of pathogens have been found: respiratory viruses, aerobic gram-positive and gram-negative bacteria, and atypical bacteria.[8] Current data on bacteriology related to AECOPD are mainly obtained from the western countries.[6] The spectrum of organisms in India might be different from those of other countries or regions making it crucial to examine the bacteriology responsible for AECOPD, which is important for the choice of empirical antibiotic treatment.[6] More than 90% of patients with AECOPD receive antibiotic therapy.[2] From time to time bacterial flora of AECOPD keeps changing and depending upon the local bacterial prevalence and resistance pattern the antibiotic is chosen.[9]

With better selection of antibiotic for empirical therapy the numbers of failure cases recorded with empirical treatment during AECOPD are reduced.[10] With proper control and prevention of these exacerbations the relentless progress of this disease can be halted and also significantly reduces the mortality and morbidity.[11] The present study was undertaken to know about the aerobic bacteriological profile and the antibiotic sensitivity pattern of AECOPD cases in our hospital.

2. Materials and Methods

This was a retrospective study based on review of data from patients who were admitted with acute exacerbation of COPD to the Karnataka Institute of Medical Science (K.I.M.S) Hubli, over a period of 1 year from January 2019 to December 2019**.** Microbiological profile of the aerobic isolates and its antibiotic susceptibility pattern was collected from the maintained records in the department of microbiology and analysis was done.

2.1. Culture methods

The samples were processed as per standard microbiological methods. Sputum samples were subjected to Gram's stain and aerobic bacterial culture by inoculation on various culture media like blood agar, chocolate agar, MacConkey agar. The isolates were identified by relevant biochemical tests. The isolates were subjected to antibiotic susceptibility testing on Mueller-Hinton agar plates by Kirby-Bauer disc diffusion method, as per CLSI guidelines. Screening for Methicillin Resistant *Staphylococcus Aureus* (MRSA) was done using cefoxitin (30 μg) disc. Resistance to ceftazidime (30 μg) disk was used as a screening method for detection of Extended Spectrum Beta Lactamase (ESBL) confirmed by double disk synergy test.

3. Results

A total of 551 sputum samples from inpatients of Medicine Department, K.I.M.S, Hubli, were sent to Department of Microbiology, K.I.M.S Hubli, for aerobic bacterial culture and antibiotic sensitivity testing. Out of 551 patient's sputum samples, 335(60.79%) were Males and 216 (39.20%) were Female patients. Among the 551 samples, total number of culture positive isolates were 282 (51.17%). The highest number of patients were in the age group of 41-50 years showing 129 (23.41%) number of positive isolates and the other age wise distribution is as shown in the Table 1. Among the 282 positive isolates, 280 samples showed Monomicrobial growth (99.3%) and 2 samples showed Polymicrobial growth (0.7%). Out of 282 isolates, Gram Negative Bacilli were 263 (93.26%) and Gram Positive Cocci were 19 (6.74%). *Klebsiella pneumoniae* 116 (41.13%) was the predominant Gram Negative Bacilli and *Staphylococcus aureus* 16 (5.67%) was the predominant Gram positive cocci followed by other organisms as shown in the Table 2.

3.1. Antibiotic susceptibility pattern

In this study 51(43.96%) of the *Klebsiella pneumoniae* isolates were found to be ESBL producers. Of the Klebsiella species, all are sensitive to amikacin (100%) and majority of the isolates sensitive to imipenem 111 (99.13%), piperacillin-tazobactam 110 (94.82%), levofloxacin 93 (80.17%), cefipime 82 (70.69%), ceftriaxone 76 (65.51%), cefazolin 73(62.92%). Majority were resistant to ampicillin 111(95.68%), followed by ciprofloxacin 83(71.56%) and amoxycillin clavulanic acid 44(37.93%).

Of the *Escherichia coli* isolates 45 (71.43%) were ESBL producers. 60(95.24%) were resistant to ampicillin, 37(58.74%) were resistant to ceftriaxone, 36(57.15%) were resistant to amoxycillin clavulanic acid, 35(55.55%) were resistant to levofloxacin, and 33(52.38%) were resistant to cefipime.

Among *pseudomonas aeruginosa* isolates all were sensitive to aztreonam (100%), 27(96.43%) isolates were sensitive to gentamicin, 26 (92.85%) were sensitive to levofloxacin, 23 (82.14%) were sensitive to piperacillin tazobactam. Higher rate of resistance were seen for ciprofloxacin 19 (67.86%). 18 (64.29%) isolates were resistant to imipenem and ceftazidime, 17 (64.17%) isolates were resistant to cefipime.

Of the *Citrobacter species* 13 (50%) were ESBL producer. 24 (94.30%) isolates were sensitive to gentamicin and piperacillin tazobactam. 23 (88.46%) were sensitive to amikacin, 22 (84.61%) were sensitive to levofloxacin, 21 (80.76%) were sensitive to ceftriaxone, 20 (70.92%), 15(57.69%) isolates were sensitive to cefazolin,

ciprofloxacin and cefipime .13 (50%) were sensitive to amoxicillin and clavulanic acid.

In case of NFGNB, all the isolates were sensitive to imipenem and amikacin. 24(96%) were sensitive to piperacillin tazobactam. 13 (52%) were sensitive to levofloxacin. 17 (68%) were resistant to amoxicillin clavulanic acid, 14(56%) were resistant to cefazolin 13(52%) were resistant to ciprofloxacin, ceftriaxone, ceftazidime and cefipime.

In case of gram positive organisms, 2(12.5%) were methicillin resistant.

The antibiotic sensitivity pattern for GNB is shown in the Table 3.

100% of *staphylococcus aureus* were sensitive to vancomycin. 14(87.5%) isolates were sensitive to clindamycin and levofloxacin. 13(81.25%) isolates were sensitive to linezolid and ciprofloxacin. 75% isolates were sensitive to erythromycin. 15(93.75%) were resistant to cotrimoxazole. 13(81.25%) were resistant to azithromycin.

CONS all the isolates were sensitive to linezolid, erythromycin, clindamycin, levofloxacin. 50% isolates were resistant to azithromycin and ciprofloxacin.

The sensitivity pattern for gram positive cocci is shown in the Table 4.

Table 1: Showing age-wise distribution

Age in years	Number(n)	Percentage(%)
11-20	33	5.98
21-30	56	10.16
31-40	90	16.33
41-50	129	23.41
51-60	108	19.6
61-70	95	17.24
71-80	21	3.84
>80	19	3.44

Table 2: Showing distribution of organism

Organism wise distribution	Number (n)	Percentage%
Klebsiella pneumoniae	116	41.13
Escherichia coli	63	22.34
Pseudomonas aeruginosa	28	9.93
Citrobacter species	26	9.22
Non fermenting GNB	25	8.87
Enterobacter species	5	1.79
Staphylococcus aureus	16	5.67
Coagulase Negative *staphylococcus*	2	0.7
Streptococcus pneumonia	1	0.35
Total Isolates	282	100

4. Discussion

COPD is a major cause of morbidity and mortality throughout the world. Early induction of empirical antibiotics can improve the outcome and reduce mortality.

Since culture techniques are time consuming, it is better to know the pattern of bacterial flora and their sensitivity in a particular geographic area.

The result of this study provides an overview of current microbiology and aerobic bacteriological profile of northern Karnataka.

Samples were collected from 551 patients with COPD. Among them 281(51.17%) showed bacterial growth. Arora et al[12] have obtained growth in 72% cases, whereas Dalvi et al[13] obtained growth in 57% of samples that is corresponding with our study. A lower frequency of isolation has been reported in a few other studies which are 13.33% and 41% (Shahanawaz et al, 2003),[14] (Narayangowda et al, 2015).[15]

Among culture positive case majority were monomicrobial growth(99.3), remaining 0.7% showed polymicrobial growth.

4.1. Age and gender distribution

It was observed that acute exacerbation of COPD is prevalent in 41-70 years of age. However among them 40-50 year of age group constitute 23.41%, 51-60 years constitute 19.6%,61-70 years constitute 17.24%.

AECOPD was common in advanced age group as respiratory tract is more susceptible due to impairment of immunological defence mechanisms, associated co morbid illness, increased duration of seasonal variation and tobacco smoking.[12]

Male(60.79%) predominance was seen in this study population compared to female (39.21%). In our country, Males are more exposed to outside environment because of their more mobility compared to females. Moreover smoking habits are more pronounced in male that constitute one of the predisposing factor for development of COPD.

Smoking and air pollution are responsible for decreased muco ciliary clearance and innate immunity.[16] It leads to increased bacterial colonisation that can give rise to increased airway inflammation and thus exacerbation. A prospective study was made by Madhavi et al,[17] who had 79% males and 21% females.

4.2. Bacteriological profiles and sensitivity pattern

Growth of pathogenic organism was obtained in was obtained in 51.17% of sputum samples. Culture positivity depends on nature of sputum, transportation time and number of organisms present in the sample.

Gram positive and Gram negative organism was isolated in 7% and 93% of study population.

Table 3: Showing antibiotic sensitivity pattern of gram negative bacilli

Antibiotic	*Klebsiella pneumoniae*				*Escherichia coli*				*Citrobacter spp*				Enterobacter spp				NFGNB			
	S	S%	R	R%	S	S%	R	R%	S	S%	R	R%	S	S%	R	%	S	S%	R	R%
CZ	73	62.93	43	37.07	35	55.55	28	44.45	15	57.69	11	42.30	3	60	2	40	11	44	14	56
PTZ	110	94.82	6	5.18	56	88.88	7	11.12	24	92.30	2	7.69	5	100		-	24	96	1	4
IPM	111	99.13	5	0.87	60	95.23	3	4.77	20	76.92	6	23.07	3	60	2	40	25	100		-
AK	116	100	0		62	98.41	1	1.59	23	88.46	3	11.54	4	80	1	20	25	100		-
LE	93	80.17	23	19.83	28	44.45	35	55.55	22	84.61	4	15.38	4	80	1	20	13	52	12	48
CIP	33	28.44	83	71.56	35	55.55	28	44.45	11	42.30	15	57.69	4	80	1	20	12	48	13	52
CTR	76	65.51	40	34.49	26	41.26	37	58.74	21	80.76	5	19.23	4	80	1	20	12	48	13	52
CPM	82	70.69	34	29.31	30	47.62	33	52.38	15	57.69	11	42.30	3	60	2	40	12	48	13	52
AMC	44	37.93	72	62.07	27	42.38	36	57.15	13	50	13	50	3	60	2	40	8	32	17	68
CAZ	65	56.03	51	43.96	18	28.57	45	71.43	13	50	13	50	2	40	3	60	12	48	13	52

CZ = Cefazolin, PTZ = Piperacillin tazobactam, IPM = Imipenem, AK = Amikacin, LE = Levofloxacin, CIP = Ciprofloxacin, CTR = Ceftriaxone, CPM= Cefipime, AMC = Amoxicillin clavulanic acid, CAZ = Ceftazidime

Table 4: Showing antibiotic sensitivity pattern of *pseudomonas aeruginosa*

Antibiotics	Sensitive (Percentage %)	Resistant (Percentage %)
AMP	3(10.71)	25(89.29)
PI	14(50)	14(50)
AMC	20(71.43)	8(28.57)
PTZ	23(82.14)	5(17.86)
CFM	11(39.29)	17(60.71)
CPM	11(39.29)	17(60.71)
CTX	13(46.43)	15(53.57)
CX	10(35.71)	18(64.29)
CAZ	10(35.71)	18(64.29)
CPZ	3(10.71)	25(89.29)
GEN	27(96.43)	1(3.57)
AK	25(89.29)	3(10.71)
OF	12(42.86)	16(57.14)

AMP = Ampicillin, PI = Piperacillin, AMC = Amoxicillin clavulanic acid, PTZ= Piperacillin Tazobactam, CFM = Cefixime, CPM = Cefipime, CTX = ceftriaxone, CX = cefoxitin, CAZ = Ceftazidime, CPZ = Cefoperazone, GEN = Gentamicin, Ak = Amikacin, OF = Ofloxacin

Table 5: Showing antibiotic sensitivity pattern gram positive organisms

Antibiotics	*Staphylococcus aureus*		Coagulase Negative Staphylococcus	
		R		R
AZM	3(18.75)	13(81.25)	1(50)	1(50)
CD	14(87.5)	2(12.5)	100	0
E	12(75)	4(25)	100	0
COT	1(6.25)	15(93.75)	-	-
VA	16(100)	0	-	-
LZ	13(81.25)	3(18.75)	100	0
CIP	13(81.25)	3(18.75)	1(50)	1(50)
LE	14(87.5)	2(12.5)	100	0
CX	14(87.5)	2(12.5)		0
AMC	13(81.25)	3(18.75)		

AZM = Azithromycin, CD = Clindamycin, E = Erythromycin, COT = Cotrimoxazole, VA = Vancomycin, LZ = Linazolid, CIP = Ciprofloxacin, LE = Levofloxacin, CX = Cefoxitin, AMC = Amoxicillin clavulanic acid

Among GNB *Klebsiella pneumoniae* 116(41.13%) was the predominant organism followed by *Escherichia coli* 63(22.34%), *Pseudomonas aeruginosa* 28(9.93%), *Citrobacter species* 26(9.22%), NFGNB 25(8.87%), Enterobacter 5(1.79%), and among Gram positive organisms *Staphylococcus aureus* 16(5.67%) was the predominant isolate followed by CONS 2(0.7%), *Streptococcus pneumoniae* 1(0.35%). The bacterial isolates depends on various factors like prevalence of bacteria in the hospital environment, in the community, antibiotic prophylaxis and severity of exacerbation. This finding is contrary to other studies reported by Seshagiri Rao, et al.[18] in 2017 who had found *Streptococcus pneumoniae* (28%) while Anand Patel, et al.[18] had found *Klebsiella pneumoniae* (59%) as commonest isolate. But otherwise their microbial profile is almost similar to the bacteriological profile noted in our study. In Kaliparambil Sugathan Roshni et al.[19] gram negative bacteria were isolated commonly in COPD patients. In contrary in a study by Rao D S,[20] *Streptococcus pneumoniae* was the most common organism isolated.

As regards the sensitivity rates of antibiotics regardless of the type of organism, it was found that the most sensitive antibiotic in the whole study was imipenem, amikacin and piperacillin tazobactam and resistance rate was high in case of ciprofloxacin and amoxicillin clavulanic acid. Erkan et al,[21] noted the poor efficacy of penicillin, ampicillin, amoxicillin–clavulanic acid, tetracycline, and erythromycin against most prevalent respiratory pathogens in acute exacerbation of COPD. Their results agree with the low sensitivity rates of these antibiotics in this study.

In this study 51(43.96%) of the *Klebsiella pneumoniae* isolates and 45(71.43%) *Escherichia coli* isolates were found to be ESBL producers and 12.5% of *Staphylococcus aureus* species isolated were methicillin resistant. Erkan et al[21] noted the poor efficacy of penicillin, ampicillin, amoxicillin–clavulanic acid, tetracycline, and erythromycin against most prevalent respiratory pathogens in acute exacerbation of COPD. Their results agree with the low sensitivity rates of these antibiotics in this study (5.5% for amoxicillin–clavulanic acid, 3.6% for erythromycin, 2.75% for tetracycline, 1.8% for penicillin, and 0.9% for ampicillin).

5. Conclusion

This study shows that *Klebsiella pneumoniae* and *Escherichia coli* are the predominant organisms associated with AECOPD. Overall the gram negative bacilli sensitive to most of the commonly used antibiotics. High rates of ESBL producers was also observed. Studies like this will help in better selection of antibiotics for empirical therapy and prevent the mortality and morbidity due to acute exacerbation of chronic obstructive disease.

6. Source of Funding

None.

7. Conflict of Interest

None.

Acknowledgements

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

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Cite this article: Mythri B A, Patil AB, Gana P, Prathibha J. Aerobic bacteriological profile of acute exacerbations of chronic obstructive pulmonary disease in a tertiary care hospital. *Indian J Microbiol Res* 2020;7(3):293-298.