

**Research Article****DRUG USE PATTERN IN MANAGEMENT OF RESPIRATORY EMERGENCIES IN MICU-A PROSPECTIVE OBSERVATIONAL STUDY**Sina Zare<sup>1\*</sup>, Miriam L Hnamte<sup>1</sup>, Merphin Philip Thomas<sup>1</sup>, Rajeswari.R<sup>2</sup>, Susheela Shekar<sup>3</sup>, Teena Nazeem<sup>4</sup><sup>1</sup> Pharm-D, Krupanidhi College of Pharmacy, Bangalore, Karnataka, 560035<sup>2</sup>Associate Professor, <sup>4</sup>Assistant Professor, Krupanidhi College of pharmacy, Bangalore, Karnataka, 560035<sup>3</sup>HOD of MICU, MVJ Medical College and Research Hospital, Hoskote, Bangalore.

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**ABSTRACT**

**BACKGROUND:** Drug utilization studies are useful tool to facilitate rational prescribing of drugs. The objective of the study is to analyze drug utilization in respiratory emergencies using WHO Prescribing Indicators, in Medical Intensive Care Unit. **PURPOSE:** To study the prescribing pattern of drugs used to treat respiratory emergencies in Medical. Intensive Care Unit (MICU) department in MVJ Medical College and Research Hospital, Hoskote. **METHODOLOGY:** The study was conducted on gaining approval for the proposed protocol from the Institutional Ethical Committee (IEC). Informed Consent (IC) was taken before commencing the study. Basic demographics, medication related details were collected using the Case Report Form (CRF). "Respiratory Distress Observation Scale" (RDOS) was used to evaluate respiratory and heart rates. WHO Prescription indicators was used to study the number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic, percentage of encounters with an injection, percentage of drugs prescribed from the essential drug list. **RESULT:** Out of the 80 patients enrolled in the study, 50 of the patients were above or equal to the age of 65, and 30 were under the age of 65. Total number of drugs prescribed to the patients was 668, out of which 324 was antibiotics, 112 were corticosteroids, 179 was Beta-2 Adrenergic Agonists & Anticholinergics and there was 53 Methylxanthines. Average drug per encounter was found to be 8.3 per encounter whereas the percentage of encounters with antibiotics was found to be 52% per encounter; which are both higher than the WHO recommendations. Out of the 80 patients who were enrolled in the study, 59 were chronic smokers versus the 21 nonsmokers. The most prevalent cause of ICU admission was COPD as 47 of the total cases were suffering from the illness itself or along with co morbid conditions (such as HTN, CKD etc). Based on the RDOS 74 patients had a rating higher than 3 at the time of admission and 77 had a rating lesser than 3 at the time of discharge from the ICU. Few to none of the cases were sent for bacterial culture sensitivity test and empirical therapy was initiated in almost all the cases. **CONCLUSION:** The management of respiratory emergencies lies on use of antibiotics, corticosteroids, nebulizers and Methylxanthines. Use of IV corticosteroids did not show any difference in the treatment outcome of the Regimens; Theophylline and Doxophylline comparison showed no significant difference in the measurement of therapeutic outcome. The average drug encounter per prescription was found to be higher than the ideal range of WHO recommendations. This along with the observation on rational use of antibiotics and use of IV route of administration which were both much higher than the ideal range recommended by WHO, suggests a change in formulating therapeutic regimens. We conclude that irrational of antibiotics and corticosteroids will only result in increase of cost of the treatment as well as the duration of therapy along with increasing the chances of patients developing resistance to antibiotic therapy. Also use of IV steroids highly affects the patient's immune system thereby enhancing the chances of further infection and relapse. Initiation of empirical therapy is advised only till the culture sensitivity tests are done. However further large scale research is needed to confirm this conclusion.

**Keywords:** Respiratory emergencies, RDOS, Drug use pattern, WHO prescribing indicators

## Introduction

Drug utilization research was defined by WHO in 1977 as 'the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.<sup>1</sup> Use of antibiotics and glucocorticosteroids is increasing in hospital wards around the globe, giving rise to the spread of multi drug resistance.<sup>2</sup> We felt the need to conduct an observational study in which the drug prescription patterns would be analyzed and compared with WHO guidelines.<sup>1,9,10</sup> In our study we observed that irrational use of antibiotics is widely practiced which could be the main reason for multi drug resistance epidemic.<sup>2,5</sup> Also, use of steroids such as Hydrocortizone, showed no significant difference in the outcome of the therapy as compared with the patients who did not receive steroids in their therapeutic regimen. Since steroids suppress the immune system, unnecessary use of steroids could result in increased susceptibility of patients to drug resistance in addition to the increased cost of the treatment.<sup>11</sup> Implementation of our findings in hospital wards and clinical practices will help in improving health care system and promote rational drug use, reduce health care cost, reduce morbidity and mortality rates as well as reducing multi drug resistance.<sup>21</sup> However, further studies with larger populations are needed to confirm our findings.

## METHODOLOGY

*Study Design and Human Ethical Clearance:* A prospective, observational study was conducted for duration of 6 months from October 2015 to March 2016 in accordance with the ethical principles of declaration of Helsinki and principles of current Good Clinical Practice (GCP).

*Approval of study protocol:* The study protocol was approved by the Institutional Ethical Committee (IEC) with ethical clearance number: Central Research/MVJ MC& RH/08/2016.

### Study Population

Study Site: The study was conducted at Medical Intensive Care Unit, MVJ Medical College and Research Hospital, Hoskote, Bangalore, South India.

### Inclusion Criteria

All patients above 18 years of age of both genders with any diagnosis or signs of respiratory emergencies.

### Exclusion criteria

The patients unwilling to participate in the study

Patients who were administered with Neuromuscular blocking agents

### Method:

1. All patients who met the inclusion criteria were enrolled in the study after taking Informed Consent (IC) before commencing the study.

2. The basic demographics, medication related details and laboratory investigation values were collected by the researchers personally using the Case Report Form (CRF).

3. All the medication orders were observed and evaluated for legibility, the use of Generic names, route of administration, dose, frequency of administration, and allergic status in medication chart using Micromedex drug database and other standard references.

4. All the cases included in the study were evaluated with "Respiratory Distress Observation Scale" (RDOS). It was measured by counting respiratory and heart rates for one minute; as well as other physical examinations. Auscultation was done if found necessary. A RDOS score  $\geq 3$  signifies a patient's need for palliation of respiratory distress and RDOS score  $< 3$  indicates that the patient is in respiratory comfort.

5. WHO Prescription indicators was used to study the number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic, percentage of encounters with an

6. injection, percentage of drugs prescribed from the essential drug list (National List of Essential Medicines).

The report was analyzed using appropriate statistical method and reported to concerned department.

### Result:

#### Demographic data

*A total of 80 patients were enrolled out of which majority of the population enrolled were found to*

be the elderly, which consisted of 50 of the patients who were above or equal to the age of 65, and 30 being under the age of 65.

The detailed demographic data is illustrated in Table 1.

Table1: Demographic data (N=80)

Gender	Percentage
Male	70
Female	24
Age	
Less than 65	37
Equal or more than 65	63
Social habit	
Smoker	74
Non smoker	26

**PREVALANCE OF DISEASE**

A total of 80 patients from the Medicine Intensive care Unit (MICU) ward were enrolled during the study period. There were 34 patients suffering from COPD 13 patients with COPD along with co-morbid conditions, 14 with bronchitis and 19 from other respiratory diseases.

**RDOS**

The patients who were enrolled in the study were rated based on the RDOS on daily basis, out of which on the day of admission 74 (93%) were above rating of 3.5 (6%) were rated below the rating of 3 and the RDOS was not applicable on only one of the patients (1%), and at the time of discharge 96% of the patients had a score of more than 3 on RDOS.

Table 2: RDOS (N=80)

RDOS	N=80	Percentage %
>3	74	93
<3	5	6
Not applicable	1	1
RDOS on discharge	N=80	Percentage %
<3	77	96
>3	00	0
	03	4

**ASSESSMENT OF DRUGS PRESCRIBED**

The medications given to manage the respiratory emergencies were observed and categorized in the following table 3.

Table3: Drugs prescribed (N=668)

Drug Class	Numbers	Percentage %
Antibiotics	324	48.5
Corticosteroids	112	16.8
Beta-2 Adrenergic Agonists + Anticholinergics	179	26.8
Methylxanthines	53	8

Table 4: ASSESSMENT OF WHO INDICATORS

Prescribing indicators	Total drugs/Encounter	Average/Percentage	Ideal range
Average number of drugs per encounter	668/80	8.3perencounter	1.6-1.8
Percentage of encounters with antibiotics	348/668	52%	(20.0-26.8%)
Percentage of encounters with IV inj	232/668	35%	(13.4%-24.1%)
Percentage of drugs prescribed by generic	638/668	4.5 %	100 %

### ASSESSMENT OF OUTCOME MICROBIOLOGICAL TESTS ASSESSMENT

Assessment of laboratory investigations for the culture sensitivity tests done on patients prior or during antimicrobial therapy was assessed and the result is shown in the following table 5.

Table 5: Microbiological test assessment (N=80)

Microbiological Test	Number of patients	Percentage (%)
Microbiological test done	12	15
Empirical use of antibiotics	68	85

### DISCUSSION

Nowadays there is an increase in the incidence of chronic diseases such as chronic obstructive pulmonary disease.<sup>5</sup> As these diseases require long-term treatment, irrational use of drugs may be possible that might lead to certain consequences. Drug utilization evaluation is an essential part of pharmacoepidemiological studies by which understanding of drug use according to the guidelines can be assessed. Knowing the more common patterns of prescribing makes it possible to elaborate training programs to adapt treatment to the current guidelines.<sup>1,9,10,12,13</sup>

In the study we found that the majority of the cases enrolled were male patients with the ratio of 70 % to 30% which suggests that men are more prone to developing respiratory emergencies than women which is the opposite of the study conducted by D S Heffernan et al ,which concluded that females are more likely than males to develop ARDS.<sup>15</sup>

Most of the enrolled patients were from the elderly population (above the age of 65) which was about 63% of the total population observed which indicates older populations are at more risk.<sup>4,16</sup>

In the study we understood that the majority of respiratory emergency cases enrolled in the study were enrolled between the months of November to January, which is the coldest months of the year as the patients enrolled were observed to be mostly of smoking habit background with 74% of the enrolled patients were chronic smokers.<sup>17,19</sup> Majority of the enrolled patients categorized under respiratory emergencies were suffering from COPD alone or along with other illnesses which included about 59% of all the patients enrolled with bronchitis being the next most common respiratory emergency with 17.5% of the enrolled cases.<sup>5,7,8,18</sup>

The patients enrolled were assessed based on RDOS starting from the day of admission till the day of discharge out of which 93% were found to be in the range of more than 3 based on RDOS rating system at the time of admission and 96% of the patients enrolled were discharged while having an RDOS rating of less than 3 which indicates a stable condition, which concludes almost all of the treatments for respiratory emergencies in the MICU department is of successful outcome.<sup>3</sup>

The therapy regimens for the management of respiratory emergencies was found to be including

of antibiotics (48%) , corticosteroids 16.8%, Beta 2 adrenergic agonists & Anticholinergics (26.8%), Methylxanthines (8%).11,14,20

Out of the antibiotics given, the most widely used antibiotics were found to be Ceftriaxone IV injection with 13.7%, Azithromycin tablet with 12.03% and Piperacillin and Tazobactam combination with 10.49%.12

The most commonly used corticosteroid given was Budesonide through nebulization with 62.48% of all the corticosteroids given, after which Hydrocortizone was widely used as an injection with 31.25%.6,7,8,12

In almost all the cases, Levosalbutamol and Ipratropium bromide nebulizers which are Beta-2 Adrenergic Agonists + Anticholinergics were given while Terbutaline syrup was given in 13% of the cases.6,7

In the Methylxanthines class, Theophylline, Doxophylline and Acebrotphylline were prescribed at almost similar percentages with 34%, 36 % and 30% respectively.6,7

The prescriptions were reviewed and assessed based on WHO indicators, and we found that average drugs given per encounter was 8.3, which is rather high as compared to the ideal range of 1.6-1.8 per encounter of WHO indicators range.1,13

Use of antibiotics were assessed, which was found to be given at the range of 52% of all the medications given, which in comparison to the ideal range which is 20-26.8% is of a large margin difference and needs to be evaluated.9,10,12,13 Percentage of encounters with IV route of administration was found to be 35% which is higher than the ideal range of 13.4%- 24.1% and requires further modifications in choosing the route of administration. Percentage of drugs prescribed in generic format was found to be 4.5%, which is of significant margin from the ideal range which is 100% use of generic names for prescribing the medications.1,13

By assessing the use of most widely prescribed medications in the most common respiratory emergencies we observed that in Cases of COPD patients, out of all the antibiotics given in all of the cases enrolled, Piperacillin & Tazobactam was the most prescribed antibiotic with encounter of

14.7% in all the cases enrolled, followed by Ceftriaxone with 12% and Azithromycin with only 3% of the prescriptions.

Similarly, for the COPD patients enrolled, antibiotic combinations were given, out of which Ceftriaxone + Azithromycin were the most common combination used in the treatment of COPD with 24% followed by Ceftriaxone + Azithromycin + Piperacillin & Tazobactam combination with 12%.

Bronchitis, which is the next most common disease in respiratory emergency, was assessed by the therapeutic regimens given, and we observed that Ceftriaxone + Azithromycin + Piperacillin & Tazobactam combination was the most widely antibiotic regimen used for the treatment of bronchitis with 29% prevalence, followed by Ceftriaxone + Azithromycin which was given at 14% rate.

In all the cases enrolled, from the Beta 2 Adrenergic Agonists + Anticholinergic agents class of drugs, Levosalbutamol and Ipratropium Bromide nebulization was given for the management of respiratory emergencies.

Terbutaline syrup was most commonly prescribed in COPD with concurrent diseases at the range of 30% followed by patients suffering only from COPD with 26% prevalence followed by 13% used in Bronchitis cases.

In the corticosteroids class of medications used in the treatment of respiratory emergencies, Hydrocortizone injection was most widely prescribed in COPD with prevalence of 52%, followed by 17% use in COPD with concurrent diseases. Budesonide nebulizer however, was used in all the enrolled cases.1,5,13,20

In the Methylxanthines class of drugs, Theophylline was prescribed most widely in COPD cases with prevalence of 53%, followed by COPD with concurrent diseases with 21% prescribed range.

Similarly Doxophylline use was assessed, and it was observed that Doxophylline was used in the majority of the COPD diseases with 45% prescribed in COPD cases and 17% prescribed in COPD with concurrent diseases.

Acebrotphylline was given mostly to COPD patients, with 31.25% given in COPD patients and 31.25 % given in COPD with concurrent diseases cases.

The outcome of all these medications in the Methylxanthines class was observed to be of

similar efficacy and the risk ratio difference was also not significant.<sup>5,14</sup>

In the study we found that empirical use of antibiotics was practiced and order for culture sensitivity test was not considered in majority of the cases (85%) and only 15% of the cases were sent for microbiological testing.<sup>1,2</sup>

The use of IV corticosteroids was assessed, in which the patients who received corticosteroids were assessed against patients who did not receive any IV corticosteroids, and the result indicated that no significant change was observed in comparing the two groups.<sup>11</sup>

In the Methylxanthines group, the Doxophylline and Theophylline use was compared, and the result indicated that the prevalence of their use in management of respiratory emergencies was similar (23%) and the outcome of therapy did not show any significant difference.<sup>14</sup>

#### LIMITATIONS OF THE STUDY

When we conducted this study we found the following limitations:

1. Treatment plan for the patient was not changed according to the severity of the disease.
2. The patients admitted in MICU are not all treated by same physicians; hence the therapy regimen differs from patient to patient.
3. Language barrier is a limitation as most of the patients enrolled in MVJ hospital only speak the local language.
4. Number of patients admitted in ICU is less.
5. Duration of study was less.

#### FUTURE OUT LOOKS

Education to the healthcare professional  
The future outlook of this study is to conduct interventional studies in order to compare the use and efficacy and also cost effectiveness of two drugs within the same class in order to prepare an efficacious hospital formulary plan.

Also, the healthcare professionals can come to a better understanding of the trend of medications used in the MICU for the management of respiratory emergencies, their effectiveness and frequency of use, for their future therapeutic planning.

#### Public awareness

The public can be benefited by being exposed to the study which reveals the risk factors for

respiratory emergencies such as Smoking and old age which can influence the public awareness about respiratory diseases and possibly preventive measures.

#### CONCLUSION

The study concludes that the population mostly at risk of developing respiratory emergencies is elderly male smokers. The management of respiratory emergencies lies on use of antibiotics, corticosteroids, nebulizers use and Methyl xanthines. The most preferred antibiotic used was Ceftriaxone IV injection and the use of Levosalbutamol + Ipratropium bromide nebulizer combination was given in every case enrolled along with Budesonide in the form of nebulizers.

The study concludes that the use of antibiotics in treatment of respiratory emergencies needs to shift from empirical therapy choices to individualization of therapy, due to the reason that long duration of antibiotics use results in antimicrobial resistance as well as increased cost of therapy.

Culture sensitivity tests need to be done more often in order to provide for a better outcome.

Use of IV corticosteroids did not show any difference in the treatment outcome of the regimens, and the use of Theophylline and Doxophylline comparison showed no significant difference in the measurement of therapeutic outcome. Hence these results can be considered in formulating therapeutic regimens in order to provide a more accurate and less costly treatment guidelines.

The average drug encounter per prescription was found to be higher than the ideal range of WHO recommendations. This along with the observation on rational use of antibiotics and use of IV route of administration which were both much higher than the ideal range recommended by WHO, suggests a change in formulating therapeutic regimens.

The study also concludes that the use of generic names for the drugs prescribed needs to be followed rather than trade names, as per WHO indicators.

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#### CONFLICT OF INTEREST

The authors declare no Conflict of Interest.

#### REFERENCES

1. World Health Organization. Introduction to Drug Utilization Research, Oslo; 2003:p 8.
2. Ramanan Laxminarayan et al., Antibiotic resistance—the need for global solutions Volume 13, No. 12, p1057–1098, December 2013 DOI: [http://dx.doi.org/10.1016/S1473-3099\(13\)70318-9](http://dx.doi.org/10.1016/S1473-3099(13)70318-9)
3. Campbell ML et al., Intensity cut-points for the Respiratory Distress Observation Scale. Palliat Med. 2015 May;29(5):436-42. doi: 10.1177/0269216314564238. Epub 2015 Jan 29.
4. Patrick Ray et al., Acute respiratory failure in the elderly: etiology, emergency diagnosis and prognosis. Crit Care.2006;10(3):R82. 2006 May24 doi:10.1186/cc4926.
5. Stephan Budweiser et al., Treatment of respiratory failure in COPD 2008 Dec. Int J Chorn Obstruct Pulmo Dis.2008 Dec;3(4):605-618.
6. Li JB et al., Retrospective analysis on acute respiratory distress syndrome in ICU. Chin J Traumatol. 2007 Aug;10(4):200-5.
7. Einarsson O et al., Airway management in respiratory emergencies. Clin Chest Med.1994 Mar;15(1):13-34.
8. Aaron Sagul et al., Acute Respiratory Distress Syndrome: Diagnosis and Management, Am Fam Physician. 2012 Feb 15;85(4):352-358.
9. Rahul M et al., Prescribing Patterns of Drugs in Acute Respiratory Distress Syndrome (ARDS): An Observational Study. J ClinDiagn Res. 2015 Feb; 9(2): FC01–FC04.
10. Thrope JM et al., Trends in emergency department antibiotic prescribing for acute respiratory tract infections. Ann Pharmacother. 2004 Jun;38(6):928-35. Epub 2004 Apr 20.
11. GC Khilnani et al., Corticosteroids and ARDS: A review of treatment and prevention evidence Department of Medicine, Pulmonary and Critical Care Division. Year : 2011 Volume : 28 Issue : 2 Page : 114-119 30-Apr-2011
12. John P. Donnelly et al., Antibiotic Utilization for Acute Respiratory Tract Infections in U.S. Emergency Departments Antimicrob Agents Chemother. 2014 Mar; 58(3): 1451–1457. doi: 10.1128/AAC.02039-13
13. Aliasghar Karimi et al., Evaluation of medicine prescription pattern using World Health Organization prescribing indicators in Iran: A cross-sectional study J Res Pharm Pract. 2014 Apr-Jun; 3(2): 39–45. doi: 10.4103/2279-042X.137058
14. MD Faiz Akram et al., Doxofylline and Theophylline: A Comparative Clinical Study J Clin Diagn Res. 2012 Dec; 6(10): 1681–1684. 2012 Dec 15. doi: 10.7860/JCDR/2012/4697.2643
15. Daithi S Heffernan et al., Gender and ARDS in Critically Injured Adults: A Prospective Study J Trauma. 2011 Oct; 71(4): 878–885. doi: 10.1097/TA.0b013e31822c0d31
16. Jean-Yves Fagon Acute respiratory failure in the elderly Crit Care. 2006; 10(4): 151. Published online 2006 Jul 25. doi: 10.1186/cc4982
17. Ruano-Ravina A et al., Dose-response relationship between tobacco and lung cancer: new findings. Eur J Cancer Prev. 2003 Aug;12(4):257-63.
18. Thomas Ferkol et al., The Global Burden of Respiratory Disease Annals of the American Thoracic Society 11(3):404-6 · March 2014 with 22 Reads DOI: 10.1513/AnnalsATS.201311-405PS
19. Carlos Iribarren et al., Cigarette smoking, alcohol consumption, and risk of ARDS - A 15-year cohort study in a managed care setting Article in Chest 117(1):163-8 · February 2000 with 2 Reads DOI: 10.1378/chest.117.1.163 · Source: PubMed
20. Andrew James Boyle et al., Pharmacological treatments in ARDS; a state-of-the-art update BMC Medicine201311:166 DOI: 10.1186/1741-7015-11-166
21. Peter J. Neumann et al., Cost-Effectiveness Analysis 2.0 N Engl J Med 2017; 376:203-205 January 19, 2017 DOI: 10.1056/NEJMp1612619