Assessment of Drug Utilization Pattern in Asthma, Chronic Obstructive Pulmonary Disease and Pneumonia: In A Rural Tertiary Care Teaching Hospital.

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ABSTRACT

Drug utilization studies are invoked as a potential tool in the evaluation in the healthcare systems as well as vigorous exploratory tools to explain the role of drugs in society. In spite of being a part of the leading causes of morbidity and mortality among the Indian population, there is lack of pioneer drug utilization studies in respiratory infections of rural populations. Hence the present study conducted with the objective to assess the drug utilization pattern in Asthma, Chronic Obstructive Pulmonary Disease and Pneumonia. A prospective and observational study was conducted in 145 patients from October 2014 to April 2015 in the medicine department of AH&RC. Relevant information was obtained from the interview as well the treatment chart of patients, by using a case report form. The most common respiratory diseases observed were chronic obstructive pulmonary disease 36.6% and its comorbidities followed by Pneumonia 22.8%. Bronchial Asthma 15.2% and rest were with associated diseases. Among the anti-asthmatic class use salbutamol +Ipratropium Combination was high (49.7%), Deriphylline (12.4 %), Montelukast (4.8%). Among corticosteroid use inhalation corticosteroid use was high (Budesonide: 48.3% followed by systemic hydrocortisone 22.8%), Cephalosporin 63.4% was the most frequently used antibiotic followed by Fluoroquinolones 31.7%. The average cost of antibiotic& total Medicine cost per patient INR was 928.88+2615.26; 1819.32. This study clearly showed that respiratory diseases drug therapy needs to be continuously evaluated to encourage the more rational prescribing, for educating the patient's drug usage, to decrease morbidity and cost of therapy for the patient.
Keywords: COPD: Chronic obstructive airway disease, RTI: Respiratory Tract infection, DUR: Drug utilization. DDI: Drug-Drug interactions

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INTRODUCTION

Respiratory tract infection (RTI) is defined as any infectious disease of the upper or lower respiratory tract. Upper respiratory tract (URTIs) infections include the common cold, laryngitis, pharyngitis/ tonsillitis, acute rhinitis, acute rhinosinusitis and acute otitis media. Lower respiratory tract infections (LRTIs) include acute bronchitis, asthma, chronic obstructive pulmonary disease, tracheitis, bronchiolitis and Pneumonia [1]. Asthma is a chronic inflammatory disorder (eg: various cells, cellular elements and cytokines) of the airways characterized by obstruction to airflow which completely or partially due to inflammatory mediators. Generally this is reversed in nature with or without specific therapy. In susceptible individuals airway inflammation may cause recurrent and persistent bronchospasm which cause symptoms like wheezing, breathlessness, chest tightness and cough particularly at night, early morning or after exercise [5]. as per the National Asthma Education and Prevention Program (NAEPP) categorized in asthma as intermittent asthma & persistent asthma. Based on severity of asthma further subdivided into mild, moderate & severe [6]. The various literatures showed an estimate of 300 million individuals is affected by Asthma worldwide, and the prevalence of asthma is increasing specially in children's. The WHO has estimated that 15 million disability adjusted life years are lost and 2, 50,000 asthma deaths are reported worldwide. Approximately 5, 00,000 annual hospitalization (34.6% in individual aged 18years or younger) is due to asthma [5]. In India, an estimate of 57,000 deaths was attributed to Asthma in 2, 00,043 (As per WHO 2004) and it was seen as one of the leading cause of morbidity and mortality in India rural Population.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recently defined COPD as "a common preventable and treatable disease characterized by persistent air flow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases". [8] Emphysema and Bronchitis are the two most common conditions that make up COPD. Chronic bronchitis is an inflammation of the lining of bronchial tubes, which carry air to and from the lungs. Emphysema occurs when the air sacs (alveoli) at the end of the smallest air passages (bronchioles) in the lungs are gradually destroyed. [9]

Pneumonia is only an infection that inflames the air sacs in one or both lungs. The air sacs may fill with fluid or pus, causing cough with pus, fever, chills and difficulty breathing. A variety of microorganisms, including bacteria, virus and fungi can cause Pneumonia. [7-9] Pharmacist roles in Drug Utilization Evaluation (DUE) program can directly improve the patient quality individually and in populations by reducing the use of inappropriate drug therapy, irrational drug use and by minimizing adverse drug reactions. [14] In diseases like Asthma, COPD and Pneumonia where a proportion of the population is suffering with or without co-morbidities, is very essential to spread a thorough awareness among the patient's medication and disease, for proper medication adherence particularly in asthma and COPD. [15]. The limited availability on pharmacoepidemolgy of respiratory infections in developed and developing countries are experiencing inappropriate and irrational drug use in their health care facilities[5]. Hence this study was carried out with objectives of assessment and prescribing pattern of antibiotics & its direct cost burden

MATERIAL AND METHODS:

STUDY SITE: Adichunchanagiri Hospital & Research Centre.

STUDY DESIGN: Prospective and Observational study.

STUDY PERIOD: This study was conducted for a period of Eight months from September 2014 to April 2015.

STUDY APPROVAL: The study was approved by the Institutional Ethical Committee, AH&RC, B.G.Nagara

STUDY CRITERIA

Inclusion Criteria:

- ♣ Inpatients diagnosed with Asthma, COPD and Pneumonia irrespective of sex.
- ♣ Patients with age ≥18 years

Exclusion Criteria:

- ♣ Patients are treated as outpatients.
- ♣ Patients with incomplete medical records

SOURCE OF DATA: Patient case sheet, Medication chart, Lab reports.

STUDY PROCEDURE

The Patients will be enrolled into the study, by considering inclusion & exclusion criteria. After their consent, the case records, laboratory reports and prescription details will be collected from the patient case sheets in a well-designed data collection form. The collected data will be reviewed for correctness/Appropriateness of drug use, benefits and other drugs and patient related aspects by referring various drug information resources(eg: Micromedex). The data will be analyzed by using Descriptive statistical analysis (Mean + SD (Min-max) are calculated along with significance (P value) by SPSS 20 [th] Version

RESULTS

Among 145 patients, 98 (67.6%) were males and 47 (32.4%) were females. Majority of the patients enrolled in the study belongs to the age group 61-70 years(31.7%) followed by 51-60 years(22.8%),71-80 years(20%),41-50 years(17.2%),>81 years(4.1%),>18-30 years(3.4%),and least was observed in 31-40 years(0.7%).Majority of the patients enrolled in the study were farmers (26.9%) followed by house wife (24.1%), business (13.1%), retired and daily labor (6.9%), and last was, students (1.4%), and interestingly some patients were not known (12.4%). Among the patients have 66.2% had past medical history of COPD (18.6%), asthma (10.3%), hypertension (6.9%),diabetes (6.2%),DM+HTN+BA (5.5%),HTN+COPD and HTN+DM+COPD (4.1%),DM+COPD (3.4%),TB+COPD (2.8%), Asthma+HTN (1.4%), TIA, TB, DM+COPD+TIA and Asthma +TB (0.7%). In which 35.5% have medication history of Antiasthmatic (8.3%), Antidiabetic (5.5%),COPD medication (4.1/5),Anti DM+Anti HTN(3.4%), AntiHTN+AntiDM+Antiasthmatic (2.8%),Anti HTN+ Antiasthmatics (2.1%),and Anti DM+Antiplatelet (0.7%).The majority of the patients hospital stay for 1-7 days (81.4%), and the remaining were hospitalized for 8-16 days (18.6%). The present study showed 91.7% were not done with culture test. Only other 8.3% were done for culture report. Most of the male study population has not undergone the culture test (93.9%) Majority of male patients (12.8%) culture specimen used were Sputum (4) followed by Blood, Urine (1) where as in female patient 12.8% had sputum test and 41(87.2%) has not gone for the culture test. Among 8.3% culture test, only 4.8% showed positive report. Culture report for the gram staining methods, Gram positive bacilli observed was 2.1% followed by gram positive cocci in 2 patients (1.4%),gram positive cocci bacilli in 1 patient (0.7%),gram positive cocci negative bacilli in 1 patient (0.7%),and normal flora in 5 patients (3.4%). Interestingly only 1.4% had gone for Antibiotic sensitivity testing. The distribution of various pulmonary disease, anti-asthmatics, antibiotics use was shown in the below (Table1,2,3)

Table 1: Distribution of pulmonary diseases

Diagnosis	N	%
Bronchial Asthma	10	6.9
Bronchial Asthma With Acute Exacerbation	12	8.3
COPD	53	36.6
• Acute Bronchitis	8	5.5
• Chronic Bronchitis	4	2.8
• Emphysema	5	3.4
• LRTI	11	7.6
• URTI	1	0.7
• PAH	15	10.4
COPD With Acute Exacerbation	33	22.8
Pneumonia	33	22.8
Bronchial asthma+pneumonia	4	2.8
Total	145	100.0

Among 145 patients enrolled in the study, 53 (36.6%) were diagnosed as COPD, [11 (7.6%) patients were found with LRTI followed by 8 (5.5%) with acute bronchitis, 5 (3.4%) with emphysema, 4 (2.8%) with chronic bronchitis and only 1 (0.7%) with URTI. Also, 1 (0.7%) patient was having mild to moderate PAH and 14 (9.7%) patients were having severe PAH or corpulmonale, followed by 33 (22.8%) were diagnosed as COPD with acute exacerbation and pneumonia, 12 (8.3%) were bronchial asthma with acute exacerbation, 10 (6.9%) with bronchial asthma and 4 (2.8%) with asthma + pneumonia.

Table2: Distribution of Antibiotics classes used

Antibiotics Used	N	%
Cephalosporin	92	63.4
• Ceftriaxone	89	69.4
• Cefixime	3	2.1
• Cephalosporin beta lactamase	5	3.4
• Ceftriaxone sulbactum		
	5	3.4
Fluroquinolones	46	31.7
• Ciprofloxacin	11	7.6
• Norfloxacin	7	4.8
• Levofloxacin	27	18.6
• Ofloxacin	1	0.7
Macrolides	15	10.3
• Azithromycin	15	10.3
• Tetracycline	2	1.4
Nitro imidazole (Metronidazole)	11	7.6
Penicillin	8	5.5
• Amoxicillin	8	5.5
• Meropenem	1	0.7
• Penicillin Beta lactamase	16	11.0
• Amoxicillin Clavulanic acid	1	0.7
• Piperacillin+Tazobacum	15	10.3
Aminoglycoside	6	4.1
• Amikacin	3	2.1
• Gentamicin	3	2.1

Among 145 patients enrolled in the study,92 (63.4%) patients were prescribed with cephalosporin [i.e. 89 (61.4%) patients were prescribed with Ceftriaxone followed by 5 (3.4%) with cephalosporin beta lactamase and ceftriaxone sulbactam and 3 (2.1%) with Cefixime] ,followed by 46(31.7%) with Fluroquinolones, 15 (10.3%) with macrolides [i.e. .levofloxacin was prescribed to 27 (18.6%) patients , followed by ciprofloxacin to 11(7.6%), Norfloxacin to 7 (4.8%) and Ofloxacin to only 1 (0.7%)], 11 (7.6%) with nitro imidazole , 8 (5.5%) with penicillin's [i.e. 16(11%) patients followed by piperacillin +tazobactam to 15(10.3%),amoxicillin to 8 (5.5%),meropenam and amoxicillin clavulanic acid to only 1 (0.7%) patient] and 6 (4.1%) with aminoglycosides[i.e. 3 (2.1%) were prescribed with amikacin and gentamycin to 3 (2.1%) patients].

In this study antibiotics were prescribed to 130 (89.7%) patients only , in which antibiotics (forms of antibiotics)are given via injection in 69 (47.6%) patients followed by inj+oral in 38 (26.2%) patients, oral in 23 (15.9%) patients and antibiotics were not prescribed in 15 (10.3%) patients. In which one antibiotic was prescribed in 62 (42.8%) patients followed by two antibiotics in 50 (34.5%) patients, three antibiotics in 12 (8.3%)patients, Four antibiotics in 5 (3.4%) patients, Five antibiotics in 1(0.7%) patients and antibiotics were not prescribed in 15(10.3) patients
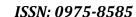
Table 3: Distribution of class of anti-asthmatic drugs

Class of anti-asthmatic drugs	N	%
Beta Agonist		
No	57	39.3
Salbutamol	14	9.7
Salbutamol+Ipatropium Bromide	72	49.7
Salbutamol+IpatropiumBromide+salmetrol	1	.7
Salbutamol+theophylline	1	.7
Total	145	100.0
Xanthophyllines		
No	123	84.8
Theophylline	1	.7
Aminophylline	2	1.4
Deriphylline	18	12.4
Aminophylline+Deriphylline	1	.7
Total	145	100.0
Leukotriene Antagonists		
No	136	93.8
Montelukast	7	4.8
Montelukast+Levocetrizine	2	1.4
Total	145	100.0

Among these patients, Beta 2 agonist were prescribed with Salbutamol+Ipratropium Bromide, 72 (49.7%) patients followed by 14 (9.7%) with salbutamol, 1 (0.7%) with Salbutamol+Ipatropium Bromide+salmetrol and salbutamol+theophylline and remaining 57 (39.3%) were not prescribed with any beta agonists.

Among Xanthophylline derivatives, 18 (12.4%) patients were prescribed with deriphylline followed by 2(1.4%) with aminophylline, 1(0.4%) with theophylline and aminophylline +deriphylline and remaining 123 (84.8%) were not prescribed with any xanthophyllines.

Among leukotriene antagonist, 7 (4.8%) patients were prescribed with montelukast followed by 2 (1.4%) with montelukast+levocetrizine and remaining 136 (93.8%) were not prescribed with any Leukotriene Antagonists. The distribution of various classes of other drugs used in this disease as showed below Table4-Table7.

Table 4: Distribution of CVS drugs

Category	Drugs	N	%
Anti Anginals	NTG	1	0.7
Cardiac Glycosides	Digoxin	5	3.4
Anti-Hyperlipidemias	Atorvastatin	9	6.2
	Rosavastatin	2	1.4
Anti-platelets	Aspirin	5	3.4
	Clopidogrel	6	4.8
	Aspirin+Atorvastatin	6	4.1

Table 5: Class of Antihistamine, Analgesic, Antifungal and Anti-ulcer and Antiemetic Used:

Class of Drugs	N	%
Antihistamines		
• No	134	92.4
• Cetrizine	4	2.8
• Levocetrizine	5	3.4
• Sinarest(CPM)	2	1.4
• Total	145	100.0
Analgesics		
• No	90	62.1
• NSAIDs – Diclofenac	3	2.1
• Opioid Analgesic - Tramadol	1	.7
• Paracetamol	43	29.7
• Ultacet-Tramadol+Acetaminophen	6	4.1
• Zix-Acelco+Para+Serratiopeptidase	2	1.4
• Total	145	100.0
Anti-Ulcer		
• No	58	40.0
• Pantoprazole – PPI	60	41.4
• Ranitidine - H2 Antagonists	21	14.5
• Omeprazole – PPI	4	2.8
• PAN + RANTAC Not simultaneously	2	1.4
• Total	145	100.0
Anti-fungal (fluconazole)	1	0.7
Antiemetic's		
• No	126	86.9
• Emeset	17	11.7
• Domperidone	2	1.4
• Total	145	100.0

Table 6: Distribution of Corticosteroids usage pattern

Corticosteroids	N	%
No	64	44.1
Yes	81	55.9
Total	145	100.0
Systemic corticosteroids		
• Hydrocortisone	33	22.8
• Prednisolone	3	2.1
Inhaled Corticosteroid		
• Budesonide	70	48.3
• Fluticasone	2	1.4

Table 7: Distribution of Corticosteroid administration

Administration Of Corticosteroids	N	%
No	64	44.1
Inhalational	46	31.7
Parenteral	9	6.2
Inhalational + Oral	2	1.4
Inhalational + Parenteral	24	16.6
Total	145	100.0

The various cough syrups used were 32.4% patients were prescribed with Ganlite P followed by 16.6% with Brozedex, 6.9% Tus Q (Bromohexine) and Mucolite.The various vitamin related supplements used ,10.3% were prescribed with becosules, zevit (B complex with Zinc) followed by 4.8% with nervilen p, and only 0.7% with shelcal(calcium supplements)

The drug interventions were made in 80 (55.2%) cases and the main intervention made about drug-drug interactions (55.2%). In which , single DDI was found in 36(24.8%) cases,2 DDI was found in 24 (16.6%),3 DDI was found in 14 (9.7%)cases,4 DDI was found in 5 (3.4%) cases,5 DDI was found in only 1 (0.7%) cases. In which 15 were accepted and modified. In the severity of DDI showed mild was in 40 (27.6%) cases, moderate severity was found in 36(24.8%) cases, 2 cases(1.4%) was found to be severe and 2 cases (1.4%) was founded moderate+ severe. Interestingly no ADR & Contraindications was observed. Only 26 patients were prescribed on inhalers and counselling was given to them on techniques of using inhalers.

The overall drug use pattern in the selected disease shown in the table8.

Table 8: Summary of distribution of drug usage pattern

Drug usage pattern	Mean + SD	Total
Total number of antibiotic prescriptions	1.54 + 0.958	223
Average number of antibiotics prescribed	1.53 + 0.958	223
Total number of drugs prescribed	10.35+ 3.155	1502
Average number of drugs per patient	10.35 +3.155	1502
Average cost of antibiotics per patient	928.88+2615.267	134687
Average cost of total medicine per patient	1819.32	2986.903

DISCUSSION

Irrational use of drug and inappropriate prescription is the two common phenomenon's in the developing countries which cause a big problem for providing effective health care facilities. However, only a few studies have been carried out because of several constraints in India. Hence Drug utilization research studies conduct in the inpatient settings are very effective in evaluating the drug prescribing trends & practices, rationality, efficiency, cost effectiveness & for developing hospital formularies. . In diseases like Asthma, COPD and Pneumonia where a lot of the population is suffering with or without comorbidities, it is very essential to spread a thorough awareness among the patients related to the medication and disease itself for proper medication adherence.

The present study shows that most of the patients enrolled in the study were males 67.6% due to the smoking habits and field work which are strongly correlated with the incidence of asthma and COPD. A similar study conducted by *Alemuddin N M et al* showed that males were prone more to respiratory diseases than females.

Among the study population, most were belonging to the age group 61-70 years and farmers (26.9%). A similar study by *Alemuddin N M et al* showed that above 50 years of age[3]

Respiratory diseases are relatively common in low socioeconomic status patients in a rural area because of the life style habits and occupational practices followed. Interestingly in our study, majority of the study population were not having any previous medical history (33.8%) and medication history (65.5%).The number of hospitalization days was 1-7 days (81.4%) in our study which was similar to a study conducted by *Chandrasekhar K et al* [5] in which the average length of stay of the patients was found to be 6.20 days. In comparison with standard guidelines many deviations and under practices of diagnosis and treatment were

observed. Sputum characteristics and culturesensitivity were not performed for most of the study population (93.9%) and (98.6%). Similar results were found in *MalpaniA K et al*.[13]

The most common respiratory diseases were Chronic obstructive pulmonary disease 36.6% and its comorbidities followed by Pneumonia 22.8%, Bronchial Asthma 15.2% and associated diseases which is contrary to the study conducted by *Maazuddin M et al* [20]where the common respiratory disease was Asthma 89.42% and COPD 10.58%. Cardiac associated comorbidites include Ischemic heart disease 6.2% and Congestive cardiac failure 4.8%.

In this study, Cephalosporin's 63.4% were the most used antibiotic followed by Fluoroquinolones 31.7%.This was contrary to the study conducted by Pooja S et al were Fluoroquinolones 28% and Cephalosporin's 22% were the most commonly used antibiotics. A high percentage of patients 42.8% were prescribed at least one antibiotic, two antibiotics were prescribed in 34.50%, three antibiotics were prescribed in 8.3% and four antibiotics were prescribed in only 3.4% cases. Similar study conducted by *Shamshy K et al* assessed that one antibiotic was more prescribed in (54.58%) cases and two antibiotics were prescribed in (28.57%) cases, and which was similar to that in our study. The mode of administration of antibiotics in our study was more through the parenteral route 47.6%, which was similar to a study conducted by *Shamshy K et al* in which 80.95% cases, drugs were administered through the parenteral route only. [17]

Among the cardiovascular drugs used Anti-platelets 12.3% and anti-Hyperlipidaemics 6.2% were used. Pantoprazole 41.4% was the common anti-ulcer drug used.

Among the study population, Corticosteroids were used in 55.9% cases. Inhalational corticosteroids (budesonide) 48.3% were the most commonly prescribed corticosteroids followed by systemic corticosteroids (Hydrocortisone) 22.8%.The inhalational route causes a high local delivery therapy hence will improve the therapeutic ratio and minimize systemic side effects. This was similar to the study done by *Shastry R et al* were Inhalational corticosteroids 16.2% and 2.9% systemic corticosteroids were used. In the anti- asthmatic drugs used, Beta agonists- Salbutamol+Ipatropium bromide (49.7%) was the most frequently used drug followed by Xanthophyllines- Deriphylline 12.4% and Leukotriene antagonists-Montelukast 4.8%.The results were similar to study conducted by *Shamshy et al* were 22.34% were anti-asthmatic drugs and contrary to Patel P D et al were methyl xanthines and combination of beta agonists were used widely.[16-20]

In this study, the most frequently used cough syrup was Ganlite P (32.4%) followed by Brozedex (16.6%) and the supplement used Becosules, Zevit (10.3%). Drug interventions were made about in 55.2% cases wherein. The major was drug-drug interactions. Single drug-drug interaction was found in 24.8% cases and double drug-drug interaction was found in 16.6% cases.15 interactions were accepted and modified by the doctors. Mild severity was observed in 27.6% cases followed by moderate severity in 24.8% cases and 1.4% severe cases were reported. Interestingly in our study, no ADR was reported. The mean of the total number of antibiotics per prescription was 1.54.The mean value of the average number of antibiotics prescribed was 1.53+0.958 and the average number of drugs per patient was found to be 10.35+3.155. The mean of the total number of drugs prescribed was 10.35.The mean of average cost of antibiotics per patient was 928.88+2615.267 and the average cost of total medicine per patient was 1819.32.[15] Among 145 study populations, 26 patients were on inhalers and counselling was provided to them on techniques of using inhalers

CONCLUSION

COPD and associated co- morbidities were the frequent reasons for hospitalization among rural people followed by Pneumonia and asthma. In our study, subjects were prescribed with antibiotics. Wherein Cephalosporin 63.4% was the most commonly used followed by Fluoroquinolones and among anti-asthmatics, 49.7% beta agonists (Salbutamol+Ipratropium bromide) followed by Xanthophyllines and Leukotriene antagonists. Among the corticosteroids, 48.3% inhalations corticosteroids (budesonide) and 22.8% systemic corticosteroids were used. Most of the study population was not assessed by sputum culture, antibiotic sensitivity and lung function test as diagnostic criteria. Based on these the present practice, suggested that need for an improvement in the current prescribing trend for better and rational utilization of drugs. Even there is need to encourage physicians to follow standard guidelines while managing respiratory tract infections. The prescription pattern was considered based on the disease status and economic status of the

patient. This study even highlights that Generic practice implementation in the therapy, will help the cost-minimization of drugs. Drug interventions were observed in about in 55.2% cases (drug-drug interactions). Patient counselling about the techniques of using inhalers was provided to 26 patients on inhalers. Hence the pharmacist contributions are very important in these. Even though, no ADR were reported in our study, boosting public health programs and health management, monitoring of drug utilization pattern, development of evidence based essential drug list, targeted in-service training and public awareness are some of the strategies which can be adopted to ensure rational drug use.

Hence, we conclude that the present hospital set up is significantly appreciable however; a series of education program should be carried out for postgraduate students, interns, nursing staff and other concerned health care professionals in order to implement quality patient care and also to assure good medication practices.

REFERENCES

[1]   www.nice.org.inNational Institute for Health and Clinical Excellence (NICE) Guidelines, United Kingdom; Respiratory tract infections-Antibiotic prescribing.
[2]   Goud KS, Kumar R, Patil V.G, Dighe D, Lalan H.N, Singh A; Indian Journal of Applied Research; May 2014; 4(5):484-87
[3]   Aleemuddin N M; *Journal of Contemporary Medicine and Dentistry;Jan*-Apr-2014; 2(1);12-17.
[4]   Abidi A, Gupta S,Kansal S, Ramgopal; International Journal of Basic & Clinical Pharmacology;2012 Dec; 1(3):184-90.
[5]   Chandrasekhar K, Saritha MK, MetiV. Asian Journal of Medical and Clinical Sciences Short Communication; May-Aug 2012; 1(2):70-73.
[6]   Sayyeda K, Ahmed Q S, Ansari N.A, Upadhyay P, Dey S, Madhwar A ; International Journal of Pharmacy and Biosciences; May-June 2013; 2(3):145-156
[7]   Shimpi D R, Salunkha P.S, Bavaskar S.R ,Ladddha G.P, Kalam A. Patel A K; International Journal of Pharmacy and Biological Science;Jan-March 2012; 2(1):117-122.
[8]   www.mayoclinic.org.inMayo Clinic; Diseases and Health Conditions; Asthma, Copd and Pneumonia.
[9]   Parvaiz A Koul; COPD Disease: Indian guidelines and the road ahead, Indian Journal of Pharmaceutical Sciences. June – Aug 2013; 3(2):96-101.
[10]   Kaur S, Rajagopalan S, Kaur N,Shafiq N ; Emergency Medicine International. 2014;1:1-5
[11]   Jayanthi MK, Sushma VN. International Journal of Pharmacy and Pharmaceutical Sciences. 2014:6(2):70-72.
[12]   Barot PA, Malhotra SD, Rana DA, Patel VJ, Patel KP. Journal of basic and clinical pharmacy. 2013 Oct 1;4(4):78;
[13]   Malpani AK, John N. N, V.L. Srividya, Paul S; International Journal of Pharmaceutical Sciences and Research; Jan 2013; 4(5):628-32.
[14]   Sharma P, Parakh R, Sharma N, Sharma N, Gautam B, Sharma D, Sharma M, Jain R; Indo American Journal of Pharmaceutical Research. 2013; 3(12):1544-51.
[15]   Donner C F. COPD a social disease: Inappropriateness and pharmaco-economics. The role of the specialist: present and future. Multidisciplinary Respiratory Medicine. 2010; 5(2):104-40.
[16]   Patel PD, Patel RK, Patel NJ; International Research Journal of Pharmacy;2012:3(7):257-60
[17]   Shamshy K, Begum IM, Perumal P.. Int J PharmTech Res. 2011;3(3):1530-6.
[18]   Soriano B J, Visick G.T, Muellerova H, Payvandi N, Hansell A.L ; Journal of American college of chest physicians.2009; 128:2099-2107.
[19]   Choudhary D K, BezbaruahB.K ; Journal of applied pharmaceutical sciences.2013, 3(8):144-48.
[20]   Mohammed M, khan MA, Mohiuddin M, Adil MSu, Mohiuddin MN, Javeedullah M, Hussain. MS. IAJPR. (2013), 3(9): 7168-7174.