ISSN: 2321-2152

IJMECE

International Journal of modern electronics and communication engineering

E-Mail
editor.ijmece@gmail.com
editor@ijmece.com

www.ijmece.com

ISSN: 2321-2152www.ijmece .com
Vol 6, Issue.3July 2018

Antimicrobial Use, Adverse Effects, and Cost of Drug Therapy in Pediatric Respiratory Tract Infections: A Systematic Review and Meta-Analysis

Dr T K V Kesava Rao[1], A Venkateswara rao[2]

Abstract

The purpose of this study is to examine the use of pharmaceuticals in the treatment of RTIs in children. A tertiary care teaching hospital conducted a cross-sectional observational study of 74 children with RTI. A systematic case record form was used to capture and analyze patient demographic and illness information, prescription history, adverse drug responses, and treatment costs. Treatment efficacy was evaluated in light of World Health Organization and Indian Academy of Pediatrics (IAP) recommendations.

The majority (54.05%) of the 74 patients were children (aged 0-1). Additionally, the majority (67.57%) of the patients were men. Pneumonia was the leading diagnosis (48.5%). 7.251.57 drugs per patient on average (from 3-16 drugs). Antibacterial drugs (100%) were the most often prescribed kind, followed by pain relievers/fever reducers (95.94%), and then respiratory drugs(86.49%). Amoxicillin/clavulanic acid (90.54%) and ceftriaxone (77.77%) were the two most common antibacterial drugs administered. Antihistamines (85.13%) and salbutamol (55.40%) were the most often given respiratory medications. The majority (75%) of prescription medications came directly from the WHO-EML, and generic names were used in 56.81% of all cases. According to the WHO and IAP recommendations, only 13.51 percent of patients received appropriate or rational medication treatment, while the remaining 35.14 percent received semi-rational drug therapy and 51.35 percent received illogical drug therapy. An adverse drug reaction (ADR) caused by an antibiotic, pain reliever, or fever reducer occurred in 16.22% of patients. The overall cost of antimicrobials was estimated at Rs. 286.17 per patient, with drugs costing an average of 314.69 Rs. The research found that antibacterials and respiratory medications were often overprescribed. Better and more prudent medication usage in pediatric patients may be possible with an increased focus on accurate diagnosis and treatment, patient education, and the availability of locally-effective recommendations.

Keywords: Infections in children's lungs; The use of antibiotics; Proper dosing; Drug treatment cost estimates; Adverse events in children

Introduction

In both industrialized and developing nations, respiratory tract infections are the leading cause of illness and death in children under the age of five [1]. Among children under the age of five, they account for 20% of deaths in India but for just 3% in the developed world [2]. Both the birth and mortality rates for children are greatest in India [2]. About 1.7 million children under the age of five died worldwide in 2010, with India accounting for almost a quarter of that number [2]. Pneumonia kills roughly 24 percent of children under 5 in the United States [2,3]. Reducing the under-five mortality rate to less than 25 per 1,000 live births by the year 2030 is one of the 'Sustainable Development Goals' announced by the United Nations in 2016. By the year 2030 [3,] it aims to reduce communicable disease outbreaks and fatalities that may have been avoided. Therefore, efforts should be made to treat as many children as possible in order to reduce their risk of death.

Professor & Principal[1] , Associate Professor[2]
PYDAH COLLEGE OF PHARMACY, KAKINADA YANAM ROAD, PATAVALA

ISSN: 2321-2152www.ijmece .com
Vol 6, Issue.3July 2018

Pathological disorders such as rhinitis, acute sinusitis, otitis media, bronchiolitis, pneumonia, and bronchitis are all classified as respiratory tract infections. They may be caused by viruses (such adenoviruses and rotaviruses) or bacteria (including H. influenzae, Streptococcus, pneumococcus, and Moraxella catarrhalis).The use of antibiotics (penicillins, erythromycin, cephalosporins, etc.), inhalants (salbutamol, ipratropium bromide), cold and flu remedies (nasal decongestants, antihistamines, etc.), and symptomatic treatment are all viable options for treating the aforementioned conditions [4].

The high prevalence of respiratory tract infections [3] may be attributed to a number of variables, the most important of which are the advent of emerging pathogenic organisms, the re-emergence of illness formerly treated, widespread antibiotic resistance, and inadequate vaccine coverage despite numerous novel initiatives. Therefore, preventing and treating these illnesses must be given high importance. All respiratory illnesses have practice recommendations, but their application and efficacy have not yet been analyzed [6]. Furthermore, the majority of regulations rest on the etiology, while treatment in India, like treatment in other impoverished nations, is mostly based on empirical evidence [7]. Drug resistance and wasteful use of antibiotics are two potential outcomes [8] of such behavior. An infected person's respiratory illness has the potential to spread to others in the community by inhalation of contaminated droplets in the air. The current research was intended to examine the prescription pattern of the medications in paediatric respiratory infection patients, side effects, and the cost of drug treatment because of the high frequency of respiratory tract infections in the paediatric age group and the dearth of studies in this area.

Methodology

Children with respiratory infections admitted to Civil Hospital, Gandhinagar, a tertiary care teaching hospital in western India, were the subjects of a prospective, observational, single-center research. Before beginning the study, the researchers submitted the protocol to the Institutional Ethics Committee (IEC) for review and approval. The study's nature and goals were communicated to the children's parents or guardians in a language they could understand. Before a patient was enrolled in the trial, written informed permission was acquired from a parent or legal guardian. Before beginning the research, the Medical Director and the head of the pediatrics department gave their approval.

Sample size: Considering, the prevalence of respiratory tract infections in paediatric patients (5%) in India [2], the sample size calculated is 73 using following formula:

Where,

$$n = \frac{Z^2 \, P \, (1 - P)}{d^2}$$

Z = Z statistics for level of confidence (95%) = 1.96

P = Expected Prevalence = 0.05 (= 5%)

d = Precision = 0.05 (= 5%)

Patient selection criteria

Patients admitted to the paediatric department (ward and ICU) of the Civil Hospital in Gandhinagar with a diagnosis of acute respiratory tract infection between March and August 2016 were included in the study. Patients could be either male or female. Patients with a HAI diagnosis or who opted for a DAMA (discharge against medical recommendation) were not included in the study.

Study procedure

Patients with respiratory infections admitted to the pediatric ward or critical care unit were screened, and those who met the inclusion and exclusion criteria were recruited in the research. From the time a patient is in until the time they are released from the hospital, they will get a daily visit during which their care will be

documented. Complete and accurate data, including demographic statistics (such as demographics, socioeconomic status, etc.) Reviewing hospital case files and conducting interviews with parents/children allowed for the collection of clinical data (history of illness, symptoms and signs, length of stay) and pharmacological therapy (dosage regimen). The organized case record form served as the repository for all the data collected. Ten individuals were used in a pilot study to evaluate the premade case record form (CRF). The case record form was then adjusted so that all patients' information could be included.

All adverse medication responses that were either reported by patients or seen by the researcher were tracked and documented for analysis. We used the WHO-Uppsala Monitoring Center (UMC) scale [9] and Naranjo's algorithm [10] to determine the likelihood that each of the ADRs was caused by the drug. ADRs were evaluated for severity using the Hartwig and Siegle scale [11] and for preventability using the modified Schumock and Thornton criteria [12]. Medication prices were collected from the hospital pharmacy (if provided by the hospital) or from private pharmacies (if not accessible in the hospital pharmacy) for the purpose of this study. The total cost of medications was figured up for a whole hospital stay.

Drug therapy was analyzed for appropriateness by comparing it to the World Health Organization's [13, 14] and the Indian Association of Paediatrics' [15] treatment recommendations. If normal treatment recommendations are adhered to, the pharmacological therapy is regarded rational; otherwise, it is deemed semi-rational if rational alternatives are employed, and irrational if neither of these conditions is met.

Analytical framework proposed

To determine (i) the demographic parameters, such as the age and gender distribution of patients, and (ii) the prevalence of various disorders leading to respiratory infections, all of the collected data was analyzed. Clinical manifestations: signs and symptoms (iv) length of time spent in the hospital (vi) analysis of antimicrobials used, type of use: empirical / definitive, its source (whether hospital supply or an outside pharmacy), and (vii) appropriateness of drug therapy. WHO-core prescription indicators analysis (viii) [16] (x) the estimation of medication costs (ix) drug-related side effects

Mathematical dissection

This information was analyzed statistically using Microsoft Excel 2010. Actual frequencies, percentages, means, and standard deviations were used to describe the data.

Results

Over the course of 6 months (March-August 2014), 74 children with respiratory tract infections admitted to the pediatric indoor unit who met the inclusion-exclusion criteria were included. Patients' ages ranged from 1 month to 11 years, with a mean age of 2.36 2.12 years. The majority of cases were infants (54.05%). Fifty patients (67.57%) were male and twenty-four patients (32.43%) were female out of the total 74. 66 individuals (or 89.19%) were in complete compliance with the CDC's recommended vaccination schedule. In table 1, we saw the patients' baseline characteristics and other pertinent information.

Parameter	**No. of patients (n=74, %)**
Age in years	
0-1	40 (54.05)
1-2	9 (12.17)
2-5	8 (10.81)
5-10	14 (18.92)
>10	3 (4.05)
Gender	
Male	50 (67.57)
Female	24 (32.43)

ISSN: 2321-2152www.ijmece .com
Vol 6, Issue.3July 2018

Body weight in Kg	
1 – 5	20 (27.02)
5.1 – 10	25 (33.78)
10.1 - 15	13 (17.57)
15.1 – 20	9 (12.16)
20.1 – 25	4 (5.41)
>25	3 (4.05)
Immunization status	
Complete	66 (89.19)
Partial	3 (4.05)
Non-immunized	2 (2.71)
Unknown	3 (4.05)

Table 1: Demographic parameters of the study population: (n=74)

Patients with upper respiratory infections (such as pharyngitis and tonsillitis) made up just 24.32 percent of the total, whereas patients with lower respiratory infections made up the vast majority (56, 75.68 percent). Table 2 shows that among LRTI, hospitalizations due to pneumonia were the most prevalent, followed by those due to bronchiolitis and WALRTI.

Table 2 displays typical symptoms seen by people suffering from respiratory disorders. Cough and cold were the most prevalent first symptoms, occurring in 94.55% of patients, followed by fever (90.54%) and shortness of breath (24.32%). In order to determine what was causing respiratory infections, doctors first took detailed patient histories and then performed a battery of laboratory tests. Sixty-nine (93.24%) patients had a complete blood count performed, followed by an x-ray. chest in 53 patients (71.62%). Hospital stays averaged out to be about 7 days, but varied from 3 to 11 days.± 2.1 days. Most people (n=58; 78.38%) only stayed in the hospital for three to seven days.

Diagnosis	**No. of patients (%)**
URTI (pharangitis, tonsilitis)	18 (24.32)
LRTI	56 (75.68)
Pneumonia	36 (48.65)
Bronchiolitis + bronchitis	10 (13.51)
Bronchial asthma	3 (4.05)
WALRTI	7 (9.46)
Symptoms	
Fever	67 (90.54)
Cough and cold	70 (94.55)
Breathlessness	18 (24.32)
Duration of stay (in days)	
1-3	4 (5.41)

3-7	54 (72.97)
> 7	16 (21.62)

Table 2: Disease related parameters in study patients: (n=74)

Analysis of drug use

Patients were given an average of 7.25 prescription medications (range: 3- 16). Of these 74 individuals, 14 (18.92%) were given less than 5 medications, whereas 53 (71.62%) were polypharmacy (5-10 medications) and 7 (9.46%) were extreme polypharmacy (>10 medications).

In all, 74 individuals were determined to have one of seven diagnoses. In 74 instances, various forms of 36 different medications were administered. Only 38 (43.18%) of the 88 formulations were administered under their brand names, whereas 50 (56.81%) were given under their generic names.

Based on the data in tables 3 and 4, it is clear that antimicrobial agents were the most often prescribed class of drugs for all patients. The range of prescription antimicrobial drugs was from one to four. In 48.65 percent of patients, just one antibiotic was given. Ninety-five point four percent of patients were prescribed amoxicillin with clavulanic acid, followed by cephalosporins (48.65 percent) and aminoglycosides (24.32 percent). Antibiotic treatment lasted anything from 1-10 days. Seventy-one (94.95%) patients needed an analgesic or antipyretic; 68 got paracetamol alone, while 3 received paracetamol + ibuprofen. Pain relievers and fever reducers were used for a period of time between one and ten days (Table 4).

Drug	No. of patients (%)
Antibiotics	**74 (100)**
Number of antibiotics prescribed	
1	36 (48.64)
2	20 (27.02)
3	16 (21.62)
4	2 (2.70)
Class of antibiotics used	
Amoxicillin + clavulanic acid	67 (90.54)
Amoxicillin	4 (5.40)
Ampicillin	6 (8.10)
Aminoglycosides (amikacin)	18 (24.32)
Cephalosporins	36 (48.64)
Ceftriaxone Cefixime Cefotaxime	28 (77.77) 3 (8.33) 5 (13.88)
Azithromycin	2 (2.70)
Antihelmintic drugs (Albendazole)	8 (10.81)
Diethylcarbamazine (DEC)	2 (2.70)
Duration of antibiotic use	1-10 days

Table 3: Analysis of antimicrobial drugs used in study patients (n=74)

Supporting medicines	No. of patients (%)
Oxygen	26 (35.13)
IV fluids	28 (37.83)
Analgesics/antipyretics	71 (95.94)
Paracetamol Paracetamol + Ibuprofen Duration of use	68 (95.77) 3 (4.05) 1-10 days
Respiratory drugs	64 (86.49)

Salbutamol	41 (55.40)
Antihistaminic drugs	63 (85.13)
Cetirizine	19 (30.15)
Chlorphenaramine maleate	41 (65.07)
Phenaramine maleate	3 (4.76)
Saline nasal drops	4 (5.40)
Dextromethorphan	12 (16.21)
Doxophyllin	2 (2.70)
Cough syrup	2 (2.70)
GIT drugs	44 (59.45)
H2 blockers	24 (54.54)
PPI	2 (4.54)
Ondensetron	34 (81.81)
Domperidone	2 (4.54)
ORS	11 (14.86)
Steroids	11 (14.86)
Dexamethasone	2 (18.18)
Hydrocortisone	4 (36.36)
Prednisolone	4 (36.36)
Budesonide	5 (45.45)

PPI - proton pump inhibitors, ORS – oral rehydration salt solution

Table 4: Analysis of supportive medicines used in the study patients: (n=74)

World health organization core indicators

As per WHO core indicators, it was observed that polypharmacy was widely practiced. Antibacterials were prescribed in all patients. Similarly, almost all patients were prescribed injections. More than half the drugs were prescribed by their generic names. A majority of the drugs prescribed were from the National Essential Medicines List (EML) 2011 (86.11%) and the WHO EML 2010 (75%). An analysis of drugs prescribed is given in Table 5.

WHO core indicators	**No. of patients (%)**
Number of drugs prescribed per encounter (mean±SD)	7.25 ± 1.57
Number of drugs prescribed by generic name (%)	50 out of 88 formulations (56.81)
Number of encounters resulting in the prescription of an antibacterial (%)	74(100)

Number of encounters resulting in the prescription of an injection (%)	74 (100)
Number of drugs prescribed from the National Essential Medicines List 2011 (%)	31 out of 36 drugs (86.11)
Number of drugs prescribed from WHO EML	27 out of 36 drugs (75)

2010 (%)	

(WHO=World health organization, EML=Essential medicines list)

Table 5: WHO core prescribing indicators for pediatric inpatients (*n*=74)

Evaluation of appropriateness

Only 10 patients' treatments (13.51%) were regarded logical when compared to the WHO respiratory illness management standards and the IAP guidelines; another 26 (35.14%) were only somewhat rational, and 38 (51.35%) were completely irrational.

Unwanted Drug Effects

There were 74 patients, and 12 of them (16.22%) had an ADR. Eight patients had diarrhea, one had severe gastritis and vomiting, and three had a maculopapular rash accompanied by itching. The World Health Organization's (WHO) causation evaluation standards and Naranjo's probability scale placed all of them in the "possible" category. All of these results may be traced back to taking the recommended antibiotics and/or painkillers and fever reducers. None of the adverse events were classed as serious, and all were assessed to be of moderate intensity. Patients with diarrhea were given ORS, those with gastritis were given intravenous pantoprazole, and those with a rash were given phenaramine maleate syrup. Domperidone or ondansetrone tablets or syrup were recommended for the treatment of nausea and vomiting. With the prescribed care, every patient eventually felt better from their ADRs.

The Price of Care

Medication for in-house patients cost an average of Rs. 314.69. Antibiotics alone accounted for a cost of Rs. 286.17 when factoring in the price of all medications. Drugs for all 74 patients cost a total of Rs 23287.06.

Discussion

The purpose of this research was to examine how pediatric patients with respiratory infections are treated pharmaceutically while in the hospital. Due to heightened vulnerability to infections during the weaning phase, the majority of recruited patients were less than one year of age. Cough, fever, and shortness of breath were the most common first symptoms, indicating the need for hospitalization. In Brazil, approximately 30 percent of hospital admissions were caused by pneumonia, and bronchiolitis was another prevalent diagnosis. [17] Culture and sensitivity tests could not differentiate between bacterial and viral etiologies, although full blood counts were performed on all patients. Treatment was based on the assumption that an elevated white blood cell count was caused by germs. This is significant since viral causes of pneumonia and bronchitis often respond better to rest and fluids rather than antibiotics.

Patients were highly polypharmacized, with an average of 7.25 medications (range: 3- 16) on their prescription lists. Antibacterials, analgesics/antipyretics, and respiratory medications were found to be the most often given treatments, similar to a research done in western Nepal [18]. Combined amoxicillin.In 90%.54 percent of cases, clavulanic acid was administered, followed by cephalosporins in 48.64 percent. The most common antibacterials provided to pediatric inpatients in these studies were penicillin and cephalosporin, which is consistent with findings from studies conducted in Kathmandu [19] and Palestine [4]. This variance in local resistance pattern may explain why these studies favored the use of older penicillin (crystalline penicillin and ampicillin) than more recently developed penicillins. These experiments were also performed around 10 years ago. Nearly half of patients were prescribed two or more antibacterials. Avoiding the time and effort required to identify the organism led to the prescription of many antibacterial drugs at once in an attempt to treat all probable infections. This practice raised the risk of side effects, medication interactions, drug resistance, and the overall expense of treatment [20].

All of the trial participants were given pain relievers, fever reducers, and oxygen as part of the research's supportive care. Patients with rhinosinusitis often take supportive drugs that target symptoms of viral URIs, especially in the early stage of illness. Although RTIs have not been shown to be effective, they may give some patients with brief relief [7,8]. Fever and discomfort from sinus pressure or general malaise are both treatable with analgesics. Although oral decongestants may help those with stuffy noses, they shouldn't be given to children under the age of two or to those with ischemic heart disease or uncontrolled

hypertension. Most patients aged 6 and above may benefit from intranasal decongestants for severe congestion, but treatment should be restricted to 3 days or less to prevent rebound nasal congestion [21]. However, antihistamines may help individuals with predisposed allergic rhinitis or chronic sinusitis [21]. This is because antihistamines thicken mucus and hinder its evacuation. An excessively high rate of antihistamine prescriptions was seen in this research (85.13%).

In this analysis, 55.40 percent of patients were given salbutamol. It is not well proven that bronchodilators are helpful for patients with pneumonia or bronchiolitis [22]. These medications were used to alleviate symptoms, especially in severe instances of wheezing. Cough-and-cold combinations accounted for over half of all respiratory medications prescribed to infants and toddlers younger than a year. According to the results of a Cochrane evaluation evaluating the effectiveness of various combinations, they are no better than a placebo for kids [21]. Use of these drugs in children less than two years old is now prohibited by the US Food and Drug Administration [23]. Overdose is a real possibility, and they haven't been shown to help with respiratory problems in kids anyhow. Antipyretics and intravenous fluids have been utilized effectively as symptomatic and supportive treatment for these individuals. Ineffective and inappropriate use of steroids in lobar pneumonia [24]. Steroids have only been recommended in situations of acute laryngo-tracheo-bronchitis (reduces laryngeal edema) and asthma.

Higher rates of adverse drug reactions (16.22%) were seen in the current research compared to prior findings from India (25). Importantly, our study's findings corroborate the well accepted fact that irrational use of antibacterials led to adverse medication responses, as was previously shown in Spain [26], Brazil [27], and Italy [28]. Half of all ADRs were considered to be unavoidable, whereas the other half occurred because patients were given the wrong medications or because precautions were ignored. The investigator reported all adverse events, and the either the patient or the treating doctor (informal reporting). One possible explanation for the low rate of reported ADRs is that treating doctors may not suspect that their patients' complaints are attributable to ADRs. Patients may not report adverse drug reactions to their doctor because they might not realize the link between their symptoms and the medication.

The survey found that the average cost of medication for each inpatient was 314.69 Indian Rupees. The cost of antibiotics alone was determined to be Rs. 286.17 out of the total price of the drugs. The sum of 23287.06 Rs represents the cost of drugs for all 74 patients. It was a large amount, but not as much as in some other nations. In Pakistan, the average cost each episode varied from $22 to $142, depending on the severity of the illness [30], whereas in Germany the total cost per hospitalized pediatric child with community-acquired pneumonia was €2579 (Rs 153,778)[29]. Possible explanations for this variance include our study's prospective nature and differences in healthcare policy among countries (reimbursements, greater monetary value for productivity). The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) collaborated in 2009 to create a Global Action Plan for the Prevention and Control of Pneumonia (GAPP) [31], which prioritizes impoverished nations and distributes resources to combat the illness.

This research has successfully brought to light the prescription patterns and adverse medication responses associated with the most frequent disorders causing respiratory tract infections in pediatric patients. The present study's limitations lie in the fact that it was done at a single center and during a very little period of time. It was also unable to do a thorough study of the direct cost, indirect cost, and disease burden to the hospital and community. In general, such drug use Research may reveal the current state of medication prescription practices, the existence of various methods to promote the wise use of medicines, and the most efficient use of available resources. Our research shows that antibiotics and respiratory medications are often administered inappropriately. It is crucial to educate both prescribers and caretakers. While it's true that physicians' time constraints in Indian hospitals may prevent them from spending enough time with patients' families, every attempt should be made to do so, especially with the assistance of paramedical staff.

Based on the results of this research, our hospital has to adopt a uniform treatment protocol that accounts for the local sensitivity pattern of the organisms we treat. The present study highlights the current treatment practice of these infections in our hospital and paves the way for further interventions that can help implement the rational use of medicines, despite the fact that culture and antibiotic susceptibility were not performed to confirm the rationality of the antibacterial used.

Conclusion

When it comes to children and respiratory diseases, pneumonia is by far the most prevalent reason for

hospitalization. Patients with respiratory infections should have their infection's source determined as soon as possible. In most cases, treatment for a viral disease is merely supportive. All medical practitioners should be concerned about the widespread misuse of antimicrobials. Selecting an Antimicrobial Drug Wisely the dosing schedule, which has been shown to decrease mortality and illness. The healthcare industry requires standardized treatment recommendations that take into account regional sensitivities. Prescriber and caregiver education on rational treatments has been shown to decrease improper antimicrobial usage, the occurrence of avoidable adverse drug reactions (ADRs), and the expense of medical care.

References

1. Epidemiology and etiology of pediatric pneumonia. 1 Rudan I1, Boschi-Pinto C1, Biloglav Z1, Mulholland K1, Campbell H1. Bull 86:408-16 in the World Health Organization.
2. 2. The International Health Regulations. 2010 Global Health Statistics. WHO;2010. France.
3. Sustainable Development Goal 3 of the United Nations Goals For a better world, here are 17 objectives. The Sustainable Development Goals are available online at http://www.un.org/sustainabledevelopment/. Access terminated on January 21, 2016
4. Parenteral antibiotic prescription patterns in Palestinian children treated at Al-Watani Government Hospital. Sawalha A, Al-Bishtawi G, Al-Khaayyat L, Sweileh W, Al-Ramahi R,J aradat N. Journal of Natural Science Research of An-Najah University, volume 20, pages 191–206 (2006).
5. The F.D.A. comes in at number five. The FDA has issued guidelines for the safe and effective use of over-the-counter cold and flu remedies. Find it at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116839.html. Last modified on June 18, 2009; seen on August 16, 2009.
6. Worrall G, Chaulk P. Expectation or practical knowledge? Family medicine clinical practice guidelines. 353–356 in J FamPract 42 (1996).
7. BMJ 317 (1998): 647–50 7 Hart CA, Kariuki S. Antimicrobial resistance in underdeveloped nations.
8. Drug prescribing patterns in an outpatient pediatric clinic in Moradabad, India; Ashraf H, Handa S, Khan NA. International Journal of Pharmaceutical Science Review and Research, Volume 3, Issue 2, Pages 1-5, 2010.
9. The Ninth World Health Organization. The World Health Organization/University of Maryland Medical Center Causation Assessment System. The document may be seen at http://www.who-umc.org/graphics/4409.pdf. [Accessed last on December 12, 2009].
10. To top it all off, we have 10 authors: Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A technique for calculating the possible side effects of a medicine. Pages 239–245 in Clin Pharmacol Ther 30, 1981.
11. Preventability and severity evaluation in reporting adverse medication reactions. Hartwig S, Siegel J, Schneider PJ. 2011. 11. Journal of Hospital Pharmacy 49

(1992): 2229–232.

12. Lau PM, K. Stewart, and M. J. Dooley. Remarks on the topic of bad medication responses leading to hospitalizations. Journal of Antibiotics 37 (2003): 303-5.
13. Chest congestion and shortness of breath. Managing common childhood diseases with minimal means: recommendations from the Pocket Book of Hospital Care for Children. WHO, Geneva, 2005.
14. Integrated Management of Childhood Illness (IMCI) guideline technical updates: evidence and suggestions for additional adjustments. Worldwide Health Organization; 2005; Geneva.
15. Review of the present state of managing and preventing community-acquired pneumonia in children under the age of five in India. Yadav KK, Awasthi S. 83–97 in Ther Adv Infectious Dis 3, 2016.
16. Sixteenthly, Richard Ofori-Asenso. A deeper dive into the WHO's prescription indicators. 2016;7(1):51-54 in the journal J Pharmacol Pharmacother.
17. Fortaleza, Brazil: Off-label and unlicensed drug use among adults. Santos DB, Clavenna A, Bonati M, Coelho HL. Journal of Clinical Pharmacology, 64, 1111-8 (2008).
18. Prescription trends among pediatric inpatients in a university hospital in western Nepal. Shankar PR, Upadhyay DK, Subish P, Dubey AK, Mishra P. A 47(2006):261 issue of Singapore Medical Journal.
19. J Nepal Health Res Counc 2 (2004): 31-6; Palikhe N. Prescribing trend of antibiotics in pediatric hospital of Kathmandu valley.
20. Vashishtha VM. The need for novel antibiotics and the spread of antibiotic resistance. Indian Pediatrics 47:505–6 (2010).
21. Over-the-counter medicines for acute cough in ambulatory children and adults: a systematic review and meta-analysis [21] by Smith SM, Schroeder K, and Fahey T. 2008 CD001831 Cochrane Database Syst Rev.
22. Review of bronchodilators for bronchiolitis. Gadomski AM, Brower M. 2010 Cochrane Database of Systematic Reviews; CD001266.
23. The FDA, which is number 23 on the list. The FDA has issued guidelines for the safe and effective use of over-the-counter cold and flu remedies. Find it at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116839.html. Last visited on August 16th, 2016 [Last accessed on August 16th, 2016].
24. Bozza FA, Bozza PT, Castro-Faria-Neto HC, Povoa P, Soares M, Salluh J. A systematic study of the use of corticosteroids in cases of severe community-acquired pneumonia. The year 2008 saw the publication of the R76 on Critical Care 12.
25. GS Iyer, PP Patel, JR Panchal, and RK Dikshit. Drug therapy for respiratory infections in children admitted to a tertiary care academic medical center: a systematic review and meta-analysis.

Global Health and Medicine 3 (2013): 140-5.

26. To cite this article: Martinez-Mir I, Garcia-Lopez M, Palop V, Ferrer JM, Rubio E, Morales-Olivas FJ. Adverse medication responses in inpatients: a prospective study. Br J Clin Pharmacol 47:681-8 (1999).

27. Pharmacoepidemiol Drug Saf. 15 (2006): 635-40. 27. Dos Santos DB, Coelho HL. Adverse drug responses in hospitalized children in Fortaleza, Brazil.

28. Adverse medication responses in children: a review of safety warnings and a prospective study by Clavenna and Bonati 28. Reference: Arch Dis Child 94, no.

29. To cite this article: Ehlken B, Ihorst G, Lippert B, Rohwedder A, Peterson G, Schumacher M, and others. The monetary toll taken by young children in Germany due to nosocomial and community-acquired respiratory illnesses. Journal of European Pediatrics 164, no. 5 (2005: 607-15).

30. Economic study of pediatric pneumonia in northern Pakistan: a systematic review and meta-analysis30 Hussain H, Waters H, Khan AJ, Omer SB, Halsey NA. 23:438-442 in Health Policy and Planning (2008).