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Pattern of Antibiotic Usage in Children Hospitalized for Common Infectious Diseases

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Abstract

Background: Antibiotic misuse is a major cause of antimicrobial resistance.
Objectives: The present study aimed at determining the pattern of antibiotic usage in previously healthy children hospitalized for common infectious diseases in a tertiary care children's hospital.
Methods: This study was the second part of a previous study in which inpatient charts of children hospitalized from October 2013 to September 2014 were reviewed to determine the rationality of drug use. Data from the first study were analyzed to define the antibiotic usage pattern in urinary tract infection, acute meningitis, community acquired pneumonia, fever without a localized source and acute gastro-enteritis. The data were checked independently by two pediatric infectious disease specialists to assess the appropriateness of prescribed antibiotics and in case of disagreement, rechecked by a third member.
Results: Hospital charts of 140 children were reviewed; 47 had been treated for urinary tract infection, 31 for pneumonia, 25 for acute meningitis, 24 for acute gastroenteritis and 13 for fever without a localized source. One-hundred and fourteen children (81.42%) received 208 prescriptions for antibiotics (1.82 antibiotics/patient). Nineteen different antibacterial drugs and 2 antivirals (acyclovir and oseltamivir) were prescribed. Most frequently prescribed antibiotic was ceftriaxone. More than 25% of prescriptions for antibiotics were needless. In 91.6% of the prescriptions the medications had been prescribed by generic names. Dosing errors were observed in less than 7% and patients received the medication for prolonged duration, 25.6% of times.
Conclusions: Nonuniformity of antibiotic usage, a high rate of needless antibiotic prescriptions, and prolonged administration found in this study call for stringent antibiotic stewardship.

Keywords: Antibiotics, Antibiotic Stewardship, Antimicrobial Resistance, Infections, Prescriptions

1. Background

The last decades have witnessed a rapidly escalating bacterial resistance to most antimicrobials. Although various biologic or biochemical mechanisms may lead to bacterial resistance, ample evidence points to the fact that antimicrobial resistance is directly linked to antibiotic usage (1-3).

While overuse and misuse of antibiotics have been observed globally, both in industrialized and developing countries, this problem has assumed immense proportions in the latter, such that antibiotics are prescribed for almost 50% of viral respiratory tract infections and viral gastroenteritis cases (4, 5). With the emergence of multidrug resistant microorganisms together with a decline in the development of new antibiotics, many researchers fear that the word is heading towards a 'postantibiotic era' when human beings may die of common infectious diseases that could have been effectively treated with easily available antibiotics (1, 4, 6).

Antibiotic prescribing errors cover a wide range, from prescribing antibiotics needlessly to prescribing the wrong antibiotic or prescribing a broad spectrum antibiotic in situations where a narrow spectrum antimicrobial was indicated, giving a wrong dose, using an inappropriate route of administration or continuing the medication for prolonged duration.

Studies on antibiotic usage for inpatients have demonstrated that antibiotics may have been prescribed unnecessarily in almost one-third of hospitalized patients; most authorities agree that effective surveillance of antibiotic usage is essential for controlling unnecessary and/or incorrect antibiotic administration to prevent antimicrobial resistance (1, 3, 6, 7).

This study addressed the issue of antibiotic usage in

children hospitalized for common acute illnesses in a university-affiliated tertiary care children's hospital.

2. Methods

This study was the second part of a previous study in which inpatient charts of children hospitalized from October 2013 to September 2014 were reviewed by trained members of the study team to determine the rationality of the drug use. This study was performed in a university-affiliated tertiary care children's hospital situated in Tehran. The previous data were analyzed to define the antibiotic usage pattern in previously healthy children, who had been hospitalized with urinary tract infection (UTI), acute meningitis, pneumonia, fever without a localized source and acute gastro-enteritis.

Case records of children with underlying chronic diseases that would make them prone to repeated or serious infections, immune deficiency and major congenital abnormalities were excluded. Recommendations from the world health organization were followed in designing this research. The WHO protocol DAP 93.1 was used to design the questionnaire for this study; patients' demographics, discharge diagnoses and hospital course were documented (8). Patients' details included clinical manifestations, laboratory and imaging results, duration of hospitalization and discharge diagnoses. Particulars of the prescribed antibiotics (type, dose, route of administration and duration of administration, and any change in treatment) were noted.

Prescriptions had been ordered, approved or changed by attending physicians (pediatric nephrologists, pediatric neurologists, gastro-entrologists, or Infectious disease specialists). Study questionnaires were filled by a third-year pediatric resident who had been trained to extract and document relevant data from the case notes and checked independently by two pediatric Infectious disease specialists (faculty members) to assess the appropriateness of prescribed antibiotics and, in case of disagreement, rechecked by a third member.

Reviewers considered the antibiotic prescription appropriate if the type of antibiotics used, the dosage and the duration of treatment were in accordance with in-hospital protocols, which are in accordance with international guidelines, recommended in pediatric texts, for example, Nelson textbook of pediatrics.

All data were then transferred to IBM SPSS statistics version 22 and percentage of antibiotics used for different patients calculated along with the rationality of prescriptions, dosing errors and treatment duration.

3. Results

Hospital charts of 140 children were reviewed. Forty-seven children had been treated for UTI, 31 for pneumonia, 25 for acute meningitis, 24 for acute gastroenteritis and 13 for FWLS, (Table 1).

One-hundred and fourteen children, (81.42%) were prescribed antibiotics; 208 prescriptions for antimicrobials had been written, making an average of 1.82 antibiotics/patient. Total of 19 different antibacterial drugs and 2 different antivirals, acyclovir and oseltamivir were prescribed (Tables 2-5). Ceftriaxone was the most frequently prescribed antibiotic (Table 6). No antibiotic was prescribed in 26 patients; 44 children received 1 antibiotic, 70 children were given antibiotic combinations with 60 received 2 antibiotics, 7 patients were administered 3 different antibiotics; 4 received 4 different antibiotics and 1child with acute meningitis was prescribed 6 different types of antibiotics.

More than 25% of the prescriptions for antibiotics were considered irrational or needless by the reviewing team composed of pediatric infectious disease specialists. In 91.6% of the prescriptions, the medications had been prescribed by generic names. Dosing errors were observed in less than 7% of the participants and the patients received the medication for prolonged duration in 25.6% (Table 6). Appropriate route of administration had been used for the prescribed drug in more than 93% of times.

4. Discussion

Overall 19 different antibiotics and 2 anti-viral medications had been prescribed for patient included in the study, with more than 80% of the patients received antibiotics with a mean of 1.8 antibiotics per patient. Only a small fraction, less than 9%, of antibiotic administrations were oral; more than 90% of antibiotic treatments were administered parenterally. As the children included in this study had been hospitalized for treatment of infectious diseases, substantial antibiotic usage was expected; however, experts recommend switching from parenteral to oral medication once the child is stable, or even initiating the treatment with oral antibiotics, especially in children with UTI and pneumonia (9-11). Overuse of injections leads to numerous adverse effects, including needle stick injuries and transmission of blood-borne infections (12-14). A point prevalence survey on antibiotic use in Croatia reported an antibiotic prescription rate of 58.8% of hospitalized patients with more than 30% receiving the drug in the oral form (15). A high rate of the parenteral antibiotic therapy was also reported from a pilot study conducted by

Table 1. Particulars of Antibiotic Treatment in Different Illnesses

Disease	No. of Patients	No. Not Given Antibiotics	No. of Antibiotic Prescriptions	Data Available	No. of Different Antibiotics	Antibiotics/Patient	Rational Prescription No. (%)
UTI	47	0	78	78	8	1.66	49 (62.8)
Gastroenteritis	24	15	8	8	2	0.33	4 (50)
FWLS	13	6	11	11	6	0.84	7 (63.63)
Acute meningitis	25	0	64	64	11	2.56	62 (97)
Pneumonia	31	5	47	45	15	1.51	34 (75.55)
Total	140	26	209	207	-	1.49	156 (75.36)

Abbreviations: FWLS, fever without localizing signs; UTI, urinary tract infection.

Table 2. List of Antibiotics Prescribed in 47 Patients With Urinary Tract Infection

Drug	Times Prescribed (%)	Generic Name, No. (%)	Rational Prescription, No. (%)	Correct Dose, No. (%)	Approved Duration, No. (%)	Approved Route, No. (%)
Ceftriaxone	31 (78.7%)	28 (90.32)	27 (87.1)	29 (93.55)	28 (90.32)	31 (100)
Amikacin	27 (57.4%)	27 (100)	9 (33.33)	26 (96.3)	14 (51.85)	27 (100)
Cefotaxime	10 (21.2%)	10 (100)	9 (90)	10 (100)	9 (90)	10 (100)
Ceftazidime	4 (8.5%)	4 (100)	3 (75)	4 (100)	3 (75)	4 (100)
Ciprofloxicin	2 (4.25%)	2 (100)	0 (0)	1 (50)	0 (0)	2 (100)
Imipenem	2 (4.25%)	2 (100)	0 (0)	1 (50)	0 (0)	2 (100)
Cefixime	1 (2.13%)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Penicillin	1 (2.13%)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)
Total	78	73 (93.58)	49 (62.8)	73 (93.58)	55 (70.51)	78 (100)

Table 3. List of Antimicrobials Prescribed for Patients Admitted with Fever Without Localizing Signs

Drugs	Times Prescribed (%)	Generic Name, No. (%)	Rational Prescription, No. (%)	Correct Dose, No. (%)	Approved Duration, No. (%)	Approved Route, No. (%)
Ceftriaxone	5 (38.46)	4 (80)	3 (60)	5 (100)	3 (60)	5 (100)
Cefotaxime	2 (15.38)	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Ceftazidime	1 (7.69)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Vancomycin	1 (7.69)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Cefixime	1 (7.69)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)
Acyclovir	1 (7.69)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Total	11 (84.61)	10 (90)	7 (63.63)	11 (100)	7 (63.63)	11 (100)

Gupta et al. at a medical emergency unit in India, where most patients received parenteral antibiotics (16).

A critical evaluation of antibiotic use in a Turkish University hospital reported a rational antibiotic usage in 77% of their patients with a figure of 1.8 antibiotics/patient, and unnecessary usage in 23%; their rate of antibiotic usage and their figures about needless prescriptions were compared broadly with ours (7).

In our study, although one single drug, namely ceftriaxone has been administered most frequently, we ob-

Table 4. List of Antibiotics Prescribed in Patients with Acute Meningitis

Drugs	Times Prescribed (%)	Generic Name, No. (%)	Rationality, No. (%)	Correct Dose, No. (%)	Approved Duration, No. (%)	Approved Route, No. (%)
Ceftriaxone	24 (96)	23 (95.83)	24 (100)	24 (100)	23 (9.83)	24 (100)
Vancomycin	25 (100)	23 (92)	25 (100)	23 (92)	20 (80)	25 (100)
Cefotaxime	3 (12)	3 (100)	3 (100)	2 (66.6)	2 (66.6)	3 (100)
Ceftazidime	2 (8)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)
Ampicillin	2 (8)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)
Chloramphenicol	1 (4)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Gentamycin	1 (4)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Meropenem	1 (4)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Rifampin	2 (8)	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Amoxicillin clavulanate	1 (4)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Acyclovir	2 (8)	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Total	64	59 (92.2)	62 (97)	61 (95.3)	55 (86)	64 (100)

Table 5. List of Antimicrobials Prescribed in Patients with Discharge Diagnosis of Pneumonia

Drugs	Times Prescribed (%)	Data Available	Generic Name, Number (%)	Rationality, Number (%)	Correct Dose, Number (%)	Approved Duration, Number (%)	Approved Route, Number (%)
Ceftriaxone	21 (67.74)	20	14 (70)	14 (70)	16 (80)	13 (65)	18 (90)
Amikacin	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Cefotaxime	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Ceftazidime	2 (6.45)	2	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Imipenem	1 (3.22)	1	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)
Vancomycin	3 (9.67)	3	3 (100)	2 (66.6)	3 (100)	2 (66.6)	3 (100)
Azithromycin	8 (25.80)	7	6 (85.71)	6 (85.71)	7 (100)	6 (85.71)	6 (85.71)
Clindamycin	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Gentamycin	1 (3.22)	1	1 (100)	1 (100)	1 (100)	0 (0)	1 (100)
Amoxicillin clavulanate	1 (3.22)	1	0 (0)	1 (100)	1 (100)	1 (100)	1 (100)
Meropenem	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Ampicillin	3 (9.67)	3	3 (100)	3 (100)	3 (100)	3 (66.7)	3 (100)
Metronidazole	1 (3.22)	1	1 (100)	0 (0)	1	0	1
Cotrimoxazole	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Oseltamivir	1 (3.22)	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Total	47	45	37 (82.2)	34 (75.55)	40 (88.8)	32 (71.1)	41 (91.1)

served the usage of a wide range of different antibiotics for treatment of common infectious diseases, which may indicate the lack of a uniform antibiotic prescription policy in the study center. Usage of a wide range of antimicrobials has been reported from other centers as well (7, 16).

Likewise, ceftriaxone or other broad spectrum cephalosporins have been cited as the most frequently used antibiotics in several other studies (15-18). Extensive use of the third generation cephalosporins has led to the emergence of extended beta-lactamase-(ESBL) producing

Table 6. Data of 19 Prescribed Antibiotics in 140 Patients

Name	Times Prescribed	Data Available	Generic Name, No. (%)	Antibiotic Needed, No. (%)	Correct Dose, No. (%)	Correct Duration, No. (%)	Approved Route, No. (%)
Ceftriaxone	87	86	75 (87.2)	70 (81.4)	78 (90.7)	70 (81.4)	84 (97.7)
Vancomycin	31	31	29 (93.5)	28 (90.3)	29 (93.5)	24 (77.4)	31 (100)
Amikacin	28	28	28 (100)	9 (32)	27 (96.4)	14 (50)	28 (100)
Cefotaxime	16	16	15 (93.7)	14 (87.5)	15 (93.7)	13 (81.2)	16 (100)
Ceftazidime	9	9	9 (100)	7 (77.7)	9 (100)	7 (77.7)	9 (100)
Ampicillin	5	5	4 (80)	5 (100)	5 (100)	5 (100)	5 (100)
Imipenem	3	3	3 (100)	0 (0)	3 (100)	0 (0)	3 (100)
Gentamycin	2	2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)
Meropenem	2	2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)
Ciprofloxicin	2	2	2 (100)	0 (0)	1 (50)	0 (0)	2 (100)
Chloramphenicol	1	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Metronidazole	1	1	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)
Clindamycin	1	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Penicillin	1	1	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)
Oral Antibiotics:							
Azithromycin	8	7	6 (85.71)	6 (85.71)	7 (100)	6 (85.71)	7 (100)
Rifampin	2	2	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Amoxicillin clavulanate	2	2	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)
Cefixime	2	2	2 (100)	1 (50)	2 (100)	1 (50)	2 (100)
Cotrimoxazole	1	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
Total	204	202	186 (92)	151 (74.7)	190 (94)	151 (74.7)	190 (94)

microorganisms; it has been noticed that this trend could be reversed by substituting these medications by using a combination of extended-spectrum penicillins and an aminoglycoside instead of cephalosporins (16).

In addition to the evolving bacterial resistance, cephalosporins and specifically ceftriaxone have been reported to cause a wide variety of adverse events ranging from urolithiasis, and hemolytic anemia to severe morbidity and mortality (19-21). In a 10-year study from Iran that extracted data from Iranian Pharmaco-vigilance database from 1998 to 2009, ceftriaxone was recognized as the most common antibiotic responsible for patient death. The authors recognized a history of allergic reactions to beta lactams, rapid injection of the drug, and off-label usage as risk factors for serious or even fatal reactions (19).

Children admitted with a discharge diagnosis of pneumonia had been prescribed 14 different antibiotics in our study, with ceftriaxone as the most frequently administered antibiotic. Although textbook references recommend the use of the third generation cephalosporins for severe community acquired pneumonia in locations, where children are not immunized against pneumococcus and H. influenzae type B and where there is a high prevalence of penicillin resistant pneumococci, authors of a recent Cochrane review about the management of community acquired pneumonia (CAP) suggest that children with severe or very severe pneumonia could be treated with penicillin/ampicillin plus gentamicin or coamoxiclavunalic acid and cefuroxime (13, 22). Only 3 of our patients with CAP received ampicillin and 1 child was given an amoxillin-clavulanic acid, while ceftriaxone was prescribed for 21 patients. Guidelines from the pediatric infectious disease society and infectious disease society of America recommend narrow-spectrum antibiotics for most children admitted for treatment of CAP (18). A large study in the United States, which compared the outcome in children hospitalized with CAP and treated either with narrow-spectrum or broad spectrum antibiotics (ampi-

cillin/penicillin vs. ceftriaxone/cefotaxime) found no appreciable difference in a length of hospital stay, admission to the intensive care unit or readmission between the two groups, however, the cost of treatment in those receiving broad spectrum antibiotics was higher (17).

A qualitative study on the use of antimicrobials in the medical department of a teaching hospital reported needless administration of antibiotics in about 23% of the cases while overprescribing of broad-spectrum antibiotics in situations, where a narrow-spectrum antimicrobial would have been sufficient was identified as the most common prescribing error (23).

It has been acknowledged that prescribing errors for in-patients can be minimized through a proper antibiotic stewardship, which combines health staff education with regular audits of prescription practices (24). Health authorities in industrial countries advocate obligatory antimicrobial stewardship in health care centers and recommend installation of electronic prescription systems in hospitals together with feedback of compliance as an essential part of any quality improvement program (25).

Results of this study identified the most common flaws in antibiotic prescriptions as follows: utilization of many different antibiotics for common infectious diseases, high usage of broad spectrum cephalosporins, especially ceftriaxone, needless and/or prolonged administration of antibiotics in more than 25% of the patients.

The present study had some limitations; the information was gathered from case notes, there is a possibility that important data about a patient's worsening condition that might have prompted the use of a broad spectrum or unusual antibiotic may not have been documented in the case note. However, because the case notes are written by the house staff and periodically checked by the senior staff, we regard that possibility as remote.

Findings of the study highlight an urgent need for regular point prevalence surveys of antibiotic usage and implementation of an efficient antibiotic stewardship.

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References

1. Kieny MP. *The evolving threat of antimicrobial resistance. Options for action. Executive Summary*. [cited 20th July]. Available from: http://whqlibdoc.who.int/publications/2012/9789241503181_eng.pdf.
2. Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev*. 2010;**74**(3):417–33. doi: 10.1128/MMBR.00016-10. [PubMed: 20805405].
3. Abera B, Kibret M, Mulu W. Knowledge and beliefs on antimicrobial resistance among physicians and nurses in hospitals in Amhara Region, Ethiopia. *BMC Pharmacol Toxicol*. 2014;**15**:26. doi: 10.1186/2050-6511-15-26. [PubMed: 24887310].
4. World Health Organization . Bulletin of the world health organization antimicrobial resistance: Revisiting the "tragedy of the commons". *Bull World Health Organ*. 2010;**88**(11).
5. Holloway K DL. *The world medicines situation 2011*. Rational use of medicines; 2015.
6. No authors listed . *Antimicrobial resistance*. [2015 November 08]. Available from: http://www.who.int/mediacentre/factsheets/fs194/en/.
7. Hosoglu S, Parlak Z, Geyik MF, Palanci Y. Critical evaluation of antimicrobial use–a Turkish university hospital example. *J Infect Dev Ctries*. 2013;**7**(11):873–9. doi: 10.3855/jidc.2921. [PubMed: 24240047].
8. Chowdhury A, Das A, Diwan V, Kafle KK, Mabadeje B. *How to investigate drug use in health facilities. International network for rational use of Drugs*. [cited 20th March]. Available from: http://apps.who.int/medicinedocs/pdf/s2289e/s2289e.pdf.
9. Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev*. 2014;**28**(7):CD003772.
10. Lodha R, Kabra SK, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database Syst Rev*. 2013;**4**(6):CD004874.
11. Neuhaus TJ, Berger C, Buechner K, Parvex P, Bischoff G, Goetschel P, et al. Randomised trial of oral versus sequential intravenous/oral cephalosporins in children with pyelonephritis. *Eur J Pediatr*. 2008;**167**(9):1037–47. doi: 10.1007/s00431-007-0638-1. [PubMed: 18074149].
12. No authors listed . *WHO injection safety fact sheet 3rd February 2012*. [cited 9th Aug]. Available from: http://www.wpro.who.int/mediacentre/factsheets/fs_20120204/en/.
13. Farsi D, Zare MA, Hassani SA, Abbasi S, Emaminaini A, Hafezimoghadam P, et al. Prevalence of occupational exposure to blood and body secretions and its related effective factors among health care workers of three Emergency Departments in Tehran. *J Res Med Sci*. 2012;**17**(7):656–61. [PubMed: 23798926].
14. Karimi M, Owlia MB. Nicolau syndrome following intramuscular penicillin injection. *J Coll Physicians Surg Pak*. 2012;**22**(1):41–2. [PubMed: 22237189].
15. Pristas I, Barsic B, Butic I, Zarb P, Goossens H, Andrasevic AT. Point prevalence survey on antibiotic use in a Croatian Infectious Disease Hospital. *J Chemother*. 2013;**25**(4):222–8. doi: 10.1179/1973947812Y.0000000065. [PubMed: 23906076].
16. Gupta M, Malhotra S, Chandra KK, Sharma N, Pandhi P. Utilization of parenteral anti-infective agents in the medical emergency unit of a tertiary care hospital: an observational study. *Pharmacoepidemiol Drug Saf*. 2004;**13**(9):653–7. doi: 10.1002/pds.927. [PubMed: 15362089].
17. Williams DJ, Hall M, Shah SS, Parikh K, Tyler A, Neuman MI, et al. Narrow vs broad-spectrum antimicrobial therapy for children hospitalized with pneumonia. *Pediatrics*. 2013;**132**(5):e1141–8. doi: 10.1542/peds.2013-1614. [PubMed: 24167170].
18. Kaliamoorthy K, Sankaralingam R, Punniyakotti S, Janardhan V, Cheekala UR. Drug utilization evaluation of third generation cephalosporins using core drug use indicators. *Pak J Pharm Sci*. 2012;**25**(2):339–42. [PubMed: 22459458].
19. Shalviri G, Yousefian S, Gholami K. Adverse events induced by ceftriaxone: a 10-year review of reported cases to Iranian Pharmacovigilance Centre. *J Clin Pharm Ther*. 2012;**37**(4):448–51. doi: 10.1111/j.1365-2710.2011.01321.x. [PubMed: 22122488].
20. Shen X, Liu W, Fang X, Jia J, Lin H, Xu M, et al. Acute kidney injury caused by ceftriaxone-induced urolithiasis in children: a single-institutional experience in diagnosis, treatment and follow-up. *Int Urol Nephrol*. 2014;**46**(10):1909–14. doi: 10.1007/s11255-014-0742-x. [PubMed: 24879561].

21. Neuman G, Boodhan S, Wurman I, Koren G, Bitnun A, Kirby-Allen M, et al. Ceftriaxone-induced immune hemolytic anemia. *Ann Pharmacother*. 2014;**48**(12):1594–604. doi: 10.1177/1060028014548310. [PubMed: 25163809].
22. Kelly MS, Sandora TJ. *Community acquired pneumonia. In nelson textbook of pediatrics*. 20th Edition ed. Elsevier; 2016. p. 2088–93.
23. Vlahovic-Palcevski V, Francetic I, Palcevski G, Novak S, Abram M, Bergman U. Antimicrobial use at a university hospital: appropriate or misused? A qualitative study. *Int J Clin Pharmacol Ther*. 2007;**45**(3):169–74. [PubMed: 17416112].
24. Huttner B, Harbarth S, Nathwani D, Escmid Study Group for Antibiotic Policies . Success stories of implementation of antimicrobial stewardship: a narrative review. *Clin Microbiol Infect*. 2014;**20**(10):954–62. doi: 10.1111/1469-0691.12803. [PubMed: 25294340].
25. Cooke J, Alexander K, Charani E, Hand K, Hills T, Howard P, et al. Antimicrobial stewardship: an evidence-based, antimicrobial self-assessment toolkit (ASAT) for acute hospitals. *J Antimicrob Chemother*. 2010;**65**(12):2669–73. doi: 10.1093/jac/dkq367. [PubMed: 20935301].