Research Article ISSN 2277-3657
Available online at www.ijpras.com

Volume 4, Issue 4 (2015):69-76

International Journal of Pharmaceutical Research & Allied Sciences

Monitoring of Adverse Drug Reactions in Pediatric Department of a Tertiary Care Teaching Hospital: A Hospital Based Observational Study

Dr. Mrutunjay Dash[1], *Dr. Monalisa Jena[2], Swati Mishra[2], Dr. Maitreyee Panda[3], Dr. Nibedita Patro[3]

1. *Department of Paediatrics, IMS & SUM Hospital, SOA University, Bhubaneswar- 751003, (Odisha*
2. *Department of Pharmacology, IMS & SUM Hospital, SOA University, Bhubaneswar 751003, (Odisha)*
3. *Department of Skin & VD, IMS & SUMHospital, SOA University, Bhubaneswar- 751003, (Odisha*

*E-mail: drmonalisajena@gmail.com

Subject: Medical Sciences

Abstract

Objective: The present study was conducted to monitor adverse drug reactions in paediatric population of a tertiary care teaching hospital of Bhubaneswar, Odisha. **Materials and Methods:** It is one year longitudinal observational study was undertaken in the Paediatric department in collaboration with department of pharmacology and Dermatology of IMS & SUM Hospital, Bhubaneswar, Odisha. The collected adverse drug reaction reports were analyzed for ADR pattern, drug groups, demographic profile (age & sex), causality, severity, and preventability of the ADR. **Results:** A total of 155 ADRs were documented during the study period among 127 pediatric patients. Out of 127 patients, male represented 37.79 % while females represented 62.20 % of total cases. Maximum number of ADRs were seen in patient of age group 2 – 11 years (57. 4%) followed by adolescent & newborn . the most common organ system affected was skin & mucous membrane followed by GI, hepatic, renal & CNS. Most common group of drugs used in paediatric department showing adverse drug reaction was drugs used in seizures (Anti epileptic drugs) (37.03%) followed by antimicrobial agents (25.92%). No definite variety of ADR was detected in our study period. There was no case of death report in our study period. There were more occurrences of ADRs with multiple drugs compared to single drug therapy. **Conclusions:** Many ADRs were seen in paediatric populations which should be properly evaluated, monitored & prevented as early & better as possible.. This indicates the need for a rigid pharmacovigilance among pediatric patients to ensure safety of drug therapy.

Keywords*: Adverse drug reaction, pediatric, pharmacovigilance, anti epileptic drugs*

Introduction:

Pediatric populations are more vulnerable for unlicensed or off label prescriptions as these medicines have not been adequately tested and/or formulated and authorized for use in appropriate paediatric age groups and the same has been seen with ADR monitoring of drugs prescribed in paediatric populations(neonates, infants, children and adolescents) in comparison to adult. [1, 2, 3] Paediatric patients constitute a vulnerable group with regard to rational drug prescribing since many new drugs are marketed without pharmacovigilance study in this age group [4], thereby increasing the risk of drug toxicity. [5] It increases our focus for more practice of pharmacovigilance for pediatric use medicines. Diseases in pediatric populations are different from their adult counterparts both qualitatively and quantitatively which in turn may affect either the benefit or the risk of therapies (or both) with a resulting impact on the risk/benefit ratio. The reason for this includes : limited availability of safety data due to the lack of clinical trials in the paediatric population; under- or over-dosing in some age groups due to the lack of pharmacokinetics data; maturation, growth and development of the paediatric population susceptible to drug-induced growth and development disorders. Pediatricians should be aware& pay a vigilant eye on the use of off label drugs especially for those categories of drugs which have clinical studies supporting their safety and/or efficacy as they increases the risk of adverse reactions. [6, 7] Adequate controlled clinical trials in children, with the notable exceptions of pediatric oncology and vaccinations are lacking because of ethical considerations. Only a vigilant post marketing surveillance detects ADRs occurring uniquely in children, for example, sulfonamide induced kernicterus in premature infants

[8], chloramphenicol induced "gray syndrome" [9] and Phenytoin induced movement disorders. [10]

There are some limitations in doing ADR monitoring in children such as:

1. ADRs may not be well noticed in children, as they are unable express.
2. Drugs may decrease growth rate (corticosteroids used for nephrotic syndrome)
3. Skin reactions are common in paeditric populations like drug reactions (antimalarials) [11]
4. Socio cultural influence in the frequency of ADRs [12]
5. Disease spectrum in developing countries like Indian children is somewhat different than in developed countries.
6. Malnutrition is another factor which affects the pharmacokinetics and ADRs.
7. Irrational multiple drug prescriptions are common in pediatric practice which also influence DRs (ventricular arrhythmias with antihistamine terfenadine in combination with antifungal agent ketoconazole) [l3]
8. Ayurvedic and homeopathic medications with allopathic drugs("shankapushpi" used as a memory enhancer has been shown to interact with phenytoin, leading to break through seizures) [14]
9. Certain drugs not recommended for pediatric use are being widely used in Indian children (eg: ciprofloxacin). In 1990, a survey showed ADRs to ciprofloxacin in pediatric practice [15] but it is well prescribed in our study population.
10. Additives such as colorings, flavorings and sugars are being widely used in liquid formulations prescribed in pediatric practice can cause rhinitis, urticaria, headache, gastrointestinal dysfunction, asthma and even anaphylactic shock. [16]

There are various criteria which differentiate between the spectrums of ADRs seen in adults & children such as frequency, nature, and severity. It is not always correct to predict the same ADRs in children that is seen with adult population [17] d/t differences in anatomical body proportions, pharmacokinetic & pharmacodynamics differences related to age and according to the above criteria's susceptibility to particular toxic effects is seen more commonly in children than adult. [18] Some ADRs are specific to the paediatric population because of the growth and development that children undergo (e.g. Reye's syndrome with acetyl salicylic acid. [19] Other ADRs are more common in children (e.g. dystonia with metoclopramide. [20]

Considering the above mentioned factors that are responsible for ADRs with different spectrum, attention has begun to focus on ADRs in the paediatric population. The aim of this study was to assess: 1) the incidence and common types of ADRs; 2) the drug classes most frequently involved in ADRs among patients 3) severity & causality assessment.

Materials & methods:

A longitudinal observational study was undertaken in the Paediatric department in collaboration with department of pharmacology and Dermatology of IMS & SUM Hospital, Bhubaneswar, Odisha from January 2014 to December 2014. Permission from the institutional ethics committee was obtained. Consent was obtained from the patient or their guardians. All the previous prescriptions and case sheets which are available were reviewed. Patients in the wards and outpatient department of pediatrics during the study period were monitored actively for occurrences of any ADRs till their discharge from the hospital. All patients of either sex in pediatric age group less than 14 years of age were included in the study. Monitoring for adverse effects was based on regular questioning & laboratory indications (complete hemogram, peripheral smear, electrolytes, and liver and renal function tests).

The collected reports were documented and analyzed for causality, severity, preventability, and demographic profile. 127 patients were enrolled for this study using self-reporting method for selection of cases using ADR reporting form by CDSCO. Following patients were excluded: [21]

(i) Patients not willing to take part in the study,

(ii) Patients dropping out the study at any stage at their will

(iii) Patients lost to follow up.

Inclusion criteria are:

(i) Patients of all age groups & either sex

(ii) Developing a suspected adverse cutaneous drug reactions following use of any medication were included in the study.

Causality of ADRs was assessed by Naranjo's algorithmic scale [22] as definite, probable, and possible by a scoring method. Severity of the ADRs was assessed by Modified Hartwig and Siegel Scale [23] which gives an overview of the severity of ADR whether it is mild, moderate, or severe in nature.

Thus the present study was undertaken: [24]

1. To collect the demographic details of the paediatric populations showing atleast one ADR

2. To identify the incidence & pattern of ADRs
3. To assess the causality & severity of the reported ADRs.

Observations & result:

A total of 500 patients were screened for the study of which 127 patients were suspected of having atleast one ADR and included in our study. In our study group 127 patients developed 155 ADRs of various types. (Table 1).Some patients developed more than one ADR (20 patients developed 2 ADRs and 4 patients developed 3 ADRs).Out of 127 patients, male represented 37.79 % (n= 48) of the cases while females represented 62.20 % (n= 79) (Table 1). Maximum number of ADRs were seen in patient of age group 2 – 11 years (57. 4%) followed by adolescent (29.13%) & newborn (11.81%) respectively. Average length of stay in hospital was noticed of 7days.

Table 1: Demographic and clinical characteristics of children (both outpatient & In patient) (n= total number of patients with ADR) (n=127)

	Number	%
Patients (N.) with ADR	127	
Age, years:		
Newborns(0 - 30 days)	2	1.57
Infants (1 month - 2 years)	15	11.81
Children (2 - 11 years)	73	57.4
Adolescents (12 - 14years)	37	29.13
Gender		
Male	48	37.79
Female	79	62.20
Others		
Length of stay, days (inpatients)	7 days	
N. of patients exposed to ≥1 drug	28	
N. drugs/patient	2.12 (total number of drugs 270)	

In most of the ADRs, the organ system affected was skin & mucous membrane followed by GI, hepatic, renal & CNS. Skin rashes in the form of erythema multiforme, pustular arshes, fixed drug eruptions, Steven Johnson syndrome, macular & mobiliform rashes (51.61%) were the commonest ADR noted followed by GI & renal toxicity. (Table 2)

Table 2: ADRs according to the organ system affected & the suspected drugs (n= 155; number of ADRs)

Types of reaction in different organ system	Suspected drugs	Total percentage
Cutaneous manifestation (80)		
Erythema multiforme	Ampicillin, Ceftriaxone¸ Vaccine induced, phenytoin	51.61%
Pustular rash	Ceftriaxone, Phenytoin	
Fixed drug eruption	Vancomycin(Figure 1), Carbamazepine, Phenytoin	
Stevens Johnson syndrome	Ceftriaxone, Carbamazepine, Lamotrigine	
Macular and morbiliform rash	Ampicillin, INH(Figure 2)	
GI system (38)		
Diarrhoea	Ampicillin, amoxicillin Cefixime	24.51%
Vomiting	Ceftriaxone , Ceftazidime	
Aphthous ulcer, oral thrush, candidiasis	Fluticasone, beclomethasone	
Hepatic (7)		4.51%
Hyperbilirubinaemia	Ceftriaxone, carbamazepine	
Hepatitis (Jaundice)	INH, Rifampicin	
Renal (12)		7.74%
Manifestations: cola colored urine, increased BUN	Vancomycin, Amikacin	

CNS manifestation(3)		
Fever	Vaccine induced (whole cell pertusis)	1.93%
Irrational behavior	Anticonvulsants (Valproic acid,Levetiracetam)	
Others (15)		9.67%
Anaphylactic shock (2)	Vaccine induced	
Growth retardation (5)	Steroids (Prednisolone, Phenytoin	
Myopathy (3)	Steroids	
Tachycardia, tremor (3)	Salbutamol	
Hypokalemia (2)	Levosalbutamol	

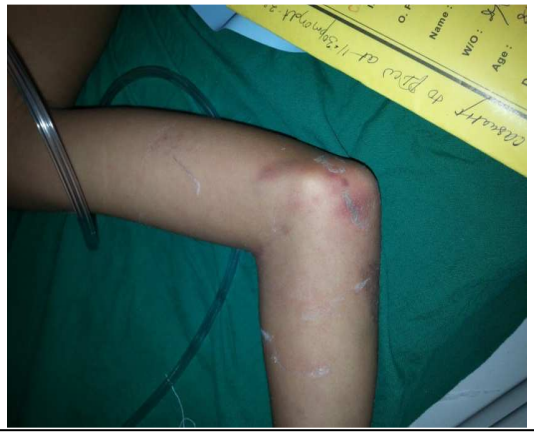

Fig 1: Fixed drug eruption with vancomycin

Fig 1: Maculopapular drug rash with INH

Most common group of drugs used in paediatric department showing adverse drug reaction was drugs used in seizures (Anti epileptic drugs) (37.03%) followed by antimicrobial agents (25.92%). Amongst the antiepileptics, most common drug showing maximum ADRs was Valproic acid followed by carbamazepine & Phenytoin whereas most common antimicrobials showing ADR was Ceftriaxone (parenteral) followed by cefixime(oral). Other antimicrobials showing significant ADRs were amikacin, vancomycin and amoxicillin & ampicillin. Other less common groups of drugs showing ADRs in paediatric populations were NSAIDs, steroid, sympathomimetics & vaccines (Table 3).

Table 3: Most prescribed drugs showing ADRs in paediatric populations (n= 270)

Groups of drugs	Total number with %
Antiepileptic agents (100)	37.03
Valproic acid	
Carbamazepine	
Phenytoin	
Leveteracetam	
Lamotrigine	
Antimicrobial agents & chemotherapeutic agents (70)	25.92
Ceftriaxone	
Cefixime	
Amoxicillin	
Amoxicillin + clavulanic acid	
Ampicillin	
Ciprofloxacin	
Amikacin	
Vancomycin	
INH, Rifampicin	
Others	
Analgesics (53)	19.62
Paracetamol	
Ibuprofen	
Diclofenac	
Corticosteroids for systemic use (27)	10
Prednisone	
Hydrocortisone	
Fluticasone, beclomethasone	
Others	
Sympathomimetics (17)	6.29
Salbutamol	
Levosalbutamol	
Vaccines (3)(Whole cell pertusis)	1.11

Assessment by modified Hartwig and Siegel scale for severity of ADRs showed highest percentage of ADRs (74%) were mild (e.g., nausea, gastrointestinal distress, oral thrush, headache, cough, etc.), which were well tolerated by the patients, 20% of ADRs were classified as moderate (e.g., sinus tachycardia with salbutamol).and remainder being severe.(Table 4)

All drug-related adverse events were evaluated according to the Naranjo's probability scale (Table 5), 20% of the events were in possible category (oral candidiasis with fluticasone; oral thrush with beclomethasone, GI distress with amoxicillin etc) and 80% under probable variety (tremor, sinus tachycardia with salbutamol, hyperbilirubinaemia with Ceftriaxone, jaundice with INH etc). No definite variety of ADR was detected in our study period. Number of serious reactions requiring hospitalization in our study was 9 around 6% of the total ADRs. They had undergone prompt management without any mortality report. Amongst the nine patient; two was a newborn with feature of severe hyperbilirubinemia with Ceftriaxone, five patients were in infancy state with 2 cases of carbamazepine with hepatotoxicity, 2 cases of steroid myopathy with purple skinned rash, one case of vancomycin with renal toxicity manifested as cola colored urine & increased blood urea nitrogen level and three cases of children 2 with salbutamol (tremor & tachycardia) and one with steroid myopathy.(Table 6) In case of outcome result of all the ADRs, 80% were cured and 20% getting better either with good vigilance, stopping the suspected drug or changing the dosing schedule or with vigorous treatment modalities. There was no case of death report in our study period. (Table 7)

Table 4: ADR classification on the basis of severity: (n=150)

Severity	Number of ADRs	Percentage
Mild	111	74
Moderate	30	20
Severe	9	6

Table 5: Causality assessment by Naranjo causality assessment score and preventability assessment by modified Schumock & Thomton scale of preventability: (n=150)

Causality	Number of ADRs	Percentage
Possible	30	20
Probable	120	80
Definite	0	

Table 6: Number of serious ADRs reports in relation to age necessitating hospitalization:

Age of child	Number of ADR Reports (n)
New born	**2**
Infants	**5**
Children	**2**

Table 7: Outcomes resulting from ADR Reports:

Outcome	Number of ADR Reports [n (%)]
Cure	80%
Getting better	20%
Death	0

Discussion:

Adverse drug reaction in paediatric population is a worrisome topic in the management of various diseases in this age group as the incidence of drug induced reaction and morbidity & mortality due to this is alarmingly increasing in our society. [25, 26] there were various studies undergoing regarding the issues of ADR monitoring, their management, prevention and outcome in paediatric population and has been found that ADRs were associated with 243 reported deaths among young children each year, in the age groups of newborn to 2 years of age. [27] In our study the scenario was little bit different as maximum number of ADRs was seen amongst the 2 – 11 years category that is around 57. 4% followed by adolescent category (29. 13%). In our study, a total of 48 (37.79%) ADRs & 79 (62.20%) ADRs were reported for male and female patients, respectively which differ from the study by M. Gallo et al where 55.5% were boys and 44.5% girls [28] and Hui Li et al where (40.41%) and (59.59%) ADRs were reported for female and male patients, respectively. [29] The average number of drugs per patient in our study was 2.13, which is consistent with the findings of other studies. [30, 31]

The most commonly affected organ system affected was the skin (52 % of ADRs) which is in accordance with various other studies. [28, 32] CADRs (cutaneous ADR) account for the majority of ADRs in hospitalized children. [33] The most frequently seen CADRs was a rash which was similar to the findings of other studies. [34, 35] Outpatient studies of CADRs estimate that 2.5% of children, who are treated with a drug, and up to 12% of children treated with an antibiotic, will experience a CADR. [36] The next system showing maximum ADRs in paeditric population of our study design was GI system followed by hepatic, renal & CNS.

Most common group of drugs showing adverse drug reaction in our study was Anti epileptic drugs (37.03%) followed by antimicrobial agents (25.92%) which is similar to some studies [37] & differ from other studies which shows antimicrobial agents [38] were the culprit drug and some shows vaccines [29] were the common drug causing ADRs in paediatric populations. In our study three cases of whole cell pertusis vaccine related ADRs were seen and all the three cases were seen in infants. The vaccine responsible was whole cell pertusis vaccine combination causing ADR in the form of excessive

cry, breath holding spells, local side induration, fever & abscess in two cases and a single case of anaphylactic shock.

Mild or moderate adverse drug reactions do not necessarily mean that a drug must be discontinued, especially if no suitable alternative is available. Severe reactions include those that may be life threatening (such as liver failure, abnormal heart rhythms, certain types of allergic reactions), that result in persistent or significant disability or hospitalization, and that cause a birth defect. In our study most of the ADRs were of mild varieties (74%) followed by moderate (20%). The severe categories were of very few around 6%. The study result was comparable to various previous results, [28] and also differs in some cases. [32]

There were no ADRs with a definite causality by Naranjo's Algorithm Scoring system due to small sample size, confined to the outpatient department (OPD) of the paediatric department & a short period of one year & unable to do the rechallenge. Most of the reactions had a probable causality score (80%) followed by possible causality score (20%) which similar to the study of R Priyadharsini et al. [32] Number of serious reactions requiring hospitalization in our study was 9 around 6% of the total ADRs. In case of outcome result of all the ADRs, 80% were cured and 20% getting better. There was no case of death report in our study period.

Conclusion

The methods for ADR detection, evaluation, and monitoring should be strengthened for a pediatric population. The role of pharmacovigilance in monitoring the safety of drugs in children should be evaluated in detection of newer and rarer ADRs. The awareness of spontaneous reporting of ADRs among health care professionals and general population should be given due considerations for preventing the morbidity and mortality among the pediatric population. In this study ADRs occurred more among children and antiepileptics were more commonly implicated. Most of the reactions were of moderate severity. This indicates the need for a rigid ADR monitoring among pediatric patients to ensure safety of drug therapy. Various pharmacovigilance awareness programs should be conducted to increase the spontaneous reporting of ADRs.

"Cite this Article"

M Dash, M Jena, S Mishra, M Panda, N Patro "Monitoring of Adverse Drug Reactions in Pediatric Department of a Tertiary Care Teaching Hospital: A Hospital Based Observational Study" Int. J. of Pharm. Res. & All. Sci. 2015;4(4):69-76

References:

1. Lawson DH. Pharmacovigilance in the 1990s. Br J Clin Pharmacol 1997; 44: 109 - 110.
2. Impicciatore P, Pandolrani C, Bosetti C, Bonati M. Adverse drug reactions in children: a systematic review of published case reports. Pediatr Perinat Drug Ther 1998; 2: 27 - 36.
3. Bonati M, Marchetti F, Zullini MT, Pistotti V, Tognoni G. Adverse drug reactions in neonatal intensive care units. Adverse Drug Reactions Poisoning Rev 1990; 9: 103 - 118.
4. Impicciatore P, Choonara I. Status of new medicines approved by the European Medicines Evaluation Agency regarding paediatric use. Br J Clin Pharmacol 1999; 48: 15- 18.
5. Conroy S, Choonara I, Impicciatore P, Mohn A, Arnell H, Rane AR et al. Survey of unlicensed and off label drug use in paediatric wards in European countries. BMJ. 2000; 320:79–82.
6. Napoleone E: Sperimentazione clinica e territorio: sicurezza ed efficacia. Rivista Pediatria Preventiva e Sociale (RIPPS) 2008, 1(suppl):26-28.
7. Napoleone E, Santuccio C, Marchetti F: "La farmacovigilanza: potenzialità e prospettive anche in pediatria". Medico e Bambino 2008, 4:214-215.
8. Silverman WA, Andersen DH, Blanc WA, Crazier DN. A difference in mortality rate and incidence of kernicterus among premature infants allotted to two prophylactic antibacterial regimes. Pediatrics 1956, 18: 614-625.
9. Lischner H, Seiigman SJ, Krammer A, Parmelee AH Jr. An outbreak of neonatal deaths among term infants associated with administration of chloramphenicol. J Pediatr 1961, 59: 21-34.
10. Chalhub E, Devivo DC, Volpe JJ. Phenytoin-induced dystonia and choreoathetosis in two retarded epileptic children. Neurology 1976, 26: 494-498.
11. Rasmussen JE. Antimalarials-are they safe to use in children? Pediatr Defmatol 1983, 1:89-91.
12. Moussa MA, Bayoumi A, Al-Khars A, Thulesius O. Adverse drug reaction monitoring in Kuwait (1981-84). J Clin Pharmacol 1985, 25:176-181.
13. Honig PK, Wortham DC, Zamani K, Conner DP, Mullin JC, Cantilena LR etal. Terfenadine-ketoconazole interaction: Pharmacokinetic and electrocardiographic consequences. JAMA 1993, 269: 1513-1518.
14. Dandekar UP, Chandra RS, Dalvi SS, Joshi MV, Gokhale PC, Sharma AV et al. Analysis of a clinically important interaction between phenytoin and shankhapushpi, an ayurvedic

preparation. J Ethnopharmacol 1992, 35: 285-288.
15. Karande S, Kshirsagar NA. Adverse drug reaction monitoring of ciprofloxacin in pediatric practice. Indian Pediatr 1992, 29: 181-188.
16. Kulkarni ML, Sureshkumar C, Venkataramana V. Colorings, flavorings and sugars in children's medicines in India. Br Med J 1993, 307: 773.
17. Titchen T, Cranswick N and Beggs S. Adverse drug reactions to non steroidal anti-inflammatory drugs, COX-2 inhibitors and paracetamol in a paediatric hospital. British Journal of Clinical Pharmacology 2005; 59: 718-723
18. Clarkson A. and Choonara I. Surveillance for fatal suspected adverse drug reactions in the UK. Ar-chives of Disease in Childhood 2002; 87: 462-466.
19. Ward M.R. Reye's syndrome: An update. The Nurse Practitioner 1997; 22: 45-46.
20. Yis U, Ozdemir D, Duman M and Unal N. Metoclopramide induced dystonia in children: Two case reports. European Journal of Emergency Medicine 2005; 12: 117-119.
21. Jena M, Mishra S, Panda M, Mishra SS. Cutaneous adverse drug reaction monitoring of different drugs in dermatology OPD of a tertiary care teaching hospital. IJCRR; Int J Cur Res Rev 2013; 05 (07): 77 – 82.
22. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30 (2):239-45.
23. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992; 49:2229-32.
24. Mishra S, Jena M, Jena B, Mishra SS. A Study of Anti-Tubercular Drug Induced Adverse Reactions in Patients Attending Pulmonary Medicine Department of a Tertiary Care Teaching Hospital. Int. J. Pharm. Sci. Rev. Res 2013; n^0 54: 308-311.
25. Berry MA, Shah PS, Brouillette RT, Hellmann J. Predictors of mortality and length of stay for neonates admitted to children's hospital neonatal intensive care units. J Perinatol 2008; 28:297-302.
26. Neubert A, Dormann H, Weiss J, Egger T, Criegee-Rieck M, Rascher W et al. The impact of unlicensed and off-label drug use on adverse drug reactions in paediatric patients. Drug Saf 2004; 27:1059-67.
27. Moore TJ, Weiss SR, Kaplan S, Blaisdell CJ. Reported adverse drug events in infants and children under 2 years of age. Pediatrics 2002; 110:e53.
28. Mariapina G, Antonio C, Maurizio B, Paolo S, Antonio I, Francesco R et al. Active surveillance of adverse drug reactions in children in five Italian paediatric wards. Open Journal of Pediatrics 2012; 2: 111-117.
29. Hui L, Xiao J G, Xiao F Y, Hong J, Wen M D, Jin F X etal. Adverse Drug Reactions of Spontaneous Reports in Shanghai Pediatric Population. PLOS ONE. 2014; 9(2): e89829
30. Buajordet I, Wesenberg F, Brørs O. and Langslet A. Adverse drug events in children during hospitali-zation and after discharge in a Norwegian university hospital. Acta Paediatrica, 2002; 91: 88-94.
31. Neubert A, Dormann H, Weiss J, Criegee-Rieck M, Ackermann A, Levy, M etal. Are computerized monitoring systems of value to improve pharmacovigilance in paediatric patients? European Journal of Clinical Pharmacology. 2006; 62: 959-965.
32. Priyadharsini R, Surendiran A, Adithan C, Sreenivasan S, Sahoo FK. A study of adverse drug reactions in pediatric patients. Journal of pharmacology & Pharmacotherapeutics. 2011; 2 (4): 277 – 280.
33. Kushwaha KP, Verma RB, Singh YD, Rathi AK. Surveillance of drug induced diseases in children. Indian J Pediatr. 1994; 61:357–365
34. Schirm E, Tobi H, van Puijenbroek EP, Monster SMH, deJong B LT. Reported adverse drug reactions and their determinants in Dutch children outside the hospital. Pharmacoepidemiol Drug Saf 2004; 13:159-165.
35. Fattahi F, Pourpak Z, Moin M, Kazemnejad A, Khotaei GT, Mamishi S et al. Adverse drug reactions in hospitalized children in a department of infectious diseases. J Clin Pharmacol 2005; 45: 1313-1318.
36. Ibia EO, Schwartz RH, Wiedermann BL. Antibiotic rashes in children: survey in a private practice setting. Arch Dermatol. 2000; 136:849–854.
37. Ruairi M G , Jennifer R M, Kim A B, Jamie J K, Matthew P, Paula R W etal. Adverse Drug Reactions Causing Admission to a Paediatric Hospital. PLOS ONE. 2012; 7 (12): e50127
38. Smyth R M, Gargon E, Kirkham J, Cresswell L, Golder S, Smyth R etal. Adverse drug reactions in children—A systematic review. PLoS One, 2012; 7: e24061.