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Original Article

Prevalence of adverse drug reactions with commonly prescribed drugs in different hospitals of Kathmandu valley

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Abstract

Objectives: To study the prevalence of adverse drug reactions (ADRs) in five different hospitals of Kathmandu Valley.

Materials and Methods: An analytical cross sectional study was designed from May 2007 to September 2007 in which prevalence of ADR was calculated. A total of 37 cases of ADRs were taken from 4287 patients and 10% of the remaining population without ADRs i.e. 425 out of 4250 patients was selected randomly. ADRs were analyzed as per the structured questionnaires designed by Canadian adverse drug reaction monitoring program. Data thus obtained were analyzed by using SPSS and Excel 2003 software and relevant statistical tools were applied.

Results: Prevalence of ADR in this study was 0.86% and male to female ratio was 0.85. 54.1% were female and 45.9% were male (P = 0.65). The highest percentage of ADRs were seen in adult patients, however the difference was statistically not significant. Maximum numbers of ADRs were reported from skin, 35.13% followed by GIT, 29.72% and then from CNS, 18.91%. Anti-infectives were associated with maximum number of ADRs followed by IV urograffin. Rashes, 35.13% were the most common type of ADRs reported followed by vomiting, 13.51% and then dizziness which was 10.81%. Regarding the outcomes attributed to ADRs, one patient died due to ADR caused by dapsone and 15 cases got hospitalized due to ADRs. The incidence of ADRs in different age groups was not significant. Similarly, there was no significant association between ADRs and sex. No significant difference was seen in case of age group less than one year as compared to two or more years of age (P = 0.78). For causality of ADRs, according to Naranjo algorhythm scale, 35% of reactions were assessed to be probable, 32% as possible and 19% were definite. Similarly, for severity assessment, 54% reports were mild, 35% were moderate and 10.81% were severe.

Conclusion: Prevalence of ADR in this study was 0.8% which is similar to other studies in other countries. All the ADRs were not toxic reactions and they were unpredictable.

Key words: Prevalence, ADRs, Drugs

Pharmacovigilance is an integral part of drug therapy. Still, it is not widely practiced in hospitals in Nepal. In various studies, adverse drug reactions have been implicated as leading cause of considerable morbidity and mortality[1]. The incidence of adverse drug reactions (ADRs) varies with studies which show incidences ranging from as low as 0.15% to as high as 30%[1–3]. ADRs are negative consequences of drug therapy. World Health Organization defines ADRs as 'any noxious, unintended and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis or therapy'. Using this definition, therapeutic failures, drug abuse and intentional or accidental poisoning (overdose) are not considered ADRs, nor are adverse events that occur as a result of intentional non-compliance or errors in drug administration[3].

Elderly patients are reported to be more susceptible to ADRs than the adult population (16.6% *vs.* 4.1%)[1]. It is estimated about 3% of all admissions to geriatric units in the U.K. are due to adverse drug effects, and that in a further 8% of admissions, an ADR is a contributory cause[1]. It has been reported that the incidence of ADR is much more in geriatric, pediatric and female patients. Females are more susceptible to gastrointestinal and cutaneous allergic adverse drug reactions[4-7]. It has been estimated that 83% of ADR in males and 93% in females are due to dose related effects[7].

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Although no specific confirmation is found in the literature for young children, it is usually stated that the incidence of ADRs is higher during the first year of life, although only objective manifestations of ADRs can be recorded in very young children.

This conclusion is attributed to the physiological immaturity of patients in this age group[8,9]. Reports on ADR monitoring in Nepal have been very few. This may be because ADRs monitoring is still in developing stage.

Based on the hypothesis that patients of 1 year of age or younger are at greater risk of developing ADRs and ADRs are more frequent in females then males, a prospective intensive events monitoring scheme was carried out to asses the extent, pattern, severity and casualty for ADRs for patients from different hospital of Kathmandu valley.

Materials and methods

The study was carried out in the four hospitals of Kathmandu valley, namely Kathmandu Medical College Teaching Hospital, Sinamangal, Tribhuwan University Teaching Hospital, Maharajgunj, Kanti Children's Hospital, Maharajgunj and Maternity Hospital, Thapathali in the same departments (Pediatric, Internal medicine and emergency). The admissions corresponded from May 2007 to September 2007. The study was analytical cross sectional in which prevalence of adverse reaction was calculated. To study the detailed history, all the 37 cases of ADRs and 10% of the remaining population without ADRs i.e. 425 out of 4250 patients were selected randomly.

Special attention was given for patients of 1–24 months old with a hospitalization period of at least 24 hours. Repeat admission of the same patient was counted as two admissions when separated by an interval of at least 1 month. Oncological patients and those with HIV infection were excluded.

Data related to any patient showing an adverse drug reaction was analyzed as per the structured questionnaires designed by Canadian adverse drug reaction monitoring program. The collected data were validated through the information on patient characteristics (sex, age, medical history, underlying diseases, etc.), drug treatment (suspected drug, dosage, route of administration, indication, date of beginning and stopping therapy, date of reaction, date of reporting and clinical details, concomitant drugs, etc.) and outcomes of the adverse event (like life threatening attributes, hospitalizations, disability etc.). Once the case was validated, an imputability score was obtained from the Naranjo Algorhythm score and Hartwig scale, based on the successive evaluation of different criteria where each possesses several degrees, and which provides grades for the causality and severity association between drug and adverse event. The evaluation followed a two-scale scheme: the Naranjo Algorhythm score and Hartwig scale. Microsoft Excel 2003 and SPSS software were used to analyze the data. Chi-square test and appropriate diagrams were used to interpret data.

Results

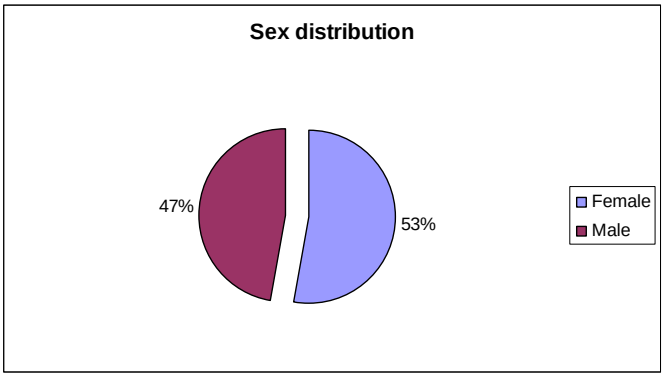

Fig 1: Sex distribution of the study population

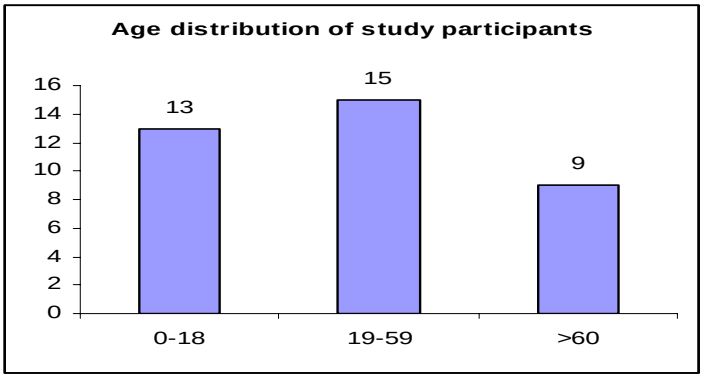

Fig 2: Age distribution of the study population

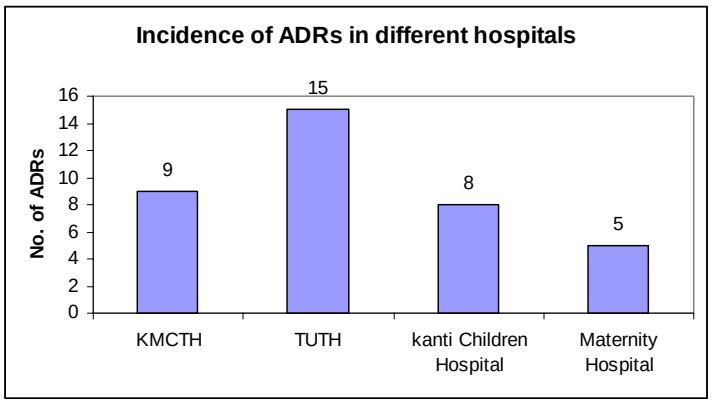

Fig 3: Incidence of ADR in four different hospitals

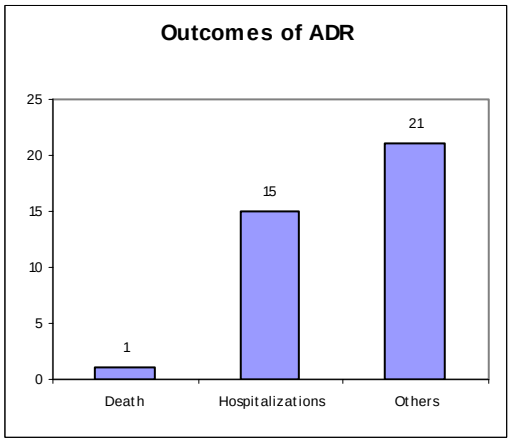

Fig 4: Outcomes of ADR

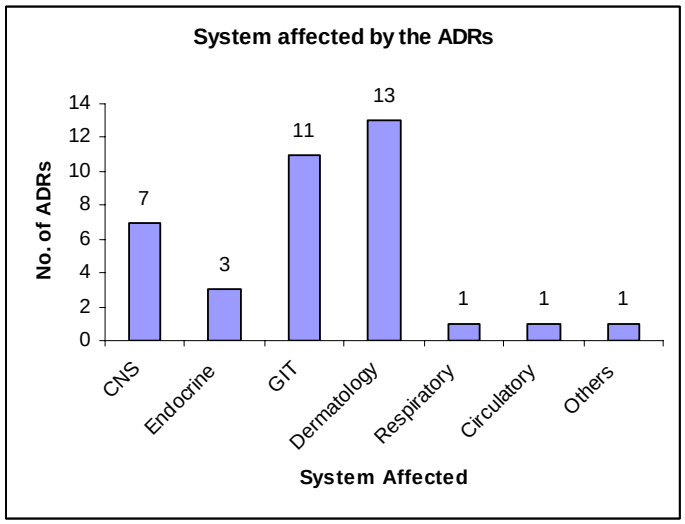

Fig 5: Systems affected by ADRs

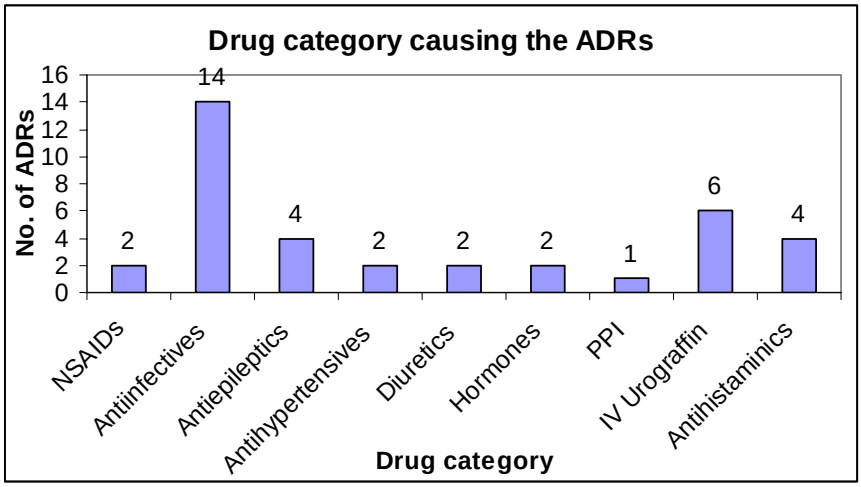

Fig 6: Drug categories causing ADRs

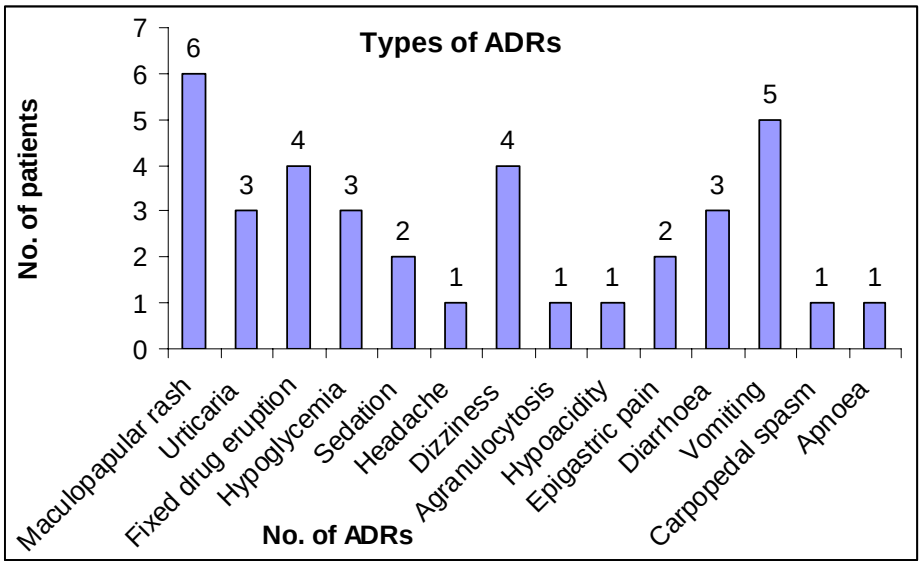

Fig 7: Different types of ADRs in study population

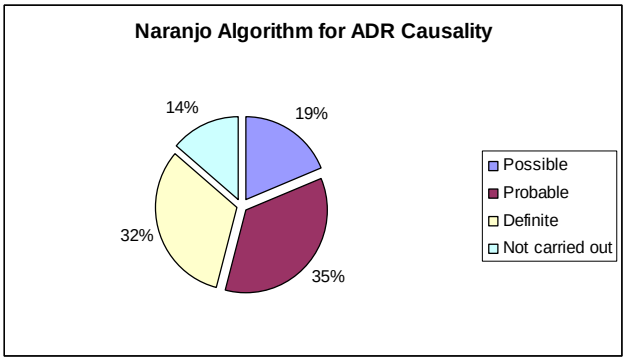

Fig 8: Naranjo Algorhythm for ADR causality

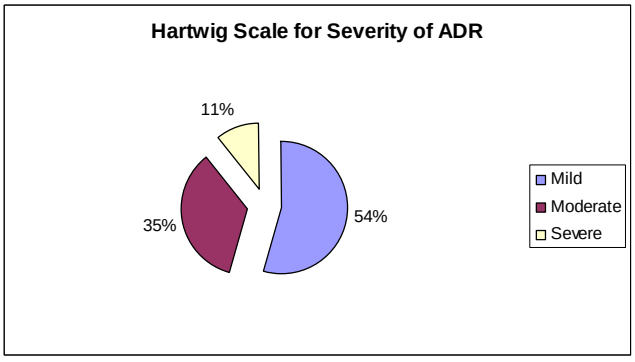

Fig 9: Severity scale for ADR

Table 1: Some rare adverse drugs reactions

Some rare ADRs	Causative drug	No. of patient
Agranulocytosis	Dapsone for 1 week	1
Steven Johnson's syndrome	Ampicillin 500mg, 6hrly per oral (First dose)	1
Anaphylaxis	Penicillin G	1
Severe bone marrow depression	Septran 400mg BD (After 3 days)	1

Table 2: Association of sex and ADRs

Sex	Adverse Drug Reaction N (%) Yes	No	Total
Female	20 (54.10%)	231 (50.10%)	233 (50.40%)
Male	17 (45.90%)	212 (49.90%)	229 (49.60%)
Total	37 (100%)	425 (100%)	462 (100%)

P = 0.65

Table 3: Association of different age group with ADRs

Age group (years)	Adverse Drug Reaction N (%) Yes	No	Total
0-1	6 (16.20%)	88 (20.70%)	93 (20.14%)
2-18	7 (18.91%)	96 (22.60%)	104 (22.50%)
19-59	14(37.80%)	126 (29.60%)	140 (30.30%)
>60	10 (27.00%)	115 (27.10%)	125 (27.10%)
Total	37 (100%)	425 (100%)	462 (100%)

P = 0.65

Table 4: Association of pediatrics age group with ADRS

Age group (years)	Adverse Drug Reaction N (%) Yes	No	Total
0-1	6 (46.20%)	92 (50.00%)	98 (49.70%)
2-18	7 (53.00%)	92 (50.00%)	99 (50.30%)
Total	13 (100%)	184 (100%)	197 (100%)

P = 0.78

During the study period, 37 ADR reports were received out of 4287 patients in four different hospitals with a prevalence of 0.86% and male to female ratio of 0.85. Among the cases of ADR 54.1% were female and 45.9% were male (P=0.65). Pediatric patients (<18 years) experienced 35.13% ADRs, followed by geriatric patients (>60 years) 24.32% and adults 40.54% ADRs (Fig 1 and 2). The highest percentage of ADRs was seen in adult patients however the difference was not statistically significant.

Maximum number of ADRs were reported from the skin 35.13% followed by GIT 29.72%, and then from CNS 18.91%. The most common drugs causing ADRs is shown in Fig 6, according to which, anti-infectives were associated with maximum number of ADRs in which ampicillin produced the highest number of reactions, followed by ciprofloxacin. The other different drugs causing ADRs were antiepileptics, NSAIDs, antihypertensives, hormones, intravenous urograffin, and antihistaminics.

Regarding the outcomes attributed to ADRs, 1 (0.27%) patient died due to adverse drug reaction caused by dapsone and 15 (40.54%) cases got hospitalized due to ADRs. 21 patients were reported as others outcomes attributed to ADRs which included disability, congenital malformation, and intervention required to prevent damage/permanent impairment, etc.

The incidence of ADRs in different age group was not significant. Similarly there was no significant association between ADRs and sex. No significant difference was seen between the ADR cases in age group less then one year as compared to two or more years of age (P=0.78). Thus, it conforms that the hypothesis of this study was not proved. According to the Naranjo algorithm scale, 35% of reaction were assessed to be probable, 32% as possible and 19%

were definite. Due to unavailability of the necessary information for imputability of scoring, we could not carry causality assessment for 10% of the study population. Similarly, severity assessment of the ADRs showed that the majority of the reactions reported were mild (54%), followed by moderate (35%) and severe (10.81%).

Table 1 Shows some rare ADRs during our study period. Among, which, one patient lead to death of the patient due to agranulocytosis due to dapsone. Different types of ADRs were studied in which rashes 35.13% the most common ADRs were reported followed by vomiting 13.51%, dizziness 10.81%. Similarly, other types of ADRs were hypoglycemia, diarrhoea, sedation, epigastric pain, agranulocytosis, headache, carpopedal spasm, apnoea and hypoacidity.

Discussion

The demographic details of our study showed female gender predominance over males for ADRs, which was similar to that of other studies reported in the literature[10]. Previous studies have shown that a larger percentage of ADRs were reported from geriatric and pediatric populations which were not similar to our results[11, 12]. In our study, we experienced a higher percentage of ADRs for adult population (40.54%), where as prevalence for ADRs in pediatric and geriatric patients were 35.13% and 24.32% respectively.

The most common systems associated with ADRs in our study were skin, gastrointestinal system and the central nervous system. This finding is consistent with many studies which have reported a higher percentage of dermatological manifestations than others. The gastrointestinal system has also been reported to be involved in the majority of ADRs[13,14,15,16,17]. In our study, anti-infectives and drugs used for radiocontrast media like IV urograffin were the most commonly involved drug classes for ADRs. Then followed by drugs affecting CNS and antihistaminics were the most commonly involved drug classes in ADRs. So, we concluded that all the adverse drug reactions were not toxic reactions and they were unpredictable.

The incidence of ADRs in different age group was not significant. Similarly there was no significant association between ADRs and sex. No significant difference was seen between the ADR cases in age group less then one year as compared to two or more years of age (P=0.78). This conforms that the hypothesis of the study was not proved.

Pharmacovigilance is not properly developed in our country. In order to minimize the problem associated with ADRs it is suggested that every hospital should have pharmacovigilance center involving medical staffs including pharmacists. Pharmacists, of late, have been encouraged to participate in the ADR monitoring programme globally and we hope that it will be beneficial to involve pharmacists in such programmes in Nepal also as this has been suggested by several studies that has been carried out in other countries[10,18] .

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