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Assessment of Adverse Drug Reactions Reported in a Tertiary Care Teaching Hospital in South India.

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ABSTRACT

The aim of the study was to detect, document, assess and report the suspected adverse drug reactions. A prospective-observational study on adverse drug reactions was conducted in a 1000 bedded multi-specialty hospital. Suspected ADRs were analyzed for causality, severity and preventability using appropriate validated scales. A total of 65 ADRs were identified in 2280 admissions during the study period. Severity of the suspected ADRs assessed using Modified Hartwig and Siegel Scale. The study revealed that 2(1.6%) suspected ADRs were severe, 5(8%) ADRs were moderate and 58(90.4%) ADRs were mild in severity. Causality assessment was done by using WHO and Naranjo scale. The assessment by Naranjo scale showed that 16 (24.8%) ADRs were possibly drug-related, whereas 43(65.6%) were classified as probably and 6(9.6%) ADRs were definitely related to the drug, while the assessment done by using WHO scale revealed that 16(24.8%) ADRs were possibly drug-related,18 (27.2%) ADRs were probably drug-related, whereas 7(9.6%) were classified as certainly related to drug. Nine patients (13.8%) were admitted due to an Adverse. Preventability of suspected ADRs assessed by using Modified Schumock and Thornton scale, revealed that 17(26%) ADRs were definitely preventable while 1 (2%) ADRs were probably preventable and 47(72%)of the drug reactions were not preventable. Intervention was required in all ADRs as it indirectly contributed to affect the patient's Quality Of Life. Our ability to anticipate and prevent such ADRs can be facilitated by the establishment of standardized approaches and active reporting of suspected ADRs.

Keywords: Adverse drug reactions, Causality, Hospital, Monitoring, Naranjo's scale, WHO scale

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INTRODUCTION

World Health Organization (WHO) defines an adverse drug reaction (ADR) as "one which is noxious and unintended, and which occurs in doses normally used in human for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological functions. According to the Centre for Health Policy Research, more than 50 percent of the approved drugs in the United States associated with some type of adverse effect not detected prior to approval[1].At least one ADR has been reported to occur in 10 to 20% of hospitalized patients[2]. Pharmacovigilance or ADR monitoring, launched by WHO in the 1960s in the wake of 'thalidomide' disaster, is currently an integrated global effort of more than 70 countries worldwide. After the "thalidomide tragedy" many countries have established drug monitoring systems for early detection and prevention of possible drug-related morbidity and mortality. The use of traditional and complementary drugs (e.g. herbal remedies) may also pose specific toxicological problems, when used alone or in combination with other drugs.

The probability of causative agent is assessed by the ADR probability designed by Naranjo et al and classified as definitive, probable, possible and suspected[3]. Allhe reported events were evaluated, after collecting adequate data from appropriate sources, as to explore the likely involvement of suspected drug in causing the reported event. In assessing the causality, concerned clinician and /or unit chief opinion was obtained. After having assessed the causal relationship between the suspected drug and the adverse reaction ,irrespective of their causality category, the reports were subjected to further analysis including their severity, predictability and preventability of reported reactions[4]. The key issue is that ADR-induced morbidity and mortality is not inevitable. As a great number of ADRs are predictable and therefore preventable. Methods for assessing ADR preventability vary, with some studies using implicit criteria while others use independent assessment by an expert review panel[5-7].

After an ADR event occurred, detected , monitored or identified, there is a need for healthcare professionals to assess casualty, preventability and severity of such suspected ADRs. This will create awareness to healthcare team to avoid such drugs causing serious ADRs and help in the speedy management of ADRs. In this context the department of pharmacy practice, after the consultations with physicians of the study hospital has planned to conduct a study to carry out the causality and severity assessment of the reported ADRs using various standard scales[8-11].

MATERIALS AND METHOD

A Prospective – Observational study was carried out for a period of 6 months from January 2013 to June 2013 in Navodaya Medical College Hospital & Research Center, Raichur.

All the patients who were experienced at least one adverse drug reactions were included in the study. For obtaining the clearance certificate , an application along with study protocol , which includes the proposed title, study site including various departments required, duration, inclusion and exclusion criteria, objective and a brief methodology about the work to be carried out was submitted to the Chairman of the Institutional Ethics Committee of Navodaya Medical College Hospital & Research Centre . The study was approved by Committee by issuing ethical clearance certificate.

A specially designed data entry format was used to enter all patients details, which include patient information, reason for admission, past medical history, social history, laboratory investigations, medications prescribed, suspected ADRs, system affected, description of the reaction, management of ADRs, dechallenge and rechallenge information, causality assessment scales, severity of the reactions etc shown in table 1,2 and 3.

An ADR reporting form which was prepared by the department of pharmacy practice aids in reporting and collection of ADRs during regular ward rounds. Forms were also made available on physicians table to encourage reporting of ADRs by them. In all the nursing stations of the study department the forms were also distributed for reporting of adverse drug reactions .

Collection of data

A total of 2280 patients admitted to the medical wards of Navodaya Medical College Hospital, Raichur, Karnataka, for a period of 6 months were observed for possible ADRs, as per W.H.O. definition. Project team include four Pharm D students .

Study wards were visited daily by the project team and patients drug charts, medical and nursing notes were reviewed for evidence of an ADR. Objective markers of ADRs, e.g. laboratory results, were identifiable from the patient notes and the hospital computer system, while subjective markers of ADRs, for example headache, nausea and rash were identified through patient notes, discussion with the ward team and, where appropriate, discussion with the affected patient.

Clinical staff were informed that the study was taking place and could also refer directly either in person or through notification cards that were made available on the wards.

ADRs were identified on the basis that they were well recognized as evidenced by their inclusion in the Summary of Product Characteristics and/or the British National Formulary, Micromedex, CIMS.

ADRs were identified by research team and confirmed by a physician. When there were doubts/disagreements, such cases were not included. ADRs that occurred outside the hospital and got admitted in our hospital were also included. Those who were identified to have ADRs were examined and the details recorded in a proforma where details of the drugs taken, observed reactions, measures taken for untoward reactions, investigations and response to measures were recorded.

Following completion of the ward based data-collection period, case note analysis was performed to assess patient outcomes and to ensure that all available details regarding the ADR had been collected. Suspected ADRs were classified in terms of causality and avoid ability according to validated algorithms and assessed for suitability for Yellow Card Reporting. ADRs were also classified as either type A or type B. We also recorded severity of the ADRs according to the Hart wig severity scale.

RESULTS AND DISUCSSION

A total of 65 ADRs were identified in 2280 admissions during the study period. Out of 65 ADRs reported male were found to be more (58%) than female(42%) as shown in Figure 1.

The result of age categorization revealed that patients of 30-59 years experienced maximum ADRs about 41(63.2%) followed by 13 (19.2%) with patients of 60 years and above and 17.6% in 10-29 years of age group is illustrated in Figure 2.

System most commonly affected were dermatological in 18 (24.8%) Patients, GI in 14(20%) patients, CNS in 11(19.2%) followed by respiratory system in 9 (17.6%) patients. The drug class mostly associated with ADR was NSAIDs in 10(13.65) cases, followed by antibiotics in 9(11.12%), anti hypertensives in 7(10.4%), cases each

Causality assessment through WHO scale indicated that 27.2 % of them were probable followed by possible(24.8%),unlikely (12.8%),unclassifiable (11.2%),unclassified (110.4) and certain (9.6%)as shown in Figure 3 .Causality assessment of suspected ADRs using Naranjo's scale showed that 65 % of them were probable and the rest of them categorized as possible(24.8%)and definite(9.6%)as shown Figure 4.

The severity of 90.4% of reactions were mild, moderate (8%) and 1.6% considered as severe are given in Figure(5).On the basis of Modified Schumock and Thrnton scale, 17(26%) and 1(2%) reactions of the suspected ADRs were definitely and probably preventable , respectively present in Figure(6). In 6(9.6%) of cases the ADRs was mnaged by withdrawal of drug and in 9(11.2%) patients the dose of drug was altered in Figure 7.

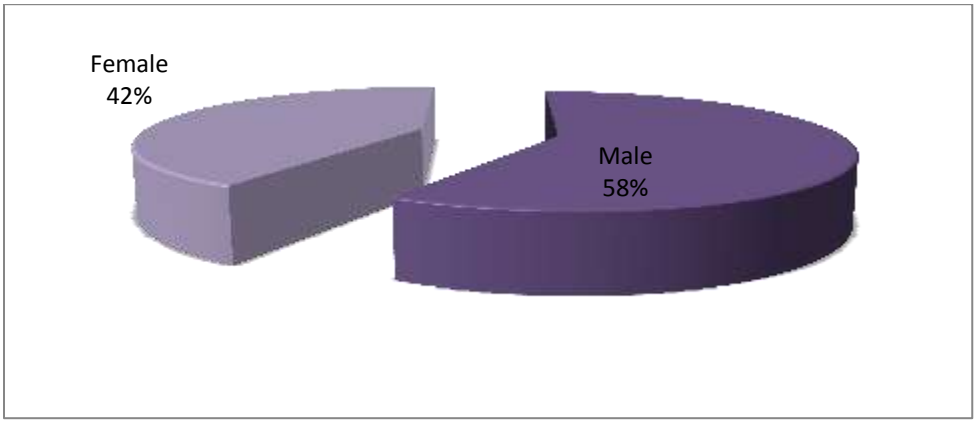

Figure 1: Gender distribution (n=65)

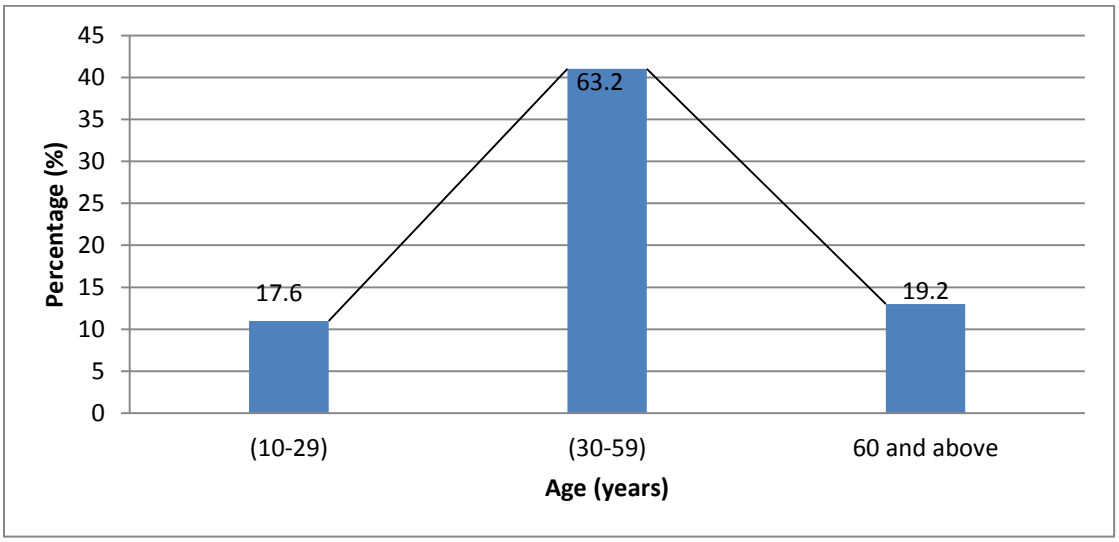

Figure 2: Age distribution (n=65)

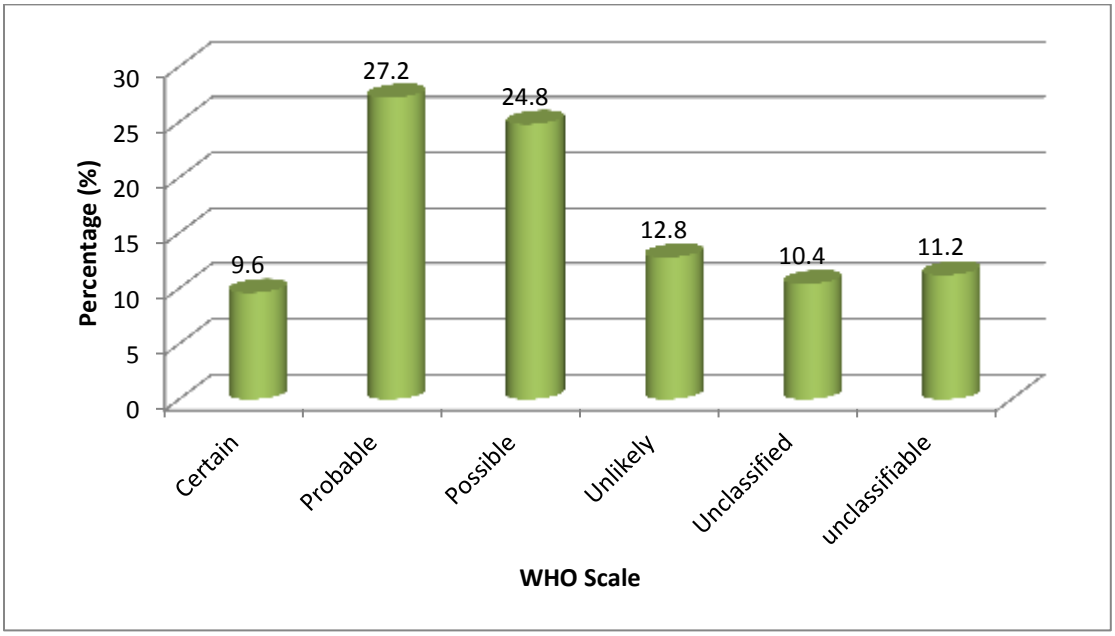

Figure 3: Causality assessment of suspected ADRs by WHO scale(n=65)

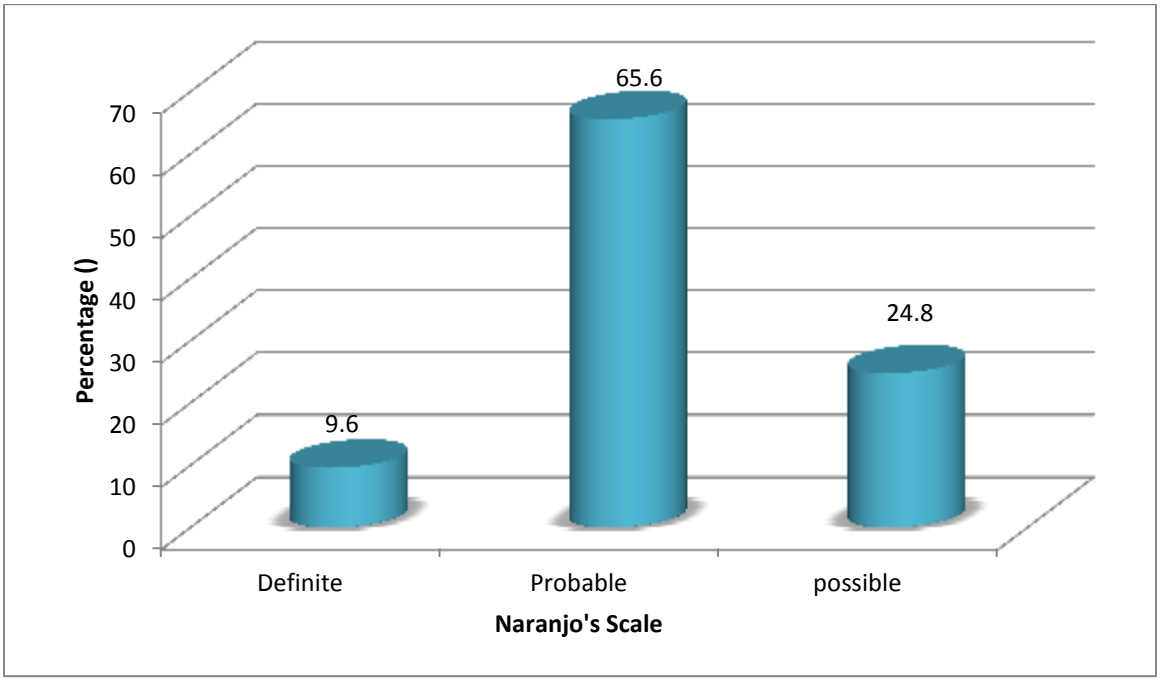

Figure 4: Causality assessment of suspected ADRs by Naranjo's scale(n=65)

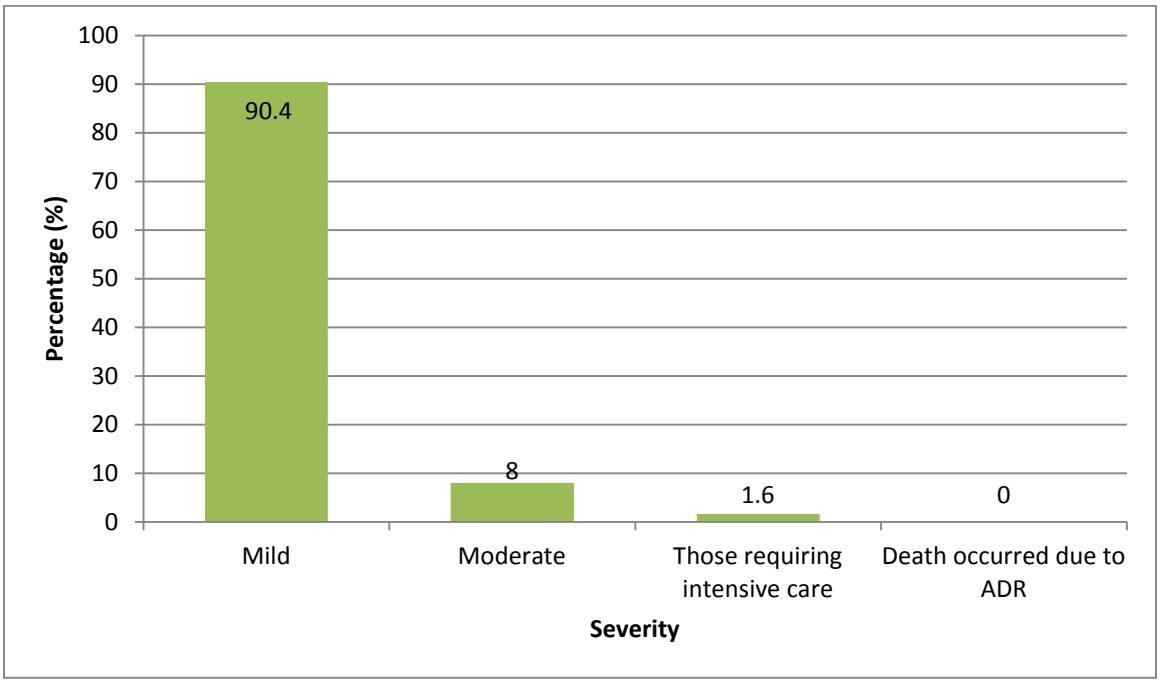

Figure 5: Severity of suspected ADRs(n=65)

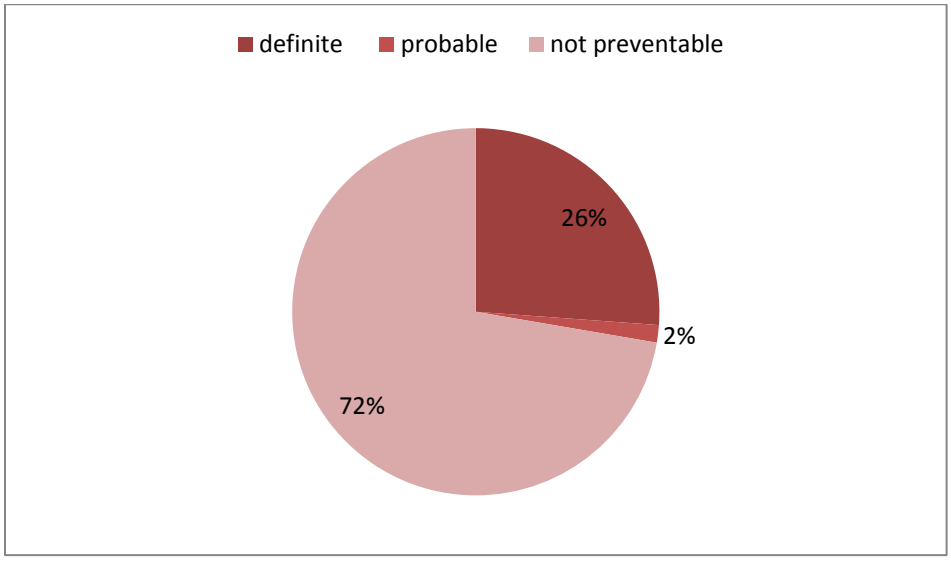

Figure 6: Preventability of suspected ADRs(n=65)

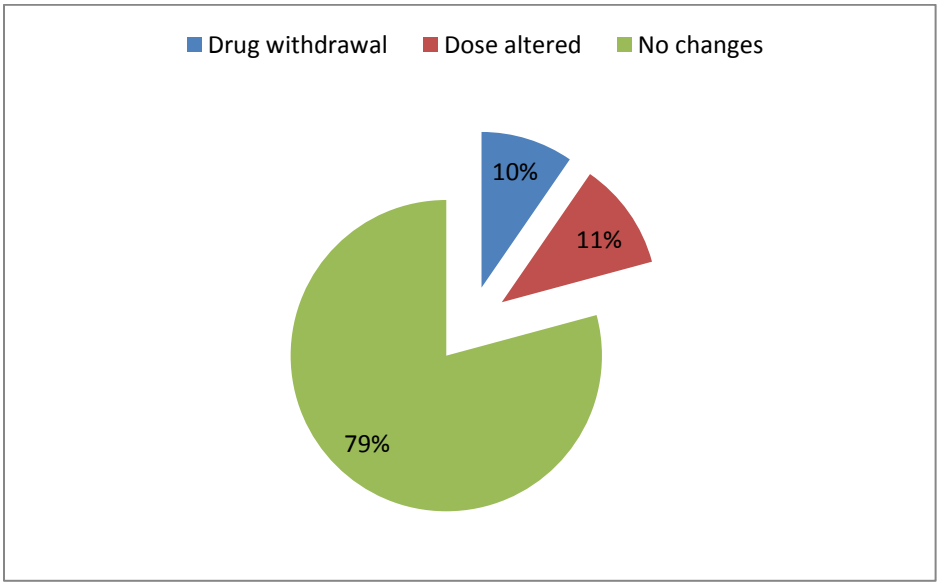

Figure 7: Management of suspected ADRs(n=65)

DISCUSSION

A prospective observational study was conducted in a 1000 bedded multi-specialty hospital .patients admitted as in-patients over a period of six months from January 2013 to June 2013 were assessed for ADR through daily ward visit by the project team. Suspected ADRs were analysed for causality, severity and preventability using appropriate validated scales.

A total of 65 were identified in 2280 admissions during the study period. The incidence of suspected ADRs were found to be 2.85%(95%CI, 2.17%-3.53%) and is comparable with study done by Rao PGM which evaluated the reports of ADRs in inpatients at south indian hospital for their incidence of ADRs was 2.85% in hospitalized patients.[2]

The result of age categorization revealed that patients of 30-59 years experienced maximum ADRs about 41(63.2%)followed by 13 (19.2%) with patients of 60 years and above and 17.6% in 10-29 years of age group. A study done by Pir Mohamed M et al.,(2004) have shown a greater percentage of geriatric population suffering from ADRs as compared to patients within age group 30-59 years in our study[12].

System most commonly affected were dermatological in 18 (24.8%) Patients, GI in 14(20%) patients, CNS in 11(19.2%) followed by respiratory system in 9 (17.6%) patients and the results are comparable matches with the international study conducted by Suh et al.,(2000) which reveals that the system most badly affected was the dermatological and Gi system[13].

The drug class mostly associated with ADR was NSAIDs in 10(13.65) cases, followed by antibiotics in 9(11.12%) , anti hypertensives in 7(10.4%), cases each. Our study results comparable with other studies like those done by Classen DC et al., which indicated that NSAIDs have cost extensive damage to human health [14].

Causality assessment was done by using WHO and Naranjo scale. Assessment by Naranjo scale showed that 43(65.6%)(955CI, 54.05%-77.15%) ADRs were probably drug related whereas 16(24.8%)(95%CI, 14.4%-35.3%) ADRs were classified probably as drug related and 6(9.6%) ADRs were definitely related to drug. While the assessment done by using the WHO scale revealed that 18(27.2%)(95%CI, 16.38%-38.02%) ADRs were probably drug related , 16(24.8%)(95%CI, 14.3%-35.3%) ADRs were possibly drug related , 9(12.8%) ADRs were unlikely drug related, where as 7(9.6%) ADRs were classified as certainly related to drug and this disagree with Davis EC et al.,(2012) study which assessed the feasibility and established methodology for conducting a large prospective study to fully assess the impact on ADR in inpatients[15].

Severity of suspected ADRs were assessed using modified Hartwig and Siegalscale , revealed that 2(1.6%)suspected ADRs were severe, 5(8%) ADRs were moderate and 58(90.4%) ADRs were mild in severity in review conducted by Joel Shuster(2005) in reporting of ADRs from the institute of safe medication practices (ISMP) in corporation with FDA's Medwatch program , in a 200 bedded community hospital reported 36 distinct admissions due to ADRs , with 90% of cases categorized as severe and 76% of events were regarded as moderate[16].

In 6(9.6%) cases the drug was withdrawn , dose altered in 9(11.2%) cases and no change was made in 45(79.2%)patients . ADRs were treated and the final outcome was measured . About 63(98.4%) patients were recovered , while in 2(1.6%) cases the ADRs decreased . no fatal cases were reported , preventability of suspected ADRs were assessed by using modified schumock

and Thorton scale , revealed that 17(26%)ADRs were definitely preventable , 1(2%) ADRs was probably preventable and 47(72%)(95%CI, 15.3%-36%)ADRs were not preventable.

Table 3 Preventability Assessment Scale(Modified Schumock and Thornton)[10]

Section A	Answering "yes" to one or more of the following implies that an ADR is DEFINITELY preventable.
	1. Was there a history of allergy or previous reactions to the drug?
	2. Was the drug involved inappropriate for the patient's clinical condition?
	3. Was the dose, route, or frequency of administration inappropriate for the age, weight or disease state?
	4. Was a toxic serum drug concentration (or laboratory monitoring test) documented?
	5. Was there a known treatment for the adverse drug reaction?
❖ If answers are all negative to the above, then proceed to Section B.	

Section B	Answering "yes" to one or more of the following implies that an ADR is PROBABLY preventable.
	Was required therapeutic drug monitoring or other necessary laboratory tests not performed?
	Was a drug interaction involved in the ADR?
	Was poor compliance involved in the ADR?
	Were preventive measures not prescribed or administered to the patient?
If answers are all negative to the above, then proceed to Section C.	

Section C	ADR is not preventable.

CONCLUSION

In conclusion our study shows that ADRs are a significant problem in hospital in-patients contributing to morbidity and resulting in considerable financial burden. Over half are definitely at potentially avoidable and steps should be taken to introduce strategies to reduce their impact. The present study hints that pharmacists' involvement may not only greatly increase the reporting rate but also quality of reporting.

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