

ORIGINAL RESEARCH ARTICLE

**Patterns of Adverse Drug Reactions in the Medical Intensive Care Unit of an Indian Tertiary Care Hospital**

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**ABSTRACT**

**Aim**

To monitor the pattern of adverse drug reactions (ADRs) in medical intensive care unit of tertiary care hospital.

**Materials and Methods**

It was a descriptive study, spread over a period of two months (5<sup>th</sup> July, 2010 to 5<sup>th</sup> September, 2010). Study commenced after getting approval from Institutional Ethical Committee (IEC). The various factors influencing the incidence of ADRs in the ICU like age, sex and polypharmacy were analysed. The most common group of drugs involved in ADRs and the most common ADRs in the ICU were also analysed.

**Results**

A total of 21 adverse drug reactions were reported during the 2 months of study in the intensive care unit. Considering the male: female ratio, there was an increased incidence of ADRs in the male compared to the female. Fifteen (71.4%) ADRs were reported in males and six (28.6%) reports were in females. Diarrhea was the commonest side effect reported in (28.57%) of all patients. Rashes were reported in (14.28%) patients. Restlessness and hypernatremia were the next common side effects reported in (9.27%) of patients. Antibiotics were the common class of drugs involved in ADRs. Adverse drug reactions were reported in 8 patients (38 %) on treatment with antibiotics.

**Conclusion**

The incidence of Adverse drug reactions is less when compared to other institutions in the west. Awareness of pharmacovigilance in the ICU could be improved by conducting training programmes and workshops for the staff on adverse reaction monitoring. This could increase the number ADR reports from the ICU which in turn could reduce the morbidity and mortality of the patients.

**Key words:** Adverse drug reactions (ADRs), unit of tertiary care hospital, Restlessness and hypernatremia, morbidity and mortality

**INTRODUCTION**

An adverse drug reaction (ADR) has been defined by World Health Organization (WHO) as “a response to a drug which is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for modification of physiological function”.<sup>[1]</sup>

A more recent definition for Adverse Drug Reactions is: "An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or

alteration of the dosage regimen, or withdrawal of the product.”<sup>[1]</sup>

Epidemiological research performed in the United States shows the occurrence of ADRs in 10-20% of all hospitalized patients. It is estimated that ADRs are responsible for 3.2-6.5% of hospital admissions.<sup>[2]</sup>

The irony in this case is the widespread prevalence of under-reporting. A study undertaken in the United Kingdom suggests the median under-reporting rate for all Adverse Drug Reactions in Hospitals is 94%<sup>[3]</sup> When the rates of Under-reporting are so high with a developed

nation like the United Kingdom, it can be assumed that a developing nation like India would have more incidence of under-reporting of Adverse Drug Reactions.

Under-reporting may also be the reason why the monitoring of Adverse Drug Reactions is not receiving as much attention as it should be. If all the Adverse Drug Reactions/Events occurring in a hospital were to be properly documented the results of the study would be alarming. It is evident that we don't pay much attention to most ADRs as the knowledge of Doctors themselves on Adverse Drug Reactions and their Reporting is inadequate (as shown by a study conducted in Nigeria).<sup>[4]</sup>

What is fascinating about Adverse Drug Reactions Monitoring is that 30-80% of them are preventable.<sup>[5]</sup> Another study in India on the incidence of Adverse Drug Reactions in patients on Anti-retro viral therapy states that 88% of all adverse drug reactions in these patients can be completely prevented.<sup>[6]</sup>

These results from previous studies only underline the importance of Adverse Drug Reaction Monitoring and Reporting. Monitoring of Adverse Drug Reactions helps in reducing the mortality and morbidity due to it.

India rates below 1% in pharmacovigilance as against the world rate of 5%. This is due to ignorance of the subject and also lack of training.<sup>[7]</sup>

Incidence of adverse drug events (ADEs) and adverse drug reactions (ADRs) is higher in the intensive care unit (ICU) than other areas of the hospital<sup>[8]</sup>

This is because patients in the intensive care unit (ICU) have multiorgan dysfunction as well as altered pharmacokinetic parameters. Hence they are susceptible to adverse drug reactions (ADRs). Predisposing factors like age, gender, number of drugs taken have been reported as significant risk factors for the development of ADRs.<sup>[9, 10]</sup>

Advancing age is not an independent risk factor for Adverse Drug Reactions<sup>[11]</sup>. Co-morbidity with advancing age becomes a risk factor. Awareness of those co-morbid conditions which predict Adverse Drug Reactions can help clinicians to identify which older adults are at greater risk, therefore, who might benefit from closer monitoring.<sup>[12]</sup> So studying the Adverse Drug Reactions/Events becomes important to give better patient care.

Few institutions in the world currently track ICU-specific ADE/ADR data. The institution of ICU-specific ADE detection and prevention strategies may improve the safety of critically ill.

There is no such pharmacovigilance system working presently in our set-up and moreover, there is paucity of data regarding ADR monitoring especially in relation to drugs used in the medical ICU. Accordingly, the present study was designed to monitor the incidence of ADRs and to assess the role of age, sex and polypharmacy in the development of ADRs in the ICU.

## AIMS AND OBJECTIVES

### Primary Objective

To monitor the pattern of ADRs in medical intensive care unit of a tertiary care hospital.

### Secondary Objectives

- To assess which group of drugs are commonly involved in the ADRs in the medical ICU.
- To analyse the involvement of age, sex, polypharmacy in the occurrence of ADRs

## MATERIALS AND METHODS

It is a descriptive study, spread over a period of two months (5<sup>th</sup> July, 2010 to 5<sup>th</sup> September, 2010).

Study commenced after getting approval from Institutional Ethical Committee (IEC). Permission to conduct the study in the medical ICU was obtained from the HOD, intensive care unit of the tertiary care hospital.

The intensivists in the ICU, the Staff nurses and the other duty nurses looking after all the three shifts in a day were requested to report all the Adverse Drug Reactions in the ICU however minor it may be.

Both new and already admitted patients at the time of commencement of study were included. Spontaneous reporting was employed to assess the ADR profile in the patients.

For spontaneous monitoring, treating physicians and nurses in the ICU were provided with reporting cards on which they were asked to record suspected ADRs.

After the initial notification of the suspected ADR by the physician, additional details were collected by review of the patient case records and interviews.<sup>[13]</sup> Regular visits to the ICU were made on a once in three days basis to collect the reported ADRs and gather more information on the ADR and the patient to whom the reaction occurred.

The information was then transferred to the proforma which was adopted from the one used by Central Drugs Standard Control organization (CDSCO) [14].

Statistical analysis was done by using Excel spreadsheets.

The various factors influencing the incidence of ADRs in the ICU like age, sex and polypharmacy were analysed. The most common group of drugs involved in ADRs and the most common ADRs in the ICU were also analysed.

### RESULTS

A total of 21 adverse drug reactions were reported during the 2 months of study in the intensive care unit. Considering the male: female ratio, there was an increased incidence of ADRs in the male compared to the female. Fifteen (71.4%) ADRs were reported in males and six (28.6%) reports were in females as seen in (Fig1).

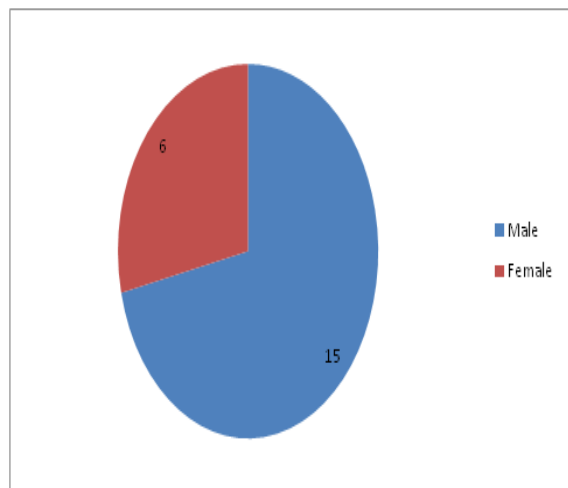


Fig 1: Sex distribution

The incidence of adverse reactions were more in the elderly as seen in (Fig 2). Out of the 21 reports, 14 (66.66%) reports were in individuals who were more than 50 yrs of age.

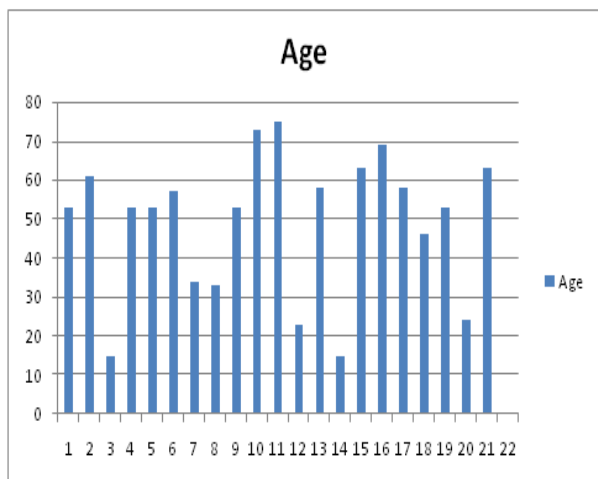


Fig 2: Age distribution

### Adverse drug reactions

6 reports of diarrhea (28.57%), 2 reports of restlessness (9.27%), 2 reports of severe hyponatremia (9.27%), 3 reports of rashes (14.28%), 1 report of severe anaphylaxis (4.76%), 1 report of hematuria (4.76%), 1 report of epistaxis (4.76%), 1 report of endotracheal bleed (4.76%), 1 report of hyponatremia (4.76%), 1 report of hypokalemia (4.76%), 1 report of hyperglycemia (4.76%) and 1 report of premature ectopic beats (4.76%) were shown in (Fig 3).

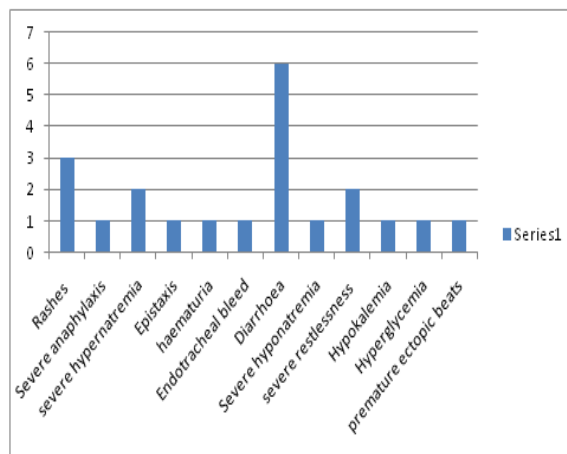


Fig 3: Adverse drug reactions

### Suspect drugs

Adverse drug reactions were reported in 8 patients (38%) on treatment with antibiotics, 3 patients (14.28%) on treatment with enoxaparin, 3 patients (14.28%) on treatment with steroids, 3 patients (38%) on treatment with sedatives midazolam, 1 patient (4.76%) on pyridostigmine, 1 patient on (4.76%) syr potchlor, 1 patient on (4.76%) mannitol and 1 patient on (4.76%) aminophylline as seen in (Fig 4).

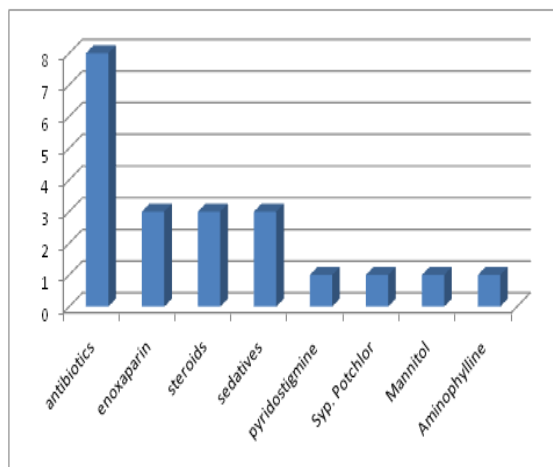


Fig: Suspect drugs

### DISCUSSION

In the 2 months of the study, 21 reports of ADRs were received from the ICU. The incidence of ADRs was 10.1% per 100 admissions as

compared to a high of 29.7% in some medical centers in the west<sup>[15]</sup>.

The main reason could be underreporting. Improving awareness about pharmacovigilance could result in increased number of reports in the ICU. The health care professionals could be requested to report every single suspected case of Adverse Drug Reaction however mild it maybe.

The incidence of ADRs was more in the men when compared to the women. Fifteen (71.4%) ADRs were reported in males and six (28.6%) reports were in females.

Fourteen ADRs were observed in patients above 50 yrs of age (66.66%). These patients were on multiple drugs and multiple organ dysfunctions. The altered pharmacokinetic parameters in these patients could have contributed to the adverse drug reactions (ADRs).

Adverse drug reactions in the elderly may be prevented by a thorough indication and prudent monitoring of pharmacotherapy. Adherence to pharmacotherapy may be improved by tailored and individual means referring to the patient's needs and expectancies<sup>[16]</sup>.

All the elderly patients who experienced ADRs had comorbid conditions like diabetes mellitus and systemic hypertension, which could have also contributed to the ADRs.

Diarrhea was the commonest side effect reported in (28.57%) all patients. Rashes were reported in (14.28%) of patients. Restlessness and hypernatremia were the next common side effects reported in (9.27%) patients. Severe anaphylaxis, hematuria, epistaxis, endotracheal bleed, hyponatremia, hypokalemia, hyperglycemia and premature ectopic beats were reported individually in separate patients.

Awareness of those co-morbid conditions which predict Adverse Drug Reactions can help clinicians to identify which older adults are at greater risk, therefore, who might benefit from closer monitoring<sup>[12]</sup>.

Antibiotics were the common class of drugs involved in ADRs. Adverse drug reactions were reported in 8 patients (38%) on treatment with antibiotics, 3 patients (14.28%) on treatment with enoxaparin, 3 patients (14.28%) on treatment with steroids, 3 patients (38%) on treatment with sedatives midazolam, 1 patient (4.76%) on pyridostigmine, 1 patient on (4.76%) sypritchlor, 1 patient on (4.76%) mannitol and 1 patient on (4.76%) aminophylline (4.76%).

Adverse drug reactions that occur in patients in the ICU may not be related to the suspect drugs. The concomitant drugs, co-morbid conditions and patients medical history could all contribute to the ADR.

Most of the ADRs in the ICU could be prevented by taking into consideration the pharmacokinetic aspects of the drugs, drug interactions and metabolic derangements that occur in the elderly. This could be achieved by improving the awareness of pharmacovigilance.

## CONCLUSION

Antibiotics were the common group of drugs involved in ADRs. Diarrhoea was the most common ADR reported.

The incidence of Adverse drug reactions is less when compared to other institutions in the west. Awareness of pharmacovigilance in the ICU could be improved by conducting training programmes and workshops for the staff on adverse reaction monitoring. This could increase the number ADR reports from the ICU which in turn could reduce the morbidity and mortality of the patients.

Adverse drug reactions were common in patients above 50 yrs of age. Most of these patients had multiorgan failure and were on multiple drugs. They also had co-morbid conditions like diabetes mellitus and hypertension. All these could have contributed to the ADRs.

Co-morbidity with advancing age becomes a risk factor. Awareness of those co-morbid conditions which predict Adverse Drug Reactions can help clinicians to identify which older adults are at greater risk, therefore, who might benefit from closer monitoring.

Moreover, monitoring of ADRs in the ICU for 2 months is not sufficient to get enough data, so it is necessary to do a study for a period of one year to collect sufficient data on the various factors involved in the ADRs.

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