Introduction
Chapter 1

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Drug therapy, a major health care approach paradoxically at time poses major health problems or even death. These unwanted outcomes of drug therapy were recognised as Adverse Drug Reactions (ADRs).

Though drugs are as old as mankind, the ADRs were recognised quiet late (1937) when, over 100 people died from renal failure as a result of consuming elixir of Sulphanilamide dissolved in diethylene glycol in USA. However Food and Drug act was passed in US as early as in the year 1906 to curb excessive adulteration of food and drugs.

To ensure safe drug therapy and prevent drug related disasters, in India the Food, Drug and Cosmetic act was passed in 1938 and Preclinical toxicity testing was mandatory for the first time. In addition drug manufacturers were required to gather clinical data about drug efficacy and safety, and to submit these data to FDA prior to drug marketing.
Introduction

Little attention was paid to ADRs until the early 1950s, when it was discovered that chloramphenicol could cause aplastic anaemia. In 1952 the first textbook on adverse drug reaction was published. In 1960, the FDA began to collect reports of ADRs and in 1961 the world experienced the infamous thalidomide disaster. In the same year the American Medical Association (AMA) as well as council on pharmacy and chemistry established the first official registry of ADRs to collect cases of drug induced blood discarsias. All the marketed drugs were kept under vigil to detect new ADRs that were missed during the earlier studies. Despite all precautionary measures ADRs do occur and some ADRs force withdrawal of the drugs from the market. To quote a few recent withdrawals, efalizumab in 2009 and sibutramine, gemtuzumab, ozogamicin and rosiglitazone in 2010. These facts emphasize the need for pharmacoepidemiology studies focusing mainly on the ADRs.

Most of the developed countries across the world like U.K., U.S.A, Australia have set up their own national ADR monitoring system since 1960s. Hospital-based ADR reporting and spontaneous reporting schemes have contributed to a large extent to these national ADR reporting system.

Lazarou and colleagues suggested that adverse drug reactions (ADRs) caused over 1,00,000 deaths in the United States. The major limitation of the present study conducted in the year 1981 has reported death rate considering likely number of admission till the year 1994.

In the United Kingdom (UK), most studies performed 30 years ago were relatively small and were often confined to individual health units meant for care
of the elderly. The largest UK study based on retrospective review of case notes probably underestimated the impact, since documentation of ADRs is poor in case notes. Thus it appears that retrospective studies based on patients records is not suitable to monitor ADRs.

Of the two most recent UK studies, one concentrated on acute medical admissions, while the other had broad inclusion criteria for drug related admissions, including drug overdoses. A prospective study regarding admission caused by ADR was carried in two large UK hospitals to determine the prevalence as well as outcome, to assess their causality and preventability.

Reports on ADRs from India though found in the literature appear to be inadequate. The literature survey identifies 1030 papers on ADR as compared to total number of 20,588 publications. However, it was in the year 1986 that a formal ADR monitoring system consisting of 12 regional centres, each covering a population of 50 million, was proposed in India.

IndianCouncil of Medical Research (ICMR) has identified five regional centres for monitoring of ADRs. It has documented to have collected around 90,000 reports from twelve centers in the country. Considering the population of India (over a billion) ADRs appear to be under reported, and therefore there is a need for setting up more number of ADR monitoring centers and strengthening the network of these centers for the exchange of information across the country.

Financial burden due to ADR related problems is estimated to be about 20.5
billion pounds every year in UK, while it is 1.5 to 4 billion dollars in US. However it is difficult to estimate the same in India due to prevailing health care system practice and want of related information.

ADRs are broadly identified as preventable and non preventable. But if the preventable ADRs are recognised for the culprit drugs, their related health injuries and distress as well as financial burden can be minimised. Poly pharmacy appears to be a rule rather than exception in the modern medical practice. Severely ill and patients with co-morbidities, on an average receive five or more drugs. It is well known that incidence of ADRs proportionately increase with the number of medications consumed. Drug usage pattern is not universal, therefore a drug with concurrent therapy with other drug is main factor that leads to unwanted drug-drug interaction. This fact emphasis the need to monitor ADRs.

Considering all variables like age, genetics, environment, drug usage pattern etc. that precipitate ADRs, emphasises the need for ADR monitoring across the globe. Such studies are never ending, since new drugs continue to enter the market now and then.

The present study therefore was planned to investigate and report incidence of ADRs, their analysis to explore the reasons for under reporting by health care personnels and to develop strategies to improve reporting in medical wards of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre a tertiary care teaching hospital to analyse ADRs regarding their causality and preventability. It was also planed to suspect and detect potential unwanted drug-drug interactions and to confirm the same through experimental studies.
1.1 Objectives for the study

The present prospective pharmacovigilance study in medical wards of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, was planned with the following objectives:

- **Primary Objectives**
  1. To find the incidence of ADRs and analyze the same regarding their causality and preventability.
  2. To study the awareness and attitude of health care professionals towards adverse drug reactions and to develop the strategies to improve reporting of ADRs by health care personnels.

- **Secondary Objective**
  1. To suspect possible adverse drug drug interactions in inpatients receiving multiple drug therapy and to confirm the same through animal experiments.