

# A Study of Adverse Drug Reactions in Patients Treated with Penicillins in a Rural Tertiary Care Hospital

Shivaraj Basavaraj Patil\*, Shrinivas R. Raikar, Bhaskar H N, M Janardhan, Y. Venkata Rao, Vahila

<sup>1</sup>Department of Pharmacology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, INDIA.

## ABSTRACT

**Background:** Adverse drug reactions (ADR) are rated as the fifth leading cause of death among all diseases. Approximately 5-8% of all hospitalization worldwide is due to ADR. **Objectives:** The present study was conducted with the aim of analyzing the pattern of Adverse Drug Reactions occurring from penicillins, their manifestations and severity. **Methods:** A non interventional observational prospective study was conducted over 2 years from Jan 2014 to Dec 2015 in KIMS Narketpally. The red boxes for dropping the filled yellow adverse drug reactions forms were installed in all the wards and outpatient departments. Additional information and missing data was obtained personally by either consulting the physician or through case sheets. **Results:** The most common penicillin implicated in causation of adverse drug reactions was combination of amoxicillin and clavulanic acid (54%), followed by Piperacillin (21%). Most of the reactions were of moderate severity. The most commonly observed adverse drug reactions were dermatological reactions (37%). Majority of the adverse drug reactions belonged to probable category (71%) according to WHO scale. **Conclusion:** Dermatological reactions are the most common adverse drug reactions occurring due to penicillin and combination of amoxicillin and clavulanic acid was the most common causative penicillin. The health care providers should make an attempt for early detections of ADRs and be vigilant about safety profile monitoring of the prescribed medicines. This will not only decrease the morbidity and mortality but also the health care cost.

**Key words:** Adverse drug reactions, Penicillin, Pharmacovigilance, Amoxicillin.

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## INTRODUCTION

Indiscriminate use of drugs, inflow of new drugs in the market, almost to the level of everyday a new drug entering the market, lack of ADR reporting culture has resulted in rise of ADR incidence.<sup>[1]</sup> An important risk factor for developing ADR is the previous occurrence of ADR. Re-exposure to offending drugs due to poor documentation can cause the patient to experience the same ADR again, thus emphasizing the importance of the accurate documentation of ADR at the time of the event and providing relevant information to the patient about the ADR will help prevent its further occurrence.<sup>[2]</sup>

Definition of an adverse drug reaction (ADR) according to WHO is a "response to a drug that 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>[3]</sup> ADRs are the fourth leading cause of death. Serious ADRs account for 6-7% of all hospital admissions.<sup>[4]</sup> ADRs are associated with

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\*Correspondence : Dr. Shivaraj Basavaraj Patil,

M.D Pharmacology, Assistant professor

Department of Pharmacology,

Kamineni Institute of Medical Sciences,

Narketpally, Nalgonda-508254, INDIA.

Mobile: 7330918988

E-mail: shivarajpatil85@gmail.com

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significant morbidity, mortality and permanent disability and are a huge economic burden on the patients due to prolonged hospitalization.<sup>[5]</sup>

According to a study conducted by Novotny *et al.*, the most troublesome classes of drugs contributing to Adverse Drug Reactions were antibiotics.<sup>[6]</sup> Among antibiotics,  $\beta$  lactams were most commonly implicated for ADRs.<sup>[7,8]</sup> So the aim of present study was to detect and analyse the ADRs due to penicillins.

**MATERIALS AND METHODS**

A non interventional observational prospective study was conducted over 2 years from Jan 2014 to Dec 2015. Prior ethics committee approval was obtained for the study. Our pharmacovigilance centre is recognized as peripheral adverse drug reaction monitoring centre under national pharmacovigilance program of India. Suspected ADR forms which have all relevant data as patient’s demographic details, all drugs received prior to onset of reaction, route of administration, dosage, frequency, date of onset of reaction and the patient’s relevant medical history were used. The ADR forms received by the centre were analysed and those ADR which were caused by penicillin group of antibiotics were included in the study. The causality assessment was done using WHO scale. The severity of reactions was assessed using modified Hartwig and Siegel scale.

**Statistical analyses:** Descriptive analyses was done and presented as percentages.

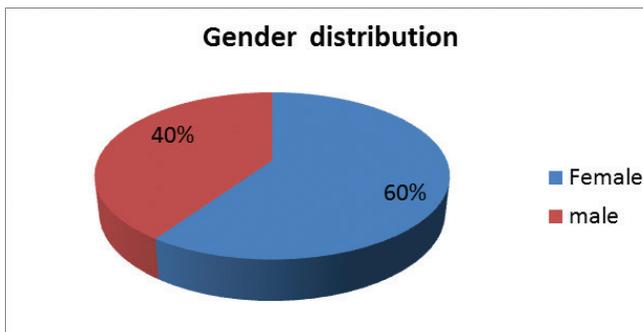
**RESULTS**

Thirty ADRs due to penicillin were reported. Mean age of patients was 38.37 years. Most of the patients were females (Figure 1). Majority of the patients belonged to 31-40 years of age group (Figure 2). Amoxicillin and clavulanic acid was the most common penicillin implicated in ADRs (Figure 3). These ADRs due to penicillin were assessed for causality using WHO scale and most of the reactions either belonged to probable or possible category (Table 1). There were no reactions assessed as certain, unlikely, conditional and unassessable.

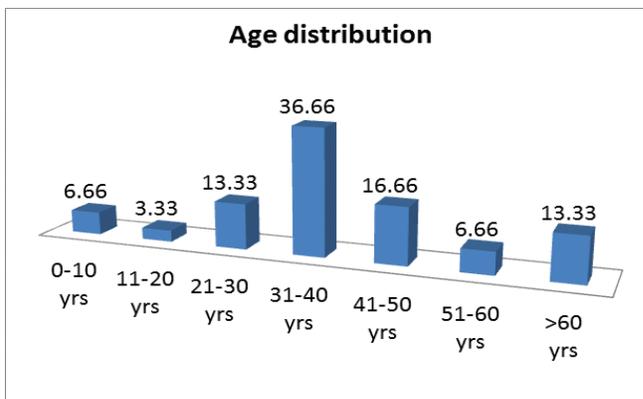
Most common system affected by ADRs was dermatological system followed by GIT system (Figure 4). Majority of the reactions were of mild to moderate severity (Figure 5). In most of the cases the drug was withdrawn once the ADR occurred (Figure 6).

**Table 1: Causality assessment of ADRs according to WHO criteria**

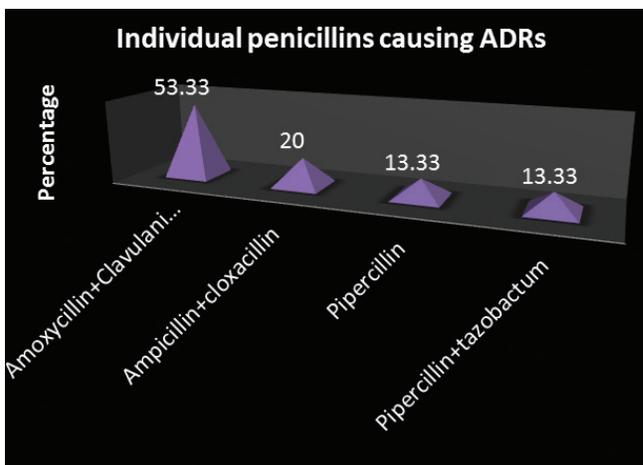
Causality assessment	Percentage of ADRs
Probable	73.33
Possible	26.67



**Figure 1:** Gender wise distribution of patients.



**Figure 2:** Age wise distribution of patients.



**Figure 3:** Figure showing individual penicillins causing ADRs.

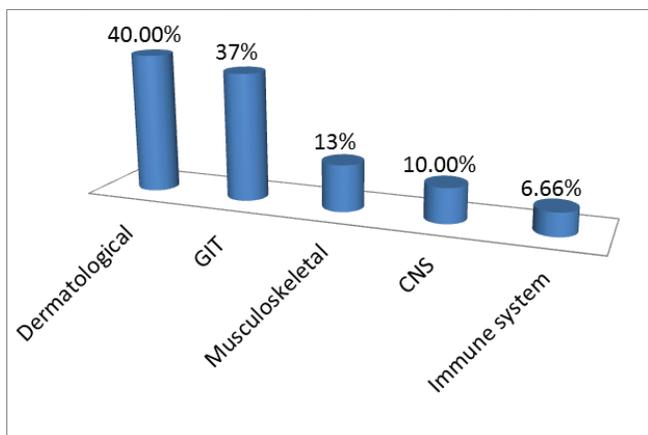


Figure 4: Figure showing organ systems affected by ADRs.

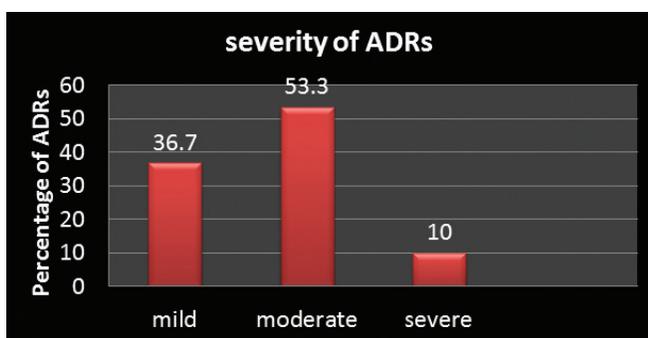


Figure 5: Severity of reported ADRs.

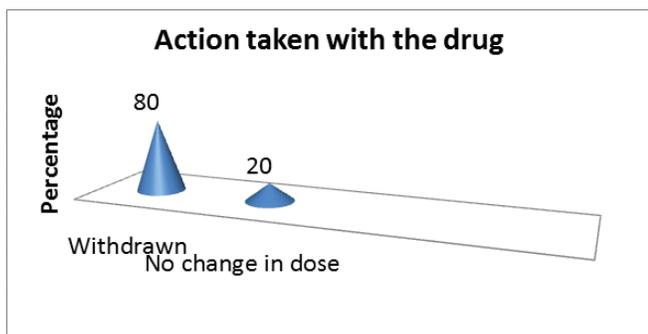


Figure 6: Action taken with the drug.

### DISCUSSION

ADRs are of major concern, affecting the patients belonging to all age groups and of either sex. They cause considerable economic burden on the society and already stretched healthcare system. The post marketing surveillance of drugs is very important in analyzing and managing the risks associated with drugs once they are available for the use of the general population.

Spontaneous reporting of ADRs has contributed significantly to successful pharmacovigilance.<sup>2</sup> It has also helped in detection of unsuspected and unusual ADRs those were previously undetected during the initial evaluation of a drug.<sup>[9,10]</sup>

In spite of these advantages, under-reporting of the adverse drug reactions remains a major draw-back. It is estimated that only 6-10% of all ADRs are reported.<sup>[10,11]</sup> The absence of organized continuing medical education programs and problematic physician attitude are other problems that add to under reporting of the adverse drug reaction.<sup>[12]</sup>

There was predominance of female sex for adverse drug reactions which was similar to a study conducted by Albin S *et al.*<sup>13</sup> The mean age of patients was 38.37 years which was less as compared to another study conducted by Jakob E. Borch *et al.*<sup>[14]</sup> Amoxicillin and clavulanic acid combination was the most common penicillin causing ADRs. But studies done by Sara *et al* and Trubiano *et al* showed amoxicillin alone as most common penicillin causing ADRs.<sup>[15,16]</sup> The reason could be increased use of amoxicillin and clavulanic acid combination than amoxicillin alone in our hospital and amoxicillin component of combination might have caused the ADRs. Most common system affected was dermatological which was in line with other studies.<sup>[13,14]</sup> This increased reporting of dermatological ADRs could be due to easy recognition of dermatological reactions than involving other organ systems.<sup>[17]</sup> Most of the reactions were of probable causality according to WHO criteria since drug rechallenge was not done in any of the cases. Most of them were moderate reactions, they resulted in an increased health care cost due to an increased length of stay and need of some medical interventions.

### CONCLUSION

Only few studies are conducted in India to study ADRs due to penicillins, so such type of studies should be conducted periodically since they help in evaluating the risk benefit ratio of drugs. Still there is underreporting of ADRs so further measures should be taken to increase the awareness among health care professionals.

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