



**A STUDY ON EVALUATING PRESCRIBING PATTERN OF ADVERSE DRUG REACTION REPORTED WITH USE OF ANTIMICROBIAL AGENTS IN TERTIARY CARE TEACHING HOSPITAL**

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### ABSTRACT

**Background:** Antimicrobials are frequently utilized in tertiary care hospitals. Rational use of Antimicrobial agents is extremely essential for improving patient safety on long run use to avoid antimicrobial resistance in hospitalized patients. Antimicrobial agents are considered one of the class of medications and common causative cause of adverse drug reactions (ADRs). A prospective observational study was carried out for duration of 4 months with sample size of 100 patients. 11 ADRs were identified during this study. Detection of the ADR was done using Naranjo Causality assessment scale. The severity of the ADRS was assessed using the Hartwig and Siegel scale. Majority of the ADRs were seen within the patients of age group 20-59 years. The most common ADR among the patients is rashes 2(18.1%), nausea 2 (18.1%), vomiting 2 (18.1%), headache 1 (9.09%), palpitation 1(9.09%), constipation 2 (18.1%), diarrhoea 1 (9.09%) In our study majority of the ADRS were due to the use of the Betalactum (38%) Anthelmintic & Antiamoebics (26%), Quinolones (12%), Macrolides (6%) others (12%). From 11 ADRs (based on the causality assessment Naranjo scale) detection of ADR being identified as 6 (54.4%) were probable, 3 (27.2%) possible, 2 (18.1 %) definite, 0% were unlikely. The severity assessment was done using the Hartwig And Siegel scale and severity of reactions appeared to be mild in 8 (72.72%), moderate in 3 (27.27%), none of reaction were severe. The present study provide source of information in regards to ADRs reported with the utilization of AMA. This would help the healthcare practioners for safe and more rational use of it in hospitalized patients.

**KEYWORDS:** Adverse drug reaction, Anti-Microbial Agents, Patient Safety, BetaLactum, Causality assessment and severity assessment.

### INTRODUCTION

Pharmacovigilance is the science and activities regarding the detection, assessment, understanding and prevention of adverse effects or the other medicine/vaccine related problem. All medicines and vaccines undergo rigorous testing for safety and efficacy through clinical trials before they're authorized to be used.<sup>[1]</sup>

#### Adverse drug reaction

WHO's definition of an adverse drug reaction, is "a response to a drug that's noxious and unintended and occurs at doses normally utilized in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function."<sup>[2]</sup> The ADRs affect the patient recovery further because of the economy related to health care. This has been the idea of starting of international drug programme by WHO. Such reactions are currently reported by use of WHO's Adverse Reaction Terminology, which will eventually become a subset of the International Classification of Diseases.

#### Antimicrobial agents

- Infectious diseases represent a serious reason behind morbidity and mortality in India and are responsible for an increase in hospital admissions, particularly in children.
- Antibiotics and other antimicrobials, therefore, constitute a vital category of medicine, both within the community and in hospitals. There's considerable evidence linking indiscriminate use of antimicrobials to altered susceptibility patterns among infectious organisms.<sup>[3]</sup>
- Antimicrobial agents include Antibiotics, Antiviral, Antifungal, Antiparasitic, and Antiprotozoal.
- Classification of antibiotics is predicated on their chemical structure (eg.  $\beta$ -Lactam, Quinolones, Sulphonamides, etc) or supported their mechanism of action (e.g. plasma membrane synthesis inhibitor, protein synthesis inhibitors, DNA or RNA synthesis inhibitor, etc).<sup>[4]</sup>
- Based on the action on bacteria, these agents are

- further classified into bactericidal and bacteriostatic.
- Bactericidal antibiotics are drugs which kill the bacteria; these agents are time or concentration-dependent. Time-dependent antibiotics ( $\beta$ -lactam, Isoniazid, Rifampin, etc.) need a specific time of interaction of antibiotics on the bacteria to kill.
  - Concentration - dependent antibiotics (Bacitracin, Aminoglycoside and Quinolones) need a minimum concentration of the chemical agent at the target site to kill the organism.
  - Bacteriostatic antibiotics are those antibiotics that inhibit the expansion and multiplication of bacteria (e.g. Macrolides, Lincosamide, and  $\beta$ -actam).
  - Antiviral drugs are a category of medication used for treating viral infections most antiviral target specific viruses, while a broad spectrum is effective against a good range of viruses. Unlike most antibiotics, antiviral drugs don't destroy their target pathogen; instead they inhibit its development.<sup>[5]</sup>
  - Antiviral drugs are one class of antimicrobials, which includes antibiotic (also termed antibacterial), antifungal and antiparasitic drugs, [or antiviral drugs supported monoclonal antibodies. Most antivirals are considered relatively harmless to the host, and so are often used to treat infections.<sup>[6,7]</sup>

#### Acyclovir

- It is antiviral medication that slows down the expansion and spread of the animal virus within the body. It is effective in treating herpes infection, and lowers symptoms of the infection. ADR include headache, nausea, vomiting, and diarrhoea.

#### Amphotericin B

- Amphotericin B is an antifungal medication used for serious fungal infections and leishmaniasis. ADR include muscle/joint pain, weakness, tingling of arm, painful urination.

#### Metronidazole

- It is an antibiotic and antiprotozoal medication used to treat bacterial infections of the vagina, stomach, liver, skin, joints, brain and neural structure, lungs, heart, or bloodstream.
- ADR include dizziness, headache, nausea, vomiting, loss of appetite, diarrhoea, constipation

#### Albendazole

- Albendazole is an anthelmintic or anti-worm medication. ADR include abdominal pain, fever, sore throat, headache, nausea vomiting dark urine.

#### Adr's associated with AMA

Classification of AMAs	Common adverse drug reactions associated with AMAs
Penicillin's	Hypersensitivity reactions which includes- rashes, anaphylaxis, fever, joint pains, angioedema, serum sickness like reaction, blood disorders, at high dose causes c.n.s. Toxicity; colitis and diarrhea
Cephalosporin	Hypersensitivity rashes, joint pains, rarely anaphylaxis; abdominal discomfort, colitis, erythema, reversible interstitial nephritis; transient hepatitis; blood disorders, dizziness etc.
Aminoglycosides	Ototoxicity, nephrotoxicity, more common in the elderly and in renal failure; may impair neuromuscular transmission and may cause transient myasthenia
Tetracycline's	Nausea, vomiting, diarrhoea, headache, dizziness, sleep disorders, rash, pruritus, anaphylaxis, increase in urea, creatinine and liver enzymes, arthralgia and myalgia, blood disorders, restlessness, hallucinations, depression, tendon damage.
Acyclovir	Headache, nausea vomiting, diarrhea
Amphotericin b	Muscle/joint pain, weakness, tingling of arm, painful urination
Metronidazole	Dizziness, headache, nausea, vomiting, loss of appetite, diarrhea, constipation
Albendazole	Abdominal pain, fever, sore throat, headache, nausea vomiting

#### METHODOLOGY

A prospective observational study was conducted to identify the adverse drug reactions associated with the utilization of Antimicrobial drugs at inpatient of various department in tertiary care teaching hospital. This study included 100 patients as sample size and given antimicrobial drugs after being hospitalized.

Information related to patient were taken from case sheets including

- Patients demographic details, vitals
- Information about the patients disease, past

medication history, personal history and comorbidities

- Antimicrobial drugs given to the patients (dose, frequency, route of administration)
- Investigating and reporting ADR

All above details were then documented in patient profile form.

All the spontaneous reported ADRs with use of Antimicrobial drugs over a period of 4 months were analyzed. The nature and type of ADRs related to AMA

were analyzed with patient related factors (age, gender, comorbidities, disease conditions, smoking, alcohol)

The pregnant, lactating, drug addicts, outpatients were excluded in this study.

The current study was undertaken to identify prescribing pattern of AMA, analyze the causality, and severity pattern of ADRs associated with AMA in various departments. The suspected adverse drug reactions were identified among the patients. Evaluating ADRs that occurred in various departments in hospital.

The assessment of the ADR was done using the Naranjo scale which helps in describing the relation between the drugs and reactions that occurred to the patient.

It consists of 10 questions that are answered as Yes, No, don't know, different point values (-1, 0, +1, or +2) are assigned to every answer. Based upon the full answers the reactions are classified as:

- Possible (Greater than 9)
- Probable (5-8)
- Possible (1-4)
- Doubtful (0 or less)

The severity assessment of ADR was done by using Hartwig and Seigel severity assessment scale which

describes the extent to which the ADRs influence the lifestyle of the patients. This scale classifies severity into the seven levels:

- Level 1 and 2 – less severe
- Level 3 and 4 – moderate
- Level 5, 6, and 7 – severe

In the level 1 and 2 requires no antidote or change of therapy, in the level 3 and 4 it may cause hospitalization of the patients for short duration i.e. 1 day or possible for readmission. Level 5, 6, 7 causes permanent damage to the patients or possibly death of the patients directly or indirectly.<sup>[8,9]</sup>

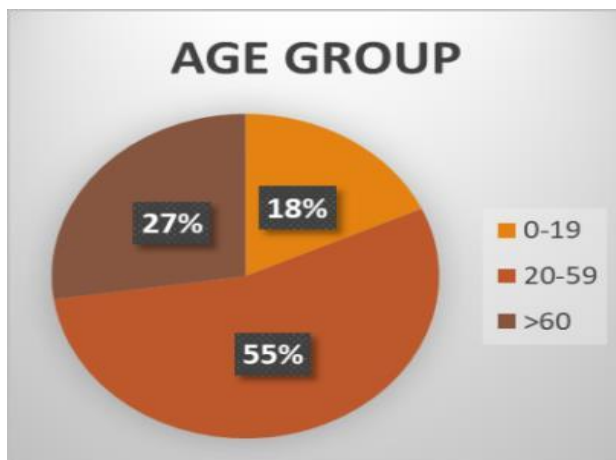
The management of the ADR was done either by decreasing, stopping or by using the alternate medicine. A pre-designed performance of central drugs standard control organization was accustomed to record the ADR's.

**RESULTS**

**Age**

The study reveals that the maximum number of ADR's were seen in the adults 6 (20-59 years), followed by 3 (>60 years) and in 2 (<19 years).

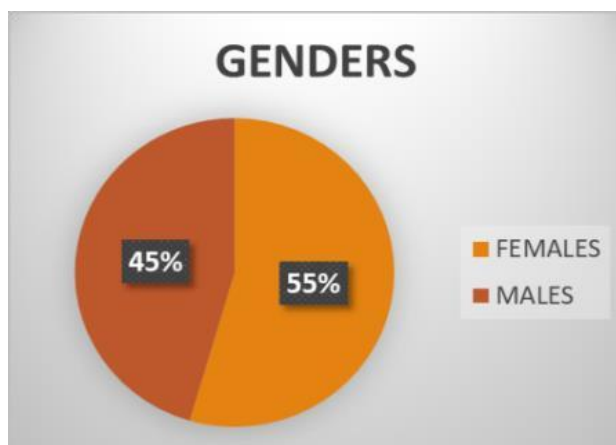
The highest percentage were seen in the age group 55% (20-59 years) while the lowest were seen in 18% (<19 years)



**Gender**

Among 11 ADRs, females experienced more number of ADR's when compared to males. The study revealed that

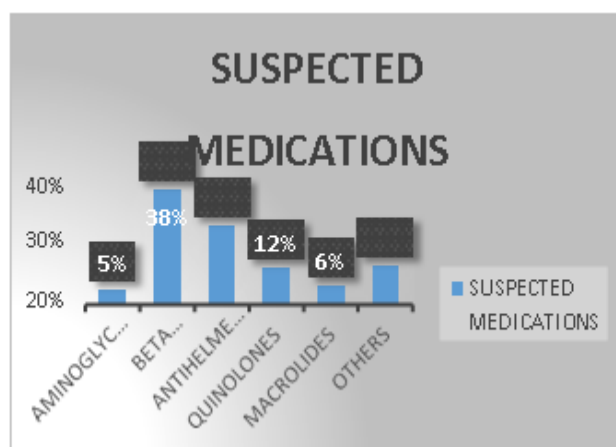
females 6 (55%) reported more number of ADR's when compared to 5 males (45%)



**Suspected medications**

Antimicrobial agents that includes betalactum antibiotics, were mostly used drugs. The study reveals that number of ADR's with suspected medications were

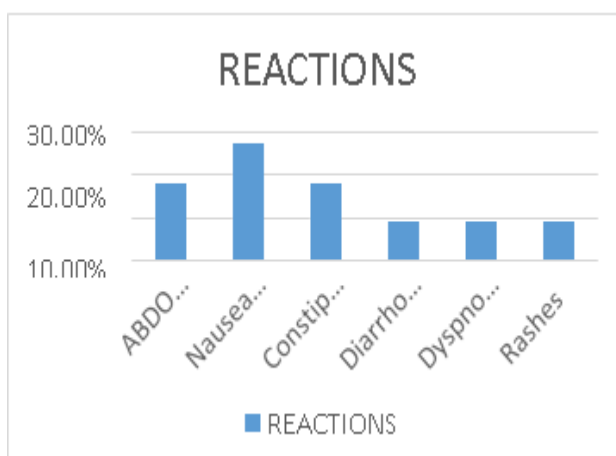
Beta Lactum (38%), followed by Anti Helmentics (26%), quinolones (12%), macrolides(6%), Aminoglycosides (5%) and others(13%)



**Adverse drug reactions**

From the study, most of the reactions that occurred were nausea and vomiting (27.2%) followed by abdominal

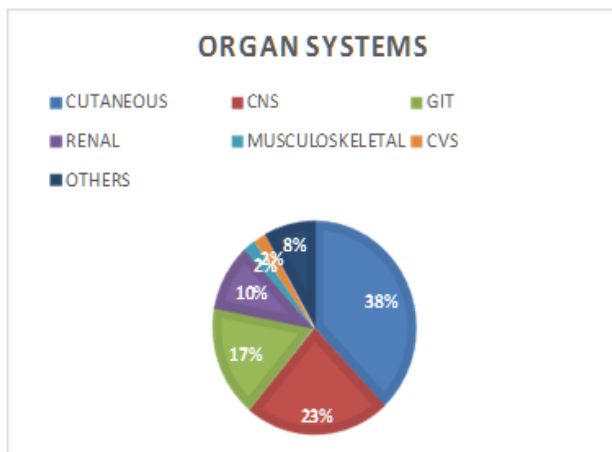
pain 2 (18.1%), constipation 2 (18.1%), diarrhea 1 (9.09%), dyspnea 1 (9.09%), rashes 1 (9.09%), others 1 (9.09%).



**Organ system involved in ADR**

From the study, most of the ADR's were found in skin

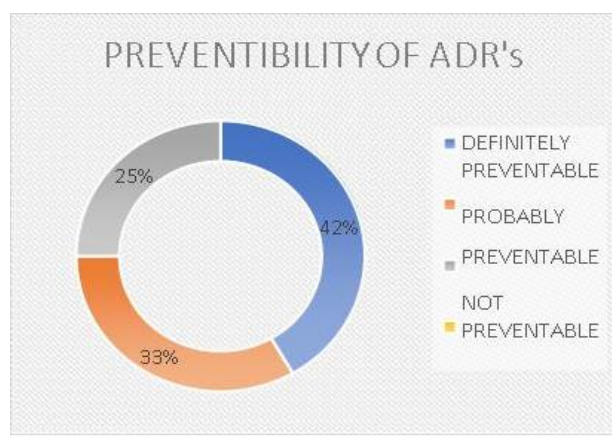
and appendages (38%) followed by CNS (23%) and GIT (17%).



**Preventibility of ADR**

ADRs were assessed for his or her preventability by using modified Shumock and Thornton method. Among

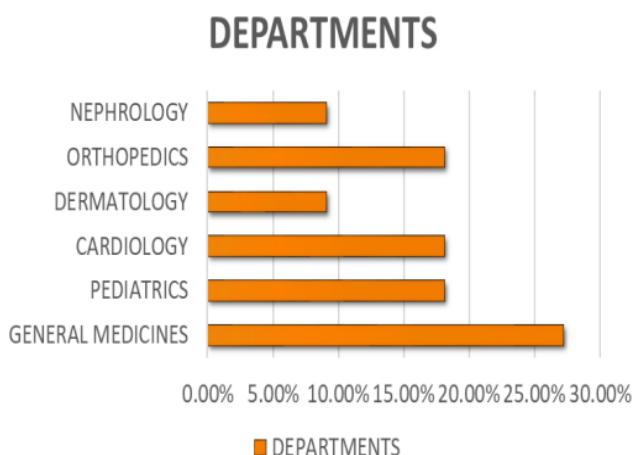
11 ADRs, 5 (45.4%) of the ADRs were definitely preventable, while 4 (36.3%) were probably preventable and three (27.27%) weren't preventable.



**Departments**

Among 11 ADRs, 3 (27.2%) ADRs were reported from the general Medicine followed by Pediatrics 2

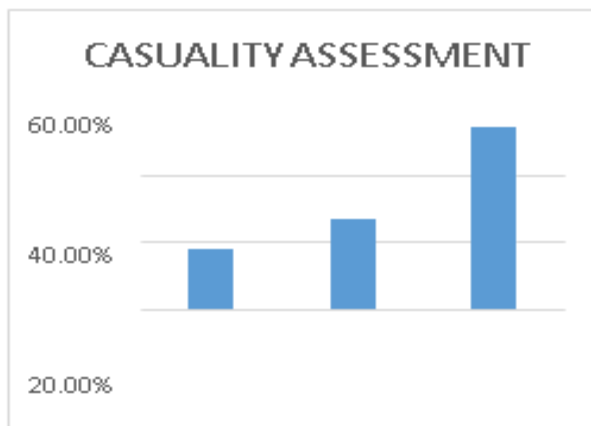
(18.1%), Cardiology 2 (18.1%), Dermatology 1 (9.09%), Orthopedics, 2 (18.1%), Nephrology 1 (9.09%).



**Casualty assessment**

According to Naranjo scale, most of the ADRs (54.5%)

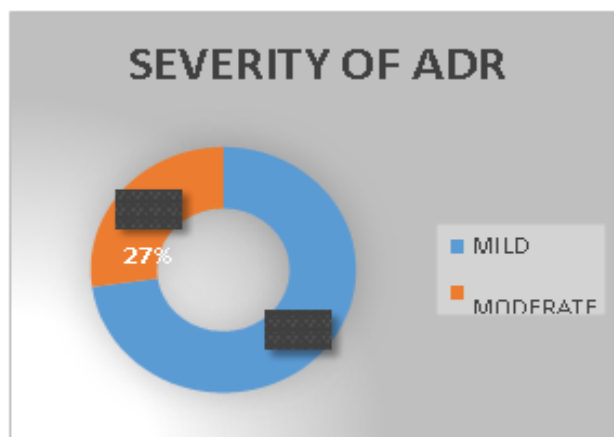
were probable, (27.2%) were possible, 2 (18.1%) were definite and 0% were unlikely.



**Severity assessment**

ADRs were assessed for their severity by Hart wig scale. Of the 11 ADRs, mild reactions accounted of 8 (72.72%)

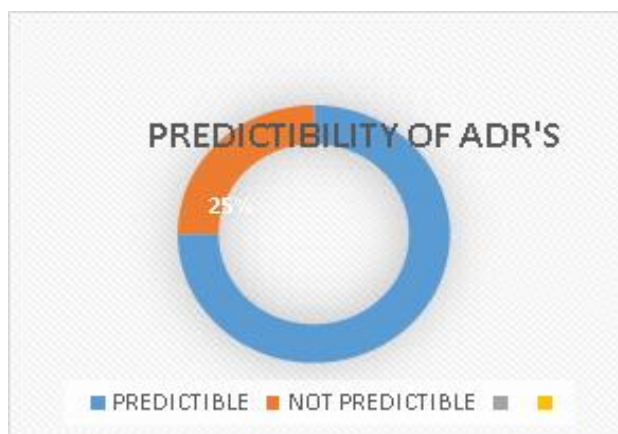
followed by 3 (27.27%) moderate reactions. None of the reactions was severe.



**Predictability**

Out of 11 ADRs, predictable 9 (81.81%) while, 3

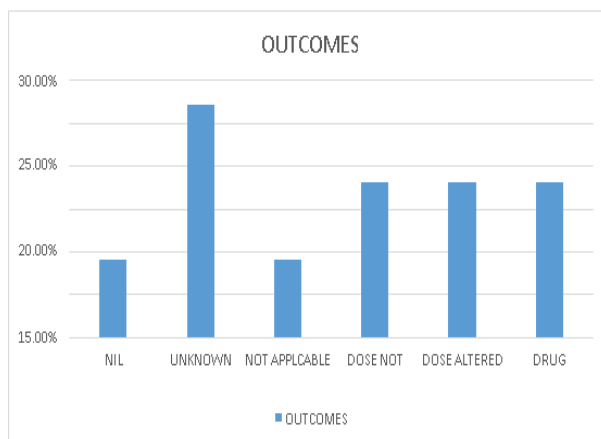
(27.27%) were notpredictable.



**Outcomes**

According to Naranjo scale, most of the ADRs (54.5%) were probable, (27.2%) were possible, 2 (18.1%) were definite and 0% were unlikely. Out of 11 ADRs, in 2 (18.1%) cases the suspected drug was withdrawn while

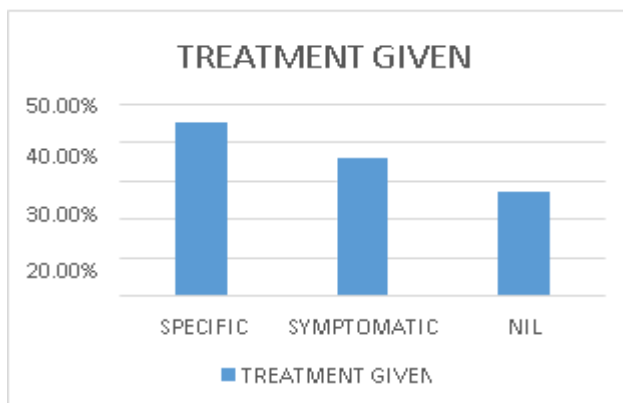
no change was made with the suspected drug in 2 (18.1%) the dose was altered in 2 (18.1%) cases., 3 (27.2%) were unknown, 1 (9.09%) wasn't applicable and dose wasn't changed in 1 (9.09).



**Treatment given**

Among 11 ADRs, specific treatment was given in 5 (45.45%) while 4 (36.36%) cases required

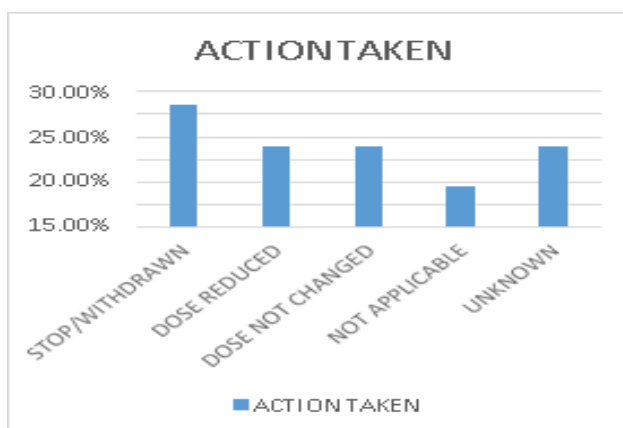
symptomatic treatment and 3 (27.27%) cases required no treatment



**Action taken**

In most of the patients, the suspected drugs were mostly

stop/withdrawn.



**DISCUSSION**

We received total of 11 ADRs during 4 months study. From this study, we found out that, females 6 (54.5%) reported more number of ADRs compared to males 5 (45.5%). The study revealed maximum number of ADRs were reported from patients of age group (20- 59years) – 6 (54.5%) followed by patients, with age group 60 years and above (60-80years) – 3 (27.2%) and children’s under 19 years – 2 (18.1%).

From the study, most of the reactions that occurred were nausea and vomiting (27.2%) followed by abdominal pain 2 (18.1%), constipation 2 (18.1%), diarrhea 1 (9.09%), dyspnea 1 (9.09%), rashes 1 (9.09%), others 1 (9.09%).

The study reveals that number of ADR’s with suspected medications were Beta Lactam (38%), followed by Anthelmintic (26%), quinolones (12%), macrolides

(6%), Aminoglycosides (5%) and others (13%).

From this study, maximum number of ADRs were reported from general medicine department 3 (27.2%) by Pediatrics 2 (18.1%), Cardiology 2 (18.1%), Dermatology 1 (9.09%), Orthopedics, 2 (18.1%), Nephrology 1 (9.09%).

Action taken in additional number of patients was mostly stop/withdrawn suspected drug 4 (36.3%) followed by dose reduced 2 (18.1%) dose not changed 2 (18.1%), not applicable 1 (9.09%), unknown 2 (18.1%)

The study revealed that number of patient recovered are 7 (63.6%) followed by recovering 2 (18.1%), not recovering 1 (9.09%), fatal 0 (0%), and unknown 1 (9.09%), According to Naranjo scale, 6 (54.5%) were probable, 3 (27.2%) were possible, 2 (18.1%) were definite and 0% were unlikely.

The severities of the reactions were done using Hart Wig Scale. Study reveals majority of ADRs were mild reactions 8 (72.72%) followed by moderate reactions 3 (27.2%) and none of the reactions was severe.

Withdrawal of the Drug 2 (18.1%) was the most line of management of ADRs, while no change was made with the suspected drug in 2 (18.1%) and also the dose was altered in 2 (18.1%) cases. Reported ADRs were assessed for preventability by using modified Shumock and Thornton method. We concluded that 5 (45.45%) of the ADRs were definitely preventable, while 4 (36.3%) were probably preventable and 13 (27.2%) weren't preventable.

Predictability of ADRs was assessed based on the incidence of the reactions and ADR reports. Results revealed that the majority of ADRs were predictable 9 (81.8%) while, 2 (27.2%) weren't predictable. Most number of the ADRs were seen within the GIT system 8 (76%) and therefore the least were seen within the other parts (24%).

## CONCLUSION

ADR reporting is an ongoing and continuous process. This type of study helps to identify and report ADR. As per the study performed, most of the ADR's were treatable by early and appropriate management. Most of the suspected drugs were unknown, the foremost limitation was under-reporting of ADR's which might be overcome by creating awareness & enhancing the culture of ADR monitoring & reporting among health care professionals for safe use of medicine. Antimicrobial drugs are the foremost widely prescribed drug so it require more ADR monitoring. AMA treatment is related to high frequency of ADR in hospitalized patients. ADR to antibiotics in inpatients are presented mainly as blood type and kind B, with a prevalence of

dose-dependent and predictable reactions. They are mild to moderate, dominantly manifested dysbacteriosis and hypersensitive reactions. Female gender, but not the age is significantly related to higher risk for ADR to antimicrobials in hospitalized patients.

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