

Preventable Drug Harms in Renal Injuries: A Prospective Observational Study in OPD and IPD Patients in Medicine Department of Civil Hospital, Nashik

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ABSTRACT


Background: Renal injuries are common clinical syndrome. Drug causes near about 20% of community and hospital-acquired episodes of renal failure. Kidneys are mainly responsible for elimination of drugs, therefore, it is susceptible to high degree of toxicity. Therefore, they are susceptible to high degree of toxicity. **Objectives:** To avoid preventable renal injuries by early prognosis, it is necessary to evaluate parameters of renal injuries in early stages of the drug exposure. **Study setting:** This study was based on case series analysis. All patients with abnormal renal function reports were included in the study. It requires long-term study, therefore, it was hard to recruit deranged renal function test patients in shorter time period of 3 months. **Materials and Methods:** Our total sample size was 180 out of which 50 (27.77%) patients were recruited within given time limit. This was a prospective observational study conducted at Civil Hospital of Nashik. All 50 patients had abnormal renal function test. Out of total 50 patients, there were 32 patients who were male (64.00%) and 19 (36.00%) patients were female. **Results:** NSAIDs were found to be the most common drugs that cause Acute renal failure. **Conclusions:** The study concludes that, by identifying renal injuries earlier, we can prevent 30% hospitalizations which are caused due to prescribed drugs.

Key words: Acute renal failure, chronic renal failure, nephrotoxicity, Nonsteroidal anti-inflammatory drugs

INTRODUCTION

Acute kidney injury (AKI) is a common clinical syndrome whose definition has standardized as a result of consensus by leading experts around the world. As a result of these definitions, reported AKI incidences can now be compared across different populations and settings. The population

incidence of less severe AKI and AKI treated with renal replacement therapy is approximately 2000-3000 and 200-300 per million populations per year, respectively. These numbers are comparable with the estimates for severe sepsis and acute lung injury. Approximately 4-5% of general intensive care unit patients will be treated with renal replacement therapy. The incidence of AKI is increasing. Intensive care unit patients with AKI have a longer length of stay and therefore generate greater costs. Patients with AKI who are treated with renal replacement therapy still have a mortality rate of 50-60%. Of surviving patients, 5-20% remains dialysis dependent at hospital discharge. As a result of these definitions, reported AKI incidences can now be compared across different populations and settings.^[1] The pattern of disease morbidity and mortality throughout the world is

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changing both in the developed and the emerging world. During the 20th century, infectious diseases were the major cause of death and disability. However, in this century, non-communicable, non-infectious diseases have become the major cause of mortality and morbidity around the world. Chronic renal failure (CRF), nephrotic syndrome (NS), nephritic syndrome, and hypertension were the four common presentations seen in 47.8%, 15.03%, 4.6%, and 4.9% of cases, respectively. Followed by Acute renal failure (ARF) (1.9%), urinary tract infection (2.9%), stone disease (4.6%), obstructive uropathy (2.1%), isolated hematuria (1.2%), and asymptomatic urinary abnormalities (0.3%). Chronic glomerulonephritis was seen in 49.4% of cases of CRF followed by diabetic nephropathy in 28.4% of cases. Of the NS cases, primary glomerulonephritis was seen 58.5% of cases, of which minimal change disease was the most common cause in 38% of cases. Of the secondary glomerular diseases, diabetic nephropathy was the most common cause of NS (53%) followed by amyloidosis (16.4%) and lupus (8.3%). Tuberculosis was the most common cause of renal amyloidosis seen in 50% of cases. Of the nephritic syndrome, post-infective glomerulonephritis was the most common cause followed by rapidly progressive glomerulonephritis being the second most common cause. In the hypertensive group, essential hypertension was the most common cause followed by renovascular hypertension.

Acyclovir, cephalosporin, ciprofloxacin, cocaine, diuretics, indianavir, lithium, mesalamine, nonsteroidal anti-inflammatory drug (NSAID),^[2] penicillin, rifampicin, penicillamine, sulfonazide, triamterene, valproic acid, streptokinase, and Chinese herbs cause acute interstitial nephritis with systemic manifestation of hypersensitivity reaction such as fever rash and arthralgias. Due to deposition of fibrin such as materials clopidogrel,^[3] cocaine,^[4] cyclosporine, indianavir, cisplatin, mitomycin, quinine, tacrolimus,^[5] and ticlopidine, these drugs cause thrombotic microangiopathy. Other drugs causing thrombotic microangiopathy include,^[6] as well as methotrexate and sulfonamide. In urinary findings, urine sediment may contain red cells and white blood cells, crystals of acyclovir are needle shaped, and indianavir are rectangular plate.^[7] Gold, lithium, NSAIDs, interleukin 2, and penicillamine these cause NS Chinese herbs; cisplatin, ifosfamide, NSAIDs, cyclosporines, nitrosurias, and analgesics these drugs cause CRF.^[8]

Drug causes approximately 20% of community- and hospital-acquired episodes of ARF.^[9] Among older adults, the incidence of drug-induced nephrotoxicity may be as high as 66%.^[10] Compared with 30 years ago, patients today are older, have a higher incidence

of diabetes and cardiovascular disease, take multiple medications, and are exposed to more diagnostic and therapeutic procedures with the potential to harm kidney function.^[11]

By identifying renal injuries earlier, we can prevent 30% hospitalizations which are due to prescribed drugs. In this way, we can save a large amount of money which is spend on these cases with avoiding unnecessary risk to patient. By identifying ADR earlier, we can provide a healthy life to our society. For preventing patient from renal injuries, we have such criteria's with which early diagnosis and treatment is possible. Many drugs can cause abnormalities in Renal Function Tests (RFTs) without any symptom which can suggest renal injuries; so, RFTs should be performed preplanned whenever a new drug is started. The cases which do not show any obvious cause, careful history (personal and family) includes medication (drug doses, administration route, previous medication, and concomitant medication) should be taken. Patient should be physically examined for any rashes or spots on body, fever, syncope, and leg and ankle edema. RFTs with other biochemical, hematological test should be performed by which we can identify renal injury with its type and pattern can initiate treatment as soon as possible. The initial treatment for these cases is usually withdrawal of suspected drug. In case, if drug is not discontinued because of polypharmacy or the underlying disease is severe, careful monitoring is important. Although renal impairment is often reversible if the offending drug is discontinued, the condition can be costly and may require multiple interventions, including hospitalization.^[12] This study provides a summary of the most common mechanisms of drug-induced renal toxicities which are caused by different drugs. It is also helpful in detection of renal injuries or toxicities caused by different drugs. This study encourages rational uses of drugs that will result in minimal harm to patients.

MATERIALS AND METHODS

This was a prospective observational study conducted at Civil Hospital of Nashik. This study was based on case series analysis. All patients with abnormal renal function reports were included in study. It requires long-term study therefore it was hard to recruit deranged renal function test patients in shorter time period of 3 months. Our total sample size was 180 out of which 50 (27.77%) patients were recruited within given time limit. This was a prospective observational study conducted at Civil Hospital of Nashik. All

50 patients had abnormal renal function test. Out of total 50 patients, there were 32 patients who were male (64.00%) and 19 (36.00%) patients were female.

RESULTS

Over a period of 2 months, a total of 50 patients were suspected for drug-induced renal injury. All 50 patients had abnormal renal function test, among these 32 were male and 18 were female. Drug-induced renal injury was more common 64% in males and 36% in females. The mean age of the male patients was 43.82 ± 7.02 ranges from 18 to 60 years and the mean age of female patients was 43.22 ± 5.08 .

NSAIDs were commonly encountered drugs (22.00%) causing renal injuries in which 8 (16%) patients had cause of dynapar and 3 (6%) patients having cause of nimesulide, followed by antibiotics (20%). Other drugs included antitubercular drugs (6.00%), aminoglycosides (22%) in which gentamycin (16%) and amikacin (6%), antimalarial drugs (6%), antiviral drugs (8%), angiotensin-converting enzyme (ACE) inhibitors (6%), and antifungal (6%) while diuretics and lipid-lowering agents account (2%), respectively, cause renal injuries to patients. Among these NSAIDs, aminoglycosides and antibiotics were most common nephrotoxic drugs.

In this study, we found that the drugs given below were commonly prescribed, which are responsible for causing drug-induced renal injury. NSAIDs are 22% causing renal injury which includes drugs such as nimesulide (16%) and diclofenac (6%). After that, antibiotics are 28% causes renal injuries including amoxicillin-clavulanic acid (6%), ciprofloxacin (4%), and cefixime (4%). Then, aminoglycosides 22% such as amikacin 16% and gentamycin 6% cause renal injuries. Antitubercular drugs are 8% responsible for renal toxicity as shown in Figure 1. Antimalarial drugs contribute 4% in renal injuries including chloroquine and artesunate. Antiviral drugs such as acyclovir (6%)

are responsible for causing renal toxicity. Other drugs responsible for renal toxicity including drugs like diuretics (2%). For the causality assessment, we use Naranjo's algorithm scale where 15% of cases which were severe are definite/certain having score above 8. While 35% cases are probable having score 5-8 and remaining 50% cases were possible shows score 1-4. and remaining 50% cases showed score of 1-4.

In Table 1, we shown drugs which were responsible for the specific pattern of renal injuries, NSAIDs account 11 cases of renal injuries in which 6 were pre-renal ARF, 4 were ARF, and 1 was CRF. Aminoglycosides account 11 cases in which 7 were pre-renal ARF, 3 were ARF, and 1 was CRF. We found 3 cases of antimalarial drugs in which 2 cases were of pre-renal ARF and 1 case of CRF. ACE inhibitor like ramipril caused pre-renal ARF in 2 cases and CRF in 1 case where acyclovir accounts for 4 cases of ARF. AKT drugs show 3 cases in which 1 case was pre-renal ARF and 2 cases were ARF. Amphotericin-B caused pre-renal ARF in 1 case and CRF in 1 case. Amoxicillin was responsible for pre-renal ARF in 3 cases and ARF in 1 case. Cefixime

Table 1: Drugs responsible for causing renal injuries

| Drugs | No. of cases | Pre-renal ARF | ARF | CRF |
|-----------------|--------------|---------------|-----|-----|
| ACE inhibitors | 3 | 2 | 1 | 0 |
| Acyclovir | 4 | 0 | 4 | 0 |
| AKT | 3 | 1 | 2 | 0 |
| Aminoglycosides | 11 | 7 | 3 | 1 |
| Amphotericin-B | 2 | 1 | 0 | 1 |
| Antimalarial | 3 | 2 | 0 | 1 |
| Amoxicillin | 4 | 3 | 1 | 0 |
| Cefixime | 1 | 1 | 0 | 0 |
| Ciprofloxacin | 2 | 1 | 1 | 0 |
| Diuretics | 1 | 0 | 1 | 0 |
| NSAIDs | 11 | 6 | 4 | 1 |
| Atrovas | 2 | 2 | 0 | 0 |
| Taxim | 1 | 0 | 1 | 0 |
| Streptomycin | 2 | 1 | 0 | 1 |

CRF: Chronic renal failure, ARF: Acute renal failure, ACE: Angiotensin-converting enzyme, NSAIDs: Nonsteroidal anti-inflammatory drugs

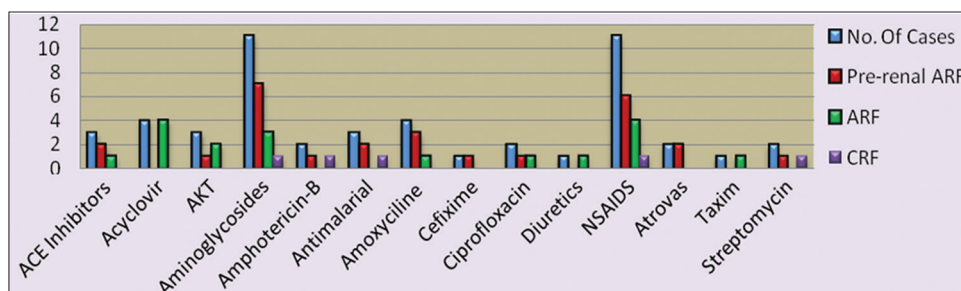


Figure 1: Graphical representation of drugs those are responsible for renal injuries

accounts for single case of pre-renal ARF, while ciprofloxacin accounts for single case of pre-renal ARF and ARF. Streptomycin accounts for pre-renal ARF and CRF in 2 cases. Furthermore, diuretics are responsible for single case of ARF. Furthermore, Atrovas causes 2 cases of pre-renal ARF and Taxim accounts for single case of ARF.

CONCLUSION

Commonly used drug causes are responsible for approximately 20% of community- and hospital-acquired episodes of ARF. NSAIDs are commonly encountered drugs (22.00%) causing ARF followed by antibiotics causing ARF (20%). Aminoglycosides (22%) causing ARF, other drugs included antitubercular drugs (6.00%) which cause CRF, after this study, we can say that by identifying renal injuries earlier, we can prevent 30% hospitalizations which are due to prescribed drugs. In this way, we can save a large amount of money which is spend on these cases with avoiding unnecessary risk to patient.

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