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ABSTRACT

Objective: Chronic kidney disease is a leading healthcare problem, with a global prevalence of 8-16%. In a recent study, the prevalence of CKD was observed to be 17.2% with 6% having CKD stage 3 or worse. Although the prevalence of anemia ranges from about 1% in stage 2 of CKD to almost 100% in end stage renal disease (ESRD), only few of them received treatment. The objectives of the current study was to identify the prevalence of anemia in CKD patients, to analyze the prescribing pattern of drugs in patients with CKD, to identify the risk factors and drug-drug interactions in the prescriptions. Methods: A prospective observational study was conducted for a period of 6 months in the inpatient department of Nephrology and Cardiology. Result: The study demonstrates the prevalence of anemia in CKD patients and it was found to be 90%. ESA therapy was administered to 30 % of patients to treat anemia and the remaining patients were treated with iron supplements and folic acid. The important risk factors identified in the study were hypertension, Type II DM, age, gender, dyslipedemia, family history, smoking and obesity. A total of 19 drug-drug interactions were identified. Among them, 47.36% of the prescriptions had major severity. Conclusion: The current study observed the prevalence of anemia in CKD patients and are prescribed with appropriate drugs according to the recommended guidelines to a greater extent and are comparable with the existing literature.
INTRODUCTION

Chronic kidney disease is a leading healthcare problem, with a global prevalence of 8-16%. In a recent study, the prevalence of CKD was observed to be 17.2% with 6% having CKD stage 3 or worse. Although the prevalence of anemia ranges from about 1% in stage 2 of CKD to almost 100% in end stage renal disease (ESRD), only few of them received treatment. Some of the most common causes of kidney damage include diabetes, hypertension, glomerulonephritis, polycystic kidney disease, kidney stones, urinary tract infections, congenital diseases and certain drugs and toxins like aminoglycosides, amphotericin and cyclosporine.¹

The National Kidney Foundation had developed a criteria for the assessment of CKD severity by dividing CKD patients into 5 different stages based on their creatinine clearance such as patients with eGFR less than 90, 60 - 89, 30 - 59, 15 - 29 and less than 15 ml/min /1.73 m² were categorized into stage 1 (normal or increased GFR ), stage 2 (early renal insufficiency), stage 3 (moderate renal failure ), stage 4 (severe renal failure ) and stage 5 (ESRD) respectively. The causes of anemia in CKD includes blood loss, shortened red cell life span, vitamin deficiencies, iron deficiency, the uremic milieu,” erythropoietin (EPO) deficiency and inflammation.² CKD patients with anemia have a major incidence of cardiovascular dysfunction, cognitive impairment and sleep disturbances. As anemia is one of the important problem in CKD patients, the objective of our study was to evaluate the prevalence of anemia in CKD patients, to analyze the prescribing pattern of drugs, to identify the risk factors and drug-drug interactions in the prescriptions.

MATERIALS AND METHODS

A prospective observational study was conducted for a period of 6 months in the inpatient department of Nephrology and Cardiology. The study was approved by hospital ethical committee (EC/2019/0503/CR/18) and written consent was obtained from all the participants. The relevant data were collected using a standard data entry format. Baseline data collection included age, sex, social history, comorbid conditions and causes of kidney disease. From the medical records, laboratory investigations such as hemoglobin, serum ferritin, serum iron, TSAT and serum folate were noted. Current use of drugs were also recorded. All the cases were analyzed to identify the prevalence of anemia, evaluate the prescribing pattern of drugs in CKD patients and identify the risk factors in the study population. Micromedex drug
database was used to identify drug-drug interactions. According to the inclusion and exclusion criteria, 100 patients were enrolled in our study.

**Inclusion criteria:**

- Patients with chronic kidney disease with stage I – V.
- Age > 18 years (both gender).
- CKD patients undergoing hemodialysis.

**Exclusion criteria:**

- Patients with other systemic illness without renal failure.
- Pregnancy.
- CKD patients undergoing peritoneal dialysis and GI bleeding.

**RESULT**

The study subjects were generally old people between the age group of 56 - 65 years. Gender distribution indicates 67% male patients and 33% females. In our study 76% of the patients were categorized under stage 5 of CKD, 11% in stage 4, 6% in stage 3, 5% in stage 2 and 2% were under stage 1 of CKD. Major causes of CKD were hypertension (86%) and diabetes mellitus (63%). The current study could identify 90 % of anemia in CKD patients (table no:1). The drugs used in the study population were analyzed and the drugs prescribed are shown in figure no: 1. Majority of the study population received vitamins and minerals (28.82%), anti-hypertensive (13.83%) and anti anginals (11.82%) followed by other categories of drugs. As the prevalence of anemia was high in the study population, iron preparations and erythropoietin stimulating agents were used for the management of anemia. In our study, 30 % of patients were treated with erythropoietin stimulating agents whereas remaining patients were treated with iron, vitamin and mineral supplements. The important risk factors identified in the current study were hypertension, Type II DM, age, gender, dyslipedemia, family history, smoking and obesity (figure no:2). The laboratory investigations analysed in our study indicate that haemoglobin levels of patient population were between a minimum of 5gm/dl and a maximum of 11gm/dl. The renal parameters (serum creatinine, urea, GFR) were found to be elevated. The most commonly used
endogenous marker for assessment of glomerular function was creatinine.

The complications associated with CKD were analyzed. Anemia was identified in 90% of the patients, 50% with heart disease, 41% with fluid overload, 22% with hyperkalemia, 15% with bone disease and 11% with hyperphosphatemia. A total of 19 drug-drug interactions were identified. Among them, 47.36% of the prescriptions had major severity, 42.10% with moderate severity and 10.52% had minor severity. The major drug interactions are discussed in table no: 2.

**TABLE NO. 1: PREVALENCE OF ANEMIA IN CKD PATIENTS (n=100)**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Category of patients</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Anemic patients</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>Non anemic patients</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

**FIGURE NO. 1: PRESCRIBING PATTERN OF DRUGS (n=100)**
### FIGURE NO. 2: RISK FACTORS (n=100)

![Risk Factors Graph]

### TABLE NO. 2: MAJOR DRUG - DRUG INTERACTIONS (n=100)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Interaction effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol + Clonidine</td>
<td>Increased risk of sinus bradycardia</td>
<td>Monitor heart rate when both drugs are given concurrently.</td>
</tr>
<tr>
<td>Aspirin+ Torsemide</td>
<td>Increased risk of renal toxicity</td>
<td>Monitor the signs of worsening renal function and assure diuretic efficacy.</td>
</tr>
<tr>
<td>Ivabradine + Levofloxacin</td>
<td>Increased risk of QT prolongation.</td>
<td>Monitor ECG</td>
</tr>
<tr>
<td>Metolazone + Aspirin</td>
<td>Reduced diuretic effectiveness and possible nephrotoxicity</td>
<td>Monitor signs of worsening renal function and assure diuretic efficacy.</td>
</tr>
<tr>
<td>Diltiazem+Cilostazol</td>
<td>Concomitant use may result in increased cilostazol exposure</td>
<td>Dosage adjustment is required for cilostazol.</td>
</tr>
<tr>
<td>Amiodarone+Ondansetron</td>
<td>Increased risk of QT prolongation</td>
<td>Avoid concomitant administration of these drugs.</td>
</tr>
<tr>
<td>Aspirin + Furosemide</td>
<td>Reduced diuretic effectiveness and possible nephrotoxicity</td>
<td>Monitor for signs of worsening renal function and assure diuretic efficacy</td>
</tr>
<tr>
<td>Ivabradine + Haloperidol</td>
<td>Increased risk of QT prolongation</td>
<td>Use caution with the concomitant administration of these drugs.</td>
</tr>
<tr>
<td>Vancomycin+Gentamycin</td>
<td>May result in nephrotoxicity</td>
<td>Monitor the signs of nephrotoxicity.</td>
</tr>
</tbody>
</table>

DISCUSSION

The current study observed the prevalence of anemia and prescribing pattern of drugs in CKD patients. The most affected population in our study were between 56 – 65 years. As age progresses, the arteries supplying the kidney narrows and there is a decrease in the GFR rate. A similar study was conducted by Havva T. et al revealed that as the age of the patient increases their quality of life scores decreases which was found to be consistent with the findings of our study. The gender distribution of the study reports more number of male patients when compared to females. Previous studies conducted by Sridhar Srimath et al reported similar results. The present study could confirm anemia as a common complication of CKD. The study could also observe patients in various categories of CKD and more number of patients under stage 5. The study findings align with the reports of study confirmed by Evans et al.

Our analysis indicates that the prevalence of anemia in CKD patients was 90 %. Similar results were confirmed by Sang-Ryol Ryu et al. The key finding of our study reveals that only 30% of patients who had anemia with CKD received ESA therapy and 90% were treated with vitamins and minerals because of the low socio-economic status. In CKD, the kidneys lose the function of producing erythropoietin hormones.

Most commonly prescribed ESA in the study population were erythropoietin alpha and darbopoietin alpha. The beneficial effects of ESA therapy include elevated haemoglobin levels, improved quality of life and cognitive functions. A similar study conducted by Ajay K Singh et al reported that the overall quality of life improved when anemia was treated with epoetin alpha, but aiming for a target value of 13.5 g/dl provided no additional quality of life benefits.

The major complications observed during our study were anemia followed by heart disease and fluid overload. A similar study conducted by Rebecca J et al stated that untreated anemia with CKD is strongly associated with cardiovascular and renal complications resulting in increased hospitalization and mortality.

CONCLUSION

The current study observed high prevalence of anemia in CKD patients and are prescribed with appropriate drugs according to the recommended guidelines to a greater extent. The
study could also observe only few patients were treated with ESA therapy. Hence patients who did not receive ESA therapy needs to be monitored for hemoglobin levels and appropriate measures are to be taken to improve the quality of life of patients. Clinicians should be receptive about the risk factors, complications and suggest appropriate therapy for the management of anemia.

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