HEMATOLOGICAL PROFILE IN PATIENTS OF CHRONIC KIDNEY DISEASE WITH ITS SEVERITY IN A TERTIARY CARE HOSPITAL, NORTH ODISHA

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Received: 01 May 2020, Revised and Accepted: 10 June 2020

INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes coupled with abnormal kidney function and a progressive decrease in glomerular filtration rate (GFR) [1]. CKD is a universal public health problem, both for the number of patients and the cost of treatment involved, especially in developing countries like India. Internationally, CKD is the 10th cause of death and the 17th cause of disability, respectively [2] with a prevalence of 8‒16% [3].

As stated by the National Kidney Foundation in India, renal diseases ranked 3rd among the life-threatening diseases after cancer and heart disease, with about 2 Lakh persons landing into terminal renal failure annually and millions more suffering from lesser forms of renal diseases [4].

The prevalence is high in India, with 229/million population suffering from end-stage renal disease (ESRD) [5]. Community-based studies planned to detect stage 3 CKD or worse show prevalence between 0.16% and 0.79%; with the actual incidence of CKD is higher than the reported number [6–8]. The ESRD incidences have been reported to be 160–232 per million populations (pmp) [5,6] with a projected ESRD prevalence of 785–870 pmp [5,9].

There is a proportional increase in the prevalence and severity of hematological impairment with increasing severity of kidney dysfunction. Studies have revealed that anemia begins to noticeable

Conclusion:
This study concluded that patients with CKD show abnormal hematological parameters. Evaluation of hematological parameters in these patients helps in classifying the type of anemia, aids in choosing the correct treatment modalities, and decreases mortality.

Keywords: Chronic kidney disease, Anemia, Hemoglobin, Red blood count, Thrombocytopenia.
hematological abnormalities in our patients with predialysis CKD and associated factors.

METHODS

The observational study was conducted in the Department of General Medicine, Pandit Raghunath Murmu Medical College Hospital, Baripada. The CKD patients who had attended the department of general medicine OPD and who were admitted to the department of general medicine, PRM MCH, Baripada between May 2018 and January 2019 were enrolled in our study.

Inclusion criteria

- All patients of CKD above 15 years of age, satisfying the following criteria, were included in the study. Criteria for diagnosis of CKD were as given by – National Kidney Foundation: K/DOQI clinical practice guidelines for CKD: Evaluation, classification, and stratification [22].

CKD is defined as the presence, for at least 3 months, of evidence of kidney damage with an abnormal GFR or alternatively, by a GFR <60 ml/min/1.73m² BSA [22].

Kidney damage is evidenced by:

- Proteinuria >300 mg/day OR
- Pathological abnormality found in histopathological study OR
- Renal imaging study (USG) showing bilateral contracted kidneys <9.0 cm with thinned parenchyma and reduced corticomedullary differentiation.

Exclusion criteria

The following criteria were excluded from the study:

- Patients aged below 15 years of age
- Patients on hemodialysis
- Pregnant and lactating women
- Aplastic anemia
- Known hematological malignancy causing secondary renal failure
- History of erythropoietin therapy during the past 3 months
- History of erythropoietin therapy during the past 3 months
- Patients suffering from recent hemorrhagic episodes were excluded from the study.

Two hundred seventy CKD patients were included in the study, divided into three groups:

- Group A – Mild CKD (n=210) (S. Creatinine =1.5–3.0 mg/dl)
- Group B – Moderate CKD (n=91) (S. Creatinine =3–6.0 mg/dl)
- Group C – Severe CKD (n=59) (S. Creatinine > 6.0 mg/dl).

Investigations

After due consideration into inclusion and exclusion criteria, detailed history and clinical examination were undertaken in all patients. All patients had undergone thorough laboratory investigations such as complete blood counts (Sysmex XS-800i), urine analysis, blood sugar, serum urea, and creatinine. Ultrasoundography of the abdomen was done on every patient. The CKD epidemiology collaboration equation, 2009, was used to calculate e-GFR. e-GFR was graded G1, G2, G3a, G3b, G4, and G5 as indicated by the KDIGO 2012 guidelines [1]. Forty healthy persons were taken as controls.

The World Health Organization defined anemia as Hb concentration <12 g/dl (females), <13 g/dl (males) classifying the severity of anemia as mild anemia (Hb concentration between 11–12.9 g/dl for males and 11–11.9 g/dl for females); moderate anemia (Hb concentration between 8 and 10.9 g/dl), and severe anemia (Hb concentration <8 g/dl) [23]. Thrombocytopenia was defined with a value of <150×10⁸/µl.

Statistical analysis

The statistical analysis was done using the Statistical Package for the Social Sciences version 21.0. The demographic features of the study population were explained using univariate analysis. Continuous variables were described as frequency and percentages. Continuous variables were presented as means and standard deviation (SD) for unpaired data; the Student’s t-test was used to compare mean values (for two groups). Pearson’s correlation was used to establish the association between eGFR and other variables. A Chi-square test was used to determine the significant associations between categorical variables. p<0.05 was considered statistically significant* and < 0.01 was considered as statistically hugely significant**.

RESULTS

During the study period, 270 CKD patients above 15 years of age, satisfying the inclusion and exclusion criteria were included in the study. All the cases were studied for the clinical presentation, risk factors, and laboratory parameters.

Out of 270 patients, 179 (66.30%) were male and 91 (33.70%) were female with M:F of 1.97:1 (Fig. 1). The average age of the patients in this study was 55.72±12.77 years. The average age of the male and female patients in the study was 55.63±13.24 and 55.89±11.84 years, respectively. The age range was from 20 to 95 years.

Fig. 2 shows that 42.59% (115) of the patients were between 46 and 60 years of age, and 26.30% (71) of the patients were between 61 and 75 years of age.

Fig. 3 shows that 35.56% CKD cases had determined etiology such as hypertension (32.22%), diabetes (4.07%), adult polycystic kidney disease (1.48%), obstructive nephropathy (1.11%), and medullary sponge kidney (0.37%); and rest of the 64.44% cases had unknown etiology.

Table 1 shows 21.85% (59), 42.59% (115), and 35.56% (96) of the patients in our study group belong to stage 3, stage 4, and stage 5 CKD, respectively.
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Fig. 4 show 120 (44.44%) patients belong to mild CKD (Group-A), 91 (33.70%) patients belong to moderate CKD (Group-B), and 59 (21.85%) patients belong to severe CKD (Group-C) in our study group.

Table 2 shows the comparisons between hematologic indices of CKD patients and healthy controls. Ht, RBC, and packed cell volume were significantly lower in the patients with CKD compared to the controls (p<0.0001), and RDW was significantly higher in the patients with CKD compared to the controls (p<0.0001).

Table 3 shows the correlation coefficient of eGFR with different variables in CKD patients. Negative Pearson’s correlation coefficient value indicate age, the level of systolic BP, diastolic BP, blood urea, serum creatinine, MCV, MCH, MCHC, and RDW increase with the decline of GFR and positive Pearson’s correlation coefficient value indicate the level of hemoglobin, RBC, PCV, and TPC decrease with the decline of GFR. On correlating eGFR with various parameters, statistical significance was observed with systolic blood pressure (r=-0.191, **p=0.0016), diastolic blood pressure (r=-0.140, *p=0.0213), B. Urea (r=-0.729, **p=0.00001), S. Creatinine (r=-0.787, **p=0.00001), hemoglobin (r=0.290, **p=0.00001), RBC (r=0.342, **p=0.00001), PCV (r= 0.315, **p=0.00001), and MCH (r= -0.150, *p=0.0136).

Table 4 shows the prevalence of anemia increased from 96.61% in Stage 3, 97.39% in Stage 4, and 100% in Stage 5 CKD, respectively. There was a hugely significant association between the severity of anemia and the stage of CKD (**p=0.000032).

Table 5 shows that 98.15% (265 cases) of the study population had anemia. The prevalence of anemia increased from 96.67% in mild CKD, 98.90% in moderate CKD, and 100% in severe CKD, respectively. There was a hugely significant association between the severity of anemia and the severity of CKD (**p=0.00001). There was decrease in level of hemoglobin, RBC, and PCV with severity of disease with hugely significant association between mild to severe and moderate to severe CKD (**p=0.0001).

Table 6 shows that 80.37% (217) of CKD patients had microcytic anemia. Normocytic anemia was seen in 17.41% (47) of CKD patients and macrocytic anemia was seen in 0.37% (1) of CKD patients. There was no significant association between the type of anemia (PCV) and the severity of CKD.

Table 7 shows that 38.52% (104 cases) of the study population had thrombocytopenia. The prevalence of thrombocytopenia increased from 30.83% in mild CKD, 35.16% in moderate CKD, and 59.32% in severe CKD. There was a hugely significant association between the prevalence of thrombocytopenia and the severity of CKD (**p=0.006).

Table 8 show that there was a hugely significant association between blood urea and serum creatinine level with mild, moderate, and severe CKD (**p=0.0001). There was decrease in level of hemoglobin, RBC and PCV with severity of disease with hugely significant association between mild to severe and moderate to severe CKD (**p=0.0001).

DISCUSSION

In our study, out of 270 patients, 179 (66.30%) were male, and 91 (33.70%) were female with M:F of 1:97:1. As per the patients enrolled in the database of “The Indian CKD Registry,” a voluntary reporting body of CKD patient’s data, initiated in June 2005, 70% of them were males [10]. The patients in the study had an average age of 55.72±12.77 years, ranging from 20 to 95 years. Most of the patients, 74.82% were above 45 years of age, but still, 25.18% of the CKD patients were below 45 years of age, which was significant in number. According to Suhnggon Kim et al. 2009, the average age of the CKD patient was with mean 50.5 years and a SD of 11.1 years [24].
We revealed that 35.56% CKD cases had determined etiology such as hypertension (32.22%), diabetes (4.07%), adult polycystic kidney disease (1.48%), obstructive nephropathy (1.11%), and medullary sponge kidney (0.37%); and rest of the 64.44% cases had unknown etiology; which is an important finding. CKD of unknown etiology has also been documented from other parts of South Asia and among South Asians living in the UK [25].

In our study, Hb% ranged from 2.8 to 14.3 g/dl, with a mean of 7.76±2.50 g/dl. The RBC count ranged from 1.19 to 5.8 × 10³/µl, with a mean of 3.27±1.03. Hematocrit ranged from 7.6% to 43.5%, with a mean of 28.48%±7.8%. These parameters are quite similar to the findings in Shastry et al. study [26]. In Shastry et al. study, Hb level ranged from 3.6 to 14.2 g/dl with a mean of 9.31±0.52 g/dl, the RBC count ranged from 1.29 to 4.22 × 10³/µl, with a mean of 3.29±0.79 and hematocrit ranged from 11.6% to 42% with a mean of 28.48±7.8%. Our study recognized that Hb, RBC, and packed cell volume were significantly lower in the patients with CKD compared to the controls (p=0.0001), which was also revealed in Shastry et al. study. We found positive Pearson’s correlation coefficient value, which indicates the level of Hb, RBC, and PCV decrease with the decline of eGFR, with statistical significance (p=0.00001). We revealed in our study that there was a decline in the level of Hb, RBC, and PCV with the severity of disease with a hugely significant association between mild to severe and moderate to severe CKD (p=0.0001). Singh et al. [27], Poudel et al. [28], Bueno and Frizzo

Table 3: Correlation coefficient of eGFR with different variables in CKD patients

| Variables   | Pearson correlation coefficient (r) | p-value |
|-------------|-------------------------------------|---------|
| Age         | -0.002                              | 0.9739  |
| Systolic BP | -0.191                              | 0.0016**|
| Diastolic BP| -0.140                              | 0.0213* |
| Blood urea  | -0.729                              | 0.00001**|
| Serum creatinine | -0.787               | 0.00001**|
| Hemoglobin  | 0.290                               | 0.00001**|
| RBC         | 0.342                               | 0.00001**|
| MCV         | -0.030                              | 0.6235  |
| PCV         | 0.315                               | 0.00001**|
| MCH         | -0.150                              | 0.1136  |
| MCHC        | -0.080                              | 0.1900  |
| RDW         | -0.062                              | 0.3101  |
| TPC         | 0.096                               | 0.1155  |

*Significance at p <0.05, ** hugely significance at p <0.01

Table 4: Associations between the severity of anemia and stage of CKD (with e-GFR)

| Severity of anemia | CKD Stage 3 | CKD Stage 4 | CKD Stage 5 | Test statistic |
|--------------------|-------------|-------------|-------------|----------------|
| Mild (11–12.9 g/dl in males) and (11–11.9 g/dl in females) | 17 | 14.17 | 8 | 8.79 | 3 | 5.08 | χ²=35.1204 df=4 |
| Moderate (8–10.9 g/dl) | 49 | 40.83 | 41 | 45.05 | 5 | 8.47 | p=0.00001** |
| Severe (<8 g/dl) | 50 | 41.67 | 41 | 45.05 | 51 | 86.44 | *Significance at p <0.05, ** hugely significance at p <0.01

Table 5: Associations between the severity of anemia and the severity of CKD (with serum creatinine)

| Severity of anemia | Mild (n=120) | Moderate (n=91) | Severe (n=59) | Test statistic |
|--------------------|-------------|---------------|--------------|----------------|
| Mild (11–12.9 g/dl in males) and (11–11.9 g/dl in females) | 17 | 14.17 | 8 | 8.79 | 3 | 5.08 | χ²=35.1204 df=4 |
| Moderate (8–10.9 g/dl) | 49 | 40.83 | 41 | 45.05 | 5 | 8.47 | p=0.00001** |
| Severe (<8 g/dl) | 50 | 41.67 | 41 | 45.05 | 51 | 86.44 | *Significance at p <0.05, ** hugely significance at p <0.01

Table 6: Associations between types of anemia and severity of CKD

| MCV (fL) | Mild (n=120) | Moderate (n=91) | Severe (n=59) | Test statistic |
|----------|-------------|---------------|--------------|----------------|
| Microcyt (<80 fL) | 96 | 80.00 | 74 | 81.32 | 47 | 79.66 | χ²=0.0786 df=2 |
| Normocyt (80–100 fL) | 20 | 16.67 | 16 | 17.58 | 11 | 18.64 | p=0.961459 |
| Macrocyt (>100 fL) | 0 | 0.00 | 0 | 0.00 | 1 | 1.69 | *Significance at p <0.05, ** hugely significance at p <0.01

Table 7: Associations between thrombocytopenia and severity of CKD

| Platelet count (lakh/ml) | Total | Mild (n=120) | Moderate (n=91) | Severe (n=59) | Test statistic |
|--------------------------|-------|-------------|---------------|--------------|----------------|
| <1.5 | 104 | 38.52 | 37 | 30.83 | 32 | 35.16 | 35 | 59.32 | χ²=14.3966 df=4 |
| 1.5–4.5 | 159 | 58.89 | 79 | 65.83 | 57 | 62.64 | 23 | 38.98 | p=0.006131** |
| >4.5 | 7 | 2.59 | 4 | 3.33 | 2 | 2.20 | 1 | 1.69 | *Significance at p <0.05, ** hugely significant at p <0.01
Table 8: Associations of hematologic indices with the severity of CKD patients

| Hematologic indices | Mild (A) (Mean±SD) | Moderate (B) (Mean±SD) | Severe (C) (Mean±SD) | p-value (A vs. B) | p-value (A vs. C) | p-value (B vs. C) |
|---------------------|---------------------|------------------------|----------------------|------------------|------------------|------------------|
| Blood urea          | 66.61±22.34         | 111.49±32.53           | 191.79±62.02         | 0.001**          | 0.001**          | 0.001**          |
| Serum creatinine    | 2.24±0.41           | 3.98±0.78              | 8.79±2.35            | 0.001**          | 0.001**          | 0.001**          |
| Hemoglobin          | 8.43±2.38           | 7.96±2.46              | 6.10±2.04            | 0.1629           | 0.001**          | 0.001**          |
| RBC                 | 3.59±1.01           | 3.33±0.97              | 2.54±0.81            | 0.0610           | 0.001**          | 0.001**          |
| MCV                 | 70.65±9.63          | 70.43±9.30             | 70.44±9.36           | 0.8677           | 0.8901           | 0.9949           |
| PCV                 | 25.21±7.46          | 23.30±7.04             | 17.81±5.85           | 0.0606           | 0.001**          | 0.001**          |
| MCH                 | 23.3±5.33           | 23.49±2.88             | 24.29±2.75           | 0.7651           | 0.0634           | 0.0929           |
| MCHC                | 33.52±4.62          | 34.04±5.27             | 0.6735               | 0.3063           | 0.5233           |                  |
| RDW                 | 16.29±2.39          | 16.61±2.42             | 0.7944               | 0.4015           | 0.3352           |                  |
| TPC                 | 1.98±0.08           | 1.72±0.06              | 0.1880               | 0.0720           | 0.5055           |                  |

*Significance at p < 0.05; ** hugely significant at p < 0.01

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