



Research Paper

Correlation between Serum Creatinine and Anemia in CKD

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ABSTRACT:

Chronic kidney disease (CKD) is failure of kidney function due to functional or structural abnormality that occurs for at least 3 months with or without the decrease in glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m².

Anemia is defined as low levels of hematocrit (Hct) or hemoglobin (Hb).¹ It is a common complication of chronic kidney disease (CKD), associated with significant morbidity.

As failure of kidney function progresses, the degree of anemia worsens, even though there is variability amongst patients. The Hct generally begins to fall when the plasma creatinine concentration is above 2mg/dl and gets lower with glomerular filtration rate (GFR) decline.¹⁻³

Anemia in CKD results from many causes, with the primary cause being decrease in erythropoiesis resulting from inadequate erythropoietin (EPO) production from kidneys. Other factors contributing to anemia in CKD would include shortened erythrocyte survival, blood loss from PUD, iron and other nutritional deficiencies, aluminum toxicity and uremic inhibitors in the bone marrow of which creatinine is one. Severe hyperparathyroidism can also cause anemia in CKD. Anemia of CKD is normocytic normochromic. Microcytic and hypochromic blood pictures suggest either iron deficiency or aluminum toxicity. Macrocytic anemia is due to folate and B12 deficiency. Both types of anemia also occur in CKD patients. The aim of this study is to correlate serum creatinine level with anemia in CKD.

KEY WORDS: CHRONIC KIDNEY DISEASE, CREATININE, ANEMIA, HEMATOCRIT, ERYTHROPOIRTIN.

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AIMS AND OBJECTIVE

To correlate SERUM CREATININE level with anemia in CKD

MATERIALS AND METHODS:

This retrospective study was carried out in Abia State University Teaching Hospital Aba, in South East Nigeria within 2015 and 2020.

Sample size was 199 patients who met the inclusion criteria, comprising of 132 males and 67 females giving a male to female ratio of 2:1. Hemoglobin, hematocrit, red cell indices, peripheral blood smears serum electrolyte, urea and creatinine levels were determined, using standard techniques. The weight of each patient was measured by simple weighing scale. The GFR was determined using the MDRD formula with the available parameters of weight, sex, race and serum creatinine level.

INCLUSION CRITERIA:

1. Patients with documented chronic kidney disease as determined by GFR of < 60mls/min/1.73m² lasting 3 months or more.

Exclusion criteria:

1. Acute or chronic inflammatory disease.

2. Malignancies of known hematological disorders.
3. Severe hemorrhagic diseases.

Data including, age, gender, serum creatinine level, hemoglobin level were obtained from records of patients folders. Data analysis was carried out using the statistical package for social science (SPSS, version 17). Pearson correlation was used for statistical analyses, and Correlation of increased serum creatinine and reduced Hb, was not statistically significant.

RESULTS:

Among the 199 CKD patients, **132(66.3%)** were males and **67(36.7%)** female with male to female ratio of 2:1. The age of the patients ranged from 18-93 years with mean age being 52 years.

The Hb levels ranged for patients with stage 1 CKD from 6g/dl to 17.9g/dl with 58 people having mean creatinine level of 0.9mg/dl. 58 people had a mean Hb of 12.1g/dl. **Pearson correlation** was used, serum creatinine level had no association with Hb level (2-tailed sig =.427). Thus correlation was not statistically significant at the 0.01 level (2-tailed).

In stage 2 CKD, mean age was 68 years. Hb levels ranged from 10.3-17.9g/dl, with a mean of 13.1g/dl. 69 people had a Mean creatinine level of 1.2mg/dl. 69 people also had mean Hb 13.1g/dl. Pearson correlation was used. Serum creatinine level had association with Hb level (**2-tailed sig=.002**). Thus correlation was statistically significant at the 0.01 level (2-tailed).

In stage 3 CKD, 26 people had mean creatinine level of 0.4mg/dl. **26** people had Mean Hb was 13.1g/dl. Pearson correlation was used. Serum creatinine level had no association to Hb level (2-tailed sig=.449). Correlation was not statistically significant at the 0.01 level (2-tailed).

In Stage 4 CKD the mean age was 57years. Creatinine level had a mean of **3.5mg/dl**. 26 people had a Mean Hb of **10.1g/dl**. Pearson correlation was used. Serum creatinine level had no association with Hb level (2-tailed sig= .878). Correlation was not statistically significant at the 0.001 level (2-tailed).

Stage 5, had 25 patients, 12 males (48%) and 13 females (52%). Mean age was 51 years. 25 people Mean Serum creatinine value was 10.0mg/dl. 25 had Mean Hb was 7.6g/dl. Pearson correlation was used. Serum creatinine level had no association with Hb Level (2-tailed sig=.113). Correlation was not statistically significant at the 0.001 level (2-tailed).

Correlation statistics:

Stage 1 CKD

| Variables | mean | Standard deviation | Frequency |
|-----------|---------|--------------------|-----------|
| Stage 1 | 0.8486 | 0.12188 | 58 |
| | 12.1138 | 3.16873 | 58 |

Inferential statistics

| Variables | | Creatinine in mg/dl | Hb (g/dl) |
|---------------------|---|---------------------|-----------|
| Creatinine in mg/dl | Pearson correlation | 1 | .106 |
| | Sig(2-tailed) | | .427 |
| | Sum of squares and cross product covariance | .847 | 2.338 |
| | | .015 | .041 |
| | Number(frequency) | 58 | 58 |
| Hb in g/dl | Pearson correlation | .106 | 1 |
| | Sig(2-tailed) | .427 | |
| | Sum of squares and cross products | 2.338 | 572.329 |
| | Covariance | .041 | 10.041 |
| | Number(frequency) | 58 | 58 |

Correlation is not statistically significant at the 0.01 level (2-tailed)

STAGE 2 CKD

Descriptive statistics

| Variables | | mean | Std deviation | Frequency |
|-----------|---------------------|---------|---------------|-----------|
| Stage 2 | Creatinine in mg/dl | 1.1838 | 0.20513 | 69 |
| | Hb in g/dl | 13.1058 | 2.07037 | 69 |

Inferential statistics

| Variables | | Creatinine in mg/dl | Hb(g/dl) |
|---------------------|-----------------------------------|---------------------|----------|
| Creatinine in mg/dl | Pearson correlation | 1 | .371 |
| | Sig.(2-tailed) | | .002 |
| | Sum of squares and cross products | 2.816 | 10.723 |
| | Covariance | .042 | .158 |
| | Number(frequency) | 69 | 69 |
| Hb in g/dl | Pearson correlation | .371 | 1 |
| | Sig(2-tailed) | .002 | |
| | Sum of squares and cross products | 10.723 | 291.478 |
| | Covariance | .158 | 4.286 |
| | Number(frequency) | 69 | 69 |

Correlation is statistically significant at the 0.001 level (2-tailed)

Stage 3 CKD

Descriptive statistics

| Variables | | mean | Std deviation | frequency |
|-----------|---------------------|---------|---------------|-----------|
| Stage 3 | Creatinine in mg/dl | 1.7508 | 0.38545 | 26 |
| | Hb in g/dl | 13.1058 | 2.87583 | 26 |

Inferential statistics

| variables | | Creatinine in mg/dl | Hb in g/dl |
|---------------------|-----------------------------------|---------------------|------------|
| Creatinine in mg/dl | Pearson correlation | 1 | -.155 |
| | Sig.(2-tailed) | | .449 |
| | sum of squares and cross products | 3.714 | -4.301 |
| | Covariance | .149 | -.172 |
| | Number(frequency) | 26 | 26 |
| Hb in mg/dl | Pearson correlation | -.115 | 1 |
| | Sig.(2-tailed) | .449 | |
| | Sum of squares and cross products | -4.301 | |
| | Covariance | -.172 | 8.27 |
| | Number(frequency) | 26 | 26 |

Correlation is not statistically significant at the 0.001 level (2-tailed)

STAGE4

DESCRIPTIVE STATISTICS

| variables | | mean | Std Deviation | frequency |
|-----------|---------------------|---------|---------------|-----------|
| Stage 4 | Creatinine in mg/dl | 3.4642 | 0.78393 | 26 |
| | Hb g/dl | 10.1008 | 2.0590 | 26 |

Inferential statistics

| Variables | | Creatinine in mg/dl | Hb (g/dl) |
|---------------------|-----------------------------------|---------------------|-----------|
| Creatinine in mg/dl | Pearson correlation | 1 | -.032 |
| | Sig. (2-tailed) | | .878 |
| | Sum of squares and cross products | 15.364 | -1.271 |
| | Covariance | .615 | -.051 |
| | Number(frequency) | 26 | 26 |
| Hb in g/dl | Pearson correlation | -.032 | 1 |
| | Sig. (2-tailed) | .878 | |
| | Sum of squares and cross products | -1.271 | 105.360 |
| | Covariance | -.051 | 4.214 |
| | Number(frequency) | 26 | 26 |

Correlation is not statistically significant at the 0.01 level (2-tailed)

STAGE 5

Descriptive statistics

| variables | | mean | Std deviation | Frequency |
|-----------|---------------------|--------|---------------|-----------|
| Stage 5 | Creatinine in mg/dl | 9.9836 | 6.17414 | 25 |
| | Hb g/dl | 7.6240 | 1.85883 | 25 |

Inferential statistics

| variables | | Creatinine in mg/dl | Hb in g/dl |
|---------------------|-----------------------------------|---------------------|------------|
| Creatinine in mg/dl | Pearson correlation | 1 | -.325 |
| | Sig. (2-tailed) | | .113 |
| | Sum of squares and cross products | 914.881 | -89.393 |
| | covariance | 38.120 | -3.725 |
| | Number(frequency) | 25 | 25 |
| Hb in g/dl | Pearson correlation | .325 | 1 |
| | Sig. (2-tailed) | .113 | |
| | Sum of squares and cross products | -89.393 | 82.926 |
| | covariance | -3.725 | 3.455 |
| | Number (frequency) | 25 | 25 |

Correlation is not statistically significant at the 0.01 level (2-tailed)

Tables:
Table 1: stage 1 CKD

| AGE | SEX | creatinine mg/dl | GFR MDRD | HB g/dl |
|-----|-----|------------------|----------|---------|
| 67 | M | 0.6 | 128 | 11 |
| 29 | F | 0.9 | 95 | 8.8 |
| 29 | F | 0.9 | 95 | 8.8 |
| 52 | M | 1.1 | 90 | 17.9 |
| 70 | M | 0.9 | 107 | 7.2 |
| 62 | M | 0.9 | 110 | 6 |
| 65 | M | 0.8 | 125 | 13.4 |
| 70 | M | 0.9 | 107 | 7.2 |
| 62 | M | 0.9 | 110 | 6 |
| 65 | M | 0.8 | 125 | 13.4 |

Correlation between Serum Creatinine and Anemia In CKD

| | | | | |
|----|---|------|-------|------|
| 85 | M | 0.91 | 102 | 14.5 |
| 62 | M | 0.82 | 122 | 13.4 |
| 47 | M | 0.9 | 116 | 16.4 |
| 76 | F | 0.7 | 108 | 7.8 |
| 45 | M | 0.72 | 152 | 13.4 |
| 36 | F | 0.9 | 91 | 14.9 |
| 74 | M | 0.7 | 142 | 10 |
| 63 | M | 0.8 | 125 | 16.4 |
| 57 | M | 0.9 | 112 | 15 |
| 39 | M | 1 | 107 | 14.8 |
| 46 | M | 0.9 | 117 | 11.6 |
| 30 | M | 0.9 | 127 | 14 |
| 36 | F | 0.9 | 91 | 14.9 |
| 30 | F | 0.9 | 95 | 13.1 |
| 29 | F | 0.9 | 95 | 7.5 |
| 79 | F | 0.6 | 124 | 12.4 |
| 40 | F | 0.8 | 102 | 11.2 |
| 39 | M | 1 | 107 | 14.8 |
| 42 | F | 0.7 | 118 | 8.9 |
| 30 | F | 0.7 | 126 | 12.8 |
| 33 | M | 1.2 | 90 | 14.9 |
| 29 | F | 0.9 | 98 | 14.5 |
| 66 | M | 0.9 | 109 | 13.7 |
| 29 | F | 0.9 | 95 | 7.5 |
| 61 | M | 1 | 98 | 14.5 |
| 44 | M | 1 | 104 | 13.4 |
| 42 | M | 0.9 | 119 | 9 |
| 50 | M | 0.9 | 91 | 10 |
| 69 | M | 0.9 | 91 | 10 |
| 69 | M | 0.9 | 108 | 14.9 |
| 60 | M | 0.9 | 111 | 13.4 |
| 41 | M | 1 | 106 | 11.9 |
| 50 | M | 0.8 | 132 | 11.9 |
| 65 | M | 0.9 | 109 | 14.5 |
| 65 | M | 0.8 | 125 | 11.6 |
| 35 | M | 0.62 | 190 | 15.9 |
| 50 | F | 0.8 | 98 | 11.3 |
| 68 | M | 0.7 | 114 | 14.2 |
| 60 | M | 0.9 | 111 | 13.4 |
| 43 | F | 0.6 | 140 | 11.2 |
| 12 | M | 0.8 | 137 | 10.9 |
| 50 | M | 0.8 | 114.9 | 13.3 |
| 72 | M | 0.9 | 107 | 13.4 |
| 50 | F | 0.8 | 98 | 11.3 |
| 40 | M | 0.9 | 120 | 14.2 |

| | | | | |
|----|---|-----|-----|------|
| 36 | F | 0.7 | 122 | 10.3 |
| 38 | M | 0.6 | 194 | 15.7 |

TABLE 2: STAGE 2 CKD

| AGE | SEX | creatinine MG/DL | GFR MDRD | HB G/DL |
|-----|-----|---------------------|-------------|------------|
| 80 | F | 0.8 | 89 | 13 |
| 80 | F | 0.8 | 89 | 13 |
| 67 | M | 1.4 | 65 | 14.6 |
| 52 | M | 1.3 | 75 | 11.9 |
| 38 | F | 1.1 | 72 | 10.4 |
| 82 | M | 1.1 | 82 | 14.6 |
| 70 | M | 1.1 | 85.6 | 11.9 |
| 60 | M | 1.1 | 88 | 11.9 |
| 60 | F | 0.9 | 82 | 10.7 |
| 67 | M | 1.4 | 65 | 14.6 |
| 60 | M | 1.1 | 88 | 14.2 |
| 60 | F | 0.9 | 82 | 10.7 |
| 82 | M | 1.1 | 82 | 14.6 |
| 52 | M | 1.3 | 75 | 11.9 |
| 38 | F | 1.1 | 72 | 10.4 |
| 70 | M | 1.1 | 85 | 11.9 |
| 52 | M | 1.1 | 90 | 17.9 |
| 34 | M | 1.6 | 64 | 13.4 |
| 41 | F | 1.2 | 64 | 12.7 |
| 70 | M | 1.1 | 85 | 13.4 |
| 38 | M | 1.3 | 80 | 13.4 |
| 76 | F | 0.83 | 86 | 8.5 |
| 47 | M | 1.25 | 80 | 11.2 |
| 60 | M | 1.5 | 61.4 | 15.7 |
| 63 | M | 1.6 | 62 | 16.4 |
| 63 | F | 1.1 | 65 | 15.5 |
| 68 | M | 1.3 | 71 | 13.3 |
| 49 | F | 1.1 | 67.9 | 14.6 |
| 58 | F | 1 | 73 | 11.9 |
| 50 | F | 1 | 75.5 | 12.8 |
| 30 | M | 1.4 | 77 | 14.3 |
| 70 | F | 1.1 | 63 | 13.7 |
| 83 | M | 1.3 | 68 | 11.9 |
| 48 | M | 1.3 | 76 | 12.8 |
| 38 | F | 1 | 80 | 11.9 |
| 54 | M | 1.1 | 90 | 15.2 |
| 40 | F | 0.9 | 89 | 9.7 |
| 75 | M | 1.3 | 69 | 14.5 |
| 70 | M | 1.3 | 70 | 12.8 |

| | | | | |
|----|---|-----|------|------|
| 37 | F | 1.1 | 71 | 12.7 |
| 59 | M | 1.5 | 62 | 11.9 |
| 59 | M | 1.4 | 67 | 17.3 |
| 45 | M | 1.5 | 65 | 10.3 |
| 40 | F | 1.1 | 71 | 11.3 |
| 54 | M | 1.5 | 63 | 12.9 |
| 61 | M | 1.5 | 61 | 15.7 |
| 55 | M | 1.4 | 68 | 16.4 |
| 83 | M | 1.3 | 68 | 11.3 |
| 38 | F | 1 | 80 | 11.9 |
| 50 | F | 0.9 | 85 | 11.9 |
| 27 | M | 0.9 | 85 | 15.7 |
| 83 | M | 1.3 | 68 | 11.9 |
| 63 | M | 1.5 | 61 | 13.9 |
| 47 | M | 1.5 | 65 | 12.8 |
| 55 | M | 1.4 | 68 | 14.8 |
| 56 | M | 1.3 | 73 | 14.9 |
| 68 | M | 1.2 | 77 | 14.6 |
| 67 | M | 1.1 | 86 | 11.6 |
| 43 | M | 1.2 | 85 | 10.7 |
| 48 | F | 1.2 | 61.7 | 14.3 |
| 74 | F | 0.9 | 79 | 13.9 |
| 35 | F | 1.1 | 73 | 12.1 |
| 56 | M | 1.2 | 81 | 14.9 |
| 78 | F | 0.8 | 89 | 6.3 |
| 80 | M | 1.2 | 75 | 12.8 |
| 70 | F | 1 | 71 | 13.4 |
| 60 | M | 1.2 | 79 | 14.9 |
| 37 | F | 1 | 80 | 14.2 |

TABLE 3: STAGE 3 CKD

| AGE | SEX | creatinine MG/DL | GFR MDRD | HB G/DL |
|-----|-----|---------------------|-------------|------------|
| 47 | M | 1.7 | 56 | 9.2 |
| 29 | M | 3 | 30 | 10.3 |
| 46 | F | 1.9 | 37 | 7.5 |
| 56 | M | 1.7 | 56 | 9.2 |
| 65 | F | 1.5 | 45 | 7.5 |
| 65 | F | 1.5 | 45 | 7.5 |
| 63 | M | 2 | 44 | 6 |
| 29 | M | 1.87 | 55 | 18.6 |
| 65 | M | 1.7 | 37 | 11.5 |
| 34 | M | 1.7 | 59 | 16.4 |
| 70 | M | 1.9 | 45 | 8.9 |
| 38 | M | 1.8 | 55 | 14.2 |

Correlation between Serum Creatinine and Anemia In CKD

| | | | | |
|----|---|-----|------|------|
| 38 | F | 1.3 | 59 | 13.4 |
| 35 | M | 2 | 49.1 | 7.8 |
| 29 | F | 1.6 | 49 | 12.7 |
| 63 | M | 2.4 | 35 | 11.9 |
| 68 | M | 2.2 | 39 | 8.5 |
| 65 | F | 1.2 | 58 | 13.3 |
| 63 | F | 1.4 | 49 | 12.2 |
| 63 | F | 1.4 | 49 | 12.2 |
| 45 | F | 1.3 | 57 | 10.1 |
| 35 | F | 1.9 | 38.7 | 10.9 |
| 73 | F | 1.7 | 38 | 10.4 |
| 58 | M | 1.8 | 50 | 11.9 |
| 70 | F | 1.3 | 52 | 10.4 |

TABLE 4: STAGE 4 CKD

| AGE | SEX | GFR MDRD | creatinine mg/dl | Hb |
|-----|-----|-------------|---------------------|-------|
| 48 | F | 29 | 2.3 | 6.7 |
| 68 | M | 23 | 3.4 | 7 |
| 48 | F | 25 | 2.6 | 7.5 |
| 75 | M | 17 | 4.3 | 10.6 |
| 52 | M | 17 | 4.6 | 10.8 |
| 42 | M | 19 | 4.4 | 8.9 |
| 75 | F | 22 | 2.7 | 10.8 |
| 37 | M | 23 | 3.8 | 7.5 |
| 56 | M | 29 | 2.9 | 9.5 |
| 29 | M | 30 | 3 | 10.3 |
| 75 | M | 17 | 4.3 | 10.6 |
| 52 | M | 17 | 4.6 | 10.8 |
| 42 | M | 19 | 4.4 | 8.9 |
| 75 | F | 22 | 2.7 | 10.8 |
| 29 | M | 30 | 3 | 10.3 |
| 56 | M | 29 | 2.9 | 9.5 |
| 65 | M | 22 | 3.62 | 8.2 |
| 75 | M | 29 | 2.8 | 12.7 |
| 65 | M | 22 | 3.65 | 8.5 |
| 34 | M | 27 | 1.6 | 13.4 |
| 58 | M | 21 | 3.8 | 16.12 |
| 85 | F | 23 | 3.8 | 11.9 |
| 67 | M | 27 | 3 | 11 |
| 55 | M | 20 | 4 | 9.7 |
| 55 | F | 19 | 4.3 | 10.6 |

Table 5: stage 5 CKD

| AGE | SEX | HB G/DL | creatinine(mg/dl) |
|-----|-----|------------|-------------------|
| 20 | F | 9.4 | 11 |
| 35 | M | 4.6 | 19.5 |
| 56 | F | 10.3 | 9.9 |
| 65 | M | 9.7 | 11.1 |
| 45 | M | 7 | 7.2 |
| 43 | M | 4.3 | 9.5 |
| 57 | M | 5.8 | 7.7 |
| 18 | M | 4.3 | 8.6 |
| 61 | F | 6.4 | 8.2 |
| 32 | F | 7.5 | 14.6 |
| 53 | M | 9.2 | 6.9 |
| 63 | M | 10 | 5.3 |
| 65 | M | 7.5 | 11.4 |
| 56 | F | 6.5 | 5.6 |
| 54 | M | 5.7 | 22.1 |
| 55 | F | 8.5 | 4.6 |
| 46 | F | 10.4 | 4.6 |
| 46 | F | 8.9 | 4.6 |
| 73 | F | 8.9 | 6.1 |
| 35 | M | 8.9 | 22 |
| 30 | F | 8.9 | 0.59 |
| 88 | F | 6.6 | 15.4 |
| 75 | M | 6.7 | 23 |
| 65 | F | 6.4 | 5.7 |
| 46 | F | 8.2 | 4.4 |

FIGURES:

FIGURE 1: STAGE 1 (Hb/Creatinine)

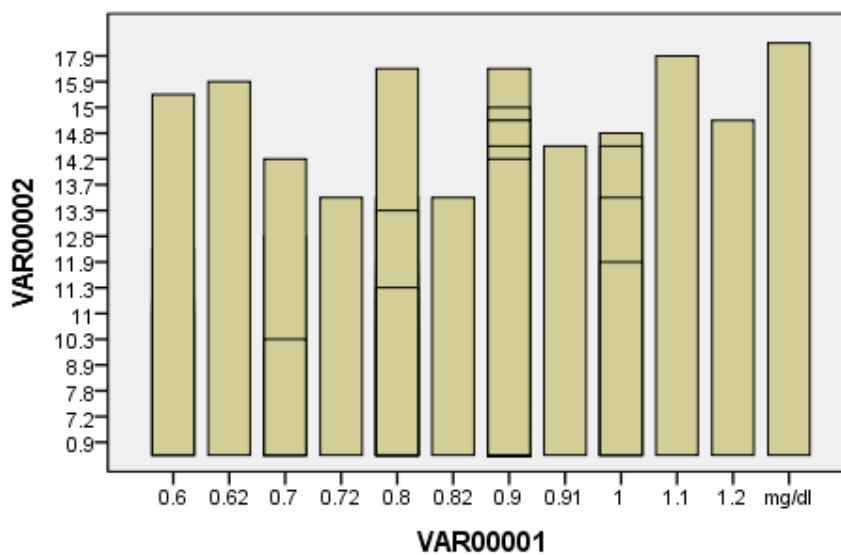


FIGURE 2: STAGE 5 CKD (HB/CREATININE)

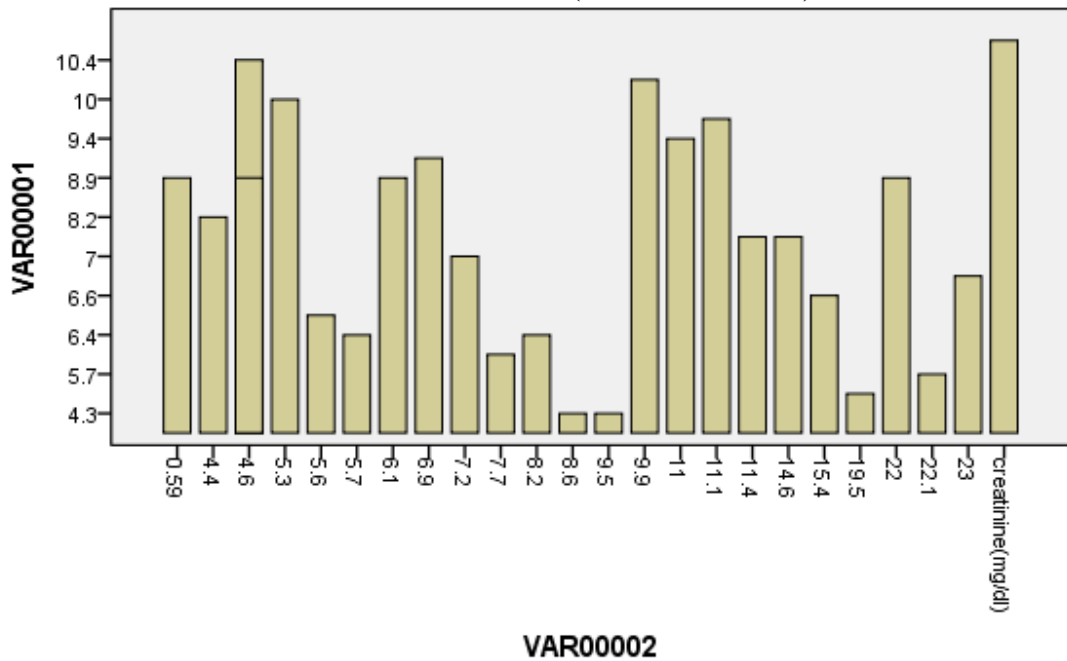
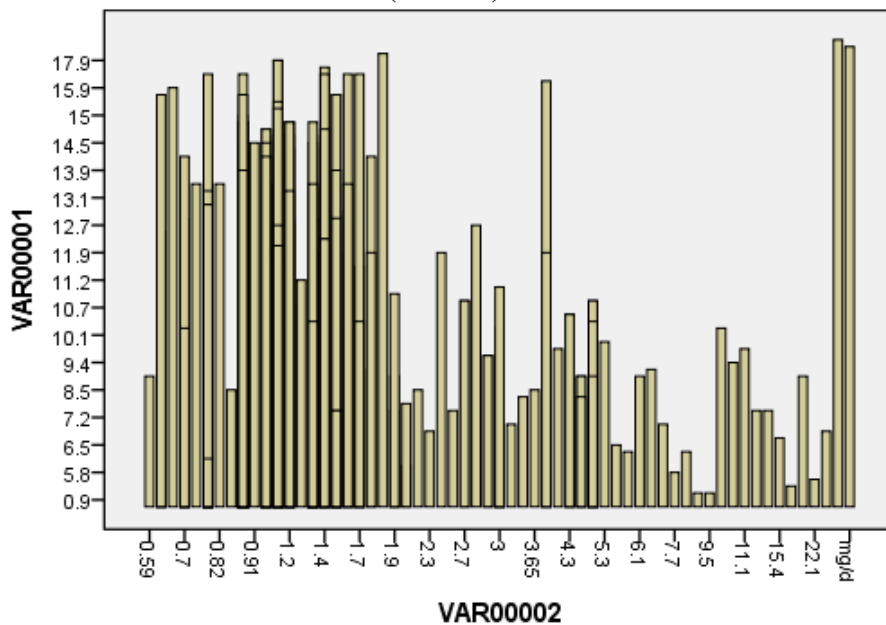


FIGURE 2: Progressing Decline in Hb levels with rise in creatinine levels (CKD1-5)



The relationship between Hb and SC (serum creatinine) levels were determined using bar chart. It showed that the correlation between Hb and SC levels was significant stage 2 CKD alone.

The relationship between Hb and SC (serum creatinine) levels thus did not correlate. Thus the correlation between Hb and SC levels was weakly significant with progressing renal failure .Figure 1, 3, 4, 5.

V. DISCUSSION:

Chronic kidney disease (CKD) is defined as failure of kidney function due to functional or structural abnormality that occurs for at least 3 months with or without decrease in glomerular filtration rate (GFR).. It is a prevalent, worldwide condition, with the number of patients affected on the rise. The global burden disease

study ranked CKD the 19th leading cause of morbidity and death in 2013¹. Worldwide, the age –standardized CKD prevalence is 10.4% in men and 10% in women and is higher in low-and middle –income countries than high income countries². For sub Saharan Africa, there was a prevalence of 13.9%¹, and 10.1% respectively³. Prevalence of CKD in West Africa was 16%, the highest in the continent. It's characterized by young aged patients, huge morbidity and premature deaths. About 90% of patients die within 90 days of starting dialysis³. Prevalence amongst middle aged group is common in women, and worsened by diabetes, ageing, obesity and albuminuria. Glomerular filtration rate (GFR) is essentially the most reliable index of kidney function in health. A decrease in GFR is a pointer to decline in kidney function and persistent or progressive GFR decline is a specific diagnostic criterion for Chronic Kidney Disease (CKD)³.

Markers of kidney function test assess the biochemical function of the kidneys. These markers may be biochemical or even radioactive. They assist in measuring GFR, as well as the concentrating and diluting property (tubular function) of kidneys. One of such is Serum Creatinine, urea, cystatin C, beta-trace protein and inulin. An increase or decrease in these markers is useful in determining the functional status of the kidneys. Creatinine is an accepted biomarker in determining GFR and it has the advantage of being excreted at a steady state, and it was also the biomarker used in our study. In our study anemia of CKD was matched with GFR, determined with serum creatinine. It is known that creatinine clearance is a precise measure of kidney function and it estimates the rate of filtration by the kidneys (Glomerular Filtration Rate)⁴.

In our study anemia of CKD was marched with GFR using creatinine as biomarker.⁴

Creatinine clearance is a precise measure of kidney function, and it estimates the rate of filtration by the kidneys (glomerular filtration rate, GFR)⁴. Creatinine clearance can be measured in two ways. It can be calculated by a formula using serum creatinine level, patient's weight and age. The formula being $140 - \text{age}$ of patient in years times their weight in kilograms (times 0.85 for women), divided by 72 times the serum creatinine level in mg/dl⁵. It can also be directly measured by collecting a 24- hour urine sample and then drawing a blood sample⁵. The creatinine levels in both urine and blood are compared. Normal creatinine clearance for healthy males is (97 – 137ml/min) and (88-128ml/min) in females⁵. Any condition that impairs kidney function will raise serum creatinine level. Such elevation should be monitored to ascertain if leading to kidney (failure/azotemia), or if it is long standing or recent. Recent elevations can be easily treated and reversed⁶. The GFR can be low even with a normal serum creatinine, especially in the elderly and in those with poor nutrition and muscle mass. It should also be noted that serum creatinine can increase after ingestion of large amount of dietary meat⁷. Kidney infections, rhabdomyolysis and urinary tract obstruction can also elevate creatinine levels. If GFR is $< 60 \text{ ml/min/1.73m}^2$, hemoglobin should be checked.

The cause of the anemia should be investigated, as it can range from erythropoietin deficiency, to deficiency of vitamin B (12) and / or folate, iron deficiency, blood loss from PUD, inflammation and malignancy⁷.

Many formulae have been used in determining GFR- Cockcroft and Gault (CG) and Modification of diet in renal disease (MDRD) formula. GFR in this study was determined with the MDRD formula, and Serum Creatinine was an important bimolecular marker.

The National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KIDQI) defines CKD based on glomerular filtration rate (GFR) and divides the disease into five stages.

Stage 1 CKD has $\text{GFR} > 90 \text{ ml/min/1.73m}^2$ Stage 2, 3, and 4 CKD are defined by GFR of 60-89 ml/min/1.73m^2 , 30-59 ml/min/1.73m^2 , and 15-29 ml/min/1.73m^2 respectively. The final stage, stage 5, occurs when GFR is $< 15 \text{ ml/min/1.73m}^2$ or when patients require dialysis⁸.

Anemia was defined by the NKF, as hemoglobin (Hb) concentration $< 12 \text{ g/dl}$ for women and $< 13.5 \text{ g/dl}$ for men⁹. The European Best practices Guidelines for the management of patients with Chronic Renal Failure defines anemia as regards age and sex. Anemia is defined as Hb concentration of $< 11.5 \text{ g/dl}$ in women, $< 13.5 \text{ g/dl}$ in men. For men less than or equal 70 years of age and $< 12 \text{ g/dl}$ in men > 70 years of age¹⁰. For patients on dialysis, Hb target value is more than or equal to 11 g/dl in women, more than or equal to 12 g/dl for men. Anemia is a common complication associated with CKD.

Anemia occurs in early development of kidney diseases and worsens with decline in kidney function. Diabetes and hypertension are the commonest causes of CKD in our environment, with reductions in Hb often occurring before onset of diabetic and hypertensive nephropathy. This is as a result of various reasons. 90% of hormone erythropoietin is produced by the kidneys. Hypoxia leads to increase in production of erythropoietin, which stimulates erythropoiesis. The kidney senses increased oxygenation as a result of formation of new erythrocytes and decreased erythropoietin production¹¹. Tuberointerstitial damage occurs even before a reduction in GFR or albuminuria is noticed.

With declining kidney function in CKD patients, there is reduction in production of erythropoietin in response to hypoxia in the kidney^{12- 13}. Also in diabetics use of medications like (methformin, fibrates, and thiazolidinediones and angiotensin-converting enzyme inhibitors) affects Hb production. Systemic inflammation associated with micro vascular disease leads to production of inflammatory mediators, like interleukins and

(TNF) tissue necrosis factor. This brings about blunting the effect of erythropoietin on the bone marrow, where erythroid precursors are stimulated¹⁴.

Other factors that could reduce Hb level in CKD patients include reduced erythropoietin production, platelet dysfunction (this leads to gastrointestinal bleeding), shortened erythrocyte survival time (30-60% of the normal span of 120 days), hemolysis due to secondary uremic toxin accumulation, blood loss due to frequent phlebotomy for laboratory studies, and PUD, loss of blood in dialysis during and after each Hemodialysis session. Malnutrition and deficiencies of iron, foliate and vitamin B12 also cause decrease in Hb level¹⁴.

Anemia in CKD causes fatigue, dizziness, shortness of breath. More adverse outcomes would include cardiovascular complications (left ventricular hypertrophy and congestive cardiac failure). Uncontrolled diabetes causes decline in kidney function with subsequent anemia. Hypoxia caused by anemia stimulates rennin-angiotensin- aldosteron system and plays a part in renal vasoconstriction. Proteinuria is worsened by increasing protein in renal tubules. It also contributes to cardiovascular disease. Anemia quickens progression of diabetic neuropathy¹⁵.

Correction of anemia has been shown to improve cardiac function by reducing exercise- induced myocardial ischemia.¹⁶ In non-dialysis patients, a stabilized renal function, plays a major role in treatment of anemia in CKD, thereby reducing hospitalization and mortality rates¹⁷. Anemia thus having such severe consequences in CKD requires early recognition and management.

VI. CONCLUSION

CKD is a prevalent condition worldwide, with an increasing number of patients every year. Commonest causes of kidney diseases are Diabetes, Hypertension, Obstructive Uropathy, Urinary tract infection (UTI), Nephrolithiasis, HIV, Hepatitis (B and C) and cystic Kidney Disease.

Anemia occurs in early development of kidney disease and gets worse with decline in renal function. Commonest cause would be reduced erythropoietin production.

Uremic toxins cause bone marrow depression, causing decline in bone marrow erythropoiesis. Urea and creatinine are amongst small molecular weight uremic toxins, others would include beta 2-microglobulin, parathormone, guanidinosuccinic acid, oxidative stress, uric-acid, peptides, leptins, p-cresylsulfate, indoxyl sulfate and hippuric acid. These uremic toxins cause nephrotoxicity, thus damaging the kidneys, leading to inability to get rid of urine and waste. Patients can thus become uremic, of which anemia is one of its complications. The aetiopathogenesis of anemia in CKD favors reduced erythropoietin production as major cause. This is as a result of less erythropoietin production (EPO). Erythropoietin signals bone marrow to produce red blood cells, thus its deficiency is the most implicated cause of anemia of CKD.

It has been associated with morbidity and mortality in CKD patients; hence therapy would include administration of erythropoiesis- stimulating agents (ESAs), which help the body in production of red blood cells. Iron can also be given, as the body needs iron to make red blood cells especially if receiving ESAs. Without enough iron, ESA treatment will not yield optimal result in improving the quality of life quality of life in patients with CKD and anemia. There is often an invalidated claim on serum creatinine correlating with depressed erythropoiesis in CKD. However our study reveals a weak correlation between low Hb with serum creatinine. Thus the anemia in CKD can be considered to result primarily from erythropoietin lack, while not underscoring other factors earlier stated.

VII. STUDY LIMITATIONS

- Variability of serum creatinine measurements can cast doubts on result accuracy. However, the inter laboratory variability is not of concern in this study as all samples were sent to the same laboratory.
- Estimating kidney function from Scr level has well- recognized limitations, including variation in creatinine production by age, gender and race. Moreover the use of MDRD or the Cockcroft Gault equations to estimate GFR could result in misclassification of subjects as regards their kidney function status due to variations in serum creatinine calibration. We based our analysis on Serum creatinine for the purpose of finding out the association between increased serum creatinine and reduce Hb in CKD.
- Finally, our data collation was drawn from records kept. Therefore we cannot rule out confounding from unmeasured factors to explain the results. These could be related, for example, to other causes of anemia such as systemic diseases and connective tissue diseases. We also cannot rule out false positive results in the anemic group because of pattern of record keeping.

WHAT IS ALREADY KNOWN IN THIS TOPIC

- Increased serum creatinine is a key indicator to kidney disease.
- Elevated serum creatinine is seen in progressing renal failure.
- Decreased renal function plays a role in anemia in CKD.

WHAT THE STUDY ADDS

- Anemia in CKD could contribute to severity in cardiovascular diseases.
- Anemia can also hasten the progression of diabetic neuropathy.
- Increased serum creatinine has a weak correlation with reduced Hb in CKD patients.

COMPETING INTREST

The authors declare no competing interest.

AUTHORS' CONTRIBUTION

JA and OC were involved in initial conception of manuscript and patient care. JA collected data while OC analyzed the data. JA and OC were involved in the writing of the manuscript. IU read and eventually approved the final draft before submission.

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BAR CHARTS

Figure 1: stage 1CKD (Hb/creatinine) ratio

Figure 2: stage 5 CKD (Hb/creatinine) ratio

Figure 3: stage 1-5 CKD (Hb/creatinine) ratio

REFERENCE

- [1]. Jager KJ, Fraser SDS. The ascending rank of chronic kidney disease in the global burden of disease study. *nephrolDial Transplant*. 2017; 32(Suppl2):ii121-8.
- [2]. Mills,KT, Xu Y, Zhang W, Bundy JD, Chen CS, Kelly TN, et al. a systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney int*.2015;88(5):950-7
- [3]. Stanifer JW, Jing B, Tolan S, Helmke N, Mukerjee R, Naicker S, et al. The epidemiology of chronic kidney disease in sub-saharan Africa: a systemic review and meta-analysis. *Lancet Glob Health*. 2014; 2(3):e174-e81.
- [4]. Hunsiker L.G. Levey A.S.
- [5]. Progression of chronic renal disease: mechanism, risk factors, and testing of interventions.
- [6]. In: Jacobson H.R. Striker G.E. Klahr S. the principles of practice of nephrology. Mosby, philadelphia, PA 1995: 622-631
- [7]. esbach J.W. Adamson J.W.anemia of end stage renal disease. 1985; 28:1-5
- [8]. MacDougall I.C. Role of uremic toxins in exacerbating anemia in renal failure. *Kidney int*. 2001;78:s67-s72
- [9]. Eschbach J.W. Varma A. Stivelman J.C.
- [10]. Is it time for a paradigm shift? Is erythropoietin deficiency still the main cause of renal anemia? *Nephrol Dial Transplant*.2002; 17:2-7
- [11]. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease evaluation, classification, and stratification. *Am J kidney Dis* 39 (suppl.1): S1-S266, 2002
- [12]. National Kidney Foundation: Clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney diseases in adults. *Am J Kidney Dis* 5 (suppl. 3):S1-S108, 2006
- [13]. S .Limori, s. Naito, Y. Noda et al., "Anemia management and mortality risk in newly visiting patients with chronic kidney disease in Japan: CKD- ROUTE
- [14]. Revised European best practice guidelines for management of anemia in patients with chronic renal failure. *Nephrol Dial Transplant* 19 (suppl.2), 2004
- [15]. Study, "Nephrology; vol.20, no.9, pp601-608, 2015
- [16]. Erslev AJ, Besrabab A: Erythropoithin in pathogenesis and treatment of anemia in chronic renal failure. *Kidney Int* 51: 622-630, 1997
- [17]. Hodges VM, Rainey S, Lappin TR, Maxwell AP: pathophysiology of anemia and erythrocytosis. *Crit Rev Oncol/Hematol* 64: 139-158, 2007
- [18]. Al-khoury S, Afzali B, Shah N, Thomas S, Gusbeth-Tatomir P, Goldsmith D, Covic A: Diabetes, Kidney disease and anemia: time to tackle a troublesome triad? *Int J clin pract* 2007
- [19]. Paefrey PS, Foley RN: The clinical epidemiology of cardiac diseases in chronic renal failure.*J Am Soc Nephrol* 10: 1606-1615, 1999
- [20]. Daugirdas JT, Blake PG, Ing TS, Eds.: Hand book of Dialysis. 4th edd. New York, Lippincott Williams & Wilkins, 2006