*Original Article*

# Evaluation of Anaemia in Predialysis Chronic Kidney Disease Patients in A Tertiary Care Centre

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**Abstract**

***Background:*** *Chronic kidney disease (CKD) is a worldwide problem. The incidence and prevalence of CKD has increased in recent year in both developed and developing countries including South-East Asia. Anaemia is a contributing factor in many of the symptoms associated with reduced kidney function.* ***Objectives:*** *The aim of this study was to determine the severity of anaemia and morphological variety of anaemia among different stages of CKD in predialysis Chronic Kidney Disease patients.* ***Method:*** *A cross sectional analysis among predialysis CKD patients were done in Nephrology department of Mymensingh Medical College Hospital and National Institute of Kidney Disease and Urology from September' 2014 to August' 2015.* ***Result:*** *A total 100 out of 147 subjects were selected as the study sample. Prediagnosed stable predialysis CKD patient with anaemia were included in this study. Mild, moderate and severe anaemia found in 27 (27%), 44 (44%) and 29 (29%) patients respectively. Among them 54% found as maximum with Normocytic Normochromic anaemia.* ***Conclusion:*** *The proportion of patients with anemia is variable among CKD stages. Degree of anemia is more marked in female as compared to male.*

**Key words:** Predialysis, Chronic Kidney Disease (CKD), Anaemia

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## Introduction

Chronic Kidney Disease (CKD) is a significant public health problem as it causes a substantial burden on the health services. Apart from its financial impacts implications is also important[1]. The incidence of CKD is higher in South Asians than in European population[2,3]. The incidence of CKD in urban area at Dhaka, Bangladesh is 26%[4]. Some studies revealed that CKD is an independent risk factor for cardiovascular disease. Some of these can be prevented or at least delayed by early detection and treatment of CKD[5]. There could be damage to glomerular or tubular function by diseases affecting the kidney, but isolated tubular defects are rare.

In all sorts of renal diseases there is loss of nephron function and thus loss of filtration which is essential for formation of urine. Tests of glomerular function are always required for diagnosis and management of renal disorders. According to the World Health Report, 2002 and Global Barden of Disease project, diseases of the kidney and urinary tract contribute to the global burden of diseases, with approximately 8,50,000 death every year and 1,50,10,167 disability-adjusted life years[6].

Anaemia is a global public health problem affecting both developing and developed countries with major consequences for human health as well as social and economic development. Anaemia is a contributing factor in many of the symptoms associated with reduced kidney function like fatigue, depression, exercise tolerance and dyspnea. In addition, anaemia has direct adverse effect on cardiovascular system (CVS) and consequences like left ventricular hypertrophy (LVH), left ventricular systolic dysfunction and coronary artery disease may occur. Accelerated progression of CKD may turn into end stage renal disease and stroke. As a result, patient with anaemia due to CKD are at risk of hospitalization, increased length of hospital stays, reduced quality of life and increased mortality.

Anaemia is extremely common in chronic kidney disease affecting up to 95% of patients with end stage renal disease. Due to its insidious onset, anaemia in CKD is often asymptomatic and is only picked up in routine blood analysis. Delayed diagnosis and treatment of anaemia associated with CKD increase the risk of cardiovascular disease[7]. Despite availability of erythropoiesis-stimulating

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protein to red cell production in CKD patients, many patients need to initiate dialysis. The recognition of anaemia of CKD should begin with an estimation of glomerular filtration rate (GFR). GFR, which can be far lower than abnormal serum creatinine, specially, in the elderly, in those with poor nutrition and muscle mass if GFR is 60 ml/min/1.73m$^2$, hemoglobin should be checked[8]. The cause of anaemia should be investigated in those individuals; this can range from erythropoietin (Epo), vitamin $B_{12}$, folic acid and iron deficiency due to CKD. Blood loss, inflammation, malignancy and aluminum intoxication also responsible for anaemia. After other cause of anaemia have been excluded, CKD is most likely etiology and it should be treated with erythropoiesis-stimulating agent (ESA), vitamin B12, folic acid and iron supplements.

**Materials & Methods**

It was a cross-sectional study done in Department of Nephrology of Mymensingh Medical College Hospital (MMCH) and National Institute of Kidney Disease and Urology (NIKDU) from September' 2014 to August' 2015 on 100 admitted CKD with anaemia patient of stage 3-5. Inclusion criteria were prediagnosed stable predialysis CKD patients who were anaemic and age group were between 18 to 70 years. Exclusion criteria were subject who did not give consent, suffering from active bleeding or having hemolytic disorder, severe cardiac and respiratory failure and anaemia of chronic disease except CKD.

After meeting inclusion and exclusion criteria a purposive sampling technique was applied. Eligible CKD patients in NIKDU & MMCH were collected. CKD patients were identified by review of their past medical records. Patient who had eGFR <60ml/min/1.73m$^2$ for more than three months was considered as CKD patient. The eGFR was calculated by serum creatinine level according to MDRD formula. In case of male CKD patients, who had hemoglobin level <13 gm/dl and in case of female CKD patients' hemoglobin level <12 gm/dl considered as anaemia. Selected patient who had given consent to take part in study, were interviewed by a standard case record form. All questionnaires were checked for completeness. Pre-coded data were entered into computer using Epi Info software version 3.5.1 and the data were transferred to SPSS (Statistical Package social science) version 20.0 for further data processing. Then categorizing of continuous variable and finally analysis. Descriptive statistics were done for social and demographic parameters. Tables were used to summaries the frequency of CKD stages, causes of CKD, severity of anaemia and morphological pattern of RBC. Pearson's Correlation Coefficient was used to determine correlation between dependent and independent categorical variable such as hemoglobin of different morphological variety of anaemia though a level set at 5% to be statistically significant. A simple bar diagram prepared to show relation between morphological variety of anaemia and hemoglobin level.

**Results**

A total of 100 patients with Chronic kidney disease were included in this study. On initial visit, detail history was taken regarding current illness and thorough clinical examination was done. Relevant investigations were done for all patients. This study identified frequency of CKD, severity of anaemia among study population, morphological anaemia and severity of anaemia according to stage of CKD. The proportion of CKD patients with anaemia was varied among different CKD stages with 70% in stage-5, 24% in stage-4 and 6% in stage-3 and none was stage-1 or stage-2 (Table-I). Among CKD study subjects, majority were moderately anaemic (44%) followed by severe anaemia (29%). Only (27%) subjects were mildly anaemic (Table-II).

**Table-I: Frequency of CKD by different stages in study population (n= 100)**

| Stages of CKD | Frequency | Percentage (%) |
|---|---|---|
| Stage-3 | 6 | 6 |
| Stage-4 | 24 | 24 |
| Stage-5 | 70 | 70 |
| Total | 100 | 100 |

**Table-II: Severity of anaemia in the study population (n= 100)**

| Anaemia | Frequency | Percentage (%) |
|---|---|---|
| Mild | 27 | 27 |
| Moderate | 44 | 44 |
| Severe | 29 | 29 |
| Total | 100 | 100 |

Among the anaemic CKD patient stage-3 normocytic normochromic anaemia (33.33%) which were followed by microcytic hypochromic (16.16%), diamorphic (16.16 %), macrocytic (16.16 %), microcytic normochromic anaemia (16.16%). 62.5%, 5%, 1%, 1%, 2% found in NN, MH, MAC, MN, Diamorphic anaemia respectively in stage-4. In case of stage-5, NN - 37%, MH - 19%, MAC - 5%, MN - 1% & Dimorphic - 8% were found (Table-III).

Among the mild anaemic subjects 50.0% had stage-3, 25.0% had stage-4, 25.71% had stage-5. Among moderate anaemic subjects 45.71% had stage-5, 45.83% had stage-4 and 16.3% had stage-5. And lastly among the severe anaemic patients 33.5% had stage-3, 29.71% had stage-4 and another 28.53% had stage-5 of CKD. Here P value is greater than the tabulated value and so the result is non-significant (Table-IV).

**Table-III: Morphological finding of anaemia by different stages of CKD among study subjects (n =100)**

| Stages of CKD | Morphology of Anaemia | | | | | | | | | | Total No. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | NN | | MH | | MAC | | MN | | Dimorphic | | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | |
| Stage-3 | 2 | 33.33 | 1 | 16.16 | 1 | 16.66 | 1 | 16.66 | 1 | 16.66 | 6 |
| Stage-4 | 15 | 62.5 | 5 | 20.83 | 1 | 4.16 | 1 | 4.16 | 2 | 8.3 | 24 |
| Stage-5 | 37 | 52.85 | 19 | 27.14 | 5 | 7.14 | 1 | 1.42 | 8 | 11.42 | 70 |
| Total | 54 | 54 | 25 | 25 | 7 | 7 | 3 | 3 | 11 | 11 | 100 |

NN: Normocytic normochromic, MH: Microcytic hypochromic, MAC: macrocytic, MN: Microcytic normochromic anaemia.

**Table-IV: Severity of anaemia by different stages of CKD among study subjects (n = 100)**

| Stages of CKD | Anaemia | | | | | | Total | Test statistics |
|---|---|---|---|---|---|---|---|---|
| | Mild | | Moderate | | Severe | | | |
| | No. | % | No. | % | No. | % | | |
| Stage-3 | 3 | 50.0% | 1 | 16.8% | 2 | 33.5% | 6 (100%) | $X^2$ test P = 0.387 |
| Stage-4 | 6 | 25.0% | 11 | 45.83% | 7 | 29.17% | 24 (100%) | |
| Stage-5 | 18 | 25.71% | 32 | 45.71% | 20 | 28.53% | 70 (100%) | |

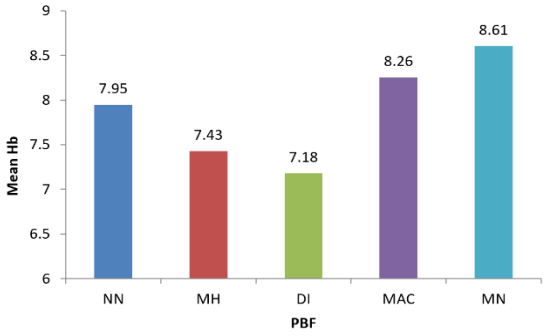


**Figure-1: Simple bar diagram showing relation between morphological variety of anaemia and mean Hb level (gm/dl) [n=100].**
NN=Normocytic normochromic, MH=Microcytic hypochromic, DI: Dimorphic, MAC=Macrocytic, MN=Microcytic normochromic

Among the study participants, mean Hb level (8.61 gm/dl) is high in microcytic normochromic anaemia followed by mean Hb level 8.26 gm/dl in macrocytic anaemia, mean Hb level 7.95 gm/dl in normocytic normochromic anaemia and mean Hb level 7.43 gm/dl in microcytic hypochromic anaemia. The lowest value of mean Hb level (7.18 gm/dl) in dimorphic anaemia.

**Discussion**

This study recruited CKD patients among patients with kidney disease seen at NIKDU, Dhaka and MMCH, Mymensingh, Bangladesh. These two hospitals serve most of the patients for the whole country, thus the study is a hospital based in tertiary care setting. In this study majority of patients were in advanced renal disease 70 (70.0%) stage 5 and 24 (24.0%) stage 4, both accounting for 94 (94.0%) of the study population. 6% patients were in stage 3 CKD [Table-I]. From the study of Muhimbili National Hospital, Dar Es Salaam, Sudan in which 78% patients were stage-5, 13% stage-4, both accounting 91% of the study population[8]. This finding is also similar to reports from other African studies which have indicated that majority of patients was also in advanced stages[9]. However, the distribution of patients in early stages, was dissimilar in the Nigerian study which revealed 7.7% for stage-1, 49 (13.5%) for stage 2 and 66 (18.1%) stage-3[10]. This difference can be partly explained by the fact that, Nigerian study had large sample size compared to this study and was a retrospective study which may explain the enrollment of patients who had early screening for CKD hence fair distribution of patient in early stage[11]. The present study being a hospital-based study only when patients in advanced stages of renal disease are referred to NIKDU & MMCH and no CKD patients in early CKD 1-2 stage were seen.

The distribution of patients among CKD stages was different from reports of studies done in USA and Indonesia. In these studies, there was almost equal distribution of patients among all stages of CKD and this can be explained by fact that in these countries' prevention was given priority, as aggressive screening programme of patients especially at risk such as diabetes mellitus and hypertension is in place, thereby early detection and decreasing progression of CKD[12].

We recruited only anaemic CKD patient, so 100% of all patient is anaemic. Very high prevalence of anaemia was observed in a study conducted in Muhimbili national hospital Dar es salam was 97.0% of 91 CKD patient[13]. In northern Tanzania

whereby the prevalence was 92.4 % among 52 CKD patients seen Kilimanjaro Christian Medical Centre compared to general population[13].

Compared to prevalence of anemia in general population in Tanzania, this was high as demonstrated from the demographic health survey of 2010 in Tanzania, where the prevalence of anaemia among women aged 15-49 years in the general population was 40%[14].

A large-scale cross-sectional USA multicenter survey study involving 5,222 patients and using 12g/dl as definition of anemia reported an overall prevalence of anemia 47.75% and progression of anemia from 26.7% in stage-3 to 75.5% in stage-5[15].

Two study, one was conducted in Indonesia and other was in Iran reported the prevalence rate of anemia in predialysis patients 73.1% and 75.0% respectively and Africa a Nigerian studies documented 77.5% and 87% prevalence of anemia in CKD patients[16].

This high prevalence of anemia among CKD patients is different study should alert clinicians that majority of patients with Chronic Kidney diseases need screening and treatment for prevention of anaemia and its complication[17].

In contrast to other studies, the prevalence and severity of anemia among CKD stages was varying as severity of kidney disease increased (Fig-1). In early stages 1-3 the prevalence was 88.9% with mean hemoglobin 9.4±3.4, stage-4 100% with mean hemoglobin 10.2±1.7 and stage-5 97.4% with mean hemoglobin of 7.9±2.4[18]. This difference may be explained by small sample size in this study and perhaps patients in early CKD stages had other contributing factors to anemia than compared to stage-4 patients (Table-II, III). Another possible explanation is improvement of hemoglobin of patients in stage-5 is on ESAs, blood transfusion and dialysis.

It is well known that the anemia of CKD is normocytic normochromic type as the loss of renal mass could be the principle mechanism[15]. In this study, the morphology of 100 anaemic CKD patients was normocytic normochromic in 54% cases, microcytic hypochromic in 25% cases, dimorphic picture (normocytic normochromic & microcytic hypochromic) in 11% cases, macrocytic in 7% cases and few (3%) had microcytic normochromic (Table-IV). Another study among CKD patients at BIRDEM academy, Shahbag, Dhaka[19] showed normocytic normochromic anaemia (93%) which was followed by microcytic microchromic (5%), 2% were anisochromic and macrocytic anaemia was absent[4]. Study at Muhabili National Hospital Dar Es Salam shows morphology of 97 anaemic CKD patients 47.4% are normocytic normochromic, 28.9% microcytic hypochromic, 16.5% dimorphic, 5% macrocytic and few 2% had microcytic normochromic anaemia[20]. Annear et al., Ketut et al. and Reza et al. showed that the anemia in CKD is generally due to EPO deficiency while microcytic anemia may reflect iron deficiency, aluminum excess or Haemoglobinopathies. Macrocytic anemia may be explained by vitamin B12 or folate deficiency or iron excess and ESAs therapy that shift immature larger reticulocyte into circulation according to anaemia management in chronic Kidney disease: National clinical guideline centre [NGCL], London Royal College of physician, 2011[21].

**Conclusion**

This study showed that moderate anemia is prevalent among CKD patients by 44%. Degree of anemia is more marked in female as compared to male. The proportion of patients with anemia is variable among CKD stages.

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