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Pattern and Severity of Anaemia in Predialysis Chronic Kidney Disease Patients in Bangladesh: A Tertiary Care Hospital Study

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Abstract

Background: Anemia is a common complication in chronic kidney disease (CKD), and is associated with a reduced quality of life, and increased morbidity and mortality. The mechanisms involved in ananaemiassociated with CKD are diverse and complex. They include a decrease in endogenous erythropoietin (EPO) production, absolute and/or functional iron deficiency, and inflammation with increased hepcidin levels, among others. Objective: The objective of our study was to investigate the prevalence and severity of anaemia in pre-dialysis patients, and chronic kidney disease patients in Bangladesh. **Material & Methods:** This was a case-control prospective study conducted with over 300 Bangladeshi non-patients as the control group A and 87 with different stages of chronic kidney disease (CKD) patients as the case group B in the department of Nephrology BSMMU from April'2004 to June 2006. The normal people who had no history of diabetes mellitus, hypertension, or CKD and were not on any medication were controlled and different stages of the CKD patients who had no history of blood transfusion, erythropoietin and parental iron infusion were cases. **Results:** Out of 300 normal populations male was 158(52.7%) and the female was 142(47.3%) and the mean haemoglobin level of the male was 13.94 g/dl and the female was 12.29 g/dl. Among males 24(15.2%) and females 55(38.7%) were anaemic and the overall prevalence of anaemia was noted at 26.3%. Of the total anaemic people, 25% was microcytic anemia. Out of 87 CKD patients, 56 (64%) were male and 31 (36%) were female. The overall prevalence of anaemia in CKD patients was 95.4%. The haemoglobin level was <11g/dl in 57.14% patients with CCr 30-59 ml/min/1.73m2 which increases to 87.5 % in patients with CCr 15-29 ml/min/1.73m2, which also increases to 94.2 % in patients with CCr <15 ml/min/1.73m2. Mean haemoglobin was observed at 8.6 g/dl, 9.54 g/dl and 11.25 g/dl in stage V, stage IV and stage III CKD patients respectively. Anaemia appeared at 43.53 ml/min/1.73 m2 of CCR. **Conclusions:** The results demonstrate that patient with reduced renal function is more likely to have anaemia and the prevalence and severity of anaemia increase with declining kidney function. CCr and TSAT is the important predictor of anaemia. In a significant number of the CKD, patient anaemia was associated with iron deficiency.

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Keywords:- Anaemia, Chronic kidney disease (CKD), Predialysis, Haemoglobin, Endogenous erythropoietin (EPO).

INTRODUCTION

There is some uncertainty over the definition of anaemia both in scientific literature and clinical practice.[1] A rational approach seems to be to define anaemia as a haemoglobin level below 5% of that total population adjusted for age and sex.[2] Anaemia refers to a state in which the level of haemoglobin in the blood is below the normal range appropriate for age and sex.[3] Normal haemoglobin levels vary with age, gender, ethnicity, smoking habits and altitude. Smoking increases haemoglobin by up to 1.5g/dl without improving oxygen exchange.[2] According to WHO anaemia is defined as haemoglobin <13 g/dl in men and <12 g/dl in women.[1] In a country like Bangladesh where most people suffer from nutritional deficiency, the mean haemoglobin in adult males and females will be much lower.[4] Globally, 30% of the total world population is anaemic and half of this 600 million people have iron deficiency anaemia.[3] Anaemia generally results from one of three different causes or a combination of Increased blood loss. Reduced RBC life span or impaired red cell population.[5] Anaemia is a frequent and serious complication of chronic renal uremia both during maintenance hemodialysis and in pre-dialysis patients. Anaemia develops from stage IV CKD and worsens in parallel with the progression of renal failure.[6] A direct relationship has been shown between the degree of anaemia as reflected by blood haemoglobin level and the degree of renal failure in pre-dialysis patients. However, contemporary epidemiological data on the incidence of anaemia and its level relative to the degree of renal failure in pre-dialysis patients are few.[7] Such data should be relevant for evaluating the current potential indication of erythropoietin therapy in pre-dialysis patients. The main consequences of renal anaemia are congestive heart failure, LVH, fatigue, reduced exercise capacity, decreased cognition, sexual dysfunction, impaired immunity, increased hospitalization and increased risk of death.[8] Appropriate treatment can reduce LVH, improve quality of life reduces other complications and halt the progression of kidney disease.[6] A Canadian multicentric cohort data suggested that by WHO definition, the prevalence of anaemia is already 25% in patients with CCr >50 ml/min. As CCr falls the proportion of patients with anaemia rises from 44% between 35 and 49 ml/min to 51% between 34 ml/min and to 87% below 25 ml/min. [9] Data from the Third National Health and Nutrition Examination Survey in the USA suggested that a decline in haemoglobin level starts at a GFR of 70 ml/min in men and 50 ml/min in women. The prevalence of renal anaemia increased from 1% to an estimated GFR of 60 ml/min to 9 and 33% at an estimated GFR of 30 and 15 ml/min respectively. In terms of absolute number, 800000 adults in the USA have haemoglobin levels <11 g/dl in association with CKD. In the UK, a study by John et al on a patient with significant CKD (defined by a median GFR of 28.5 ml/min) identified a prevalence of 1295 adults per million populations with significant anaemia.[10] New data suggested that in the UK the overall prevalence of anaemia as defined by K/DOQI in people with stage III CKD and below is ~ 4800 per million population.[11] Much remains unknown about anaemia in a patient with mild to moderate chronic renal

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insufficiency.[12] The importance of iron status in the pathophysiology and treatment of anaemia among patients with end-stage renal disease has been well described.[13] However, little is known about the iron status of patients with a less severe reduction in renal function. However, there was wide variation between an individual with a number of the patients, with a CCr of 80 ml/min who were anaemic and conversely with a CCr of 20 ml/min who were not anaemic.[14] They also found that those with CCr 20-30 ml/min, 46% of women and 19% of men had TSAT < 20%, 47% of women and 44% of men had S. ferritin <100ng/ml and the subjects with higher CCr also had similar iron status. About a third of CKD patient has been found to be iron deficient at the time of the first dialysis.[15] In this study, only a minority of the subject with renal anaemia met the K/DOQI ferritin and TSAT target. Haemoglobin targets for CKD patients traditionally have been based on haemoglobin values found in a population of young or middle-aged Caucasians living at low altitudes (<1500 m), and without concurrent diseases.[1] The haemoglobin level at which therapy with an erythropoiesis-stimulating agent should be initiated, as well as its target haemoglobin level, remains, controversial.[16] Recent trials recommend a target haemoglobin level between 11 and 12 g/dl in CKD patients.[17] The recommended S. Ferritin target level in ESA- treated CKD patients receiving iron supplementation is 100-500 µg/l.[18] Parental iron supplementation should be initiated when S. ferritin <100 µg/l or TSAT <20%.[18] The population of Bangladesh is around 140 million. The population density is over 9000 per square kilometre about 80% of the population of Bangladesh lives in rural areas. They are suffering from a high rate of illiteracy, malnutrition, poor socioeconomic condition, and lack of adequate health care knowledge and facilities. Near about 18 million people have CKD. In a study over 16 pre-dialysis patients found that 62.5 %, had low or absent stainable marrow iron and 37.5% had normal iron while none had an iron overload.[19] In a recent survey of patients with ESRD in Bangladesh on maintenance hemodialysis, the mean haemoglobin was 7.3g/dl in the year 2001 (N=960) and 7.8g/dl in 2002(N=1253).[4] But no study has been conducted till now on anaemia in the normal population and pre-dialysis patients in Bangladesh. This study has been designed to determine the prevalence of anaemia in the normal population and chronic kidney disease, the relationship between the level of haemoglobin and degree of renal failure assessed by serum creatinine and CCr, the pattern of anaemia and iron status in predialysis CKD patients.

OBJECTIVES

General objective:

The general objective of the study was to investigate the prevalence and severity of anaemia in pre-dialysis patients, and chronic kidney disease patients in Bangladesh.

Specific Objectives:

- To highlight the pattern of anaemia in pre-dialysis chronic kidney disease (CKD) patients.
- To find out the correlation between the severity of anaemia with the different stages of chronic kidney disease (CKD).

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MATERIAL AND METHODS

This was a case-control prospective study conducted with over 300 Bangladeshi non-patients as the control group A and 87 with different stages of chronic kidney disease (CKD) patients as the case group B in the department of Nephrology BSMMU from April'2004 to June 2006. Every normal people who came to BSMMU indoors for a different purpose and the staff of the BSMMU were offered included in this study. Those who had no history of DM, hypertension, or CKD, were not on any medication and agreed to informed consent were included in the control group. And different stages of tprediabeticents who had no history of blood transfusion, erythropoietin and parental iron infusion were predialytic CKD patients in Nephrology indoor in BSMMU as a cases group was recruited as the study population. A purposive sampling technique was followed for sample selection.

Inclusion Criteria:

- Age >18 years and <70 years.
- Apparently normal, healthy Bangladeshi people who had no history of diabetes mellitus, hypertension, or chronic kidney disease and who were not on any medication and serum creatinine were normal (As a control).
- Patient with chronic kidney disease with the different stages.

Exclusion criteria:

- Age <18 years and >70 years.
- Any emergency patients attending in nephrology OPD or indoors.
- Chronic kidney disease is associated with any bleeding disorder chronic obstructive pulmonary disease, chronic liver disease and malignancy.
- Hemolytic anaemia or family history of hemolytic anaemia.
- Pregnancy and breastfeeding mother.
- Bleeding and coagulation abnormality.
- Patient received a blood transfusion and epoetin therapy.

CKD pre-dialysis patients were studied who met the inclusion criteria and agreed to informed consent were included. CKD patients were examined for general physical and systemic examinations that are height, weight, BP, oedema, and anaemia. The normal population underwent general physical examination and systemic examination for height, weight, anaemia, BP and oedema. The normal population was investigated for serum creatinine, haemoglobin level, total and differential count of white blood cells, peripheral blood film, mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration. Creatine clearance was calculated by the Cockcroft-Gault equation. CKD patients were investigated for serum creatinine, haemoglobin level, erythrocyte sedimentation rate, total and differential count of white blood cells, peripheral blood film, mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration and urine for routine and microscopic examination, stool for routine and microscopic examination and serum iron, serum ferritin, total iron-binding capacity. Haemoglobin level, erythrocyte sedimentation rate, total and differential count of white blood cells, peripheral blood film, mean corpuscular volume, mean corpuscular haemoglobin and

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mean corpuscular haemoglobin concentration is measured in the autoanalyzer and rechecked manually in the department of clinical pathology, BSMMU. Serum iron and total iron-binding capacity were estimated in calorimetric principle using an automated device and transferrin saturation was calculated. Serum ferritin was determined by an enzyme-linked immunosorbent assay. In selected cases endoscopy of the stomach and duodenum, serum C-reactive protein, serum parathyroid hormone, serum bilirubin, plasma protein electrophoresis, haemoglobin electrophoresis and bone marrow examination was performed. In this study, anaemia was considered when haemoglobin levels were <13 g/dl for men and <12 g/dl for women. For categorical analysis; stage-III CKD was defined by a CCr of between 30 ml/min and 60 ml/min, stage-IV CKD by a CCr of between 15ml/min and 29 ml/min and stage-V CKD by a CCr of less than 15 ml/min. Data were processed and analyzed using computer software SPSS version 11.5. The test statistics used to analyze the data were descriptive statistics, Chi-square test, Fisher's Exact Probability Test, and Student's t-Test. The descriptive statistics were frequency, mean and standard error of the mean. The data measured on a continuous scale were presented as mean and standard deviation from the mean and compared using the student's t-Test. Categorical data were expressed as percentages and evaluated using Chi-square or Fisher's Exact Probability Test. The level of significance was 0.05. P-value <0.05 was considered significant. The summarized information was then presented in form of tables, charts and graphs.

RESULTS

[Table 1] showed, that a maximum (27.3%) of normal respondents of the study group were within the 28-37 years age group followed by 27.0% within the 38-47 years age range, 24.3% within the 18-27 years age range, 14.7% within 48-57 years and 6.7% within 58 to 67 years age group. In group, B maximum patients (29.9%) were within the 48 to 57 years age range followed by 27.6% within the 28-37 years age group, 21.8% within the 18 to 27 years age range, 12.6% within 38-47 years age group and 8.0% within 58 to 67 years age range. The mean age of the normal respondents of the study group was 37.62 years with a standard deviation of ±12.12 years. On the other side mean age of the patient group was 39.96 years with a standard deviation of ±12.77 years. No statistically significant difference was observed between groups in terms of age.

[Table 2] showed, that out of all normal respondents of group A 158 (52.7%) were male and 142 (47.3%) were female. On the other side, 56 (64.4%) patients in group B were male and 31 (35.6%) were female. The male and female ratio for group A was 1.11: 1 and in group B 1.81:1. No significant difference was observed between groups in terms of sex distribution.

[Table 3] showed the mean body surface area (BSA) of the normal male was 1.62±0.11 m2 and for female were 1.47±0.17 m2 and the patient group were 1.57±0.18 m2 for male and 1.46±0.18 m2 in female respectively. The mean haemoglobin level of the normal male was 13.94±1.33 g/dl and female were 12.29±1.15 g/dl and the mean haemoglobin level of CKD male patient was 9.26±2.03 g/dl and female were 9.09±1.93 g/dl respectively. There are

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significant differences in haemoglobin levels in both groups. The mean serum creatinine levels in normal people were 1.05±0.11 mg/dl and 6.98± 4.53 mg/dl in CKD patients. The mean corrected CCr were 85.66±14.93 ml/min/1.73 m2 in normal males and 77.85±16.23 ml/min/1.73 m2 in normal females and the mean corrected CCr were 16.57± 12.59 ml/min/1.73 m2. There were significant differences between the two groups in respect of S. creatinine and CCr.

[Table 4] showed, among the normal male 15.2 % (24) were anaemic and 38.7 % (55) were anaemic and among the CKD patient 96.4% (54) males were anaemic and 93.5 % (29) females were anaemic that and 6.5% (2) of female and 3.6% (2) of male had normal haemoglobin level. Overall, out of all respondents of group A 26.3% had anaemia and the rest 73.7% were normal. In CKD patients 95.4% were anaemic and rests only 4.6% were normal in terms of anaemic status.

[Table 5] showed, Based on MCV in group A 10.33% of individuals were microcytic and the rest 89.77% were normocytic. In the CKD group 46.0% were microcytic, 51.7% normocytic and macrocytic were 0.

[Table 6] showed, In group, A maximum, 63.3% of males had corrected CCr levels within 60 to 90 ml/min/1.73m^2 followed by 35.4% above 90 and 1.3% within 30 to 60 ml/min/1.73m^2. In female 73.2% had Corrected CCr level within 60 to 90 followed by 18.3% had >90 and 8.5% had within 30 to 60 ml/min/1.73m^2. Overall, out of 300 normal people having corrected CCr < 60 ml/min/1.73 m^2 were 8.5% (12), 60-90 ml/min/1.73 m^2 were 73.2% (204) and more than 90 ml/min/1.73 m^2 18.3% (26).

[Table 7] showed out of all patients (87) maximum of 59.8% (52) had severe renal failure in terms of corrected CCr < 15 ml/min/1.73m^2 followed by moderate renal failure as defined by corrected CCr 15-29 ml/min/1.73m^2 were 27.6% (24) and mild renal failure as defined by corrected CCr 30-60 ml/min/1.73m^2 were 12.6% (11).

[Table 8] showed different levels of Hb, creatinine, corrected CCr, serum ferritin and TSAT level in different grades of renal failure patients. The mean haemoglobin level of severe renal failure was 8.60□1.83 g/dl and moderate renal failure was 9.54□ 1.94 g/dl and mild renal failure was 11.25□1.29 g/dl. The mean serum creatinine level of severe renal failure was 9.58□ 4.05 mg/dl, moderate renal failure was 3.69□1.15 mg/dl and mild renal failure was 1.86□0.32 mg/dl. The mean corrected CCr was 8.97□ 2.76 ml/min/1.73 m2, 19.36□3.33 ml/min/1.73 m2 and 43.53□ 9.59 ml/min/1.73 m2 in severe, moderate and mild renal failure respectively. The mean serum ferritin level was 364.53□246.14 µgm/l, 278.85□192.90 µgm/l and 259.19□148.84 µgm/l in severe, moderate and mild renal failure respectively. The mean TSAT level was 16.29±9.98(%), 16.45±4.12(%) and 19.86±3.57(%) in severe, moderate and mild renal failure respectively.

[Figure 1] showed that the mean serum creatinine level in mild renal failure was 1.86□ 0.32 mg/dl, 3.69□1.15 mg/dl in moderate renal failure and 9.58□4.05 mg/dl in severe renal failure.

[Figure 2] showed that the mean serum haemoglobin level in mild renal failure was 11.66 g/dl, 9.82 g/dl in moderate renal failure and 8.65 g/dl in severe renal failure in males

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and in the case of females mean serum haemoglobin level in mild renal failure was 10.17 g/dl, 9.37 g/dl in moderate renal failure and 8.52 g/dl in severe renal failure. The haemoglobin level was progressively decreased from mild to severe renal failure and the decrement was similar in both sexes and there was no significant difference between males and females.

Table 1: Age distribution of the study groups (N=387)

Age group (in years)	**Group**	
	Normal Population Group A	**CKD Patient Group B**
18-27 yrs.	73 (24.3)	19 (21.8)
28-37 yrs.	82 (27.3)	24 (27.6)
38-47 yrs.	81 (27.0)	11 (12.6)
48-57 yrs.	44 (14.7)	26 (29.9)
58-67 yrs.	20 (6.7)	7 (8.0)
Mean age ±SD	37.62±12.22 (18-67)	39.96±12.77(18-67) *

Table 2: Sex distribution of study groups

Sex	**Group**	
	Group A	**Group B**
Male	158 (52.7)	56 (64.4)
Female	142 (47.3)	31 (35.6)

Table 3: Mean distribution of BSA, Hb level, serum creatinine and corrected CCr level of the normal population (N=387)

	Group	
	Group A	**Group B**
BSA		
Male	1.62±0.11	1.57±0.18
Female	1.47±0.17	1.46±0.18
Hb (g/dl)		
Male	13.94±1.33	9.26±2.03
Female	12.29±1.15	9.09±1.93
Serum creatinine (mg/dl)	1.05±0.11	6.98± 4.53
Corrected CCr	85.66±14.93	16.57± 12.59

Table 4: Distribution of the respondents of both groups by Anaemic status (N=387)

Anaemia status	**Groups**		**p-value***
	Group A	**Group B**	
Male			
Anaemic (<13 g/dl)	24 (15.2)	54 (96.4)	0.001
Normal (≥13 g/dl)	134 (84.8)	2 (3.6)	

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Female			
Anaemic (<13 g/dl)	55 (38.7)	29 (93.5)	0.001
Normal (≥13 g/dl)	87 (61.3)	2 (6.5)	
Overall anaemic status			
Anaemic	79 (26.3)	83 (95.4)	
Normal	221 (73.7)	4 (4.6)	

Table 5: Distribution of MCV and Hb level of normal male (N=387)

MCV	**Group**	
	Group A	**Group B**
Microcytic	31 (10.33)	40 (46.0)
Normocytic	269 (89.67)	47(54)
Macrocytic	0 (0)	0(0)

Table 6: Distribution of the patients by corrected CCr in group A by sex (N=387)

Corrected CCr (ml/min/1.73m2)	**Male**	**Female**	**Total**
30-60	2 (1.3)	12 (8.5)	14 (4.7)
60-90	100 (63.3)	104 (73.2)	204 (68.0)
>90	56 (35.4)	26 (18.3)	82 (27.3)

Table 7: Severity of renal failure measured by corrected CCr (n=87)

Corrected CCr (ml/min/1.73m2)	**Frequency**	**Percentage**
Severe (<15)	52	59.8
Moderate (15-29)	24	27.6
Mild (30-60)	11	12.6

Table 8: Distribution of the patients by serum level of Hb, creatinine, ferritin, TSAT and renal failure N=387)

Renal failure	**Mean±SD**				
	Hb (g/dl)	**Creatinine (mg/dl)**	**Corrected CCr**	**Serum Ferritin**	**TSAT level**
Severe (n=52)	8.60± 1.83	9.58± 4.05	8.97± 2.76	364.53± 246.14	16.29± 9.98
Moderate (n=24)	9.54± 1.94	3.69± 1.15	19.36± 3.33	278.85± 192.90	16.45± 4.12
Mild (n=11)	11.25± 1.29	1.86± 0.32	43.53± 9.59	259.19± 148.84	19.86± 3.57

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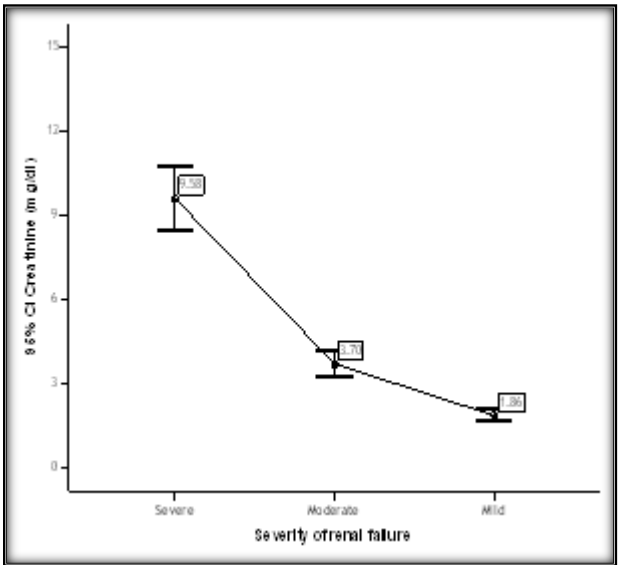

Figure 1: Mean serum creatinine level in different grades of CKD patients (n=87)

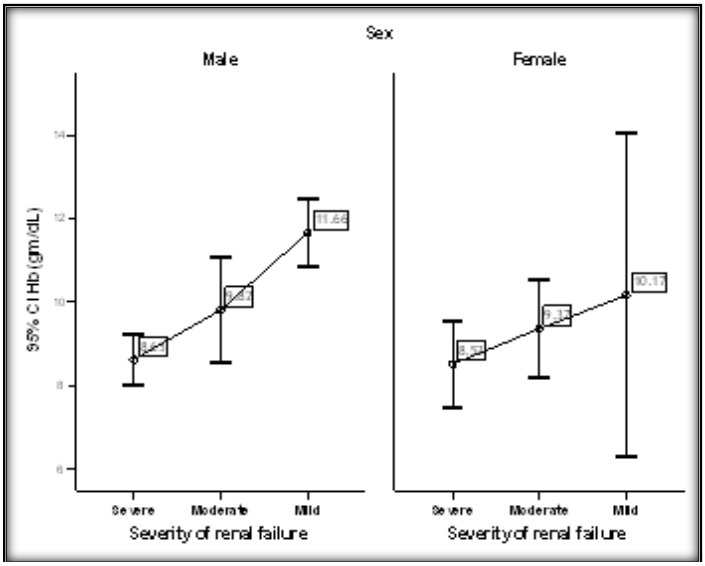

Figure 2: Mean serum Hb level in different grades of CKD patients by Sex (n=87)

Table 9: Prevalence of anaemia in different grading of renal failure (n=87)

Overall

Chronic renal failure	**Hb level**	
	≤11 g/dl	**>11 g/dl**
Severe (n = 52)	49 (94.23)	3 (5.77)
Moderate (n = 24)	21 (87.5)	3 (12.5)
Mild (n = 11)	4 (57.14)	7 (42.86)
Total (87)	74	13

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Out of 87 CKD patients, 52 were severe renal failure, among them, 49 (94.23%) had haemoglobin levels <11gm. Out of 24 moderate renal failure patient, 21(87.5%) had haemoglobin level <11g/dl and out of 11 renal failure patient, 4(57.14%) had haemoglobin level < 11g/dl.

Male

Chronic renal failure	**Hb level**	
	≤11 g/dl	**>11 g/dl**
Severe	37 (80.4)	2 (20.0)
Moderate	7 (15.2)	2 (20.0)
Mild	2 (4.3)	6 (60.0)
Total	46 (100.0)	10 (100.0)

Female

Chronic renal failure	**Hb level**	
	≤11 g/dl	**>11 g/dl**
Severe	12 (42.9)	2(40.0)
Moderate	14 (50)	2(40.0)
Mild	2 (7.1)	1(20.0)
Total	28 (100.0)	5 (100.0)

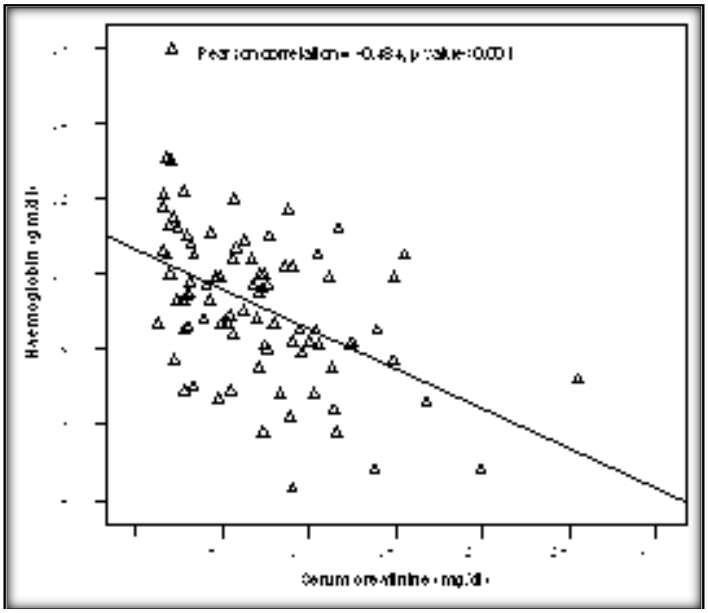

Figure 3: Correlation of serum Hb and serum creatinine level in CKD Patients (n=87)

The above scatter plot shows the correlation between Hb level and serum creatinine level of CKD patients. The figure showed Pearson correlation = -484 which indicates a negative correlation between these two variables and it is highly significant (p-value < 0.01).

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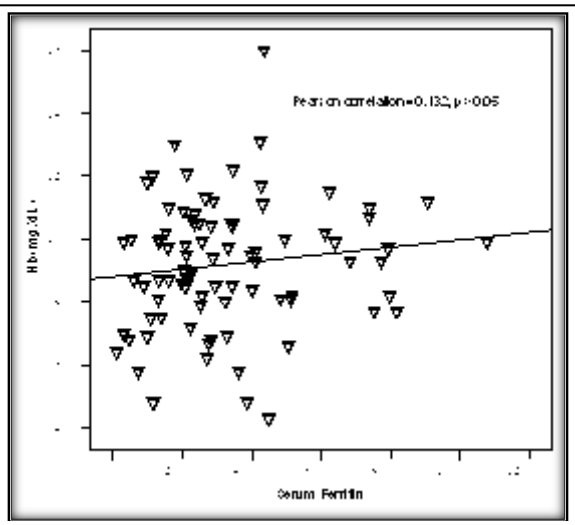

Figure 4: Correlation of serum Hb and serum ferritin level in CKD patients (n=87)

The above scatter plot shows the correlation between Hb level and serum ferritin level of CKD patients. The figure showed Pearson correlation = 0.132 which indicates a positive correlation between these two variables and it is not significant (p-value > 0.05).

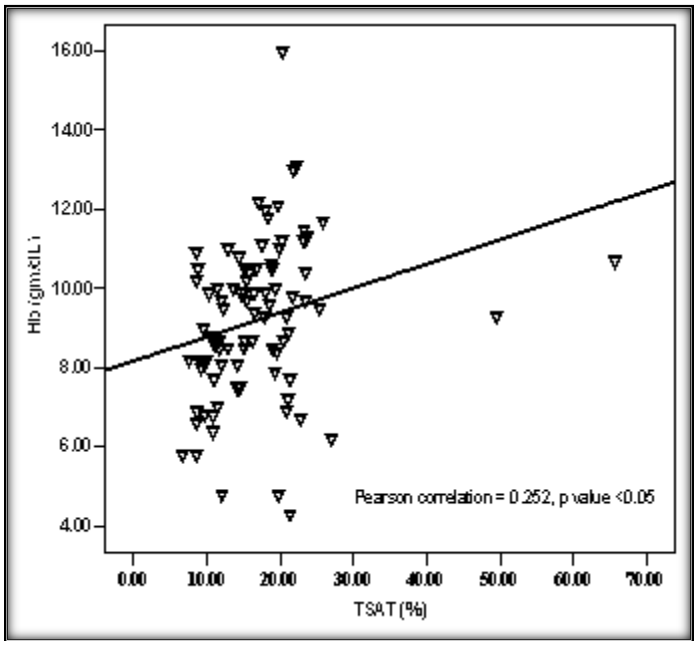

Figure 5: Correlation of serum Hb and TSAT level in CKD patients (n=87)

The above scatter plot shows the correlation between Hb level and TSAT of CKD patients. The figure showed Pearson correlation = 0.252 which indicates a positive correlation between these two variables and it is significant (p-value < 0.05).

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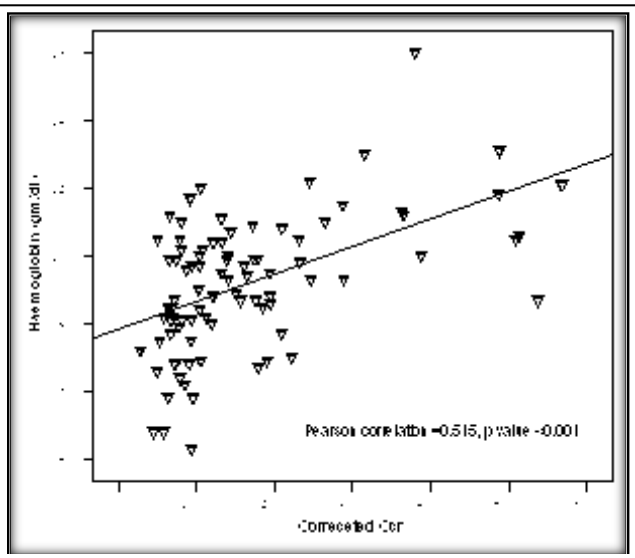

Figure 6: Correlation of serum Hb and corrected CCr level in CKD patients (n=87)

The above scatter plot shows the correlation between Hb level and serum corrected CCr level of CKD patients. The figure showed Pearson correlation = 0.515 which indicates a positive correlation between these two variables and it is highly significant (p-value < 0.001).

DISCUSSION

The definition of anaemia has attracted considerable interest recently because of epidemiologic studies that suggest that anaemia may be associated with poorer outcomes in a variety of disorders.[20] In many studies, the definition of anaemia used is that suggested by the WHO expert committee nearly 40 years ago.[21] The sample studied during the second National Health and Nutrition examination survey NHANES-II (1976-1980) was selected statistically as representative of the entire population of the United State. Among 11547 subjects were used to calculate a 95% reference range. In the adult population (10-44 years) the lower limit of normal was 13.2g/dl in men and 11.7 g/dl in women. Anaemia was noted in 3% of adult men and 4.6% of adult women. NHANES-III showed the lower limit of normal Hb of men aged 20-59 years was 13.4 g/dl and above 60 years was 12.4 g/dl and in females aged 20-49 years was 11.9 g/dl and more than 50 years 11.6 g/dl.[22] The Scripps - Kaiser database collected in the Sandiago area between 1998 to the 2002 year conducted over 6709 populations aged 20-59 years set the lower limit of normal haemoglobin was 13.4 g/dl and aged over 60 years is 12.8 in men and 11.9 in females aged 20 to 49 years and above 50 years the mean haemoglobin level was 11.9 g/dl. With these two data they found that overall, 22% of normal people are anaemic.[23] One prospective community cohort study, the Atherosclerosis Risk in Communities (ARIC) study involved 14410 normal individuals aged between 45 and 64 years and showed that 4.8% of men and 13% of women were anaemic.[24] A previous study showed that among 215 north Indian rural populations aged 16-70 years, the overall prevalence of anaemia was 47.9 (N=215) 50 %

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(N=136) among females and 44.3%(N=78) among males.[25] Low socioeconomic status, illiteracy and lower body mass index were associated with a high prevalence of anaemia.[25] Williams found that the lower limit of normal haemoglobin was 14.0g/dl in men and 11.6g/dl in females.[26] Jandl found the lower limit of haemoglobin was 14.2g/dl in men and 12.2g/dl in women.[27] A previous found that the lower limit of the haemoglobin was 13.2g/dl in men and 11.6g/dl in women respectively.[28,29] Rapaport stated that the lower limit of mean haemoglobin levels was 14 g/dl and 12 g/dl in the case of the female.[30] In 1985, World Health Organization (WHO) report, it was estimated that 15 - 20 per cent of the world population had iron deficiency anaemia.[31] Despite the lack of new prevalence data, estimates of the global prevalence of iron deficiency anaemia have increased to more than two-thirds of the world population.[31] WHO reported that 6% man and 35% of woman were anaemic in India (Vellore) and 64% of the woman was anaemic in Delhi conducted over 100 female in Vellore and 95 female in Delhi.[31] WHO also reported that 14% of males and 29%of women are anaemic in Israel.[31] According to a previous study, it had been shown that 17% of females are anaemic in Sweden conducted over 414 females.[32] Another study showed that 4.5% of the woman had anaemia in Australia, in a study conducted over 1024 females.[33] A previous study showed that of 72 Senegalese women that 58% of the women are anaemic.[34] In our prospective observational study, we found that the mean haemoglobin level was 13.94±13 g/dl in males and 12.29±1.15 g/dl in females. Among the males 15.2% and 38.7% of females were anaemic. Overall, 26.3% of people were anaemic. This finding was higher than Europe and America but lower than Indian and African peoples but our mean haemoglobin level in urban areas was almost equal to the lower limit of Europe and American people. This finding may not be representative of our whole population as most of our people live in rural areas and the socio-economic condition is very poor. By this finding, we can follow the WHO criteria for the definition of anaemia and the target haemoglobin levels in CKD patients recommended by K/DOQI guidelines and European Best Practice Guideline (EBPG) mostly in urban areas but for the rural area, further studies are needed to comment. Richard Bright 1836 first described the association between anaemia and chronic renal failure.[35] By a prospective observational study conducted over 403 predialysis patients found that the haemoglobin level was less than 11 g/dl in 62 patients with an Scr more than 400 µmol/l and 58% of the patient with an estimated CCr less than 20ml/min/1.73m^2. The proportion of anaemia was higher in the female patient than in the male for any given CCr value.[36] They showed that the overall proportion of patients with Hb less than 11 g/dl gradually rose with decreasing CCr values from less than 15% of patients spent with CCr 15-19.9 ml/min/1.73m^2 and to 61% for CCr levels less than 15 ml/min/1.73m^2. They showed a positive correlation between the individual CCr and haemoglobin values in males and females and which was highly significant and is in general agreement with our findings. The PRE-dialysis survey on anaemia management (PRESAM) involving 4333 patients from different countries showed that at the first visit to the dialysis centre the mean haemoglobin concentration was 10.0±2.1 g/dl and 68% of patients had a

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haemoglobin concentration ≤11.0g/dl. The mean haemoglobin concentration at the start of dialysis was 9.5±1.7g/dl and 80% of the patient had a haemoglobin level <11g/dl. The haemoglobin concentration at the first visit to the dialysis centre was positively correlated with CCr (r=43, p<0.01). But there was great variability and patients with CCr as low as 20 ml/min had a range of haemoglobin concentrations from severe anaemia to normal (from 4.8 to 14.2g/dl).[37] Patients with CCr >50 ml/min had a mean haemoglobin concentration of 12.0 g/dl, those with 40 – 50 ml/min had a mean haemoglobin concentration of 12.39 g/dl, those with a rate of 30-40 ml/min had a mean haemoglobin concentration 11.0 g/dl, those with 20-30 ml/min had a haemoglobin concentration 9.8 g/dl, those with a CCr<10 ml/min had a mean haemoglobin concentration of 9.0 g/dl. They also showed that 56 % were iron deficient, 37 % absolutely and 19 % functional.[37] The study showed that who did not receive epoetin before dialysis and received transfusion in the month prior to dialysis, haemoglobin concentration on the first visit to a dialysis centre was closely related to CCr. Data from the Third National Health and Nutrition Examination Survey in the USA suggested that a decline in haemoglobin level starts with a GFR of 70 ml/min in men and 50 ml/min in women. The prevalence of renal anaemia increased from 1% to an estimated GFR of 60 ml/min to 9 and 33% at an estimated GFR of 30 and 15 ml/min respectively. A Canadian multicentric cohort data suggested that by WHO definition, the prevalence of anaemia is already 25% in patients with CCr >50 ml/min. Our findings are consistent with the TSAT and haemoglobin value but differed with the S. ferritin. Kazmi et al conducted a study over 604 patients with chronic renal insufficiency and they found a direct correlation between predicted glomerular filtration rate and Hct and an inverse correlation between S. creatinine level and Hct. Anaemia was noted early in CRI; 45% of patients with S. creatinine level of 2 mg/dl or less had an Hct <36% and 8% had an Hct <30%. They also found that 54% of patients with TSAT <20%,[38] which was consistent with our findings. A study showed that haemoglobin level starts to decline at a much lesser degree of renal impairment and on average is significantly reduced at GFR level of less than 60 ml/min/1.73m^2.[38] In a recent survey of patients with ESRD in Bangladesh on maintenance hemodialysis the mean haemoglobin was 7.3g/dl in the year 2001 (N=960) and 7.8g/dl in 2002(N=1253).[39] But no study has been conducted till now on anaemia in predialysis patients in Bangladesh. Samad et al conducted a study over 16 predialysis patients and found 62.5 %, had low or absent stainable marrow iron and 37.5% had normal iron while none had an iron overload. A study conducted over predialysis CKD patients that 17 out of 20 had low iron, only 3 patients had normal iron and none had an iron overload.[40] Our prospective observational study provides comprehensive information as to the level of haemoglobin with respect to graded values of Scr and CCr in adult predialysis patients. In the whole series, we observed that the prevalence of anaemia in a population with the normal renal function was 38.7 % and the overall prevalence of anaemia in CKD patients was 95.4%. The prevalence of anaemia was 38.7 % in normal population, which increases to haemoglobin level <11g/dl was 57.14 % in patients with CCr 30 -59 ml/min/1.73m^2 which increases to 87.5 % in patients with CCr 15-29 ml/min/1.73m^2, which also increases to 94.2 % in patients with

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CCr <15 ml/min/1.73m^2. We also observed that 46 % of patients with CKD had microcytic anaemia and 73.6 % of patients with CKD had TSAT <20 %. These findings were consistent with the different studies stated earlier. With respect to the influence of gender, our observations are in agreement with the data from the USRDS registry report and Junger et al with a higher proportion of anaemia in female patients but in variance with Hsu et al WHO reported that any given level of renal function men had a higher decrease in haemoglobin than women. Bangladesh Renal Registry Report (1986-1996) noted that the causes of the renal failure were glomerulonephritis 47%, diabetic nephropathy 24% and hypertension 30% which was the general agreement with our findings and reflects the higher prevalence of glomerulonephritis in our country.[39]

CONCLUSIONS

The prevalence of anaemia in the urban area of Bangladesh is higher than USA and Europe but lower than in India and Africa (Senegal). Anaemia appears early in CKD patients in stage-III CKD. Further study is needed for the evaluation of haemoglobin levels in the rural areas of Bangladesh as most of the people reside in rural areas. This study provides a description of the association between kidney function and haemoglobin level across the entire range of kidney function. The results demonstrate that patient with reduced renal function is more likely to have anaemia and the prevalence and severity of anaemia increase with declining kidney function. CCr and TSAT is the important predictor of anaemia. In a significant number of the CKD, patient anaemia was associated with iron deficiency.

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