



CHRONIC KIDNEY DISEASE; STUDY ON PATTERNS OF ANEMIA IN RELATION TO GLOMERULAR FILTRATION RATE (GFR) IN PATIENTS

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ABSTRACT...Chronic kidney disease is usually related with anemia and the level of anemia correlates with the severity of renal failure. A chronic kidney disease is complicated by anemia and anemia may contribute to adverse clinical outcomes. No large-scale population data are available for patients with chronic kidney disease regarding prevalence of anemia, subpopulations at risk, and relationships between anemia and renal dysfunction. **Objectives:** The objective of this study is to determine the frequency of different patterns of anemia in relation to glomerular filtration rate in patients suffering from chronic kidney disease stage II and above patients. **Material & Methods:** **Study Design:** Cross sectional study. **Setting:** Medical and Nephrology wards of Liaquat University Hospital Hyderabad / Jamshoro. **Period:** 20th January 2013 to 19th December 2013. **Results:** During the study period, total 339 patients of chronic kidney disease with stage II and above patients were enrolled. The mean age \pm Standard Deviation and range) of patients was 50.65 ± 11.86 (16 to 80 years, n = 339). 211 (62.2%) were male and 128 (37.8%) were female. (Male to Female Ratio 1:6). Mean Hemoglobin \pm SD was 7.16 ± 3.89 (3.0 to 17.0 g/dL). The frequency of anemia was present in 285 (84.1%) patients with mean Hb \pm SD 6.02 ± 2.1 (g/dL). The mean weight \pm SD was 56.50 ± 9.84 (40 to 81 kg). The mean serum creatinine \pm SD was 5.63 ± 2.48 (0.9 to 12.0 mg/dL) and we observed that most frequent pattern of anemia was normocytic-normochromic anemia in 216 (77.0%) patients, hypochromic-microcytic in 61 (18.0%) and macrocytic in 17 (5.0%) patients. We also found that as anemia increased progressively with declining GFR with mean hemoglobin concentration of 11.78 ± 2.8 g/dL in CKD stage 2, 10.14 ± 3.6 g/dL in CKD stage 3, 6.8 ± 3.6 g/dL in CKD stage 4, 7.44 ± 4.0 g/dL in CKD stage 5. **Conclusion:** Frequency of anemia increases with the progression of stage of chronic kidney disease (decreased GFR) and anemia was most common in stage 5 patients of chronic kidney disease. Most frequent pattern of anemia is normocytic normochromic anemia.

Key words: Chronic kidney disease, end stage renal disease, chronic renal disease, anemia,

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INTRODUCTION

Anemia is best explained by the World health Organization (WHO) as a hemoglobin concentration underneath 13.g/dL for adult males and post-menopausal ladies a hemoglobin below 12.0g/d for premenopausal women.¹ According to above explanation, almost 90 percent of patients with a glomerular filtration rate (GFR) short of what 25 to 30 mL / min have anemia, numerous with Hemoglobin levels below 10 g/dL.² Without treatment, the anemia of chronic kidney disease (CKD) cause number of physiologic abnormalities and pathological problems including decreased tissue oxygen delivery and utilization,³ , cardiac

enlargement, increased cardiac output ,angina, ventricular hypertrophy, congestive heart failure,^{4,5} decreased cognition and mental acuity, menstrual issues, decreased nocturnal penile tumescence, and impaired immune achievements.⁶ Normocytic normochromic anemia is most overwhelming s finding of Chronic Renal Disease patients, in additions, anemia may result in growth retardation and decreased intellectual efficiency in pediatric patients. These physiological and pathological abnormalities have significant impact on quality of life, and patient's survival is decreased in patients with chronic renal disease.⁷

The prevalence of anemia was elevated too for the hemoglobin level below 12 g/dl in different stages of chronic kidney disease that is 42%, 33%, 48%, 71%, and 82%, in stages from 1 to 5 respectively. The prevalence of anemia was also elevated for the hemoglobin level below 11 g/dl (the minimum hemoglobin level at which treatment should be started with erythropoietin) that is 21%, 17%, 31%, 49%, and 72% respectively for stages 1 to 5.⁸

The most frequent morphologic findings were normochromic-normocytic (80%), hypochromic-microcytic (15%) and macrocytic (5%) in the study of Afshar R et al.⁹ It is also like was watched that 25% patients have anemia even in earliest phases of chronic kidney disease in study by Levin et al.¹⁰ No study has been conducted in our population and few data regarding anemia in chronic renal disease is accessible in Pakistan. By more timely identification and management, anemia and its physiologic consequences can be counteracted.

This study will help to determine the incidence and prevalence of anemia in chronic renal disease in our population to reduce the mortality and morbidity. The aim of this study is to determine the different patterns of anemia in relation to glomerular filtration rate in chronic kidney disease stage II and above patients.

MATERIAL & METHODS

This cross sectional study was carried out on 339 patients in the Medical and Nephrology wards of Liaquat University Hospital Hyderabad / Jamshoro from 20th January 2013 to 19th December 2013. Those patients who had Chronic Kidney Disease for >3 months duration (Stage II and above patients), age > 14 years and have not received treatment for anemia and other disturbed blood profile were included while patients suffering from leukemia, lymphoma and other malignancies, pregnant ladies, smokers, severe lung and cardiac disease, known cases of polycythemia because of any reason were not included in the study.

Chronic Renal Disease diagnosed patients from

different medical and nephrology wards according to the consideration and avoidance criteria were included in this study, after informed consent from patient or closest relative after full explanation of research work. Detailed history and intensive clinical examination were done. Patients were organized as indicated by their current glomerular filtration rate and who has not gotten treatment of anemia. Patients proforma containing demographic data, co-morbidities, current treatment, patients weight, laboratory workup included complete blood picture, Erythrocyte Sedimentation Rate, Urea, creatinine estimate glomerular filtration rate, Random Blood Sugar, urine analysis and ultrasound of kidneys, were filled by the researcher. Glomerular filtration rate is assessed by the help of Cockcroft-Gault formula.

$$eC_{cr} = (140 - \text{Age} \times \text{Weight (in kg)} \times [0.85 \text{ if female}]$$

$$\frac{\text{72} \times \text{Serum Creatinine (in mg/dl)}}{\text{}} \text{---}$$

eCcr = estimated creatinine clearance or GFR

In order to study the frequency of anemia in chronic renal disease patients, we have stratified them according to eGFRs into five stages according to the K/DOQI initiative as follows.

Stage 1	GFR above 90ml/min with proteinuria and abnormal ultrasound of kidneys
Stage 2	eGFR 60-90 ml/min with proteinuria and abnormal ultrasound of kidneys
Stage 3	eGFR 30-59 ml/min
Stage 4	eGFR 15-29 ml/min
Stage 5	eGFR <15ml/min

DATA ANALYSIS

The data were entered and analyzed in statistical program SPSS version 16.0. Quantitative data (frequencies and percentage such as gender, patterns of anemia (normocytic, microcytic, macrocytic) and stages of chronic kidney disease were presented as n (%). Numerical variables like age (in years), weight (in kg), hemoglobin (g/dL), serum creatinine, MCV, GFR etc. were presented as Mean \pm Standard deviation. Stratification of age, gender and weight was done to see the

effect of these outcome variables through chi-square test. All data were calculated on 95% confidence interval. P value ≤ 0.05 was considered as statistically significant level.

RESULTS

This cross sectional study was conducted in Medical and Nephrology wards of Liaquat University Hospital Jamshoro / Hyderabad to determine the frequency of different patterns of anemia in relation to glomerular filtration rate in patients suffering from chronic kidney disease stage II and above patients.

During study period, total 339 patients of chronic kidney disease with stage II and above patients were enrolled in this study based on inclusion and avoidance criteria.

Table-I shows the age distribution of patients, minimum age being 16 years and maximum age was 80 years. The mean age \pm Standard Deviation range) of patients was 50.65 ± 11.86 (16 to 80 years, n = 339). Out of 339 patients, 211(62.2%) were male and 128(37.8%) were female. (Male to Female Ratio 1:6).

In this study, mean Hemoglobin \pm SD was 7.16 ± 3.89 (3.0 to 17.0 g/dL).

In the present study, the frequency of anemia was present in 285(84.1%) patients with mean Hb \pm SD 6.02 ± 2.1 (g/dL).

The mean weight \pm SD was 56.50 ± 9.84 (40 to 81 kg). The mean serum creatinine \pm SD was 5.63 ± 2.48 (0.9 to 12.0 mg/dL).The mean MCV \pm SD was 79.53 ± 11.15 (55 to 120 fl). In the present study, the average GFR was 80.5 ± 12.3 ml/min/1.73 m².

In this study, most common pattern of anemia was normocytic-normochromic anemia in 216(77.0%) patients, hypochromic-microcytic in 61(18.0%) and macrocytic in 17(5.0%) patients.

Characteristics	n(%)	Mean \pm SD (Range)
Age (in Years)	-	50.65 ± 11.86 (16 to 80 years)
Gender:		
Male	211(62.2%)	-
Female	128(37.8%)	-
Hemoglobin(g/dL)	-	7.16 ± 3.89 (3.0 to 17.0 g/dL)
Anemia:		
Positive	285(84.1%)	-
Negative	54(15.9%)	-
Weight in kilograms	-	5.50 ± 9.84 (40 to 80 kg)
Serum creatinine (in mg/dL)	-	5.63 ± 2.48 (0.9 to 12.0)
MCV(fl)	-	79.53 ± 11.15 (55 to 120 fl)
Glomerular filtration rate (GFR)	-	80.5 ± 12.0 (15 to 90 GFR)
Patterns of Anemia:		
Normocytic (70 to 100)	261(77.0%)	-
Microcytic (< 70)	61(18.0%)	-
Macrocytic (> 100)	17(5.0%)	-
Stage of CKD:		
60 to 90 (Stage 2)	41(12.1%)	-
30 to 59 (Stage 3)	54(15.9%)	-
15 to 29 (Stage 4)	74(21.8%)	-
< 15 (Stage 5)	170(50.1%)	-
Hemoglobin (g/dL):		
60 to 90 (Stage 2)		11.78 ± 2.8
30 to 59 (Stage 3)		10.14 ± 3.6
15 to 29 (Stage 4)		6.8 ± 3.6
< 15 (Stage 5)		7.44 ± 4.0

Table-I Baseline characteristics of the patients (n=339)

In this study, the patients were stratified according to their GFR. Greater number of the patients i.e. 170 (50.1%, n = 339) with advanced renal disease were observed in stage 5 in this study, 41(12.1%, n = 339) patients in stage 2, 54(15.9%, n = 339) patients in stage 3, 74(21.8%, n = 339) were in stage 4.

In this study, we observed that as anemia worsens progressively with decreasing GFR with mean hemoglobin concentration of 11.78 ± 2.8 g/dL in CKD stage 2, 10.14 ± 3.6 g/dL in CKD stage 3, 6.8 ± 3.6 g/dL in CKD stage 4, 7.44 ± 4.0 g/dL

in CKD stage 5.

In this series, microcytic anemia was strongly associated with the age group 41 to 50 years (p 0.001). Out of 339 patients, 106(31.3%) patients

were in the age group 41 to 50 having 20(32.8%) microcytic anemia. Out of 211(62.2%) male patients, most 14(82.4%) had macrocytic anemia whereas in 48(78.7%) females patients had microcytic anemia.

Variables	Patterns of anemia			Total	P value
	Normocytic (70 to 100) (n = 261)	Microcytic (< 70) (n = 61)	Macrocytic (> 100) (n = 17)		
Age (in groups):					
15 – 30	17(6.5%)	9(14.8%)	4(23.5%)	30(8.8%)	
31 –40	36(13.8%)	18(29.5%)	6(35.3%)	60(17.7%)	
41 – 50	82(31.4%)	20(32.8%)	4(23.5%)	106(31.3%)	
51 – 60	83(31.8%)	12(19.7%)	2(11.8%)	97(28.6%)	0.001
61 – 70	36(13.8%)	2(3.3%)	1(5.9%)	39(11.5%)	
71 – 80	7(2.7%)	0(0.0%)	0(0.0%)	7(2.1%)	
Gender:					
Male	184(70.5%)	13(21.3%)	14(82.4%)	211(62.2%)	<0.0001
Female	77(29.5%)	48(78.7%)	3(17.6%)	128(37.8%)	
Patients weight (in kg):					
< 60	186(71.3%)	61(100.0%)	15(88.2%)	262(77.3%)	<0.0001
> 60	75(28.7%)	0(0.0%)	2(11.8%)	77(22.7%)	

Table-II. Stratification of age, gender and weight and their outcome(n = 339)

DISCUSSION

Anemia is a most frequent finding of CKD and may lead to adverse clinical consequences and anemia worsens with progression chronic renal disease. The prevalence of anaemia and renal dysfunction in previous studies varied from 40% to 69.7%, depending on diagnostic criteria used and study populaces.^{10,11}

In non-hospitalised patients this prevalence varies from 4% to 23% and is usually related with chronic renal disease, increased age and more extreme clinical features.^{11,12}

Anand *et al* found 28% and 16% mortality in anaemic and non-anaemic patients, respectively, with hospital admission rates of 56% and 33%, during a mean follow-up period of one year.¹² Most of studies have indicated connection of anaemia to adverse clinical outcomes in patients with HF.^{13,14,15} Sales *et al* reported 16.8% mortality in patients with anaemia versus 8% in patients without anemia.¹³

The results of this study shows that the overall fre-

quency of anemia was present in 84.1% patients. This high prevalence of anemia in CKD in this study may be because of greater number of patients in advanced renal disease (60.8%) in whom the mean hemoglobin concentrations were 7.44 g/dL and 6.8 g/dL, respectively for Chronic kidney Disease stages 5 and 4. This was similarity to the study of Ijoma C *et al*.¹⁶ who showed 77.5% prevalence of anemia in whom the mean hemoglobin concentrations were 7.15 g/dL and 8.60 g/dL, respectively, for CKD stages 5 and 4 whereas Reza Afshar *et al*⁹ observed anemia in 85% of patients.

In the present study, the frequency of anemia i.e. 12.1%, 15.9%, 21.8%, 50.1% respectively in patients of chronic kidney disease from stage 2 to 5, this prevalence is same to the findings in the study of Shaheen F *et al*.⁸ but marginally lower in our study because of difference in the geographic variation and population.¹⁷ McClellan *et al*.¹⁸ in a, cross-sectional, large scale, US multi-center survey study involving 5,222 patients and using 12 g/dL as definition for anemia reported

an overall anemia prevalence of 47.75% and progression of anemia from 26.7% in CKD stage 3 (GFR from ≤ 60 mL/min/1.73 m²) to 75.5% in CKD stage 5. However, Valderrábano et al.¹⁹ studying 4,333 patients before dialysis in a study involving 779 participating centers in 21 countries, showed a greater prevalence rate of 68% for anemia though the study used 11 gm/dL for definition of anemia.

The prevalence of iron deficiency anemia among Chronic kidney disease patients has decreased because of early recognition and treatment.²⁰ In this study, most frequent pattern of anemia was normocytic-normochromic anemia in 77.0% patients and hypochromic-microcytic in 18.0% and macrocytic in 5.0% patients. In the study of Afshar R et al. conducted in Iran discovered that the patterns of anemia consisted of: normochromic-normocytic (80%), hypochromic-microcytic (15%) and macrocytic anemia (5%) in their studies.⁹ In comparison to Bhatta S et al.²³ study conducted in Nepal that reported that normocytic normochromic anemia in 77.5% patients, Microcytic hypochromic anemia in 15% while macrocytic normochromic anemia in 7.5% patients. These results correlate well to this study.

In past studies, the burden of anemia therapy was estimated.^{21,22} Furthermore, if we estimate the burden of CKD population with hemoglobin below 11 g/dL in the USA according to the study by Kazmi et al.² (estimated number of all CKD patients: 13.0 million Americans), the anemic population in need of treatment with erythropoietin will be 11.8 million.

CONCLUSION

The conclusion of this study is that frequency of anemia increases with the progression of stage of chronic kidney disease (decreased GFR) and anemia was most common finding in stage 5 patients of chronic kidney disease. The most common pattern of anemia is normochromic normocytic anemia in chronic kidney disease.

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REFERENCES

- Orun E, Yalcin SS, Aykut O, Orhan G, Morgil GK, Yurdakok K, et al. **Breast milk lead and cadmium levels from suburban areas of Ankara.** *Sci Total Environ.* 2011 Jun 1;409(13):2467-72.
- Kazmi WH, Kausz AT, Khan S, Abichandani R, Ruthazer R, Obrador GT et al. **Anemia: An early complication of chronic renal insufficiency.** *Am J Kidney Dis.* 2001 Oct;38(4):803-12.
- Igaki N, Takashima M, Ohyama M, Oh S, Kida A, Yanase K et al. **The beneficial effect of effective control of anemia on hyperinsulinemia and hypoxemia in a hemodialysis patient with corrected transposition of the great arteries.** *Clin Exp Nephrol.* 2004 Jun;8(2):163-7.
- Gosmanova EO, Le NA. **Cardiovascular Complications in CKD Patients: Role of Oxidative Stress.** *Cardiol Res Pract.* 2011 Jan 2;2011:156326.
- Taddei S, Nami R, Bruno RM, Quatrini I, Nuti R. **Hypertension, left ventricular hypertrophy and chronic kidney disease.** *Heart Fail Rev.* 2011 Nov;16(6):615-20
- Kralova S, Leva L, Toman M. **Changes in lymphocyte function and subsets in dogs with naturally-occurring chronic renal failure.** *Can J Vet Res.* 2010 Apr;74(2):124-9.
- Iseki K. **Role of chronic kidney disease in cardiovascular disease: are we different from others?** *Clin Exp Nephrol.* 2011 Aug;15(4):450-5.
- Shaheen F, Souqiyeh MZ, Al-Attar BA, Karkar A, Al Jazairi AM, Badawi LS et al. **Prevalence of anemia in predialysis chronic kidney disease patients.** *Saudi J Kidney Dis Transpl* 2011;22:456-63.
- Afshar R, Sanavi S, Salimi J, Ahmadzadeh M. **Hematological profile of chronic kidney disease (CKD) patients in Iran, in pre-dialysis stages and after initiation of hemodialysis.** *Saudi J Kidney Dis Transpl* 2010;21:368-71.
- Tang Y, Katz SD. **Anemia in chronic heart failure: prevalence, etiology, clinical correlates, and treatment options.** *Circulation* 2006;113:2454-61.
- Silverberg DS, Wexler D, Blum M, Keren G, Sheps D, Leibovitch E, et al. **The use of subcutaneous erythropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestive heart failure improves cardiac and renal function and functional cardiac class, and markedly reduces hospitalizations.** *J Am Coll Cardiol* 2000;35:1737-44.
- Anand I, McMurray JJV, Whitmore J, Warren M, Pham A, McCamish MA, et al. **Anemia and its relationship to clinical outcome in heart failure.** *Circulation* 2004;110:149-54.

13. Sales ALF, Villacorta H, Reis L, Mesquita ET. **Anemia as a prognostic factor in a population hospitalized due to decompensated heart failure.** Arq Bras Cardiol 2005;84:237-40.

14. O'Meara E, Clayton T, McEntegart MB, McMurray JJ, Lang CC, Roger SD, et al. **Clinical correlates and consequences of anemia in a broad spectrum of patients with heart failure: results of the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) Program.** Circulation 2006;113:986-94.

15. Latado AL, Passos LC, Darze ES, Lopes AA. **Comparison of the effect of anemia on in-hospital mortality in patients with versus without preserved left ventricular ejection fraction.** Am J Cardiol. 2006;98:1631-4.

16. Ijoma C, Ulasi I, Ijoma U, Ifebunandu N. **High prevalence of anemia in predialysis patients in Enugu, Nigeria.** *Nephrology Reviews* 2010; 2:e14:61-65.

17. Obrador GT, Roberts T, St Peter WL, Frazier E, Pereira BJ, Collins AJ. **Trends in anemia at initiation of dialysis in the United States.** Kidney Int 2001;60(5):1875-84.

18. McClellan W, Aronoff SL, Kline Bolton W, et al. **The prevalence of anemia in patients with chronic kidney disease.** Curr Med Res Opin 2004;20:1501-10.

19. Valderrabano F, Horl WH, Macdougall IC, et al. **Pre-dialysis survey on Anemia management Nephrol Dial Transplant** 2003;18:89-100.



20. Suega K, Bakta M, Dharmayudha TG, Lukman JS, Suwitra K. **Profile of anemia in chronic renal failure patients.** Acta Med Indones (serial online) 2005;37(4):190-4.

21. Hsu CY, McCulloch CE, Curhan GC. **Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey.** J Am SocNephrol 2002;13(2):504-10.

22. Suega K, Bakta M, Dharmayudha TG, Lukman JS, Suwitra K. **Profile of anemia in chronic renal failure patients: comparison between Pre-dialyzed and Dialyzed patients at the Division of Nephrology, Department of Internal Medicine, Sanglah Hospital, Denpasar, Bali, Indonesia.** Acta Med Indones 2005;37(4):190-4.

23. Bhatta S, Aryal G, Kafle RK. **Anemia in chronic kidney disease patients in predialysis and postdialysis stages.** Journal of Pathology of Nepal 2011;1:26 - 29.

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