FUNCTIONAL IRON DEFICIENCY ANAEMIA IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT

Introduction: Anemia is one of the major harms in hemodialysis patients, which is caused by inadequate production of erythropoietin. Functional iron deficiency (FID) anemia is a type of anemia, characterized by lack of functional iron. There are many markers identified for assessing FID in patients of chronic kidney disease(CKD). Of these the most sensitive marker is percentage of hypo chromic red cells (%HRC).

Objective: To observe the frequency of functional iron deficiency in patients of chronic kidney diseases by percentage of hypo chromic red cells.

Methodology: This study was carried out in the Ibnae –Sienna Hospital Multan from March 2016 to September 2016. All those CKD patients who were on hemodialysis and on erythropoietin stimulating agent (ESA) were included in the study. However, those patients who had history of chronic infections like tuberculosis or any history of malignancy were not included in this study. For this study, 150 patients on hemodialysis and on ESA were recruited. Hemoglobin (Hb), mean cell volume (MCV) and %Hypo were measured on the Sysmex XE 5000.

Results: A sum of 150 hemodialysis patients on ESA were enrolled in this study. Of these 57.3%were males while 42.7% were females. The average age of patients was 48.71±11.92 years. Functional iron deficiency was observed in 28.7% of patients on hemodialysis.

Conclusion: Percentage of hypochromic red cells (%HRC) is the most sensitive marker for diagnosis of FID. Timely diagnosis will help in reducing treatment related complications and improve quality of life.

Key words: Functional iron deficiency; Chronic kidney disease; Haemodialysis; Percentage of hypochromic red cells.

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem. One of the main complications of CKD is anemia which occurs mainly because of reduced erythropoietin production by kidneys. However, during treatment with Erythropoiesis stimulating agent (ESA) some patients develop functional iron deficiency anemia. Functional iron deficiency is characterized by presence of adequate iron stores but slow rate of iron mobilization to site of erythropoiesiswhen ESA started. In other words, iron transport fails to keep up with increase rate of erythropoises.[1]

There are certain diagnostic markers for functional iron deficiency. The main diagnostic marker is percentage of hypo chromic red cells(%HRC). % of hypo chromic red cell <5%is considered normal. The cutoff of more than 6% is considered diagnostic for functional iron deficiency. The sensitivity of this parameter to detect FID is 91.7%.[2]

Functional iron deficiency causes resistance to erythropoiesis treatment. Thus, early diagnosis can prevent this problem. Also, these patients respond better to intravenous iron therapy rather thanoral therapy.Aim of my study is to diagnose functional iron deficiency early. %HRC implements its diagnosis. %HRC is the best available method to verify FID.Since timely diagnosis will improve the quality of life.

MATERIAL AND METHODS

Study design: cross sectional study

Setting: This study was carried out at department of Haematology, Ibnae –Sienna Hospital Multan

Duration of study: from March 2016 to September 2016.

Sample technique: Consecutive (Non-Probability) Sampling.
Sample size: Sample size will be 150 using 42.9% prevalence of functional iron deficiency anemia.

INCLUSION CRITERIA
Patients of chronic kidney disease on ESA
Age from 18 to 70 years
Both males and females patients
On maintenance heamodialysis for more than 3months.

EXCLUSION CRITERIA:
Patients of CKD not on ESA
History of chronic infectious disease like tuberculosis.
History of malignancy

RESULTS

Demographic data:
A sum of 150 hemodialysis patients on ESA were enrolled. Of these 57.3%were males while 42.7% were females. The mean of dialysis vintage was 22.55 ± 12.15 months. Average age of study patients was 48.71+11.92 years.

Hemoglobin levels:
According to KDIGO in CKD anemia is defined as Hb<11g/dl.

When a %HRC cut-off value of >6% was applied, 43 participants (28.7%) were diagnosed with FID. Almost all of these patients were anemic. Functional iron deficiency was observed in males more than females.

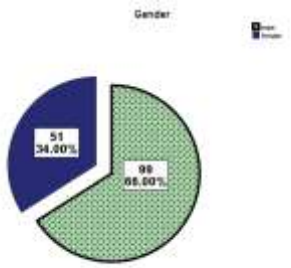
Ferritin
Out of 43 participants diagnosed with functional iron deficiency 5 participants had ferritin below 200ug/dl. About 2 participants had high iron stores (>800ug/dl). 30% of patients had absolute iron deficiency anemia. Of which majority were females 27%.

Stratification of gender was done to determine the effect of gender on the frequency of FID. In male patients, FID occurred in 33 patients while in female patients FID occurred in only 10 patients. (Table 1).

Stratification of Age of patients was also done. (Table 2). Stratification of patients on the basis of duration of dialysis was also performed. In patients with DD <24 months, FID occurred in 15 patients versus in 28 patients with DD>24 months(Table 3).

Descriptive Statistics of Mean Age of Patients.

	Mean	Std. Deviation
Age (years)	48.71	11.92



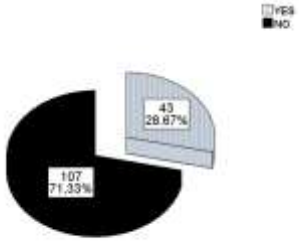
Frequency of Gender distribution.

Descriptive Statistics of Mean Hemoglobin Levels (g/dl).

	Mean	Std. Deviation
Hemoglobin	9.145	1.1289

Table 1: Descriptive Statistics of Duration of Dialysis (Months).

	Mean	Std. Deviation
Duration of Dialysis (months)	22.55	12.15



Frequency of Functional Iron Deficiency.

Table 2: Stratification of Gender to Determine the Effect of Gender on FID.

Gender	Valid	Frequency	Percent	P-value
Male	**YES**	33	33.3	**0.07**
	NO	66	66.7	
Female	**YES**	10	19.6	
	NO	41	80.4	

Table 3: Stratification of Age to Determine the Effect of Age on Functional Iron Deficiency (FID)

Age Group	Valid	Frequency	Percent	P-value
Age <50 Years	**YES**	22	32.8	**0.31**
	NO	45	67.2	
Age > 50 Years	**YES**	21	25.3	
	NO	62	74.7	

Stratification of Duration of Dialysis(DD) to Determine the Effect of Duration of Dialysis on Functional Iron Deficiency (FID)

Age Group	Valid	Frequency	Percent	P-value
DD <24 Months	YES	15	23.8	0.26
	NO	48	76.2	
DD <24 Months	YES	28	32.2	
	NO	59	67.8	

DISCUSSION

Chronic kidney disease is becoming widespread in South Asian countries like Pakistan. There are multiple causes for this spread. Most of the people have inadequate health-care provision due to either lack of health education, primary healthcare, inadequate funding on the part of the government and, most importantly, the increasing prevalence of risk factors Diabetes and hypertension[3]. Other causes like glomerulonephritis and renal stones are prevalent due to infections and dry weather conditions[4,5,6,7]

There are many mechanisms responsible for anemia in CKD of which disordered iron metabolism is a major contributor.

Functional iron deficiency is defined as decreased rate of iron delivery to the developing red cells despite adequate iron stores. The development of FID in CKD is most commonly related to the use of erythropoietin stimulating agents (rHuEPO). [8,9,10]

Serum ferritin and tranferrin saturation is used worldwide to diagnose iron deficiency. However these two analytes are not recommended to determine the rate of delivery of iron to erythron. There are many markers identified to diagnose functional iron deficiency ,most sensitive of which is percentage of hypochromic red cells(%HRC).

According to this study significant proportion of patients with chronic renal disease has functional iron deficiency anemia. A study conducted in Iran with sample size of 184 patients functional iron deficiency anemia was diagnosed in 41.1 percent of participants. Majority of cases were seen in males.[11,12]

In multiple studies conducted in Iran from 2006-2013 (Hojjat, Medanloo Farahani Tayebi, Nazemian and Savari,)functional iron deficiency was prevalent in males too.

According to this study the prevalence of functional iron deficiency in Pakistan is similar to that of middle east countries, but more than European countries.[13,14]

On the basis of this study implementing %HRC will be helpful in diagnosis and will decrease cost on further testing investigations like serum transferrin saturation and transferrin receptors. Limitations of this study, includes the effect of reticulocytosis on %HRC. Increase reticulocytes results in falsely increase level of percentage of hypo chromic red cells.

Another factor is that this analyte is largely available for research work only. Since it is not routinely used, there is no daily running of in house controls of this parameter, therefore the quality control challenge remains.Also this analyte is not available on all blood analyzers.

CONCLUSION

In our study functional iron deficiency (FID) was present in many patients. The new analyte, percentage of hypo chromic red cells is helpful for identification of Functional iron deficiency anemia. It appears to give financial as well as clinical advantage tothe patients of chronic kidney disease on hemodialysis. Percentage of hypochromic red cells will help divert the iron therapy in a more useful way, solving the problem at utilization level, rather than storage level in all cases of CKD with FID

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