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A Study of Hematological Profile in Patients of Chronic Renal Failure Undergoing Hemodialysis at a Tertiary Health Care Institute

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Abstract

The complete blood count, peripheral blood smear, bleeding time, clotting time and renal function tests of 114 patients of chronic renal failure who had required hemodialysis for a period of at least 3 months prior to the commencement of this study were studied. The purpose of this study was to investigate the derangements in the haematological profile of chronic renal patients undergoing hemodialysis and to correlate the same with the duration and severity of the renal failure. The principal finding in the study was a 100% prevalence of anemia among chronic renal failure patients, which was predominantly of the normocytic normochromic type. Red blood cell count was reduced in nearly all (93%) of study patients. There was also a strong negative correlation (r = -0.74) between haemoglobin and duration of hemodialysis. However, a significant proportion of cases showed abnormal cells in the peripheral blood cells such as burr cells, schistocytes and pencil cells, suggesting other contributing factors to the anemia. Female patients also showed a significantly greater prevalence of increased red cell distribution width (>15%) as compared to males (p = 0.001) and a lower prevalence of normocytic normochromic anemia as compared to males (p = 0.009). White blood cell counts, platelet counts, and bleeding and clotting times were largely within normal limits, and none of these variables showed a statistically significant association with the duration of hemodialysis, or serum creatinine, or serum blood urea nitrogen. The inference from the study is that anemia is a major comorbidity in end-stage renal failure patients, with many factors contributing to it, and detailed workup and effective treatment of anemia is necessary in this group of patients.

Keywords: Anemia, Bleeding Time, Clotting Time, Complete Blood Count, Hemodialysis, Normocytic Normochromic

1. Introduction

The prevalence of Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD) is rising rapidly throughout the world, including India. It is estimated that as of 2015, 55,000 Indians are on hemodialysis, with the number rising by 10-20% each year[1].

The US National Kidney Foundation's Kidney Dialysis Outcomes Quality Initiative (K/DOQI) guideline defines CKD as kidney damage or estimated glomerular filtration rate (eGFR) of < 60 ml/min/1.73 m2 for > 3 months. Kidney damage is defined as pathological abnormalities or markers of damage including blood, urine or imaging tests[2].

Rajapurkar MM, et al[3] found diabetic nephropathy to be the predominant (31% of cases) cause of CKD in patients from all over India.

NKF/KDOQI guideline (2002) defines anemia in Chronic Kidney Disease when the hemoglobin level is < 13.0 g/dl in adult males and 12.0g/dl in adult females[2].

The major cause of anemia in CKD is lack of erythropoietin (EPO) synthesis in the diseased kidneys. As renal disease progresses, specialized peritubular cells that produce EPO are depleted or injured, resulting in inappropriately low EPO comparative to the degree of anemia, which is usually of the normocytic normochromic type[4].

The coagulation profile of CKD patients may also be

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affected as CKD advances. In a study by Subhan-ud-din and Shahida A.R. Shah[5], bleeding time (BT), prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count and D-dimer levels were evaluated in 100 CKD patients. 93% of the patients had elevated D-Dimer levels, and platelet count was reduced compared to controls, however, BT, PT and aPTT time were not significantly different from controls.

2. Materials and Methods

A total of 114 cases were studied. All of the patients had been undergoing hemodialysis for ESRD for at least 3 months prior to the commencement of the study and were in the age range of 18-75 years. None of the patients had any known acute illness or chronic haematological disorder.

The CBC of each patient was done on a 5-part Beckman Coulter automated hematology analyzer. Peripheral blood smears were made and stained with Field's and Leishman stain, and examined for RBC, WBC and platelet morphology.

Predialyis serum creatinine (sr. creat) and serum blood urea level (sr. BUL) were also obtained for each patient.

The bleeding time of each patient was recorded by giving a 5mm deep puncture on the fingertip followed by pressure on a blotting paper at 30 second intervals. The time taken for bleeding to stop was noted.

The clotting time was recorded by aspirating blood (from the 5mm puncture given for the bleeding time) into a thin capillary tube. The tube was intermittently tilted below the horizontal, and the time taken for the blood to stop flowing was noted.

3. Results

3.1 Age, Sex, History, Duration of Dialysis and RFTs

The total number of cases in the study was 114. The mean age of the subjects was 43.36+/- 11.24 years, with a range of 18-75 years. 65.79% of the study subjects were male.

95.61% of the study subjects had hypertension, and 60.53% had diabetes mellitus. Only 16.67% had comorbidities likely to contribute to CKD, such as chronic glomerulonephritis, renovascular disease, obstructive uropathy etc.

The mean duration of hemodialysis was 1.78+/-0.81 years, with a range of 0.5-4 years.

The mean predialysis serum creatinine value was 7.87+/-2.25 mg/dl, with a range of 3.1 – 20mg/dl.

The mean serum BUL was 130.33+/-34.83 mg/dl, with a range of 78-252 mg/dl.

3.2 Anemia

Anemia as defined by WHO criteria[6] was present in 100% of the subjects. The mean Hb level was 7.39+/-1.7mg/dl. 5.26% of the patients had mild anemia, 55.26% had moderate anemia and 39.47% had severe anemia according to WHO criteria[6].

As seen, 77.19% of the study subjects had normocytic normochromic anemia, and males had a greater prevalence of normocytic normochromic anemia than females, which was statistically significant (p = 0.009).

Females had a greater prevalence of abnormal RBCson peripheral smears than males, especially of pencil cells.

The mean RBC count was 2.78+/0.74 millions/cmm.

Table 1. Prevalence of various types of anemia

Anemia based on Morphology	Females (39)		Males (75)		Total (114)	
	No.	%	No.	%	No.	%
Dimorphic Anemia	11	28.21	6	8.00	17	14.91
Microcytic Hypochromic	4	10.26	3	4.00	7	6.14
Macrocytic Anemia	0	0.00	2	2.67	2	1.75
Normocytic Normochromic Anemia	24	61.54	64	85.33	88	77.19
Total	**39**	**100.00**	**75**	**100.00**	**114**	**100.00**

Chi sq. = 11.58, p value = 0.009*

Table 2. Prevalence of various type of abnormal red blood Cells

Abnormal RBCs	Females (39)		Males (75)		Total (114)	
	No.	%	No.	%	No.	%
Pencil Cells	10	25.64	2	2.67	12	10.53
Fragmented RBCs	5	12.82	4	5.33	9	7.89
Burr Cells	14	35.90	23	30.67	37	32.46
Macro-Ovalocytes with Hypersegmented Neutrophils	4	10.26	4	5.33	8	7.02
Normocytic Normochromic RBCs	24	61.54	64	85.33	88	77.19

Table 3. Prevalence of normal and increased RDW

Red Cell Distribution Width (RDW)	Females (39)		Males (75)		Total (114)	
	No.	%	No.	%	No.	%
>15% (Anisocytosis)	26	66.67	26	34.67	52	45.61
Normal (10-15%)	13	33.33	49	65.33	62	54.39
Total	**39**	**100.00**	**75**	**100.00**	**114**	**100.00**

Chi sq. = 10.59, p value = 0.001*

Table 4. Pearson correlation between severity of anemia and duration of dialysis, serum creatinine & serum BUL among study patients

		Duration of Dialysis	Creatinine	BUL	Haemoglobin
Duration of Dialysis	Pearson Correlation	1	.379**	.489**	-.743**
	Sig. (2-tailed)		.000	.000	.000
	N	114	114	114	114
Creatinine	Pearson Correlation	.379**	1	.665**	-.383**
	Sig. (2-tailed)	.000		.000	.000
	N	114	114	114	114
BUL	Pearson Correlation	.489**	.665**	1	-.518**
	Sig. (2-tailed)	.000	.000		.000
	N	114	114	114	114
Haemoglobin	Pearson Correlation	-.743**	-.383**	-.518**	1
	Sig. (2-tailed)	.000	.000	.000	
	N	114	114	114	114

**. Correlation is significant at the 0.01 level (2-tailed).

93% of the study patients had a low RBC count (below 4 millions/cmm).

The mean red cell distribution width was 15.08+/-2.39%. Females had a greater prevalence of increased RDW (>15%) compared to males, and this difference was statistically significant (p = 0.001).

The above table shows strong negative correlation between haemoglobin and duration of dialysis (r = -0.74, p = 0.00), weak negative correlation between haemoglobin and creatinine(r = -0.38, p = 0.00) and moderate negative correlation between haemoglobin and BUL (r = -0.52, p = 0.00).

Pearson correlation test also showed moderate negative between RBC count and duration of dialysis (r = -0.59, p = 0.00) and serum BUL, (r = -0.48, p = 0.00) & weak negative correlation between RBC count and serum Creatinine (r = -0.37, p = 0.00).

An ANOVA test showed that mean duration of dialysis, serum creatine and serum BUL were all significantly higher (p < 0.05) in patients having fragmented RBCs and burr cells in their peripheral smears as compared to patients without these cells.

3.3 WBCS

The mean WBC count was 7968+/-4843/cmm. 15.79% of the patients had leukocytosis (total WBC count > 11000/cmm) (which was neutrophilic leukocytosis in all cases) and 16.67% of the patients had leukopenia (total WBC count < 4000/cmm). Also, 6.14% of patients showed eosinophilia (defined as absolute eosinophil count > 500/cmm), 3.51% had relative lymphocytosis (greater percentage of lymphocytes than neutrophils), and 4.39% had hyper segmented neutrophils (defined[7] as more than 3% of neutrophils with five lobes, and/or atleast one neutrophil with 6 or more lobes)

On Pearson correlation, no correlation was found between WBC count and duration of dialysis (r = 0.16, p = 0.08), serum creatinine (r = 0.11, p = 0.24) or serum BUL(r = 0.14, p = 0.15). Also, on ANOVA, duration of dialysis (p = 0.83), serum creatinine (p = 0.93) and serum BUL(p = 0.69) did not differ significantly between patients having various types of WBC morphology.

3.4 Platelets

The mean platelet count was 2.26+/- 1 lakh/cmm. Thrombocytopenia (platelet count < 1.50 lakhs/cmm) was present in 13.16% of patients, while thrombocytosis (platelet count > 4.50 lakhs/cmm) was present in 1.75% of patients. 9.65% of patients showed macroplatelets on peripheral smears.

On Pearson correlation, there was no correlation between platelet counts and duration of dialysis (r = 0.022, p = 0.82), serum creatinine (r = 0.024, p = 0.79) and serum BUL (r = -0.052, p = 0.58). Unpaired t-test also

showed no association between presence or absence of giant platelets and duration of dialysis (p = 0.54), serum creatinine (p = 0.96) and serum BUL (p = 0.39).

3.5 Bleeding and Clotting Times

The mean bleeding time was 6.75+/- 1.79 minutes. 10.53% of the patients had an abnormal bleeding time (> 9 mins). There was no significant difference between patients with normal and abnormal bleeding times with respect to duration of dialysis (p = 0.96), serum creatinine (p = 0.96) and serum BUL (p = 0.69)

The mean clotting time was 4.95 +/- 0.99 minutes. 13.16% of patients had an abnormal clotting time (> 6 mins). There was no significant difference between patients with normal and abnormal clotting times with respect to duration of dialysis (p = 0.06), serum creatinine (p = 0.57) or serum BUL (p = 0.66).

4. Discussion

The majority of study subjects were males (65.79%), similar to studies by ArunS et al[8], Chinwuba et al[9], MN Islam et al[10], and Bhattacharjee K et al[11].

The mean age in this study was 43.36 +/- 11.24 years, similar to Chinwuba et al[9] and MN Islam et al[10] respectively.

4.1 Etiology of CKD

Hypertension and diabetes mellitus were identified as the main causes for CKD in this study; 109 (95.6%) of the patients had hypertension and 69 (60.5%) had diabetes mellitus. This was similar to studies by Bhatta S et al[12], and George SV et al[13]. However, Chinwuba et al[9] found the prevalence of hypertension (22.5%) and diabetes mellitus (15.1%) to be lower than that of chronic glomerulonephritis (37%) among CKD patients in that study.

4.2 Anemia

In this study, all the patients were anemic. The mean haemoglobin level was 7.39+/- 1.7g/dl. This finding was in concordance with the studies by Bhatta S et al[12], Barde R et al[14], Hakim et al[15] and Bhattacharjee K et al[11].

The prevalence of mild, moderate and severe anemia by WHO criteria[6] was 5.26%, 55.26% and 39.48% respectively.

In this study, 77.19% of all the patients had normocytic normochromic anemia, similar to the studies by Arun S et al[8], Mudiyammanavara NR, et al[16], George SV et al[13], Bhattacharjee K et al[11] and Reza A et al[17], but contrasting with studies such as Tennankore KK et al[18], which found a prevalence of MCV > 97 fl of 61%, and MCV > 102 fl of 30%, and Talwar et al[19] which found a 60% prevalence of microcytic hypochromic anemia among CKD patients.

Duration of dialysis, serum creatinine and serum BUL were significantly higher in patients with fragmented RBCs (p<0.05) and burr cells (p<0.05). Burr cells are known to increase in proportion to the severity of uremia[20] while fragmented RBCs suggest a hemolytic component, which could be due to reasons like decreased adenosine triphosphatase activity in the RBC membrane[21], decreased red cell survival in uremia[22], or even toxins in the dialysate itself such as copper, nitrates and formaldehyde[23].

4.3 WBCs

The mean WBC count in this study was within the normal range. 15.79% of the patients had neutrophilic leukocytosis. Other studies such as George SV et al[13] and Rathod SG[24] also show a considerable number of ESRD patients showing neutrophilic leukocytosis. This may be due to the high incidence of latent or secondary infection in these patients.

4.4 Platelets

The mean platelet count in this study was within the reference range. 13.16% of the patients had thrombocytopenia while 1.75% had thrombocytosis.

Gafter U et al[25] found the mean platelet count among ESRD patients to be significantly reduced (1.75+/- 0.065 lakhs/cmm) compared to controls.

Another study by Dorgalaleh et al[26] found the mean platelet count in CKD patients to be 1.72+/-0.9 lakhs/cmm and reduced compared to controls. Other studies show platelet dysfunction in many cases of ESRD which predisposes the patients to bleeding[27,28].

4.5 Bleeding and Clotting Times

The mean bleeding and clotting times in this study were within the reference ranges. 10.53% of the patients had an increased bleeding time (> 9 mins) while 13.16% of the patients had an increased clotting time (> 6 mins).

A study by Butt M et al[29] found increased bleeding time in 33% of patients on hemodialysis, which is higher than in this study, although hemodialysis improved the bleeding time in many patients. Subhan-ud-din and Shahida A.R. Shah[5] found that, no stage III CKD patients and only 10% of stage IV CKD patients had an abnormal bleeding time. Also the PT and aPTT were normal in all the patients in that study. By contrast, Ramaprabha P et al[30] found a significant elevation of PT, aPTT and plasma fibrinogen

levels in ESRD patients as compared to controls, as well as a decrease in platelet count.

One study[31] showed improvement of the bleeding time consequent to correction of anemia with ESAs (Erythropoeitin Stimulating Agents). So the overall inference is that there is a bleeding tendency in ESRD, despite normal platelet count.

5. Conclusion

This study showed a 100% prevalence of anemiain patients on hemodialysis. It was predominantly of the normocytic normochromic type, suggesting EPO deficiency as the primary cause. However, in some cases, the presence of abnormal cells such as fragmented RBCs, pencil cells and macro-ovalocytes suggest other contributory factors, such as hemolysis, iron deficiency or folate/vitamin B12 deficiency. Neutrophilic leukocytosis in some patients may be explained by the tendency towards latent or secondary infections. Although the platelet counts, bleeding and clotting times were largely normal in this study, some studies suggest otherwise. In the light of this study, there is a need for nephrologists to monitor the haematological profile of CKD patients on dialysis, and treat any derangements in the same, so as to improve outcome for these patients.

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