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General Medicine

HAEMATOLOGICAL PROFILE OF CHRONIC RENAL DISEASE PATIENTS ON ANTIHYPERTENSIVE MEDICATIONS UNDERGOING HEMODIALYSIS

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KEYWORDS :

INTRODUCTION

Chronic renal disease (CRD) is a patho-physiologic process with multiple etiologies, resulting in the intransigent attrition of Nephron number and function and frequently leading to end-stage renal disease (ESRD). In turn, ESRD represents a clinical state or condition in which there has been an irreversible loss of endogenous renal function, of a degree sufficient to render the patient permanently dependent upon renal replacement therapy (dialysis of transplantation) in order to avoid life – threatening uremia [1].

CRD is considered as a serious public health problem throughout the world with high cost of medical care especially in countries like India which represents a substantial burden in third world nations (2). CRD is diagnosed as glomerular filtration rate (GFR) < 60ml/min per 1.73m2, accompanied by symptoms of uremia largely and need a maintenance dialysis therapy or even a kidney transplant (3).

Among the various risk factors, the three leading risk factors for CRD are hypertension, diabetes, and obesity. It has been shown that the prevalence of CRD-associated anemia is around 50%. According to WHO guidelines, anemia is defined as a hemoglobin (Hb) level lower than 13 g/dL in men and post-menopausal females, and lower than 12 g/dL in pre-menopausal females. Anemia has also been found in diabetics even with a GFR of more than 60 ml/min (4). Although anemia may be found at different CRD stages, a strong correlation exists between the incidence of anemia and the degree of CRD severity (5). It is well known that hematological parameters are reduced in CRD. Erythrocyte indices are the most affected one because maximum production of erythropoietin take place in the juxta glomerular apparatus of kidney. Apart from decreased erythropoietin, it might also be due to vitamin B12, iron and folic acid deficiencies resulting from dietary insufficiency or blood loss, or due to decreased erythrocytes life span (6). The various other causes of anemia in CRD may include gastrointestinal bleeding; severe hyperparathyroidism and systemic inflammation (7). The CRD associated anemia is treated by recombinant human erythropoietin. This way of treatment has replaced transfusions and led to major improvement of the survival rates of CRD-associated anemic patients (8).

Other affected hematological parameters in CRD include total leukocyte Count and its differential counts, platelet count, bleeding time and prothrombin time (9). Thrombocytopenia is regarded as a consequence of hemodialysis. Platelet count tends to be decreased in both predialysis and hemodialysis patients (10). However, its occurrence is rare in patients undergoing hemodialysis using biocompatible membranes.

The present study has been undertaken to determine the hematological profile of CRD patients taking antihypertensives and to compare the hemodialyzed and pre-dialyzed patients with normal healthy controls.

MATERIALS AND METHODS

This is a cross sectional study done on the chronic kidney disease patients on maintenance hemodialysis. The study was carried out in the Hakeem Abdul Hameed Centenary hospital, a tertiary care hospital attached to Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, New Delhi between January-2017 to December-2017.

The study population included the patients attending dialysis unit of HAHC hospital. The selection of patients was based on previous diagnosis with chronic kidney disease, based on KDIGO guidelines (CKD is defined as either kidney damage marked by albuminuria and GFR less than 60 mL/min per 1.73 m2 for ≤3 months)(3). Source of data was patient's dialysis unit records and personal interview with the patient and/or his relative with follow ups. A pre-tested structured questionnaire was used to elicit the information regarding the socio-demographic characteristics of the disease, drug history and lab investigations.

BLOOD SAMPLES

Anticoagulated Blood samples were taken for haematological investigations such as haemoglobin, RBC , TLC, DLC, ESR and Platelet count.

INCLUSION CRITERIA

All the patients suffering from chronic kidney disease more than 15 years of age were included in the study.

EXCLUSION CRITERIA

Patients suffering from any disease other than CRD that could affect their haematological parameters such as malignancy, inherited or acquired blood diseases, acute or chronic inflammation, connective tissues diseases, dehydration, or recent hemorrhagic episodes and pregnant females were also excluded from the study.

RESULTS

There were total 100 patients enrolled in the study. Among the study population 72% patients were males and 28% were females, the maximum number of patients were from the age group 41-60 years (60%) followed by the patients of age group 21-40 years (20%) (Table 1).

Table No.1: Age & gender distribution of hemodialysis patients.

Age (year)	Male	Female	Total No
< 20	01	02	03
21 - 40	16	02	18
41- 60	42	18	60
>60	13	06	19
Total	72	28	100

Primary cause of ESRD leading to dialysis:

The most common primary etiology for ESRD leading to dialysis was patients suffering from both diabetes and hypertension 43% followed by hypertension alone 22% and diabetes mellitus 18% (Table- 2).

Table No.2: Primary cause of ESRD leading to dialysis.

Primary cause	Number of patient	% of patient
Hypertension	22	22 %
Diabetes mellitus	18	18 %
Diabetes mellitus with hypertension	43	43%
Drug intake	10	10 %
Kidney stone	5	5 %
Chronic glomerulonephritis	2	2 %

Chronic comorbidity in dialysis patients:

Among the presence of co-morbidity, hypertension with diabetes mellitus topped the list (55%) followed by hypertension (30%), diabetes mellitus (10%) and coronary artery disease (5%) (Table-3).

Table No.3: Chronic comorbidity in dialysis patients.

Co-morbid conditions	Number of patients	% of patients
Hypertension	30	30 %
Diabetes mellitus	10	10 %
Hypertension with Diabetes mellitus	55	55 %
Cardiovascular disease	05	05

Hematological parameters in hemodialysis patients and its relationship with hemodialysis:

Data presented in table-4 shows that the RBC count, hemoglobin levels and platelets counts are significantly reduced (p-value < 0.05) in the patients of chronic renal failure and the process of hemodialysis further decreases the level of all the above mentioned hematological parameters whereas there is slight increase in total leucocyte count in the patient of CRF but a significant leukocytosis is induced by the process of dialysis (table-4). Another significant change noted was in the value of ESR which is significantly high (p-value <0.05).in the patients of chronic renal failure and dialysis also has significant role in decreasing ESR value in these patients.

Table-4: Haematological profiles (mean ± SD) of pre-dialyzed-CKD, post-hemodialyzed healthy control subjects and its relationship with hemodialysis:

Parameters	Control	Pre-dialysis	Post-dialysis
Hb (gm/%)	12.6±0.88	8.52±0.22	7.82±1.78
RBC (million/mm3)	4.83±0.36	4.17±0.8	3.05±0.99
TLC (thousand/mm3)	5.7±1.75	6.04±0.42	6.82±0.45
Platelet count (Lac/mm3)	2.62±0.55	1.72±0.45	1.59±0.57
ESR	14.8±0.66	52.3±0.31	40.19±0.21

Effect of chronic kidney disease on hematological parameters and its relationship with hemodialysis:

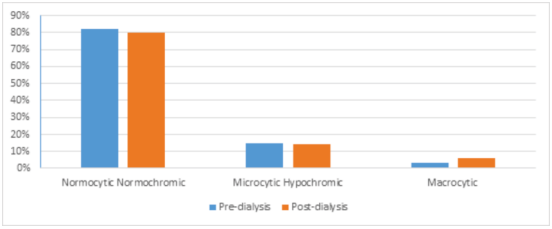
Although there is some leukocytosis in the patients of chronic renal failure there is not much effect of CRF on DLC except that an increase in number of monocytes was detected (table-5)

Table-5: Differential leucocyte count in patients of CRF and its relation with hemodialysis:

Differential leucocyte count (Mean Value)	Control (%) (Mean value)	Pre-dialysis (%) (Mean value)	Post-dialysis (%) (Mean value)
Neutrophil	62	65.17	66.27
Lymphocytes	22	21.21	20.12
Monocyte	04	11.21	10.42
Eosinophil	2.5	1.10	1.12
Basophil	0.1	0.31	0.12

Morphology of RBCs – Morphologically the most common type of anemia was normocytic normochromic (80%), microcytic hypochromic (15%) and macrocytic anemia (5%) (Figure 2). Macrocytosis in hemodialyzed patients was seen slightly more than predialyzed (5.9 vs. 4.8%).

Figure 1. Frequency of different morphologic features of anemia in hemodialyzed and pre-dialyzed patient



DISCUSSION

In the present study 72%(number) patients were males and 28% were females, the maximum number of patients were from the age group 41-60 years.

The primary etiology for ESRD leading to dialysis was patients suffering from both diabetes and hypertension 43% followed by hypertension alone 20% and diabetes mellitus 20% and this finding high point the alarming need of poor control of blood pressure and blood sugar and the primary healthcare providers should take into account the development of various preventive measures so as to avoid its complications.

Effect of hemodialysis on haemoglobin and RBCs –

In CRD patients the levels of haemoglobin oscillate above or below the recommended levels within brief spell of time even though the calculated mean hemoglobin remains within the target range of 11 to 12 g/dl [11]. Most of the patients of CRD suffered from anemia and its severity progresses as the disease progresses.

The present study suggested that patients with CRD patients on regular hemodialysis exhibit varied degrees of diversification in hematological parameters. In these patients the red blood cells count and hemoglobin levels were appreciably reduced in contrast to the pre-dialysis levels. The major cause of the reduction in RBCs count in post-dialysis patients is diminished production of erythropoietin. The main hormone, Erythropoietin is the primary humoral regulator of the RBCs production and is also required for retaining the RBCs survival by impeding the DNA cleavage taking place in CFU-Es. If there is not sufficient erythropoietin, then this will lead to expeditious DNA cleavage resulting into cell death. The survival of RBCs is inversely proportional to the blood urea nitrogen concentration in CRD patients. The hemolytic factor has been suggested to be a contributory factor involved in the reduction of RBCs which is usually eliminated through the kidneys (12). The hemoglobin concentration and hematocrit generally provide an accurate reflection of the extent to which the circulating red cell mass is reduced. Hemodialysis have a significant impact on these parameters. Uremic plasma leads to an increment in the expression of phosphatidyl serine over the extrinsic surface of RBC which intensifies the detection of these catastrophic red blood cells by macrophages, resulting in their destruction and reduced survival (13).

Effect of hemodialysis on white blood cells:

The present study showed an increase in the WBC count in the CRD patients as the disease advances and also post dialysis. The exact mechanism through which CRD causes a slight increase in total leucocyte count is not clear. The probable explanations include that in patients of CRD going through dialysis procedure, the blood is getting exposed to the artificial membranes leading to the activation of complement system in vivo. The complement is specifically C3a or C5a, generated by the classic complement activation pathway. This complement activation causes neutrophil aggregation and adherence to the endothelial surface with the fall in total leucocyte count eventually. This can also be because of up regulation of various cytokines such as interleukin-6 (IL-6) and tumor necrosis factor – α (TNF- α) in the blood which contribute to chronic inflammation in the already existing uremic state[14]. This implies activation of the acute phase proteins such as C - reactive

protein which may also be the cause of significantly raised ESR value found in our study[15].

Effect of hemodialysis on platelet count:

The present study suggested that in the CRD patients the platelet count was notably reduced in contrast to predialysis levels. Thrombocytopenia is a common side effect of hemodialysis[16].The membranes of dialyzer is responsible for platelet adhesion, aggregation, and activation[17]. Hemodialysis resulting into platelet activation which has been manifested by raised levels of platelet factor 4 and thromboxane[18,19]. In CRD patients, there is diminished production of erythropoietin resulting into reduction in total platelet count[20]. Erythropoietin potentiates the effect of megakaryocyte colony stimulating factors, acetylhydrolase (PAF-AH) and paraoxonase (PON1)[21]. Some studies have also concluded that occurrence of thrombocytopenia following hemodialysis were interconnected with complement activation, precisely C3a, along with the platelet activation[22]. Many other studies also found a statistically significant decrease in platelet count of CKD patients thus, corroborating with our study[23,24,25,26].

Morphology of anemia-

The morphologic feature of anemia on peripheral smear examination consisted of: normocytic -normochromic (80%), microcytic-hypochromic (15%) and macrocytic anemia (5%)). Macrocytosis in hemodialyzed patients was seen slightly more than predialyzed (5.9 vs. 4.8%). (Figure-1)

CONCLUSION-

Chronic Renal Disease is associated with varied degrees of changes in the hematological parameters that requires heedful evaluation and management for the patients.

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