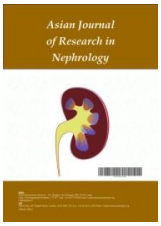

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Assessment of Full Blood Count Parameters in Patients with End Stage Renal Disease (ESRD) on Regular Haemodialysis

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Authors' contributions

This work was carried out in collaboration among all authors. Author CK designed the study, corrected the proposal and literature survey, supervised and guided methodology and analysis and finally corrected and modified the manuscript up to this final version. Authors TA, SR and PK wrote the protocol, managed the literature survey, carried out data collection, performed the initial analysis and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Haematological profile is commonly affected in chronic kidney disease and this becomes more apparent as the disease progresses. The aim of this study was to assess full blood count (FBC) parameters in a cohort of Sri Lankan patients with End Stage Renal disease (ESRD) on regular haemodialysis.
Materials and Methods: This comparative cross-sectional study included hundred (100) patients with ESRD on regular haemodialysis, who were recruited from haemodialysis units of Colombo South Teaching Hospital (CSTH) and National Institute of Nephrology Dialysis Transplantation (NINDT) in Sri Lanka. Full blood count and serum ferritin were done in all the patients. Data were analysed statistically by using SPSS (version 19.0) data base.
Results: The cohort of hundred individuals included 60% male and 40% female patients. In this cohort, majority (n=83, 83%) were either severely or moderately anaemic with a haemoglobin less

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than 10.9g/dL(WHO cut off) despite erythropoietin treatment. Majority had a normal mean corpuscular volume (MCV) (n=63, 63%), but 96 (96%) patients had an increased red cell distribution width-coefficient variation (RDW-CV) indicating anisocytosis. Ninety (90%) patients had a normal total white cell count and ninety nine (99%) patients had a normal absolute reticulocyte count. Thrombocytopenia was noted in 29(29%) patients. There was no statistically significant correlation between serum ferritin and the two indices MCV and MCH

Conclusion: In our cohort, patients showed varying abnormalities in haematological parameters which were comparable to previous studies. Most importantly, anaemia and thrombocytopenia are anticipated in these patients, so that regular monitoring of haemoglobin and platelet count is indicated in chronic renal failure patients undergoing haemodialysis.

Keywords: Chronic kidney disease; end stage renal disease; haemodialysis; anaemia; thrombocytopenia.

1. INTRODUCTION

End Stage Renal Disease (ESRD) is the final stage of chronic kidney disease (CKD) characterized by progressive and irreversible deterioration in renal function. The body fails to maintain fluid and electrolyte balance resulting in uraemia in patients who fail to survive without renal transplantation or regular haemodialysis [1].

In haemodialysis, the blood is allowed to flow through a special type of filter that removes waste and extra fluids [2]. Haemodialysis influences the transport of water through the erythrocyte membrane and induces morphologic and functional modifications [3,4]. As a renal replacement therapy, haemodialysis can help to feel better and live longer, but it is not a cure for kidney failure [5].

Red blood cell production and survival is low in chronic renal failure due to erythropoietin deficiency. This is because majority of erythropoietin is synthesized in the kidney except 10% in liver and other organs [6]. Therefore anaemia is a common feature that can be observed in most of the patients of CKD. Chronic blood loss, haemolysis and bone marrow suppression by retained uremic substances are also causes for the anaemia in CKD [7,8]. The toxic uremic environment in chronic renal failure accounts for the decreased RBC life span. The contribution to mechanical damage caused by haemodialysis process to the shortened life span is not clearly observed, but reductions up to 70% in total RBC survival have been reported in uremic patients [9]. Gastrointestinal bleeding, sever hyperparathyroidism and systemic inflammation can also be considered as causes of anaemia in patients of CKD [10].

A research done by Mohammad Asaduzzaman et al., on chronic kidney disease patients undergoing haemodialysis concluded that CKD patients undergoing haemodialysis are at risk of anaemia, as well as thrombocytopenia, septicaemia, bacteraemia and inflammatory tendency. Another study was conducted by Yasir A.H Hakim et al., (2016) to evaluate the effect of haemodialysis (machine) in complete blood count with focus on haemoglobin, platelet and T-WBC count. 199 patients with end stage renal failure were included in the study. Authors commented that platelet count and haemoglobin concentration were reduced and white blood cell count was increased after haemodialysis.

Changes in red blood cell (RBC) indices are observed in CKD and may be caused by vitamin B12, iron and folic acid deficiencies, which are consequences of dietary insufficiency or blood loss or by decreased erythrocytes' lifespan in CKD patients[8,11].

A hospital based, cross sectional comparative study was conducted by Mohammed Nasim Uddin Chowdhry et al., (2017) to observe the effect of haemodialysis on red cell indices and haematocrit in CKD patients. The study population included 40 patients of diagnosed CKD. Authors concluded that there were significant changes, especially, regarding MCV, in patients receiving maintenance haemodialysis, along with consequent changes in MCHC.

RDW is usually used for diagnosis of anaemia, especially as a marker in iron deficiency anaemia and elevated level reflects an increased size variation of red blood cells which indicates altered erythrocytes [12,13]. As anaemic conditions are commonly present in ESRD patients RDW has been found as a predictor of such conditions.

White blood cell (WBC) count and platelet count were within normal limits in CKD subjects [14]. Eosinophilia is reported in some studies [15]. Though thrombocytopenia is a known potential side effect of haemodialysis it is rarely seen in patients who undergo haemodialysis using biocompatible membranes [16]. Platelet count tends to be decreased in both pre-dialysis and haemodialysis in CKD patients in some studies [17].

As there is limited literature regarding the haematological profile of patients with ESRD in Sri Lankan setup, our aim is to assess FBC parameters in a cohort of patients with end stage renal disease on regular haemodialysis.

2. MATERIALS AND METHODS

This comparative cross-sectional study included hundred (100) patients with ESRD on regular haemodialysis, who were recruited from haemodialysis units of Colombo South Teaching Hospital (CSTH) and National Institute of Nephrology Dialysis Transplantation (NINDT) in Sri Lanka. Study population was selected after considering inclusion and exclusion criteria.

2.1 Inclusion Criteria

1. Patients with end stage renal disease on regular haemodialysis and erythropoietin for three months or longer.
2. Age more than 18 years.

2.2 Exclusion Criteria

1. Patients not undergoing optimal dialysis. eg:-< 2 dialysis sessions per week.
2. Any blood transfusion during last 3 months.
3. Previously diagnosed haematological disorders other than iron deficiency anaemia.
4. Patients with any clinically evident inflammatory and infectious diseases, malignancies and haemoglobinopathies.

The blood samples for FBC were analysed in the Mindray BC6800 analyser in the manual mode within 6 hours of collection. The analyser was calibrated according to the international standards and quality control samples were run daily prior to the analysis. Serum ferritin was done by the chemilunest method in the Immulite biochemistry analyser.

Selected patients according to the inclusion and exclusion criteria were divided into two groups as male and female and FBC parameters were analysed separately in the two groups. Haematological values for normal adults (predominantly from Europe and North America) (Dacie and Lewis practical haematology, 7th edition) were considered for the analysis. Deviation of each parameter from the above standard normal values was assessed. All the statistical analysis was done using SPSS data base.

3. RESULTS

In this study, hundred (100) patients with ESRD on regular haemodialysis and erythropoietin for 3 months or longer were included. All the patients had an estimated GFR (eGFR) value less than 15 mL/min. There were 60% male participants and 40% female participants (Table 1). In the male participants, majority were above 50 years (n=38, 63.33%) but in females, majority of the patients were below 50 years of age (n=24, 60%).

All the male and 52.5% (n=21) female participants had RBC counts below the standard level (normal range 4.5-5.5x10^{12}/L). In both male and female groups, majority of patients were moderately anaemic (n=39, 65% in male, n=26, 65% in female). Severe anaemia with haemoglobin below 8g/dL was noted in18.33% (n=11) males and 17.5% (n=7) females (Table 2). In this study, 98.33% (n=59) male and 92.5% (n=37) female patients had a haematocrit below the normal range (NR 40-50% in males and 36-46% in females).

In this cohort, majority of patients had a normal MCV (Table 3) and a low MCH (Table 4). Also, 65% (n=39) males and 85% (n=34) females had a low MCHC (below 31.5g/dL). RDW was above normal (above 14) in 96.67% (n=58) of males and 95% (n=38) of females indicating RBC anisocytosis was a prominent feature.

Majority of patients which included, 90% males (n=54/60) and 90% females (n=36/40) had a normal WBC count (4-10x10^{9}/L). Only 29% of patients showed thrombocytopenia in our study cohort (Table 5).

All the male and 97.5% (n=39) female patients had a normal absolute reticulocyte count (0.02-0.2x10^{12}/L) despite anaemia and erythropoietin treatment.

The association of MCV and MCH with serum ferritin values were further analysed using the

data shown in Tables 6 and 7. In our study, majority (n=61,61%) had a low serum ferritin value(<200 ng/mL), out of which only 27 patients had a low MCV and 44 (72.13%) patients had a low MCH. According to those data, Pearson correlation between MCV and serum ferritin level was 0.213 and between MCH and serum ferritin level was 0.216 in males. Pearson correlation between MCV and serum ferritin level was 0.219 and between MCH and serum ferritin level was 0.281 in females. Therefore, there was no significant correlation between those two parameters and serum ferritin level in our study population.

4. DISCUSSION

This comparative cross sectional study had been carried out to assess the FBC parameters in a cohort of Sri Lankan patients with End Stage Renal Disease (ESRD) on regular haemodialysis. In this study, we observed that most of the patients had low RBC counts and low haemoglobin levels. Majority of the patients were either severely or moderately anaemic with the haemoglobin level less than 10.9g/dL despite erythropoietin treatment. This finding was in concordance with the studies by Mohammad Asaduzzaman et al., Yasir A.H Hakim et al., Anwar Habib et al., and Akbar Dorgalaleh et al. Anemia was mainly normocytic with normal MCV (63%) similar to the finding in the study by Mohammed Nasim Uddin Chowdhry et al., in which majority had normal MCV.

Majority of patients in this study had low MCHC and it was also in agreement with the studies by Nasim Uddin Chowdhry et al. and Akbar Dorgalaleh et al.

According to the results in our study, a large number of participants (96%) had a hematocrit below the normal range, similar to the studies by Mohammed Asaduzzaman et al., Mohommed Nasim Uddin Chowdhry et al., and Akbar Dorgalaleh et al. In this patient cohort, majority (96%) had high RDW-CV value (>14%) indicating RBC anisocytosis was a prominent feature. A study of haematological profile in patients with chronic renal failure by Arjun Chakravarti et al., had revealed that females showed a significantly higher prevalence of increased RDW (>15%) as compared to males (p=0.001). But in this study, we had observed an equal prevalence of increased RDW in both sex groups.

Significant thrombocytopenia had been observed in some studies [6,18,19]. But contrasting with those findings, in the present study, majority of subjects (71%) had a normal platelet count despite regular dialysis and only 29% of participants showed thrombocytopenia. Majority of the participants showed a WBC count within the reference range in our study. Most of the studies had showed variable WBC counts and some increased counts may be due to the high incidence of latent or secondary infection in patients [20]. In the present study, patients with any clinically evident inflammatory and infectious diseases were excluded and that might be the reason for our findings.

There was no reticulocyte response in majority of the study population despite erythropoietin treatment. This may be due to iron restricted erythropoiesis due to absolute iron deficiency or functional iron deficiency as patients were mainly on oral iron supplements. A study by Abdulrahaman Y et al. had revealed that the reticulocyte count was significantly lower among the CKD patients compared to healthy controls.

In our study, majority had low serum ferritin indicating a state of iron deficiency. However, microcytosis (low MCV) could not be appreciated in the majority with hypochromasia (low MCH) detected in a greater number of patients.There was no statistically significant correlation between serum ferritin and the two red cell indices MCV and MCH.

Table 1. Distribution of dialysis patients among different age and sex groups

Age	Sex				Total	
	Male	% (Male)	Female	% (Female)	number	%
18-30	2	3.33	6	15		
31-40	11	18.33	8	20	19	19
41-50	9	15	10	25	19	19
51-60	18	30	9	22.5	27	27
61-70	17	28.33	6	15	23	23
71-80	2	3.33	1	2.5	3	3
81-90	1	1.67	0	0	1	1
Total	60	100	40	100	100	100

Table 2. Distrubution of haemoglobin according to WHO cutoff values

Hb(g/dL)	Male		Hb(g/dL)	Female		Total	
	Number	%		Number	%	Number	%
Below 8 Severe anaemia	11	18.33	Below 8 Severe anaemia	7	17.5	18	18
8-10.9 Moderate anemia	39	65	8-10.9 Moderate anaemia	26	65	65	65
11-12.9 Mild anaemia	10	16.67	11-11.9 Mild anaemia	5	12.5	15	15
Above 13	0	0	Above 12	2	5	2	2

Table 3. Distribution of MCV among study participants

MCV(fL)		Male		MCV(fL)		Female		Total	
		Number	%			Number	%	Number	%
Below	83	23	38.33	Below	83	14	35	37	37
Standard	83-101	37	61.67	Standard	83-101	26	65	63	63
Above	101	0	0	Above	101	0	0	0	0

Table 4. Distribution of MCH among study participants

MCH(pg)		Male		MCH(pg)		Female		Total (%)	
		Number	%			Number	%	Number	%
Below	27	35	58.33	Below	27	25	62.5	60	60
Standard	27-32	25	41.67	Standard	27-32	15	37.5	40	40
Above	32	0	0	Above	32	0	0	0	0

Table 5. Distribution of Platelet count among study participants

PLT(10^9/L)		Male		PLT(10^9/L)		Female		Total (%)	
		Number	%			Number	%	Number	%
Below	150	19	31.67	Below	150	10	25	29	29
Standard	150-450	41	68.33	Standard	150-400	30	75	71	71
Above	450	0	0	Above	400	0	0	0	0

Table 6. Association between MCV and serum ferritin level

SF(ng/mL)	MCV(fL)	Male	Female	Total	
				Number	%
<200	<83	17	10	27	44.26
	>=83 ,<101(normal range)	20	14	34	55.74
>=200	<83	6	4	10	25.64
	>=83, <101 (normal range)	17	12	29	74.36

Note:200ng/mL is the recommended cutoff value for serum ferritin in hemodialysis patients. (National Kidney Foundation of America)

Table 7. Association between MCH and serum ferritin level

SF(ng/mL)	MCH(pg)	Male	Female	Total	
				Number	%
<200	<27	24	20	44	72.13
	>=27,<32 (normal range)	13	4	17	27.87
>=200	<27	11	5	16	41.03
	>=27,<32 (normal range)	12	11	23	58.97

5. CONCLUSIONS

Overall, our main findings on haematological parameters of patients with ESRD are comparable to previous studies. In our study, we mainly found that majority of patients with ESRD are either moderately or severely anaemic with a normal MCV and significantly decreased levels of MCH and MCHC. A significantly increased RDW was observed similar to most of the other studies. Reticulocyte response was not evident despite erythropoietin treatment, most probably due to iron restricted erythropoiesis due to absolute or functional iron deficiency which we did not analyse by a full work up of iron studies in this study. Thrombocytopenia is also a possible finding in these patients. Based on these results of this study, we suggest that clinicians should be alert of these possible changes in haematological parameters when managing this type of chronic patients.

6. LIMITATIONS

The nutritional status and conditions with malabsorption were not taken into consideration in the study.

CONSENT

Blood samples were taken for full blood count (EDTA tube) and serum ferritin (plain tube) after their informed written consent, before starting the regular haemodialysis session for the given week.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s) from the hospitals.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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