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Clinico-Laboratory profile of macrocytic anemia in patients admitted in tertiary care hospital, Chennai- A cross sectional study.

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ABSTRACT

Background:Macrocytosis is a common finding encountered in automated coulters and evaluation of clinical, biochemical and haematological parameters in macrocytic anemias will provide a clue to diagnosis. This study was done to evaluate the clinical and laboratory parameters and distribution of macrocytic anemia in our hospital and we also studied the mean difference between the gender and laboratory parameters of macrocytic anemia.

Methods: A cross sectional study was conducted in Saveetha medical college a tertiary care hospital, Chennai. 50 patients presenting with macrocytosis were taken in to study. A detailed clinical history and physical examination was done in all cases. Complete blood count (CBC), peripheral blood examination and reticulocyte distribution width – coefficient of variation (RDW-CV) was done in all cases.

Results: Majority of study participants (48%) were in age group of 41-60 years with male: female ratio 2.1:1, with 70% vegetarian diet. The most common presentation of the patient was easy fatigability (56%) and commonest sign was pallor (86%). The laboratory findings suggestive of macrocytic anemia were the mean hemoglobin levels 9.04+_1.85mg/dl, mean MCV 104.07+_3.72fl, mean RDW-CV 15.61+_2.61%, with peripheral smear suggestive of megaloblastic anemia in 64 % and 28% had bicytopenia, while 8% had pancytopenia. The mean difference between the gender and RBC count, MCV, MCHC, WBC count were statistically significant with p value<0.05.

Conclusion: Macrocytic anemia can be easily detected by correlating preliminary clinical findings and laboratory findings and RDW-CV is one of the diagnostic tool that can be utilized before going to advanced tests.

Keywords: Clinical, Laboratory profile, Macrocytic anemia, RDW-CV.

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INTRODUCTION

Macrocytic anemia refers to macrocytosis (mean corpuscular volume (MCV) greater than 100 fL) in the setting of anemia. It is divided into two forms, megaloblastic (hyper segmented neutrophils) and non-megaloblastic. The megaloblastic form is due to impaired DNA synthesis from folate and/or vitamin B12 deficiencies, while the non-megaloblastic moiety occurs from multiple mechanisms. [1][2]

Macrocytosis affects 2% to 4% of the population, 60% of whom have anemia. Various etiological factors of macrocytic anemia are alcoholism, folic acid deficiency, vitamin B12 deficiency and medications. Autoimmune causes are more common in middle-aged women. Hypothyroidism and primary bone marrow disease account for more cases of macrocytic anemia in older patients. The prevalence of vitamin B12 deficiency increases in patients older than 60 years.[3][4]

Macrocytic anemia would be wrongly diagnosed as iron deficiency anemia in many of the situations because of similar presentation of variety of anemias. Hence laboratory findings with complete blood count, mean corpuscular volume (MCV), red cell distribution width - coefficient of variation (RDW-CV), White blood cell count (WBC), platelet count with hemoglobin estimation will further help to diagnose the macrocytic anemia. With this background, our objective was to assess the clinico-laboratory findings of macrocytic anemia in patients admitted in tertiary care hospital, Chennai India. Based on this aim of our study is to evaluate the clinical and laboratory parameters in patients with macrocytic anemia and to find the mean difference between the gender and laboratory parameters of macrocytic anemia.

METHODOLOGY

This study was done as a cross sectional study which was done over a period of 3months on 50 patients with age ≥15 years who were admitted with macrocytic anemia in Saveetha medical college a tertiary care hospital, Chennai.

Macrocytic anemia was diagnosed in patients with a mean red blood corpuscular volume >95 fl and anemia with a hemoglobin of < 13 gm/dl in male patient and < 12 gm/dl in female patient. Patients above the age of 15 years with macrocytic anemia were included in the study. Whereas

patients with decompensatedliver disease, chronic kidney disease, Hemolytic anemia, Hemorrhagic disease and Post splenectomy and pregnant patients were excluded.

After obtaining Institutional Ethical Clearance, and with patient consent. All the patients were evaluated for clinical presentation and examination of signs was done. Further, they were investigated with a complete hemogram, which includes estimating hemoglobin level, red blood cell indices (MCV, MCH, MCHC), red cell distribution width –coefficient of variation (RDW-CV), total leucocyte count, differential leucocyte count, platelet count, and examination of peripheral smear was done.

RESULTS

The mean age of study participants was 49.48+-14.4 years and 33 (64%) were male and 17 (34%) were females. Among 33 male, 48.5% were in the age group of 41-60 years and among 17 female 47.1 % were in the age group of 41-60 years as shown in table 1.

Table 1:Baseline characteristics of the study participants

Baseline characteristics	Gender		characteristics Gender Total		
Age in years	Male N (%)	Female N (%)	N (%)	P value	
15-25	4(12.1%)	1 (5.9%)	5 (10%)		
26-40	2 (6.1%)	3 (17.6%)	5 (10%)	0.57	
41-60	16 (48.5%)	8 (47.1%)	24 (48%)	0.57	
>60	11 (33.3%)	5 (29.4%)	16 (32%)		
Vegetarian diet	24 (72.7%)	11 (64.7%)	35(70%)	0.74	
Mixed diet	9 (27.3%)	6 (35.3%)	15(30%)	0.74	
Alcohol consumption	5(15.2%)	3(17.6%)	8(16%)	1	

The following symptoms and signs were observed in the patients with macrocytic anemia. (Table 2) The most common symptom being easy fatigability and most common sign being pallor.

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Symptoms	Frequency (%)	Signs	Frequency (%)
Easy fatigability	28 (56%)	Pallor	42 (84%)
Anorexia	10(20%)	Glossitis	2 (4%)
Breathlessnesson exertion	5(10%)	Jaundice	3 (6%)
Palpitations	6 (12%)	Hepatomegaly	2 (4%)
Weight loss	1 (2%)	Splenomegaly	1(2%)
Total	50 (100%)	Total	50 (100%)

Most of the patients (64%) had hemoglobin levels between 6-10mg/dl and 30% had more than 10mg/dl and 6% had Hb levels below 6mg/dl..

The mean difference between the gender and hematological parameters was done with one –way ANOVA test. The mean RBC count, MCV, MCHC, WBC count were statistically significant with p value<0.05, indicating that the patients with macrocytic anemia have mean difference in above parameters between gender. The mean RBC count were reduced in both the genders and mean MCV values were raised above the normal limit (83-101fl), the mean RDW-CV were also raised in both the genders above the normal limit (11.6-14%) suggestive of macrocytic anemia. Other hematological parameters are listed in the below table 2.

Table 3:The mean differencebetween the gender and hematological parameters among macrocytic anemia patients.

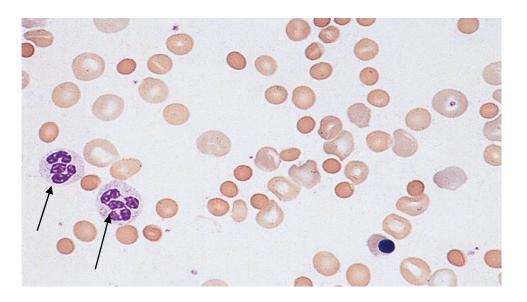
Sl	Hematological	Male	Female	Total	p-
no	parameters	(Mean+_SD)	(Mean+_SD)	(Mean+_SD)	value
1	HB (g/dl)	9.09+_2.06	8.93+_1.39	9.04+_1.85	0.081
2	RBC count	3.42+_1.28	3.43+_1.47	3.43+_1.33	0.001*
3	MCV (fl)	103.17+_3.05	105.8+_4.34	104.07+_3.72	0.015*
4	MCH	32.379+_1.80	33.353+_2.17	32.71+_1.97	0.09
4	MCHC (g/dl)	31.33+_1.18	31.35+_2.08	31.34+_1.53	0.001*

5	WBC	8309.39+_4544.91	8084.71+_3445.76	8233+_4168.02	0.032*
6.	Platelet count	189787.88+_100594.09	152000+_82537.8	176940+_95707.33	1.77
7	RDW-CV (%)	15.53+_2.84	15.76+_2.19	15.61+_2.61	0.08
8	Neutrophil count	5273.33+_3384.56	5221.76+_3481.88	5255.80+_3382.35	0.03*
9	Lymphocyte count	2111.21+_1403.032	2175.29+_1541.57	2133+_1436.13	0.02*
10	Monocyte count	458.48+_278.72	374.12+_238.172	429.80+_266.24	1.13
11	Eosinophil count	439.39+_551.63	299.41+_281.96	391.80+_478.72	0.95
12	Basophil count	23.94+_39.52	18.82+_11.66		0.27

^{*}p value <0.05 is considered as statistically significant

Peripheral smear findings of all 50 participants revealed that the most common finding were the presence of macrocytes (80%), anisocytosis (70%), and macroovalocytes (55%). Hypersegmented neutrophils were present in 48% patient. Other findings such as tear drop cells, Howell–Jolly bodies, polychromatocytes, nucleated RBCs, and target cells were also reported but were less frequent.

Figure 1: Peripheral smear of the participant-arrows showing hypersegmented neutrophil with > 4 lobes suggestive of megaloblastic anemia.



DISCUSSION

In our study, patient population male and female percentage is 64% and 34% respectively. Male to female ratio was 2.1: 1. About 48% of the patients were of the age 41-60 years, and 32% were above 60 years. In comparison, Salma hag et al [5] study showed 17.6% of

patients in age group 41-60 and 12.5% in age group above 60 years. In contrast to our study, this study also included patients below the age 15 years. Vineetha Unnikrishnan et al [6] and Arya et al [7] had more Male: Female ratio as that of our study. But studies done by Tejas Shah et al[8] and Uma Khanduri et al[9] showed female predominance.

In our study 15 (30%) of the patients were on mixed diet and 35 (70%) had vegetarian diet were commonly found to be affected. Contrast results were observed in Arya et al [7], where 84% were on mixed diet and 16% were vegetarian diet and non-vegetarians were commonly affected. The study conducted by Iqbal SP et al [10] showed Vitamin B12 deficiency in 94% of non-vegetarians. The data collected from Andrews L et al [11] and SR Kankonkar et al [12] showed that vitamin B12 deficiency is higher in vegetarians compared to non-vegetarians.

The majority of patients 42(84%) were nonalcoholic while 8 (16%) were alcoholic. In concordance with the study conducted by Arya et al [7] found 29.2% alcoholic by using Michigan Alcoholism Screening test and - glutamyl transferase levels. Alcoholism is a well-known cause of macrocytic anemia. Chronic consumption of more than 80 grams of alcohol per day has adverse effects on the hematologic system [13].

In our study majority of patients 28 (56%) had fatigue as presenting complaints while 10 (20%) had anorexia, 6(12%) had palpitations, 5(10%) had breathlessness on exertion and 1 (2%) had weight loss as the chief complaints. The most common sign among the patients was pallor (84%) followed by 6% had jaundice, 4% had glossitis & hepatomegaly each and 2% had splenomegaly. While in a study by Deepankar P [14],pallor was the most common finding in the study group and present in 96% patient, skin hyperpigmentation was present in 48% and oral ulcer in 26% of patients.

In the study by Tejas Shah et al [8] 63% had pallor, 32% had skin hyperpigmentation and 12% had icterus. In the study by Salma Haq et al [5] 84% had pallor, 28% had jaundice and hepatomegaly and 48% percent had splenomegaly. In a study by Vineetha Unnikrishnan [6] 35% had jaundice, 31.7% had splenomegaly,28.3% had hepatomegaly and 23.3% had skin changes. In a study by Arya et al [7], majority of patients- 86 (81.1%) had fatigue as presenting complaint while 71 patients had breathlessness, 63 had loss of appetite, 42 had fever, 36 had vomiting, 35 had yellow discoloration of sclera, 33 had neurological manifestations, 26 had bleeding

manifestations, 27 had abdominal pain, 23 had swelling of feet,15 had oral ulcers,14 had diarrhea, 16 had palpitations, and 11 had weight loss as presenting complaint.

On laboratory investigation, the hematological parameter hemoglobin was in the range of 9.04 ± 1.85 g/dl, followed by total count (8233 ± 4168 / cumm), platelet count (176940 ± 95707 / cumm), RDW-CV ($15.61 \pm 2.61\%$), MCV (104.072 ± 3.72 fl), MCH (32.71 ± 1.97 pg/cell), MCHC (31.34 ± 1.53 g/dl). A total of 32 patients had hemoglobin in the range of 6-10 gm/dl, followed by 2 patients in the range of 6-6gm/dl. Thrombocytopenia was detected in 18 (36%) patients. Arya et al [7] in their study reported the hemoglobin in the range of 6.42 ± 2.09 g/dl, followed by total count (7375 ± 6907 / cumm), platelet count (123686 ± 100097 / cumm), PCV (19.89 ± 6.38 %), reticulocyte count (2.08 ± 2.31 %), MCV (108.24 ± 7.10 fl), MCH (34.78 ± 4.08 pg/cell), MCHC (32.36 ± 2.77 g/dl). The thrombocytopenia detected was 72.2%, which was comparable higher than our study. Khanduri et al [15] in their study reported MCV ranging from 77 to 123 and reticulocyte count was found to be higher (more than 2) in 42% case. Chanarinet al [16] described 60% of patients with Hb<10 gm/dl.84% of patients with raised MCV level. In the study by Deepankar P et al [14], mean hemoglobin value of study group was 7.16 ± 2.41 (female -6.40 and male -7.46). 88% of the participants had Hb level <10gm/dl, and 53% of the patients had value of <6gm/dl.

On presentation, in our study population a majority of 14 patients (28%) had bicytopenia, while 4 (8%) had pancytopenia. In contrast to our study, Arya et al [7] reported 47.16% bicytopenia and 53% had pancytopenia, Tejas Shah et al [8] reported 48% of patient with pancytopenia. In another study by Uma Khandhuri et al [15], pancytopenia was reported in 62% of patients. The study by Salma Haq et al [5] reported pancytopenia in 41% and bicytopenia in 60%.

Peripheral smear of the participants in our study showed macrocytosis in 80%, anisocytosis in 70%, and macroovalocytes in 55%, and hypersegmented neutrophil in 48%, which was quite similar from the Deepankar P et al study.[14]Unnikrishnan et al. in their study found that all the 26 patients with MA had hypersegmented neutrophils and/ or macro-ovalocytosis in peripheral smear.[6]Niazi and Khan found macrocytosis (68.5%), hypochromia (31.5%), anisopoikilocytosis (65.9%), and hypersegmentation of neutrophils (51.5%) on peripheral smear examination.[17] Mwanda and Dave found anisocytosis, macro-ovalocytes in 83% cases, and hypersegmented neutrophils in 51% cases in peripheral smears.[18]

CONCLUSION

Our study showed a male preponderance. Diet and alcoholism did not influence much in our study. The mean difference between the gender and RBC count, MCV, MCHC, WBC count were statistically significant. The RBC indicators -Mean Corpuscular Volume and qualitative marker of anisocytosis -Red Cell Width are important markers as they are early indicators of macrocytic anemia. These markers usually precede the onset of anemia. So they help the clinicians to diagnose and effectively treat the reversible condition, Megaloblastic anemia and to easily differentiate from the most common iron deficiency anemia.

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