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STUDY OF CLINICAL PROFILE OF MEGALOBLASTIC ANEMIA.

General Medicine

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ABSTRACT

Background: Megaloblastic anemia encompasses a heterogenous group of anemias characterized by the presence in the bone marrow of large blood cell precursors called Megaloblasts. Megaloblastic anemia is most often due to hypovitaminosis, specifically vitamin B12 (Cobalamin) and folate, which are necessary for the synthesis of DNA. Overt neurological manifestations of megaloblastic anemia are well documented but there is paucity of data on the existence of subclinical neurological manifestations in Megaloblastic anemia. Hence, we have undertaken this study, to assess the clinical profile of the patients with the megaloblastic anemia. **Methods:** Present study was prospective in nature conducted among 100 megaloblastic anemia patients. All patients fulfilling inclusion criteria and exclusion criteria were taken up for the study. Study was carried out over a period of 1.5 years. **Results:** Majority of the patients was in the age group of 31-40 years and most of them were male. Anisopoikilocytosis (86%) was the commonest peripheral blood smear findings amongst study population. Out of 100, 29 patients had axonal neuropathy, 10 patients had demyelinating neuropathy and 1 had axonal as well as demyelinating neuropathy. **Conclusion:** Besides bedside neurological examination, further Nerve conduction study examination is helpful for the evaluation of neuropathies and studies can be considered to monitor the progression of disease and understanding of the varied spectrum of neurological manifestations of megaloblastic anemia.

KEYWORDS

Megaloblastic anemia, peripheral blood smear, Nerve conduction study, neurological manifestations.

INTRODUCTION:

Megaloblastic anemia encompasses a heterogenous group of anemias characterized by the presence in the bone marrow of large blood cell precursors called Megaloblasts.[1] This condition is due to impaired DNA synthesis leading to an asynchronous maturation between the nucleus and cytoplasm of erythroblasts, explaining the large size of megaloblasts.[2] Megaloblastic anemia is most often due to hypovitaminosis, specifically vitamin B12 (Cobalamin) and folate, which are necessary for the synthesis of DNA. The average Indian Vegetarian diet is deficient in cobalamine.[3] Cobalamin deficiency causes subacute combined degeneration of the posterior and lateral grey column of the spinal cord due to methionine deficiency. Methionine is needed for the production of myelin. Myelin deficiency causes demyelination and gliosis of the grey column, which is further aggravated by the neurotoxicity of methylmalonic acid.

Vitamin B12 is first bound within the duodenum and jejunum to intrinsic factor produced by gastric parietal cells and is then absorbed in the terminal ileum. Our body stores 2 to 3 mg of vitamin B12 in the liver (sufficient for 2 to 4 years).

The most common cause of vitamin B12 deficiency is pernicious anemia caused by autoimmune gastric atrophy and leading to intrinsic factor production reduction. 8 Vitamin B12 deficiency may also develop following gastrectomy, ileal resection or ileitis of any cause. The other causes of impaired vitamin B12 absorption include Zollinger-Ellison syndrome, Blind loop syndrome, fish tapeworm infestation and pancreatic insufficiency.

Prevalence of megaloblastic anemia reported by various Indian studies ranges from 02% to 40%.[4-6] Overt neurological manifestations of megaloblastic anemia are well documented but there is paucity of data on the existence of subclinical neurological manifestations in Megaloblastic anemia. Hence, we have undertaken this study, to assess the clinical profile of the patients with the megaloblastic anemia.

OBJECTIVES:

To study the clinical profile, upper gastro-intestinal endoscopic findings & nerve conduction study of megaloblastic anaemia.

MATERIALS AND METHODS

This was a facility based prospective observational study, protocol of which was approved by the Institutional Ethical committee of the medical college and is consistent with all the ethical standards. Written informed consent was taken from all study subjects.

Megaloblastic anemia cases diagnosed by using any of the following methods or in combination as per availability a) Serum Vit.B12 levels, or b) Bone Marrow studies or c) Hemogram with PBS & willing to participate in the study were included. All consecutive patients fulfilling inclusion and exclusion criteria were taken up for the study until the required sample size was fulfilled. Sampling method used was universal. Study was carried out over a period of 1.5 years from December 2020 to June 2022.

Exclusion criteria were Patients <18 years, pregnant and lactating women, patients already on vit.B12 and/or folic acid supplements, patients who have been already transfused, patient with decompensated ALD, patients of iron deficiency anemia, hemolytic anemia, sickle cell anemia, thalassemia, dimorphic anemia. Detailed history regarding onset and progression of symptoms. Then all the patients were subjected to lab investigations such as Upper Gastro intestinal Endoscopy, Fundus Examination, NCV examination, LFT, RFT, hemogram, retic count, ultrasonography, MRI Brain, urine analysis, thyroid function test, homocysteine levels etc. Considering the confidence level 95%=z (which is 1.96) with error of margin 10%. Where p is prevalence of cases from previous study that is 40%[4-6] and q is 100-p=60 Thus, using formula sample size(n)=z2 PQ/E2 n=1.96 x 1.96 x 40 x 60/(10x10) n=92.1984=93. We have rounded this to nearest whole number i.e. 100.

Data was collected in pre-structured proforma (Annexure I- case record sheet) which was pilot tested and after ensuring it's validity. Quantitative data was then tested by Mean and Standard Deviation, difference between more than two means tested by 'ANOVA' test. P value <0.05 was considered significant.

RESULTS:

In the current study, majority 29 (29%) of the cases were from the age group of 31-40 years followed by 26 (26%) from the age group of <30 years and least i.e. 09 (9%) from the age group of >60 years with the mean age of 40.89 ± 14.89 years. Male predominance was seen in the current study with 68% males & 32% females. Majority of study population had been taking mixed diet (63%). Mean serum Ferritin and Vit.B12 level was 937.29 ± 1056.10 and 116.44 ± 19.24 respectively. H. Pylori gastritis was present in 17 cases. (Table 1)

Table 1. Distribution of patients according to baseline characteristics.

Baseline characteristic		Frequency (no.)	Percentage (%)
Age groups	<30	26	26

	31-40	19	19
	41-50	29	29
	51-60	17	17
	>60	09	09
Gender	Male	62	62
	Female	38	38
Type of diet	Mixed	63	63
	Vegetarian	37	37
Serum Ferritin	Mean + SD	937.29	1056.10
Serum Vit.B12	Mean + SD	116.44	19.24
H. Pylori gastritis	Yes	17	17

In the present study, common complaints amongst study population were generalized weakness (89%) followed by breathlessness on exertion (67%), lower limb edema (41%) and anorexia (37%). (Chart 1)

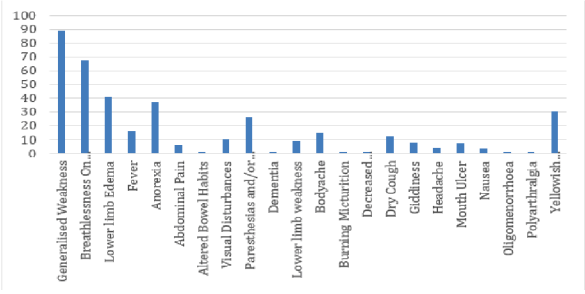

Chart 1. Distribution of patients according to presenting complaints.

Neurological examination of study population revealed that abnormal vibration/ proprioception was observed in 31% of the study population, loss of deep tendon reflexes in 28 % and gait disturbances in 16 patients. (Table 2)

Table 2: Distribution of patients according to neurological findings.

Neurological Findings	Frequency	Percent
Abnormal Vibration / Proprioception	31	31
Abnormal pinprick sensation	8	8
Gait Disturbances	16	16
Loss of Deep tendon Reflexes	28	28

In our study, Mean Hemoglobin, Hematocrit, MCV, RBC Count, WBC Count and Platelet Count was 6.01 ± 2.18, 16.48 ± 8.43, 110.1 ± 23.9, 2.53 ± 2.46, 4517 ± 1729,

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121876 ± 87453 respectively. (Table 3) On upper GI scopy we have seen gastritis (17%) was observed amongst 17% study population, duodenitis in 7%, esophagitis in 4% and normal findings in 64%. (Chart 2)

Table 3. Mean CBC parameters amongst study population.

Mean CBC parameters	Mean	Std. Deviation
Hemoglobin (gm/dl)	6.01	2.18
Hematocrit (%)	16.48	8.43
MCV (fl)	110.1	23.9
RBC Count (x106/µl)	2.53	2.46
WBC Count	4,517	1,729
Platelet Count (cells/ µl)	121,876	87,453

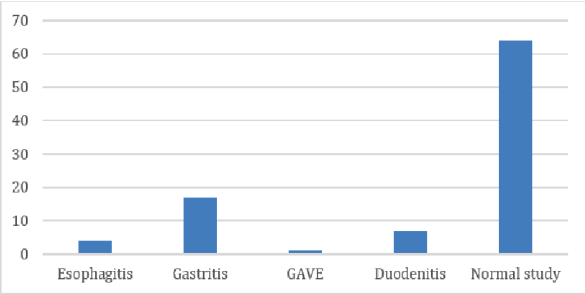

Chart 2. Upper GI Scopy findings amongst study population.

Anisopoikilocytosis (86%) was the commonest peripheral blood smear findings amongst study population followed by macrocytic picture (79%), microcytosis in 57%, macro ovalocytosis in 55% and hyper segmented neutrophils were present in 31%. Normocytic blood picture was seen among 51%. (Chart 3)

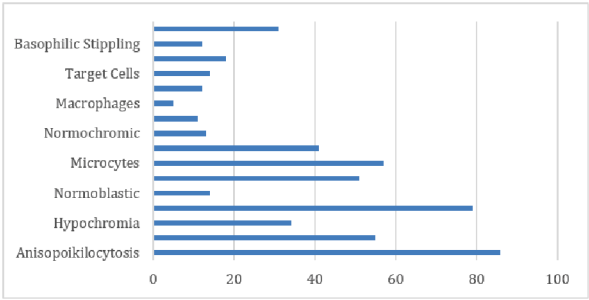

Chart 3. Peripheral blood smear findings amongst study population.

Out of 100, 40 patients had abnormal NCV findings. Out of which 29 patients (72.5%) patients had axonal neuropathy, 10 (25%) patients had demyelinating neuropathy and 1 (2.5%) had axonal as well as demyelinating neuropathy. (Table 4)

Table 4. NCV study Findings.

Cases	Axonal neuropathy	Demyelinating neuropathy	Mixed	Normal
Frequency	29	10	01	60
Percentage	72.5	25	2.5	60

DISCUSSION:

The prevalence of megaloblastic anemia (MA) reported by various Indian studies ranges from 02% to 40%.93-98 MA remains the commonest cause of macrocytic anemia and pancytopenia.

In the present study, 31 to 40 years (29%) was the most common age group amongst study population followed by less than 30 years (26%) with the mean age of 40.89 ± 14.89 years. This finding was comparable with the study conducted by Navjyot Kaur et al.[7] in which the mean age of MA patients was 36.15 ± 17.6 years and the Highest incidence of MA was noted in the age group between 16 and 20 years.[7] In India, it affects all age groups and is possibly related to an inadequate diet.[8,9] There was male predominance (62%) amongst study population. This is in line with the Navjyot Kaur et al.[7] This observation may be due to the fact that females tend to be more iron deficient and in presence of iron deficiency, the MCV won't rise above 100 fL even with co-existent Vit B12 or folic acid deficiency.

In the present study, weakness/fatigue (89%) was the most common clinical features followed by breathlessness on exertion (67%), edema (41%) and anorexia (37%). These findings were comparable with Navjyot Kaur et al.[7] in which easy fatigability was the commonest symptom (87.5%) followed by anorexia (70%), breathlessness on exertion (60%) and palpitations (47.5%).[7] This finding was also in agreement with Pandya and Patel.[10] in which symptoms of anemia such as weakness, fatigue, exertional dyspnea, palpitations, dizziness, and aches and pains all over the body are commonly present; These symptoms are comparable with other Indian studies.[11,12] Majority of study population had mixed diet. This finding was comparable with the study conducted by Navjyot Kaur et al.[7]

In this study, anisopoikilocytosis (86%) was the most common peripheral blood smear findings amongst study population followed by macrocytosis (79%), microcytosis (57%), macro ovalocytes (55%) and normocytic (51%) picture. These findings were comparable with the study conducted by Navjyot Kaur et al.[7] in which hyper segmented neutrophils were noted in 57.5% (23/40) patients while ovalo-macrocytosis was documented in 45% (18/40) patients.108

In the present study, Gastritis (17%) was the most common upper GI Scopy findings amongst study population followed by Esophageal varices (7%) Esophagitis (4%). This finding was in agreement with the study conducted by Navjyot Kaur et al.[7], in which Fourteen (14/40) patients tested positive for Helicobacter Pylori infection. Gastric atrophy, malabsorption and deficiency of intrinsic factors (required for vitamin B12 absorption) are the reasons for developing MA.

In the present study, Mean Hemoglobin, Hematocrit, MCV, RBC Count, WBC Count and Platelet Count was 6.01 ± 2.18, 16.48 ± 8.43, 110.1 ± 23.9, 2.53 ± 2.46, 4517 ± 1729, 121876 ± 87453 respectively. This finding was comparable with the study conducted by Navjyot Kaur et al.[7], in which Mean Hb in MA patients was 6.39 g/dL (± 1.95) and MCV recorded was 117.5 fL (± 5.082) with a mean red cell distribution width (RDW) of 21.53 (± 4.63). 108

The most common sensory neurological finding was in the form of abnormal vibration/ proprioception (31%) followed by abnormal pin prick sensation (8%). The most common motor finding was loss of deep tendon reflexes (28%) followed by gait disturbances (16%). One study done by Edward Hilton et al.[13] comparing neurological manifestations of 369 patients found that 45% patients had paresthesia's and numbness. Whereas motor involvement in the form of gait ataxia in 12.3%123 Another study by Burhan Turgut et al.[14] which included nerve conduction study in megaloblastic anemia which included 128 patients found that 54% had abnormal vibration / proprioception. Abnormal pin prick sensation was found in 21% of patients. Motor involvement in the form of gait disturbance was found in 32% patients and loss of deep tendon reflexes was seen in 10% of patients.

Out of 100, 40 patients had abnormal NCV findings. Out of which 29 patients (72.5%) patients had axonal neuropathy, 10 (25%) patients had demyelinating neuropathy and 1 (2.5%) had axonal as well as demyelinating neuropathy. This was consistent with study done by Puri V. et al.[15] study comparing NCV finding of megaloblastic anemia which found that 76% of the patients had axonal peripheral neuropathy and 24% had demyelinating neuropathy.

CONCLUSION:

From this study we can conclude that the megaloblastic anemia has wide spectrum of clinical manifestations and is more commonly present in middle aged males. It is more frequently found in the study population which was having mixed diet, stating the need of further evaluation for the causes of malabsorption with the help of investigations like upper gastrointestinal endoscopy. Besides bedside neurological examination, further Nerve conduction study examination is helpful for the evaluation of neuropathies and studies can be considered to monitor the progression of disease and understanding of the varied spectrum of neurological manifestations of megaloblastic anemia.

Declaration: 3
There was no source of funding in our study and there was no any conflict of interest.

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