https://doi.org/10.29309/TPMJ/2023.30.10.7735

The Professional Medical Journal
www.theprofesional.com
2023, Volume, 30 Issue, 10

ORIGINAL ARTICLE

Study of clinico-pathological profile in patients with megaloblastic anemia

Muhammad Bilal Ghafoor[1], Faiza Sarwar[2], Sana Khan[3], Shameela Majeed[4], Farah Yasmeen[5], Misbah Ashraf[6], Sumrah Abbasi[7], Abdus Sami[8], Nimra Riyaz[9]

Article Citation: Ghafoor MB, Sarwar F, Khan S, Majeed S, Yasmeen F, Ashraf M, Abbasi S, Sami A, Riyaz N. Study of clinico-pathological profile in patients with megaloblastic anemia. Professional Med J 2023; 30(10):1270-1274. https://doi.org/10.29309/TPMJ/2023.30.10.7735

ABSTRACT… Objective: To determine the clinico-pathological profile in patients with megaloblastic anemia. **Study Design:** Cross Sectional study. **Setting:** Department of Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. **Study Period:** June 2022 to July 2023. **Material & Methods:** The study subjects were 100 patients suffering from megaloblastic anemia. Using convenient sampling technique, blood samples were analyzed for complete blood count (CBC) and peripheral blood morphology followed by serum B12, serum and red cell folate levels and the bone marrow examination. SPSS version 23 was utilized to analyze the data. The results of variables including age, gender, clinical features and hematological profile were analyzed. **Results:** Out of 100 diagnosed patients of megaloblastic anemia, 51 (51%) were males, whereas 49 (49%) were females. Anemia alone was present in 18(18%), 11(11%) had anemia along with leucopenia, 14 (14%) faced anemia with thrombocytopenia, 57(57%) had pancytopenia while 16(16%) were pallor. Moreover, 01(01%) of the studied patients presented with fatigue and bleeding while 02 (2%) got weight loss. 10(10%) had fatigue accompanying with Pallor. 19(19%) faced pallor associated with fatigue and bleeding. 14(14%) had pallor accompanying with fatigue, Jaundice and weight loss. 37(37%) had pallor along with fatigue, bleeding, weight loss and jaundice. **Conclusion:** Males were more frequently affected by megaloblastic anaemia than females. The frequent clinical features appreciated were fatigue, pallor, weight loss, bleeding, and jaundice. Common cytopenia was pancytopenia, followed by bicytopenia.

Key words: Clinico-pathological Profile, Hematological, Megaloblastic Anemia.

INTRODUCTION

Megaloblastic anemia is regarded as presence of macrocytosis in the peripheral blood along with megaloblasts and precursor cells in the bone marrow.[1] Megaloblasts possess morphological and functional abnormalities due to the deficiency and abnormal function of vitamin B12 or folate.[2] A megaloblast bears characteristic chromatin array and increased asynchrony of nuclear and cytoplasm with reasonably immature nucleus for cytoplasmic hemoglobinization.[3] Megaloblastic anemia is prevalent in the developing countries including Pakistan.[4] The pervelance of this anemia vary from 02% to 40% in various studies. It is charecterized with macrocytic anemia and pancytopenia with varied clinical and pathological presentation leading to neuro-developmental deterioration.[5] Deficiency of cobalamin and folate or conditions causing impaired DNA synthesis results in megaloblastic anemia. It may be inherited or acquired abnormalities. Dietary deficiency of (vitamin B12) happens less often than deficiency of folate. Due to insufficient intake, malabsorption of vitamin B12, intrinsic factor or parietal cells deficiency, ileac malabsorption in patients with enteritis or ileac resection, biologic competition comprising bacterial overgrowth and tapeworm infestation.[6] Parasitic infections like Diphyllobothriumlatum (Fish tapeworm), gastrectomy, and drugs including oral contraceptives, anticonvulsants, alcoholism and vegetarian diet are common causes of vitamin B 12 deficiency.[7] Vitamin B12 deficiency also causes gastrointestinal, neurological and psychiatric disorders and plays a vital role in myelination of nerves by acting as a coenzyme in the methylmalonyl CoA mutase reaction.[8] Main causes of folate deficiency are reduced intake

1. MBBS, M.Phil, CHPE, Ph.D Scholar, Associate Professor Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
2. MLT, M.Phil, Ph.D, Medical Technologist Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
3. MBBS, FCPS, Medical Officer Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
4. MBBS, M.Phil, CHPE, Assistant Professor Pathology, Watim Medical & Dental College, Rawat, Pakistan.
5. MBBS, Medical Officer Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
6. MLT, Medical Technolopgist Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
7. MBBS, Medical Officer Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
8. MBBS, Medical Officer Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.
9. MLT, M.Phil, Medical Technologist Pathology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan.

Correspondence Address:
Dr. Muhammad Bilal Ghafoor
Department of Pathology,
Sheikh Zayed Medical College/
Hospital, Rahim Yar Khan, Pakistan.
drbilal.ryk@gmail.com

Article received on: 07/06/2023
Accepted for publication: 22/08/2023

from diets lacking folate, alcoholism, decreased absorption of nutrients in the small bowel, e.g. celiac disease, inflammatory bowel disease, tropical sprue and increase demand in pregnancy, hemolytic anemia, and puber.[9] Cobalamin and folate are cofactors in several important metabolic pathways in the cell. Folate deficiency during pregnancy can result into neural tube defects and various other developmental disorders in the fetus.[10] it is also related with low weight birth and delivery of premature babies.[11] Clinical features of megaloblastic anemia are varying from symptoms of severe anemia like fatigue, anorexia to neurological and neuropsychiatric manifestations.[3] Finding of megaloblastic anemia include increased mean corpuscular volume (MCV) on complete blood count.[12] After skin hyperpigmentation and jaundice, pallor was the commonest finding on general examination.[13] In young children symptoms include poor and delayed growth, difficulty in movement, delayed developmental, irritability, degeneration, hypotonia and involuntary movements.[14] Deficiency of vitamin B12 and folate are crucial for the synthesis of pyrimidine and purine nitrogenous bases during DNA replication.[15] It is a general belief that an increase in severity of this anemia results in development of thrombocytopenia subsequently leucopenia and pancytopenia.[16]

Considering the available resources and limited facilities, this study was intended to correlate and compare the clinical and pathological parameters in diagnosed cases of megaloblastic anemia.

OBJECTIVE

To determine the clinico-pathological profile in patients with megaloblastic anemia.

MATERIAL & METHODS

This cross-sectional study was conducted on 100 diagnosed patients of megaloblastic anemia at Pathology Department of Sheikh Zayed Medical College/Hospital Rahim Yar Khan from June 2022 to July 2023 after approval from ethical committee (245/IRB/SZMC/SZH). The diagnosis of megaloblastic anemia was confirmed by bone marrow examination and blood tests including peripheral blood film, serum B12, serum and red cell folate levels. Variables like age, gender, clinical and pathological profile including hemogram, RBC indices, morphology of peripheral blood cells and bone marrow findings were the part of the study. The data was analyzed using SPSS version 23.

RESULTS

Total 100 patients of megaloblastic anemia were the part of this study. The mean age in patients was 21±14 years.

Gender	Frequency (%)
Male	51 (51.0%)
Female	49 (49.0)
Total	100 (100.0)

Table-I. Gender wise distribution of study subjects

Clinical Findings	Frequency (%)
Pallor	16 (16%)
Fatigue	01 (1%)
Bleeding	01 (1%)
Weight Loss	02 (2%)
Fatigue + Pallor	10 (10%)
Pallor+ Fatigue + Bleeding	19 (19%)
Pallor+Fatigue+Jaundice + weight loss	14 (14%)
Pallor+ Fatigue+ Bleeding, Weight loss + Jaundice.	37 (37%)
Total	100 (100%)

Table-II. Clinical findings of study subjects

Hematological Features	Frequency (%)
Anemia	18 (18%)
Anemia+Leucopenia	11 (11%)
Anemia+Thrombocytopenia	14 (14%)
Pancytopenia	57 (57%)
Total	100 (100%)

Table-III. Pathological features of study subjects

Variable	Gender	N	Mean±SD	P-Value
Age	Male	51	22.3±15.7	0.360
	Female	49	19.7±12.9	0.358
Hb	Male	51	7.51±2.5	0.54
	Female	49	7.81±2.4	0.54
TLC	Male	51	11.5±40.05	0.34
	Female	49	5.9±8.5	0.33
Platelets	Male	51	96.39±111.2	0.39
	Female	49	116.41±121.1	0.39
MCV	Male	51	91.62±9.6	0.25
	Female	48	93.61±7.5	0.25
MCH	Male	51	31.59±3.8	0.06
	Female	49	33.41±5.8	0.06
MCHC	Male	51	34.92±3.3	0.20
	Female	49	36.13±5.8	0.21

Table-IV. Descriptive statistics of variables age, Hb, TLC, Platelets, MCV, MCH, and MCHC

DISCUSSION

Megaloblastic anemia is a pathological non-

malignant disorder due to defect in DNA synthesis happening in hematpoietic cells of the bone marrow. Current study involved 100 patients of megaloblastic anemia. Megaloblastic anemia was present in 51% males and 49% females. A study from peshawar, pakistan reported analogous findings.[17] Present study reported clinical findings including pallor (16%), fatigue (01%), bleeding (01%), weight loss (02%), while (10%) of the study subjects presented with fatigue and pallor, (19%) with pallor, fatigue and bleeding, (14%) pallor, fatigue, Jaundice and weight loss, and pallor, (34%) fatigue, bleeding, weight loss and Jaundice. Pathological features in the present study showed anemia alone (18%), anemia with leucopenia (11%), anemia associated with thrombocytopenia (14%) and 57% have pancytopenia. In comparison a study at India revealed the gender wise distribution discovered the male preponderance. Pallor (75.72%) was the most common clinical feature in thrombocytopenia patients, followed by generalized weakness (68.93%), dyspnoea (36.89%), fever (29.12%), weight loss (26.21%), hepatomegaly (23.30%), splenomegaly (18.44%), lymphadenopathy (7.76%), bone tenderness (7.76%), and bleeding manifestations (4.85 %). Megaloblastic anemia (47.6%) was most commonly seen on peripheral smear followed by normocytic normochromic picture.[18]

Another study from India reported megaloblastic anemia in 18% of patients.[19] Similar study reported male to female ratio in megaloblastic anemia patients as 1.4:1 with generalised weakness 81% , fever 38.75%, shortness of breath 37.5% and anorexia 35% and common clinical finding was pallor 96.25%, hyperpigmentation 37.5% and jaundice 32.5%. In present study fever and hyperpigmentation is not detectable. In pathological features anemia is found in 17.50% cases, anemia with leucopenia in 3.75%, anemia in association with thrombocytopenia in 26.25% cases and pancytopenia in 52.50% cases.[20] Another study in comparison reported 66% males and 34% females. Most common clinical features in the study were fatigue (96%), anorexia (64%), pallor (100%), skin pigmentation (32%), weakness (15%), jaundice (12%), weight loss(10%). In pathological features pancytopenia was detected in 48% of the patients, anemia with leucopenia in 4%, anemia accompanying with thrombocytopenia in 12% and isolated anemia in 36% of the studied patients.[21] A research done by Tariq Aziz in pakistan in 2010 showed that the megaloblastic anemia was discovered in 59% females while males made up rest of the 41%. The common clinical features include pallor 98%, weakness 98%, shortness of breath 88% and Jaundice 30%. In pathological features 40.9% cases had pancytopenia, 37% cases possessed bicytopenia, 22.1% cases were with isolated anemia.[22]

Another study conucted in 2018 at Jammu region reported that among the study participants 39.21% were males and 60.79% were females. Clinical examination of this study showed pallor in 86.24% cases. Fever was seen in 74.50 % of patients and bleeding was noted in 13.72% of study subjects. Pathological features included anemia in 31.38% cases, anaemia associated with leucopenia in 5.88% cases, anaemia accompanying with thrombocytopenia in 27.45% and pancytopenia in 35.29% of the studied patients.[23]

CONCLUSION

Megaloblastic anemia is common among males compared with females Fatigue, pallor, weight loss, bleeding and jaundice were often seen clinical features. Pancytopenia and bicytopenia were the two most frequent cytopenias. Early diagnosis and prompt addressal of the illness with vitamin B12, folate and diet plan can protect the patients from devastating sufferings.

REFERENCES

1. Oltean, A., Chincesan, M.I., Baghiu, M.D., Molnar, E., and Marginean, C.O. **Megaloblastic anemia in children: Case series from a single institution and literature review.** RO J Pediatr. 2018; 67(4):171-76. doi: 10.37897/rjp.2018.4.2

2. Jain, M., And Dolai, T.K. **ABC of the peripheral smear.** J Indian Med Assoc. 2020; 118(11): 19-23.

3. Torrez, M., Chabot-Richards, D., Babu, D., Lockhart, E., and Foucar, K. **How i investigate acquired**

megaloblastic anemia. Int J Lab Hematol. 2022 Apr; 44(2):236-247. doi: 10.1111/ijlh.13789. Epub 2022 Jan 3.

4. Younas, A., Younas, M., Ijaz, A., Haroon, Z.H., and Basharat, N. **Rogers syndrome-thiamine responsive megaloblastic anemia syndrome: Case Report.** Pak j pathol 2022; 33 (2): 69-72. https://doi.org/10.55629/pakjpathol.v33i2.711.

5. Jain, S., and Bhagwat, GP. **Pancytopenia: Clinical and haematological profile from a tertiary care centre in central India.** National J Lab Med 2022; 11(2):05-10. DOI: 10.7860/NJLM/2022/45917:2588.

6. Sobczyńska-malefora, A., Delvin, E., Mccaddon, A., Ahmadi, KR, and Harrington, DJ. **Vitamin B12 status in health and disease: A critical review. Diagnosis of deficiency and insufficiency clinical and laboratory pitfalls.** Crit Reviews Clin Lab Sci 2021; 58(6):399-429. https://doi.org/10.1080/10408363.2021.1885339.

7. Khan, M.I., Munir, A.H., and Fatima, S.H. **Pattern of clinical and hematological profile in patients diagnosed as megaloblastic anemia in a tertiary care centre.** TPMJ 2019; 26(6): 934-938. https://doi.org/10.29309/TPMJ/2019.26.06.3600.

8. Calderón‐Ospina, C.A., and Nava‐Mesa, M.O. **B Vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin**. CNS neuroscience & therapeutics . CNS Neurosci Ther. 2020; 26:5-13. doi.org/10.1111/cns.13207.

9. Powers, J.M. **Nutritional anemias. In Lanzkowsky's Manual of Pediatric Hematology and Oncology.** (Elsevier), 2022;61-80. https://doi.org/10.1016/B978-0-12-821671-2.00024-6.

10. Wang, L., and Ren, A. **Linking apoptosis and caspases in fetal neural tube defects.** In Factors Affecting Neurodevelopment. (Elsevier). 2021; 73-82. https://doi.org/10.1016/B978-0-12-817986-4.00007-9.

11. Obeid, R., Holzgreve, W., and Pietrzik, K. **Folate supplementation for prevention of congenital heart defects and low birth weight: An update.** Cardiovasc Diagn Ther. 2019 Oct; 9(Suppl 2): 424-33. doi: 10.21037/cdt.2019.02.03

12. Khan, M.I., and Waqar, S. **Sensitivity of mean corpuscular volume in detecting megaloblastic anemia.** Pak J Pathol. 2018: 29(2):34-36.

13. Belabbes, F., Houda, Y., Al Bouzidi, A., Bennani, Y., and Ahnach, M. **Polyneuropathy, Organomegaly, Endocrinopathy, M-protein, and Skin Changes (POEMS) Syndrome and Idiopathic Portal Hypertension: A Rare Association.** Cureu 2022; 14: 2-8. DOI: 10.7759/cureus.24923.

14. Obeagu, E.I., Babar, Q., and Obeagu, G.U. **Megaloblastic Anaemia-A Review.** Int. J. Curr. Res. Med. Sci. 2021; 7(5): 17-24. DOI: http://dx.doi.org/10.22192/ijcrms.2021.07.05.004.

15. Guéant, J.-L., Guéant-Rodriguez, R.-M., Kosgei, V.J., and Coelho, D. **Causes and consequences of impaired methionine synthase activity in acquired and inherited disorders of vitamin B12 metabolism.** Critical Reviews Bio Mol BioL 2022; 57(2):133-155. doi.org/10.1080/10409238.2021.1979459.

16. Ashcheulova, T., and Gerasimchuk, N. **Clinical blood analysis: Methodical instructions for English medium students.** 2021.

17. Munir, A.H., Khan, M.I., and Rahman, S. **Frequency of hematological disorders in Peshawar by bone marrow aspiration and trephine biopsy examination.** Pak J Surg 2019; 35(3): 230-233.

18. Kanetkar, S., Patil, N., and Nagar, V. **Clinico-Hematological Study of Thrombocytopenia on the Basis of Bone Marrow Examination in a Tertiary Care Hospital.** Journal of Pharmaceutical Research International 2022; 2(19): 24-32.

19. Deepankar, P., Roshan, R., Gupta, H.K., and Buxi, G. **Relative prevalence of vitamin B12 and folic acid in megaloblastic anemia and its clinical–etiological profile in a tertiary care center.** Int J Sci Study 2018; 6(3):23-30.

20. Momin, M., Reddy, K., Prusty, S., and Aluri, A. **Clinical, haematological and bone marrow aspiration evaluation in Megaloblastic anemia-study of 80 cases in a tertiary care hospital.** Telangana. Int. J. Curr. Res. Biol. Med. 2017; 2(8): 1-7. DOI:10.22192/ijcrbm.

21. Pandya, H.P., and Patel, A. **Clinical profile and response in patients with megaloblastic anemia.** Int J Med Sci Public Health 2016; 5(2):304-306..

22. Aziz, T., Ali, L., Ansari, T., Liaquat, H.B., Shah, S., and Ara, J. **Pancytopenia: Megaloblastic anemia is still the commonest cause.** Pak J Med Sci 2010; 26(1):132-136.

23. Kaur, A., Raina, S.K., Kaul, K.K., and Mahajan, D. **Clinico-Hematological profile of megaloblastic anaemia in children in Jammu Region-One year retrospective study.** Ind J Bas App Med Res 2018; 7(2):424-429.

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	M. Bilal Ghafoor	Conception of study, Designing, Literature reveiw and supervision of study.	
2	Faiza Sarwar	Manuscript writing, Analysis and interpretation.	
3	Sana Khan	Collection of data, Literature review.	
4	Shameela Majeed	Literature review, Analysis & Critical reivew.	
5	Farah Yasmeen	Data collection, Methodology.	
6	Misbah Ashraf	Data collection, Experimentation.	
7	Sumrah Abbasi	Data analysis & Discussion.	
8	Abdus Sami	Data analysis & Discussion.	
9	Nimra Riyaz	Laboratory tests quality management & facilitation.