

Original Article

Unveiling the Spectrum of Megaloblastic Anemia: Insights from a Multifaceted Study at Abbas Institute of Medical Sciences, Muzaffarabad

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ABSTRACT

Background: This study aimed to determine the frequency of Megaloblastic Anemia cases presenting in the outpatient department (OPD) and wards of AIMS Hospital in Muzaffarabad, AJ&K.

Methods: Conducted at the Pathology department of Abbas Institute of Medical Sciences from May 2022 to October 2022, this case-control study analyzed 125 cases from OPD and wards. Patient interviews, venous blood sample collection, and complete blood picture (CP) analysis, including peripheral film (PF) tests and Vitamin B12 and folates levels reports, were conducted using a Hematology analyzer. Statistical analysis using SPSS version 25.0 was employed.

Results: Statistical analysis revealed a mean age of 3.656, with females having a higher frequency of Megaloblastic Anemia, especially during childbearing age. Males had a higher frequency in children and the elderly. The residential distribution showed a balance of village and city dwellers, whereas the patient category breakdown showed a higher frequency in the young age group.

Conclusion: The study highlighted Megaloblastic Anemia's serious public health significance, its causes, and the observed trends in the study population. Surgical interventions, particularly abdominal surgeries, were identified as potential contributors. Analyses of peripheral smears revealed varying degrees of anemia severity, with most cases being moderate. The study concluded that Megaloblastic Anemia is more common in females, especially during childbearing age, and in males, especially in children and the elderly. These findings highlight the importance of targeted interventions and nutritional education programs in addressing the specific demographic trends observed in this study population.

Keywords: Megaloblastic anemia, Pathology, EDTA, Case control study

INTRODUCTION

Megaloblastic anaemia, which is caused by the formation of aberrant nucleated red cells called megaloblasts in the bone marrow, arises from a dietary vitamin B12 or folic acid shortage, poor absorption, or increased needs. A substantial impairment in bone marrow activity results from a vitamin deficit of this kind. Marrow cells multiply but do not mature properly, and erythropoiesis is largely rendered ineffective(1, 2). Young red cells (reticulocytes) are less plentiful, anaemia sets in, and even platelets and granulocytes (white cells with granules in the cellular material outside the nucleus) are less numerous. Macrocytic anemia is caused by mature red cells that are generated from megaloblasts that are larger than usual(3). The characteristics of hemolytic anemia result from the defective and inadequate erythropoiesis, which is linked to an accelerated breakdown of red blood cells (caused by the destruction of red cells at a rate substantially greater than normal)(4, 5).

The formation of deoxyribonucleic acid (DNA) requires the red, cobalt-containing vitamin B12, which is present in animal food(6). Vitamin B12 deficiency causes DNA synthesis to be disturbed, which in turn affects the ability to produce red blood cells. In contrast to other vitamins, it is only produced by specific bacteria and molds in the lumen (first stomach chamber) of sheep and cattle when traces of cobalt are present in their feed(7, 8). Humans must consume food from an animal source to passively obtain vitamin B12.

Furthermore, unless a certain stomach secretion called intrinsic factor is present to bond with vitamin B12, this vitamin cannot be effectively absorbed from the human intestinal system(9, 10).

Pernicious anaemia, which primarily impacts elderly people, is the most frequent cause of vitamin B12 deficiency(11, 12). Due to an immunological mechanism including the formation of antibodies against the stomach lining, the stomach may not secrete intrinsic factor in people with this condition. Such antibodies' propensity to develop may run in families. Monthly injections of vitamin B12 are administered to patients with pernicious anaemia. Although oral vitamin therapy is a possibility, low absorption makes it ineffective(13).

Rare are further types of vitamins B12 deficiency. Complete vegetarians (vegans) whose diets are deficient in vitamin B12, people whose stomachs have been completely removed and who therefore lack a source of intrinsic factor, people infected with the fish tapeworm *Diphyllobothrium latum*, people with intestinal cul-de-sacs or partial obstructions where competition between the tapeworms and bacteria for vitamin B12 deprives the host, and people with primary intestinal diseases that affect the absorption capacity of the host are all at (ileum)(14, 15). These circumstances are also likely to lead to the development of further dietary deficiencies, such as those in iron and folic acid(16, 17).

Folic acid shortage causes blood abnormalities that are comparable to those that occur with vitamin B12 deficiency. The nutrient folic acid, generally known as folate, is present in green vegetables but is also produced by specific gut flora. A very inadequate diet or, as previously indicated, persistent intestinal malabsorption are the usual causes of deficiency(18, 19). The demand for this vitamin rises significantly during pregnancy. In cases of chronically accelerated red cell synthesis, there is also an increase in demand. Some individuals who take anticonvulsant medications also experience this form of insufficiency, and there is some evidence to suggest that vitamin absorption may be compromised in these circumstances(20, 21).

Neurological signs of vitamin B12 insufficiency are visible. Paresthesia and balance issues are the main signs and symptoms(22). Peripheral neuropathy in patients with vitamin B12 deficiency can cause lancinating symptoms, which typically affect the lower extremities. Less commonly, optic atrophy-related visual problems may start to occur. When the Romberg test is positive, (Romberg test positive denotes sensory ataxia as the cause of postural imbalance sustaining balance standing in an upright position) the clinical examination typically reveals a loss of vibratory sensation and proprioception(23). Less frequently Babinski reflex, hyporeflexia, and clonus. There are other psychiatric disorders, one of which is a sort of dementia. After replacement therapy, these neurological conditions might not fully recover(24, 25).

MATERIAL AND METHODS

This study was conducted at the Pathology department of Abbas Institute of Medical Sciences (AIMS), the largest civil and teaching hospital of AJ&K, using a case-control study design. It took place from May 2022 to October 2022. Venous blood samples were collected in EDTA vials. Patients of all age groups and both genders, males and females, attending the General OPD or in indoor settings during this period, were included (26). A total of 125 blood samples from clinically suspected cases of anemia were collected. The inclusion criteria were individuals attending the OPD or admitted to the wards suspected of having anemia. The exclusion criteria included hemolyzed, insufficient, unlabeled, or clotted blood samples. The data was analyzed using SPSS software version 25.0(27, 28).

RESULTS

Demographic Characteristics and Descriptive Statistics of Study Participants

The descriptive statistics provide valuable insights into the study population's characteristics across various variables. The 125 participants' average age is 3.656 years, with a median of 4.000 years, indicating a slightly right-skewed distribution. In terms of gender, the mean is 1.704, where 1 represents male and 2 represents female. The skewness of -0.905 indicates a mild leftward skewness in the gender distribution, indicating a slight female predominance in the sample. The mean for patients' residential areas is 1.488, with 1 representing the village and 2 representing the city. The skewness of 0.049 indicates a symmetrical distribution. Finally, the mean of the patients' category variable is 1.992, with 1 corresponding to CHILD, 2 to YOUNG, and 3 to OLD. The skewness of 0.010 indicates a near-normal distribution. These statistics provide a concise overview of the central tendency, variability, and distribution shape within each variable, aiding in the understanding of the demographic characteristics of the study cohort.

		AGE GROUPS	Gender	Patients' Residential area	Patients Category
N	Valid	125	125	125	125
	Missing	0	0	0	0
Mean		3.6560	1.7040	1.4880	1.9920
Median		4.0000	2.0000	1.0000	2.0000
Mode		3.00	2.00	1.00	2.00
Std. Deviation		1.23852	.45833	.50187	.67795
Skewness		.140	-.905	.049	.010
Std. Error of Skewness		.217	.217	.217	.217

Table-1: Demographic Characteristics and Descriptive Statistics of Study Participants

Gender Distribution of Study Participants

The data presented here shows the frequency of megaloblastic anemia cases reported at Muzaffarabad's Abbas Institute of Medical Sciences. Blood samples were collected from both the general outpatient department (OPD) and indoor settings from 125 patients suspected of anemia. SPSS software version 25.0 was used for the statistical analysis.

According to the findings, 29.6% of the 125 cases were male and 70.4% were female. The patients' ages are distributed as follows: 2.4% were under one year old, 15.2% were between one and twelve years old, 31.2% were between thirteen and twenty-five years old, 24.8% were between twenty-six and forty-one years old, 18.4% were between forty-two and sixty-five years old, and 8% were between 61 and eighty-five years old. In terms of residence, 51.2% of patients lived in villages, while 48.8% lived in cities. Furthermore, 23.2% were children, 54.4% were young, and 22.4% were elderly.

The study's findings show that females have a higher prevalence of megaloblastic anemia than males, with most females affected during childbearing age. The higher frequency in males is observed in children and elderly males. These findings highlight gender and age disparities in the prevalence of megaloblastic anemia, highlighting the importance of targeted interventions and public awareness campaigns.

When these findings are compared to those of other similar studies, they can provide valuable insights into the demographic distribution and prevalence of megaloblastic anemia in various populations, contributing to a more complete understanding of the condition.

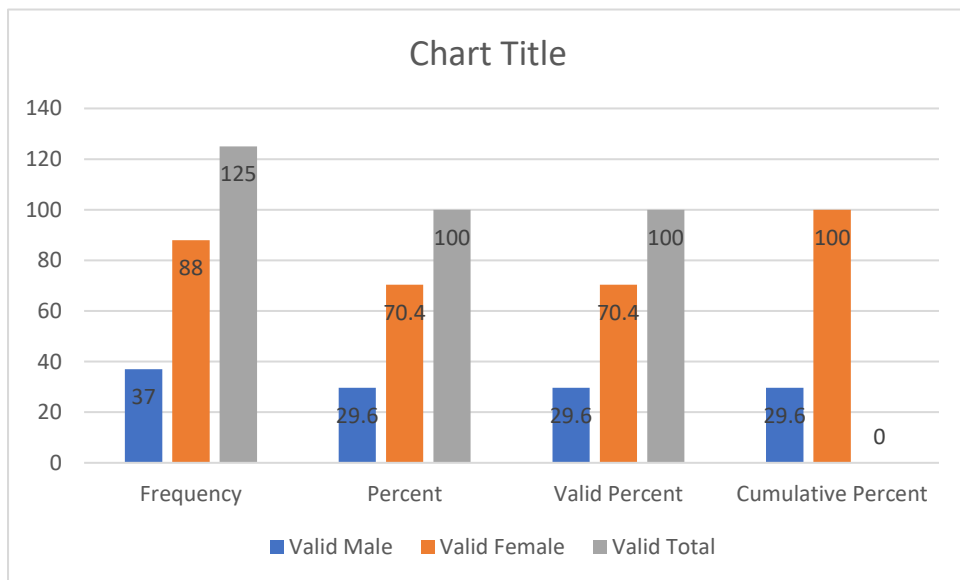


Fig.1. Gender Distribution of Study Participants

Age Distribution of Study Participants

The distribution of age groups in the 125-person study population reveals a diverse range of participants. The majority, or 31.2% of the sample, is between the ages of 13 and 25. Individuals aged 26 to 41 years make up 24.8% of the population. Participants aged 42 to 60 years old and those aged 1 to 12 years old account for 18.4% and 15.2% of the total, respectively. 2.4% of the sample

is made up of people under the age of one year. Finally, 8.0% of the population is between the ages of 61 and 85. The cumulative percentages show a progressive distribution across these age groups, emphasizing the study population's diverse age composition.

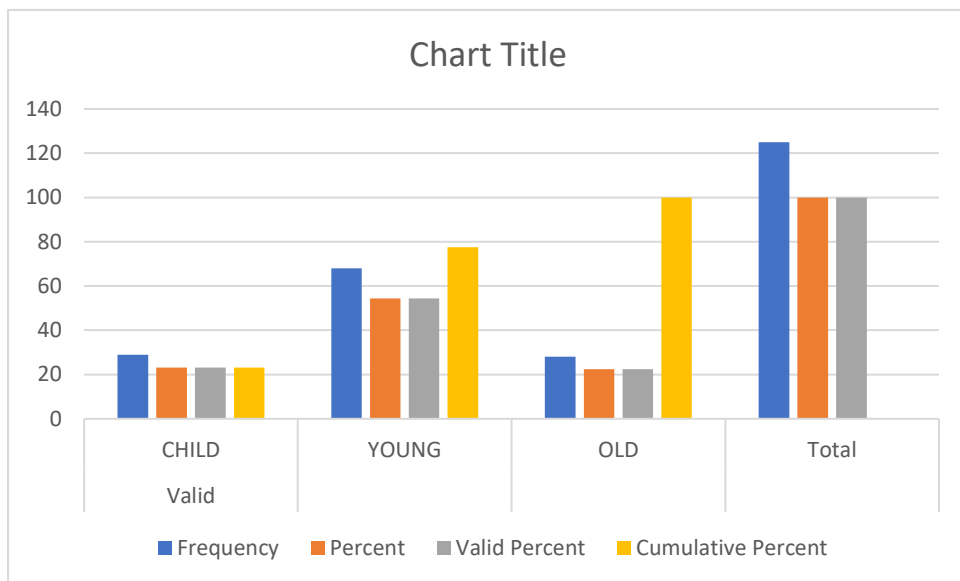


Fig.2. Age Distribution of Study Participants

Residential Area Distribution of Study Participants

The data shows a distribution of participants based on their residential locations, which are classified as "Village" and "City." The majority of people, 51.2%, live in villages, with the remaining 48.8% residing in cities. The cumulative percentages show that these two categories account for the entire study population of 125

participants. This suggests that the study has a relatively balanced representation of both urban and rural settings, allowing for a comprehensive analysis that takes into account the potential influence of different residential environments on the variables under investigation.

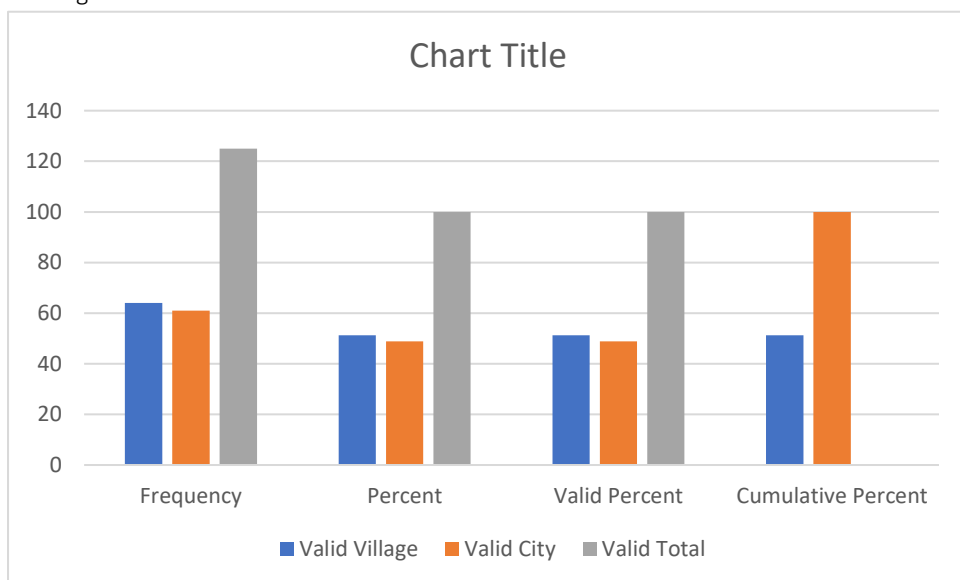


Fig.3. Residential Area Distribution of Study Participants

Age Category Distribution of Study Participants

The age distribution of participants, labeled "CHILD," "YOUNG," and "OLD," reveals a diverse composition within the study population. Individuals classified as "YOUNG" make up the largest segment, accounting for 54.4% of the total sample. Following that, the "CHILD" group accounts for 23.2%, while the "OLD" group accounts for 22.4%. The cumulative percentages

show that the entire study population of 125 people falls into one of these three age groups. This distribution enables a thorough examination of the research variables at various stages of life, ensuring a diverse representation of ages in the study and providing insights into potential age-related patterns or differences in the outcomes under investigation.

Fig.4. Age Category Distribution of Study Participants

DISCUSSION

The study was conducted at Abbas Institute of Medical Sciences Muzaffarabad from May 2022 to October 2022 to determine the frequency of Megaloblastic Anemia cases presenting in the OPD and wards of AIMS Hospital Muzaffarabad, AJ&K. A total of 125 cases were studied, with 37 males (29.6%) and 88 females (70.4%). Most cases (48.8%) were found in people aged 31 to 45. Comparing our results with other similar studies, a study conducted in Pakistan found a higher frequency of Megaloblastic Anemia in females (70%) compared to males (30%)(29). Another study conducted in Saudi Arabia reported a higher frequency in males (54.4%) compared to females (45.6%) (30). However, these studies do not provide a direct comparison with our study in terms of age groups and residential areas.

Our research discovered that 61.2% of patients lived in cities, while 38.8% lived in villages. This suggests that the distribution of Megaloblastic Anemia cases is not consistent across residential areas. When compared to other studies, a study conducted in rural Pakistan discovered a higher prevalence of Megaloblastic Anemia (65%) in rural areas compared to urban areas (35%) (31).

29 (23.2%) of the patients were children, 68 (54.4%) were young, and 28 (22.4%) were elderly. This distribution indicates that Megaloblastic Anemia affects different age groups, with the young having the highest prevalence. In comparison, a study conducted in Pakistan discovered a similar distribution, with the highest prevalence observed in the 10-19 age group (42.5%).

Our study discovered a higher frequency of Megaloblastic Anemia in females than in males, with a similar distribution across age groups. This suggests that targeted interventions and public awareness campaigns should be directed toward females, particularly those of childbearing age and those undergoing abdominal surgery. Efforts should also be made to improve nutrition and address potential nutrient deficiencies, particularly in rural areas and among the elderly.

CONCLUSION

In conclusion, the study conducted at Abbas Institute of Medical Sciences Muzaffarabad from May 2022 to October 2022 discovered that females had a higher frequency of Megaloblastic Anemia than males. Most female cases were observed during childbearing age, whereas the highest frequency of male cases was found in children and older-aged males. The study also revealed that most Megaloblastic Anemia patients lived in villages and were undergoing abdominal surgeries, which could potentially lead to nutrient malabsorption and the development of the condition.

Organizing awareness seminars, securing government funds for food supplements, educating parents about childhood anemia, posting WHO guidelines in hospitals, providing doctors with comprehensive diet plans for childbearing age and post-surgery patients, and fostering coordination between health and food departments to fortify public food supplies with folic acid supplements are all recommendations for preventing this fatal disease. These targeted measures aim to raise public awareness, provide nutritional support, and collaborate on anemia prevention efforts.

REFERENCES

1. Sayar EH, Orhaner BB, Sayar E, NesrinTuran F, Küçük M. The frequency of vitamin B12, iron, and folic acid deficiency in the neonatal period and infancy, and the relationship with maternal levels. *Turk Pediatri Ars.* 2020;55(2):139-48.
2. Oo TH. Diagnostic difficulties in pernicious anemia. *Discov Med.* 2019;28(155):247-53.
3. Morkbak AL, Hvas AM, Milman N, Nexø E. Holotranscobalamin remains unchanged during pregnancy. Longitudinal changes of cobalamins and their binding proteins during pregnancy and postpartum. *Haematologica.* 2007;92(12):1711-2.
4. Margalit I, Cohen E, Goldberg E, Krause I. Vitamin B12 Deficiency and the Role of Gender: A Cross-Sectional Study of a Large Cohort. *Ann Nutr Metab.* 2018;72(4):265-71.
5. Khurshid A, Fatima S, Altaf C, Malik HS, Sajjad Z, Khadim MT. Thiamine Responsive Megaloblastic Anaemia, Diabetes Mellitus and Sensorineural Hearing Loss in a Child. *J Coll Physicians Surg Pak.* 2018;28(9):S169-s71.
6. Wickramasinghe SN. Diagnosis of megaloblastic anaemias. *Blood Rev.* 2006;20(6):299-318.
7. Zulfiqar AA, Andres E. Association pernicious anemia and autoimmune polyendocrinopathy: a retrospective study. *J Med Life.* 2017;10(4):250-3.
8. Wazir SM, Ghobrial I. Copper deficiency, a new triad: anemia, leucopenia, and myeloneuropathy. *J Community Hosp Intern Med Perspect.* 2017;7(4):265-8.
9. Green R, Datta Mitra A. Megaloblastic Anemias: Nutritional and Other Causes. *Med Clin North Am.* 2017;101(2):297-317.
10. Green R. Vitamin B(12) deficiency from the perspective of a practicing hematologist. *Blood.* 2017;129(19):2603-11.
11. Nykjaer A, Fyfe JC, Kozyraki R, Leheste JR, Jacobsen C, Nielsen MS, et al. Cubilin dysfunction causes abnormal metabolism of the steroid hormone 25(OH) vitamin D(3). *Proc Natl Acad Sci U S A.* 2001;98(24):13895-900.
12. Birn H, Fyfe JC, Jacobsen C, Mounier F, Verroust PJ, Orskov H, et al. Cubilin is an albumin binding protein important for renal tubular albumin reabsorption. *J Clin Invest.* 2000;105(10):1353-61.
13. Stouten K, Riedl JA, Droogendijk J, Castel R, van Rosmalen J, van Houten RJ, et al. Prevalence of potential underlying aetiology of macrocytic anaemia in Dutch general practice. *BMC Fam Pract.* 2016;17(1):113.
14. Wickramasinghe SN. Morphology, biology and biochemistry of cobalamin- and folate-deficient bone marrow cells. *Baillieres Clin Haematol.* 1995;8(3):441-59.
15. Tefferi A, Pruthi RK. The biochemical basis of cobalamin deficiency. *Mayo Clin Proc.* 1994;69(2):181-6.
16. Rusak E, Chobot A, Krzywicka A, Wenzlau J. Anti-parietal cell antibodies - diagnostic significance. *Adv Med Sci.* 2016;61(2):175-9.
17. Hesdorffer CS, Longo DL. Drug-Induced Megaloblastic Anemia. *N Engl J Med.* 2015;373(17):1649-58.
18. Gudgeon P, Cavalcanti R. Folate testing in hospital inpatients. *Am J Med.* 2015;128(1):56-9.

19. Lindenbaum J, Rosenberg IH, Wilson PW, Stabler SP, Allen RH. Prevalence of cobalamin deficiency in the Framingham elderly population. *Am J Clin Nutr.* 1994;60(1):2-11.
20. Toh BH. Diagnosis and classification of autoimmune gastritis. *Autoimmun Rev.* 2014;13(4-5):459-62.
21. Saif ur R, Zafar L, Imran T, Ghafoor A, Durrani AA, Ahmed TA. Frequency of intrinsic factor antibody in megaloblastic anaemia. *J Coll Physicians Surg Pak.* 2014;24(3):157-9.
22. Norman EJ, Morrison JA. Screening elderly populations for cobalamin (vitamin B12) deficiency using the urinary methylmalonic acid assay by gas chromatography mass spectrometry. *Am J Med.* 1993;94(6):589-94.
23. Porter FS, Rogers LE, Sidbury JB, Jr. Thiamine-responsive megaloblastic anemia. *J Pediatr.* 1969;74(4):494-504.
24. Devalia V, Hamilton MS, Molloy AM. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol.* 2014;166(4):496-513.
25. Bizzaro N, Antico A. Diagnosis and classification of pernicious anemia. *Autoimmun Rev.* 2014;13(4-5):565-8.
26. Borgna-Pignatti C, Azzalli M, Pedretti S. Thiamine-responsive megaloblastic anemia syndrome: long term follow-up. *J Pediatr.* 2009;155(2):295-7.
27. Stamm RA, Houghton LA. Nutrient intake values for folate during pregnancy and lactation vary widely around the world. *Nutrients.* 2013;5(10):3920-47.
28. Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med.* 2013;368(2):149-60.
29. Saif-ur-Rehman LZ, Imran T, Ghafoor A, Durrani AA, Ahmed TA. Frequency of Intrinsic Factor Antibody in Megaloblastic Anaemia. *prevention.* 8:9.
30. Margalit I, Cohen E, Goldberg E, Krause I. Vitamin B12 deficiency and the role of gender: a cross-sectional study of a large cohort. *Annals of Nutrition and Metabolism.* 2018;72(4):265-71.
31. Hariz A, Bhattacharya PT. Megaloblastic Anemia. *StatPearls.* Treasure Island (FL) ineligible companies. Disclosure: Priyanka Bhattacharya declares no relevant financial relationships with ineligible companies.: StatPearls Publishing
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