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Insights in Blood Disorders

The Demographic Characteristics Associated with Megaloblastic Anemia in Central Sudan

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ABSTRACT

Background: *Many populations in Sudan may have diets low in vitamin B12 and folate due to limited access to diverse foods due to the ongoing extended war. This study aimed to assess the demographic characteristics associated with megaloblastic anemia in central Sudan.*

Methodology: *This is a descriptive prospective study conducted in El-Obeid Teaching Hospital, El-Obeid, North Kordofan State, Sudan. Two hundred participants were selected for this study (100 were with clinical symptoms mimicking anemia, and 100 were*

apparently healthy volunteers as an internal control for comparing hematological parameters).

Results: *This study investigated 200 Sudanese individuals, aged 21 to 95 years, with a mean age and standard deviation of 52±16. Most of the study subjects were aged 60-69 years, followed by the age ranges 45-59 and 35-44 years, representing 22%, 21%, and 20%, respectively. Out of the 200 participants, 34% were males and the remaining 66% were females. B12 deficiency was detected in 84% of patients. Folate deficiency was detected in 13.6% of patients.*

Conclusion: *The prevalence of B12 deficiency is among the highest compared to other reports. Folate deficiency is among the reported prevalence rates worldwide. Both B12 and folate deficiencies were seen among younger adults, which oppose the global findings. B12 deficiency was more prevalent among males; hence, folate deficiency was more common among females. Megaloblastic anemia in Sudan necessitates a coordinated approach to nutritional interventions, healthcare, public health, and policies to reduce poverty and enhance health.*

Keywords
Megaloblastic Anemia, B12, Folate, Sudan.

Introduction
Megaloblastic anemia (MA) is a broad classification of macrocytic anemias distinguished by bone marrow megaloblasts. DNA synthesis is stopped, which prevents nuclear division. Fewer abnormalities impair cytoplasmic maturation, which is dependent on RNA and protein production. Megaloblasts are enormous because the maturation of the erythroblast nucleus and cytoplasm occurs at different times. This impacts hematopoiesis and fast-regenerating tissues, like gastrointestinal cells. Megaloblastic anemia is typically caused by hypovitaminosis, particularly vitamin B12 (cobalamin) and folate deficiencies, which are required for DNA synthesis [1].

Megaloblastic anemia is prevalent; however, data on its prevalence are insufficient. Furthermore, population diversity may depend on universal folate supplementation in food products, the prevalence of chronic conditions such as pernicious anemia and H. pylori infection, as well as cultural and individual dietary practices [2].

Vitamin B12 insufficiency is common and causes megaloblastic anemia and brain damage. Pernicious anemia has been linked to atrophic gastritis-induced malabsorption and B12 deficiency. Dietary restrictions may cause B12 deficiency. The same effect as cobalamin deficiency on folate metabolism is methionine synthase reduction. It causes 5-MTHF accumulation and DNA synthesis issues. Low MTHFR activity may inhibit 5-MTHF formation, directing folate metabolism to thymidylate and increasing DNA synthesis [3].

B12 and folate are needed for folate-mediated one-carbon metabolism (FOCM). FOCM regenerates methionine and synthesizes thymidylate via methyl transfer. Megaloblastic anemia and neurocognitive impairments can result from folate and B12 deficiency. Since the US requires folic acid fortification, folate deficiency is rare, but B12 deficiency is widespread, especially in vegetarians/vegans and older people. Folate fortification improves folate status and minimizes birth abnormalities. Fortified foods and folic acid supplements have raised the number of people above the tolerance level. Megaloblastic anemia has long been linked to folate and B12, yet high serum folate may aggravate neurocognitive consequences and metabolic impairments (altered glucose homeostasis, type 2 diabetes in offspring) caused by B12 deficiency [4]. Pernicious anemia is an uncommon autoimmune disorder that impairs the absorption of vitamin B12 (cobalamin), leading to vitamin B12 deficiency and megaloblastic anemia. The condition impacts individuals across all age groups, with a particular prevalence among those aged 60 and above. Despite advancements in understanding, physicians encounter challenges in diagnosis due to the condition's complexity, diverse clinical manifestations, and the limitations of existing diagnostic methods. Upon diagnosis, rapid B12 therapy typically resolves anemia; however, lifelong supplementation and monitoring are necessary [5].

Despite the limited availability of data concerning megaloblastic anemia in Sudan, it remains a notable health issue within the country. In Sudan, as in various other regions, megaloblastic anemia can be influenced by a multitude of demographic factors, including dietary habits, socioeconomic conditions, and the accessibility of healthcare services. The factors contributing to this deficiency in Sudan appear to be deeply embedded in inadequate dietary intake, a critical concern in a nation grappling with widespread malnutrition [6]. Therefore, this study aimed to assess the demographic characteristics associated with megaloblastic anemia in central Sudan.

Materials and Methods
This is a descriptive prospective study conducted in El-Obeid Teaching Hospital, El-Obeid, North Kordofan State, Sudan. Two hundred participants were selected for this study (100 were with clinical symptoms mimicking anemia, and 100 were apparently healthy volunteers as an internal control for comparing hematological parameters). Out of the 100 individuals with indications of anemia, abnormal hematological changes were observed in 44 patients who underwent further estimations of serum Vit-B12 and folate. After consent to participate, the participant's essential identification information was obtained. A blood sample was taken as a part of the required investigation by the hospital.

Statistical Analysis
The data for this study was initially compiled in a data sheet and then entered into a statistical software program for social sciences (SPSS). Frequencies, percentages, means, and cross-tabulations were computed. A chi-square test was performed utilizing a 95% confidence interval. A P-value less than 0.05 is considered

statistically significant.

Results

This study investigated 200 Sudanese individuals, aged 21 to 95 years, with a mean age and standard deviation of 52±16. Most of the study subjects were aged 60-69 years, followed by the age ranges 45-59 and 35-44 years, representing 44/200 (22%), 42/200 (21%), and 40/200 (20%), respectively. Out of the 200 participants, 68/200 (34%) were males and the remaining 132/200 (66%) were females. The distribution of males and females among age groups was relatively similar. Most individuals were from urban residences, 121/200 (60.5%). According to occupation, most participants were housewives, followed by teachers and employees, constituting 55/200 (27.5%), 31 (15.5%), and 27 (13.5%), in this order, as indicated in Table 1, Figure 1.

Table 1: Distribution of the study subjects by sex and age.

Variable	Males	Females	Total
Age			
<35 years	1	38	39
35-44	8	32	40
45-59	10	32	42
60-69	27	17	44
70+	22	13	35
Total	68	132	200
Residence			
Rural	31	40	71
Urban	34	87	121
Total	65	127	192
Occupation			
Students	0	6	6
Employees	7	17	24
Retired	22	5	27
Teachers	3	28	31
Self-employed	17	9	26
Farmers	15	1	16
Housewives	0	55	55
Others	3	2	5
Total	67	123	190

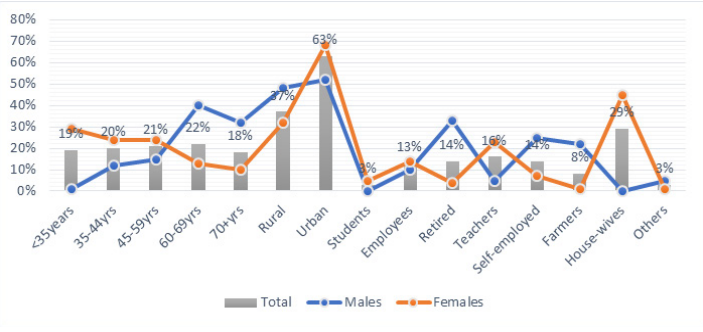


Figure 1: Description of the study subjects by demographic characteristics.

Vitamin B12 was measured for 44/200 (22%) participants. Of the 44 individuals, B12 deficiency was detected in 37/44 (84%) patients. No high B12 measure was detected. B12 deficiency was detected in 11/12 (91.7%) males and 26/32 (81.3%) females. The risk of B12 deficiency among males, the relative risk (RR), and the 95% confidence interval (95% CI); RR (95% CI) = 1.1282 (0.8890 to 1.4319), P = 0.3212, and z statistic = 0.992.

Most cases with B12 deficiency were detected among the age group 45-59 years, followed by 35-45 and < 35 years, representing 11/44 (25%), 8 (18.2%), and 8 (18.2%), in that order. Most cases were married, 33/44 (75%). Most cases were urban inhabitants, 27/44 (61.4%). The risk of B12 deficiency is associated with urban residence; the RR (95% CI) = 1.1323 (0.8164 to 1.5704), P = 0.4567, as indicated in Table 2, Figure 2.

Table 2: Distribution of demographic characteristics by B12 status.

Variable	Low n=37	Normal n=7	Total n=44
Sex			
Males	11	1	12
Females	26	6	32
Age			
<35 years	8	1	9
35-44	8	3	11
45-59	11	2	13
60-69	5	0	5
70+	5	1	6
Marital Status			
Single	3	0	3
Married	33	7	40
Widow	1	0	1
Residence			
Rural	10	3	13
Urban	27	4	31

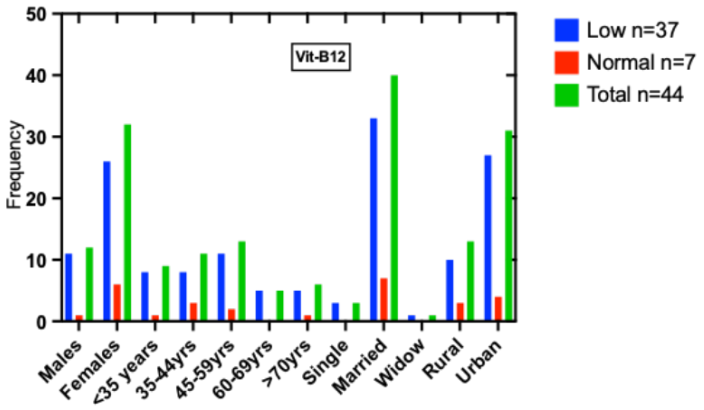


Figure 2: Description of the cases by demographic characteristic by B12 status.

Table 3, Figure 3, summarized the distribution of study subjects by B12 status and education & occupation. Most patients with B12 deficiency were with a graduate level of education, followed by primary and secondary levels, constituting 14/44 (31.8%), 9 (20.5%), and 8 (18.2%), in this order. Most patients were housewives, 10/44 (27.7%), followed by teachers, 6 (13.6%).

Table 3: Distribution of study subjects by B12 status and education & occupation.

Variable	Low n=37	Normal n=7	Total n=44
Education			
Primary	9	0	9
Intermediate	2	0	2
Secondary	8	3	11
Graduate	14	3	17
Illiterate	4	1	5
Occupation			
Students	3	0	3
Employees	5	2	7
Retired	5	0	5
Teachers	6	1	7
Self-employees	2	0	2
Farmers	1	0	1
Housewives	10	4	14
Others	5	0	5

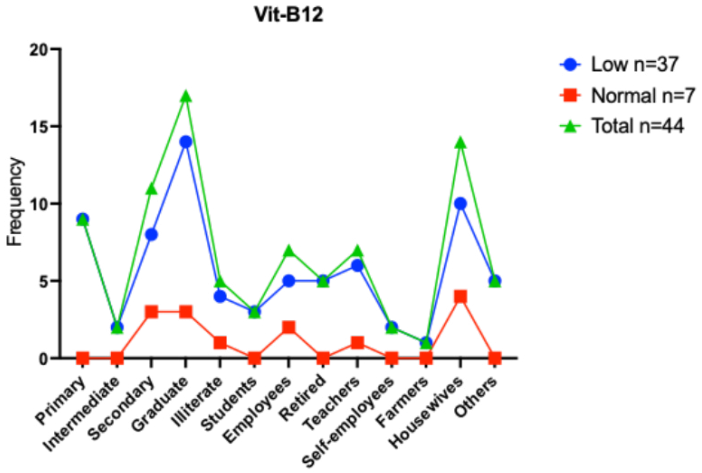


Figure 3: Description of study subjects by B12 status and education & occupation.

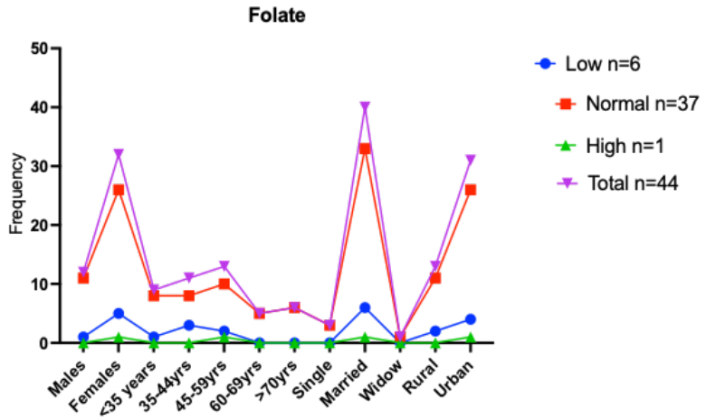
Abnormal folate levels were detected in 7/44 (15.9%) patients; 6/7 (85.7%) had folate deficiency, and 1/7 (14.3%) had a high folate level. Folate deficiency was detected in 5/32 (15.6%) females and 1/12 (8.3%) males. The risk of folate deficiency among females, RR (95% CI) = 1.9355 (1.9355), P = 0.5260, z statistic = 0.634. Most patients with low folate levels were aged under 45 years, 4/6 (66.7%). The risk of folate deficiency is associated with the age under 45 years, RR (95% CI) = 1.2 (0.2575 to 5.5928), P = 0.8164, and z statistic = 0.232. All patients were married 6/6 (100%). About 4/6 (66.7%) were urban residents, and 2/6 (33.3%) were rural inhabitants, as indicated in Table 4, Figure 4.

The distribution of the cases by education and occupation was summarized in Table 5, Figure 5. All cases with folate deficiency were with secondary 3/6 (50%) or graduate level of education 3/6 (50%). Most patients with low folate were housewives, 3/6 (50%), followed by employees, 2/6 (33.3%).

Table 4: Distribution of demographic characteristics by folate status.

Variable	Low n=6	Normal n=37	High n=1	Total n=44
Sex				
Males	1	11	0	12
Females	5	26	1	32
Age				
<35 years	1	8	0	9
35-44	3	8	0	11
45-59	2	10	1	13
60-69	0	5	0	5
70+	0	6	0	6
Marital Status				
Single	0	3	0	3
Married	6	33	1	40
Widow	0	1	0	1
Residence				
Rural	2	11	0	13
Urban	4	26	1	31

Figure 4: Description of demographic characteristics by folate status.



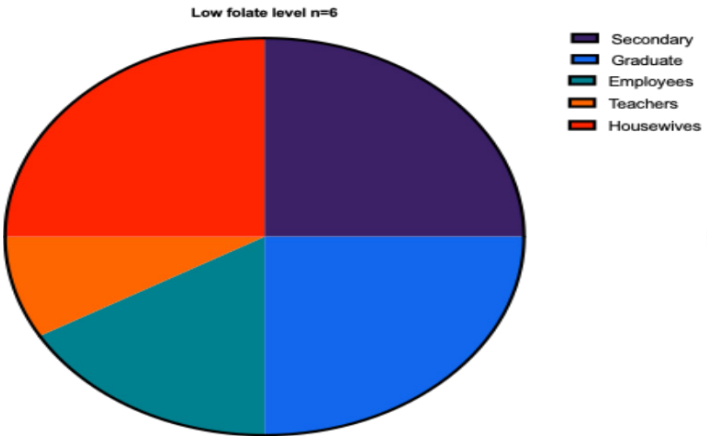


Figure 5: Description of study subjects by Folate status and education & occupation.

Table 5: Distribution of study subjects by folate status and education & occupation.

Variable	Low n=6	Normal n=37	High n=1	Total n=44
Education				
Primary	0	8	1	9
Intermediate	0	2	0	2
Secondary	3	8	0	11
Graduate	3	14	0	17
Illiterate	0	5	0	5
Occupation				
Students	0	3	0	3
Employees	2	5	0	7
Retired	0	5	0	5
Teachers	1	6	0	7
Self-employees	0	2	0	2
Farmers	0	1	0	1
Housewives	3	10	1	14
Others	0	5	0	5

Discussion

Megaloblastic anemia continues to be a notable health issue in Sudan, influenced by various demographic characteristics of the Sudanese population. The present study aimed to investigate the relationship between megaloblastic anemia associated with vitamin B12 and folate deficiency and the demographic characteristics of the patients. The prevalence of low B12 among the studied individuals was notably high at 85%, in contrast to findings from various regions globally, as indicated in the results. The prevalence of vitamin B12 deficiency is considerable and exhibits global variation, with notably higher rates observed in older individuals, reaching as high as 40-80% in certain developing nations [7]. Factors contributing to vitamin B12 deficiency include prolonged metformin treatment in individuals with type 2 diabetes mellitus (T2DM) [8], poor diet (especially among vegans) [9], pernicious anemia [10], and other related issues [11,12].

The results of the current study indicate that B12 insufficiency is more prevalent among younger persons than older adults. Nevertheless, the vast majority of research links vitamin B12 deficiency to older persons [13]. This suggests that the majority of cases in this study may be linked to adverse dietary factors resulting from the ongoing armed conflict in Sudan, which affects the life patterns of the entire population. Healthy older individuals demonstrate neurological alterations at both extremes of the measurable "normal" B12 range. These findings question the existing comprehension of optimal serum B12 levels and indicate the need to reassess the formulation of suitable nutritional guidelines [14].

The present investigation found that males are more likely to have B12 insufficiency. Men are more likely than women to be vitamin B12 deficient, with studies showing higher prevalence and more severe deficits in males, even after controlling for food and weight. However, the gender disparity varies by population and age, with older females exhibiting higher deficiency rates in some studies. While the symptoms are generally the same for both genders, specific illnesses, such as pernicious anemia, are more common in women [15].

The majority of patients with B12-associated anemia were from low socioeconomic backgrounds, characterized by low education levels and financially disadvantaged occupations. Socioeconomic health inequalities represent a significant global public health issue. It remains unclear to what degree socioeconomic inequalities contribute to impaired vitamin status and whether this relationship is mediated by dietary factors. Low socioeconomic status correlated with decreased levels of vitamin B6, vitamin B12, and particularly, folic acid [15].

The incidence of folate insufficiency was 13.5%, which is comparatively lower than reported in much prior research [16]. A previously reported prevalence rate of folate deficiency stands at 37.9% (n: 413/1088) [17].

Folate is essential for the metabolic control of amino acids and nucleic acids, as well as one-carbon metabolism. Folate must be received from diet, and supplementation is particularly suggested in people at risk of deficiency owing to specific disorders. Folic acid is the vitamin's synthetic form, which is commonly found in meals and supplements. Cell metabolism in the body converts it into the bioactive folate derivative (6S)5-MTHF. Folate deficiency is linked to several health conditions, including neurological diseases, and can raise the risk of cardiovascular disease [18].

The current study data indicated that folate insufficiency was more prevalent among younger persons. Folate deficiency is prevalent among elderly adults (over 65) due to factors such as diminished dietary intake and intestinal malabsorption. In advanced age, insufficient folate levels correlate with a heightened risk of cognitive deterioration, dementia, depression, and overall mortality [19]. Our recent findings indicate that folate insufficiency is more prevalent in females than in males. Similar findings were previously documented [17]. The limited number of individuals with folate insufficiency precludes the establishment of a reliable prognosis based on other demographic variables.

The current study offers significant updates on the scarce information concerning megaloblastic anemia in Sudan; nonetheless, it is limited by the small number of cases analyzed.

Conclusion

The prevalence of B12 insufficiency is among the highest compared to previous reports. The prevalence of folate insufficiency in this study is comparable to that reported worldwide. Both B12 and folate deficits were observed in younger persons, contradicting the global findings. Males were more likely to have B12 deficiency, so females had higher folate deficiency. Megaloblastic anemia

remains a major health concern in Sudan, necessitating attention from healthcare practitioners, lawmakers, and public health officials. Addressing dietary inadequacies through education, supplementation programs, and greater access to healthcare services may help to lower the prevalence of this illness in the general population.

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