

## Clinical Aspects of B12 and Folate Insufficiency in Anemic Patients: A Report from War Hot Zone of Sudan

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### ABSTRACT

**Background:** The continuous conflict in Sudan greatly impacts the population's diet and elevates the risk of important vitamin deficiencies. This study sought to evaluate clinical variables linked to vitamin B12 and folate deficiency in the hot zone of the armed conflict.

**Methodology:** This study is a descriptive prospective analysis carried out at El-Obeid Teaching Hospital in El-Obeid, North Kordofan State, Sudan. Two hundred participants were selected for this study, comprising 100 individuals exhibiting clinical symptoms of macrocytic anemia (cases) and 100 healthy volunteers (controls).

**Results:** The 200 participants were aged 21 to 95 years, with a mean age of 52±16 and standard deviation. Most study participants were 60–69 years old, followed by 45–59 and 35–44 years old (22%, 21%, and 20%, respectively). About 66% of participants were females, and 34% were males. B12 deficiency affected 84% of individuals. Folate deficiency affected 13.6% of patients. 73% of cases ate mixed food, 27% were vegetarian, and all control groups ate mixed food. The most common symptoms were foot numbness (86%), dizziness (70%), epigastric discomfort (55%), and recurrent diarrhea (43%).

**Conclusion:** This study indicates that B12 insufficiency is more common than folate. The B12 deficiency level in Sudan is higher than the global level. Vitamin supplementation is necessary for people under prolonged armed conflict.

## Keywords

Megaloblastic Anemia, B12, Folate, metformin, Sudan.

## Introduction

Megaloblastic anemia is a type of macrocytic anemia that occurs as a result of vitamin B12 (cobalamin) or folate deficiency. Megaloblastic anemia is common worldwide, but there was insufficient evidence on its epidemiology. Megaloblastic anemia becomes more common as people become older, and poverty increases the risk. Vitamins B12 and folate operate as coenzymes in DNA synthesis; therefore, deficits can result in poor DNA synthesis and, as a result, unproductive hematopoiesis in the bone marrow [1]. Erythroblasts require vitamin B12 and folate to proliferate and differentiate. Vitamin B12 or folate deficiency affects purine and thymidylate syntheses, as well as DNA synthesis, resulting in erythroblast apoptosis and the formation of bigger cells with an immature nucleus and copious cytoplasm [2]. Vitamin B12 shortage can result from dietary deficiencies, malabsorption diseases, or autoimmune illnesses that impair intrinsic factor production. Severe B12 deficiency can induce persistent nerve damage, amnesia, confusion, balance problems, heart abnormalities, and an increased risk of stomach cancer, particularly when combined with pernicious anemia [3]. Folate deficiency is caused by a variety of genetic, physiological, biochemical, nutritional, and pharmacological variables that influence intake, absorption, metabolism, or total requirements [4]. Folate deficiency occurs primarily in low- and middle-income nations, particularly among women of reproductive age and communities without access to subsidized foods. Socioeconomic level, education, and dietary diversity all increase the risk of folate deficit [5]. Severe folate deficiency can lead to pancytopenia, mucocutaneous and gastrointestinal signs, cardiovascular problems, and neuropsychiatric symptoms such as sadness, sleeplessness, irritability, cognitive decline, and psychosis.

Folate deficiency during pregnancy dramatically raised the incidence of neural tube abnormalities, premature birth, fetal growth limitation, and placental abruption [6].

Although megaloblastic anemia exists in Sudan, there has been little research on it; therefore, the findings of this study will aid in early detection, lowering the risk of consequences. The purpose of this study was to evaluate the clinical symptoms associated with B12 and folate deficiency in North Kordofan State.

## Materials and Methods

This study is a prospective descriptive investigation carried out at El-Obeid Teaching Hospital, located in North Kordofan State, Sudan, spanning from December 2023 to June 2025.

This study includes two hundred participants: one hundred exhibiting clinical symptoms of anemia with an MCV greater than 100 fl, and one hundred apparently healthy volunteers serving as internal controls. Following the acquisition of consent to participate, the essential identification information of the

participant was collected. A blood sample was collected as part of the necessary investigation conducted by the hospital. For the analysis of hematological parameters and subsequent evaluations of serum vitamin B12 and folate levels.

## Results

The study comprised 200 Sudanese individuals ranging from 21 to 95 years old, with a mean age  $\pm$  standard deviation of  $52 \pm 16$ . Most of the study participants were aged 60–69 years, followed by 45–59 and 35–44 years, accounting for 44/200 (22%), 42/200 (21%), and 40/200 (20%), respectively. Most cases occurred between the ages of 45 and 59, with ages 60–69 and over 70 accounting for 25%, 21%, and 19%, respectively. Most controls were under the age of 35, followed by those aged 60–69 and 35–44, who accounted for 26%, 23%, and 18%, respectively. The gender distribution of cases and controls within each age group was relatively similar, with 66% females and 34% males among the study subjects. Furthermore, 65% of the study population lived in cities, with the remaining 34% in rural areas, as shown in Table 1 and Figure 1.

**Table 1:** Illustrates the study's subjects' ages, genders, and locations.

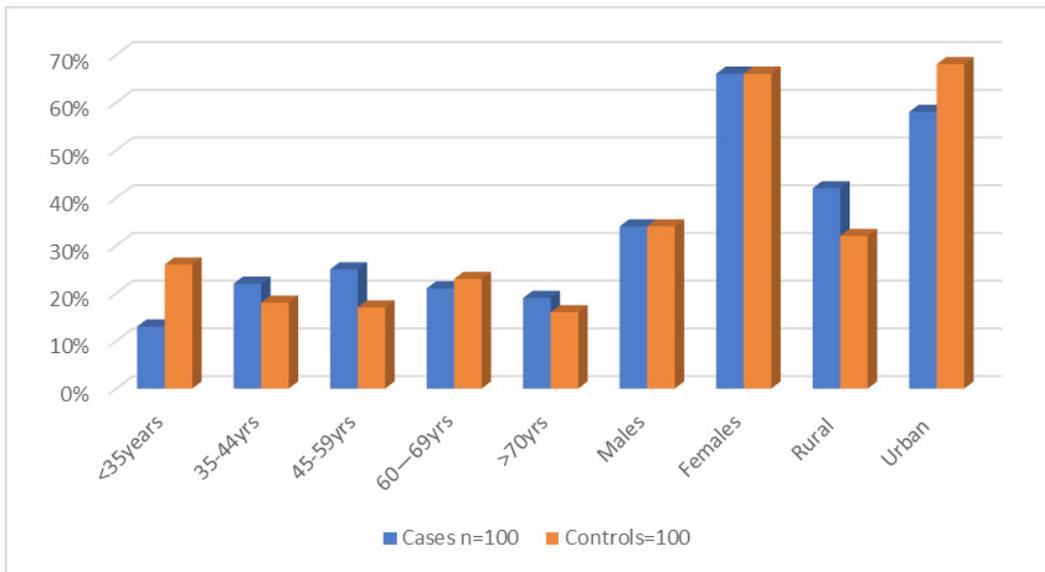
Category	Variable	Cases n=100	Controls n=100	Total
Age	<35 years	13	26	39
	35-44	22	18	40
	45-59	25	17	42
	60–69	21	23	44
	$\geq 70$	19	16	35
		100	100	200
Sex	Males	34	34	68
	Females	66	66	132
Residence	Rural	42	29	71
	Urban	58	63	121
		100	92	192

Vitamin B12 deficiency was diagnosed in 84% of patients, with a mean of  $155.6 \pm 96.8$ . Low folate levels were discovered in 13.7% (mean  $8.1 \pm 4.7$ ), while excessive folate levels were detected in 2.3% of subjects. Out of 100 patients with megaloblastic anemia, 55% reported epigastric discomfort, 86% reported foot numbness, 43% reported chronic diarrhea, and 70% reported dizziness, as shown in Table 2 and Figure 2.

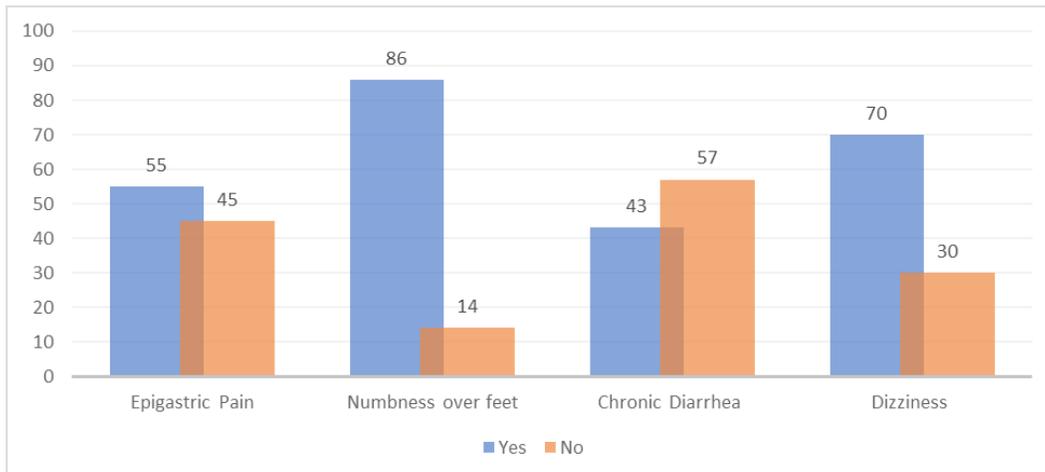
**Table 2:** Distribution of megaloblastic anemia participants based on clinical symptoms.

Variable	Yes	No
Epigastric Pain	55	45
Numbness over feet	86	14
Chronic Diarrhea	43	57
Dizziness	70	30

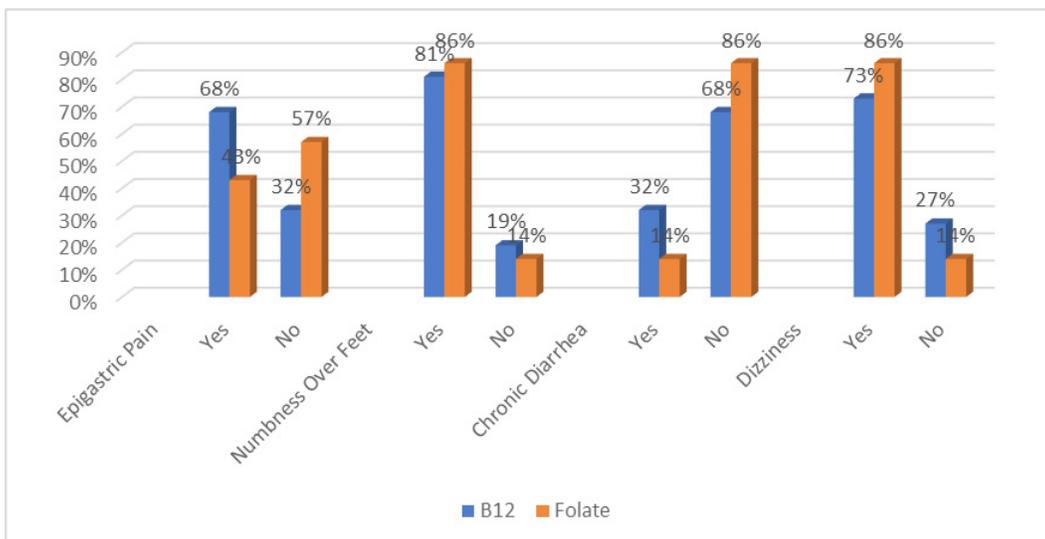
Out of 44 participants, 37 had B12 deficiency. 68% of them had epigastric discomfort, 81% had numbness in their feet, 32% had chronic diarrhea, and 73% had dizziness. Out of 44 subjects



**Figure 1:** Describes the subject's age, gender, and demographic information.



**Figure 2:** Shows the distribution of megaloblastic anemia cases based on clinical symptoms.



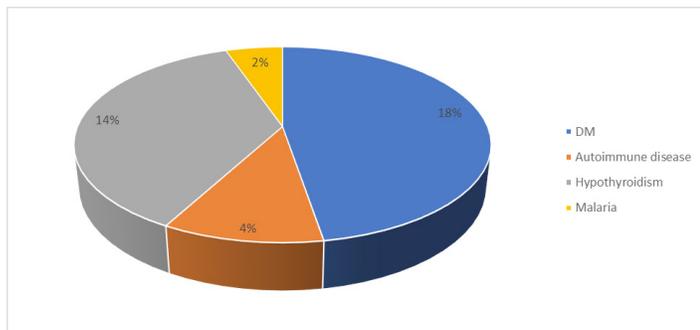
**Figure 3:** Description of B12 and folate-deficient participants based on clinical symptoms.

tested for folate insufficiency, 43% reported epigastric pain, 86% reported tingling in their feet, 14% reported chronic diarrhea, and 86% reported dizziness. As seen in Table 3. Figure 3. 73% of patients ate mixed foods, the remaining 27% were vegetarian, while the entire control group ate mixed foods.

**Table 3:** Shows the distribution of B12 and Folate insufficiency patients by clinical symptoms.

Variable	B12 n=37	Folate n=7
<b>Epigastric Pain</b>		
Yes	25	3
No	12	4
<b>Numbness Over Feet</b>		
Yes	30	6
No	7	1
<b>Chronic Diarrhea</b>		
Yes	12	1
No	25	6
<b>Dizziness</b>		
Yes	27	6
No	10	1

In terms of comorbidities, DM accounts for 18% of cases and 22% of controls. Furthermore, hypothyroidism affects 14% of cases and 9% of controls in this sequence. Malaria affects 2% of cases and 11% of controls, respectively. 44% of patients had hypotension, 38% had normal blood pressure, and 18% had hypertension. About 17/18 (94%) of patients received metformin treatment compared to 4/22 (18%) of the controls, as shown in Figure 4.



**Figure 4:** Distribution of subject according to comorbidities.

## Discussion

Consuming a balanced diet rich in essential vitamins is paramount for safeguarding against serious health issues. In Sudan, the recent conflict has led to a proliferation of various nutritional deficiency disorders. Megaloblastic anemia represents a form of nutritional anemia that arises due to a deficiency in vitamin B12 and folate. This research seeks to evaluate the clinical factors linked to deficiencies in B12 and folate within North Kordofan State.

This study comprises 200 Sudanese participants, with 50% categorized as cases and the remaining 50% as controls. The participants' ages ranged from 21 to 95 years, with a mean age of 52±16. The distribution of gender revealed a composition

of 66% female and 34% male within both the case and control groups. Approximately 65% of the participants in the study were from urban environments. The prevalence of V-B12 deficiency was significantly higher than that of folate deficiency, recorded at 84% compared to 13.7%, respectively. The occurrence of B12 deficiency was less common in adolescents and children [7]. The prevalence of vitamin B12 and folate deficiency is notably elevated in elderly male patients [8].

Among 100 cases of patients with megaloblastic anemia, the most frequently observed clinical features include numbness in the feet (86%), followed by dizziness (70%), epigastric pain (55%), and chronic diarrhea (43%). A significant proportion of individuals with B12 deficiency experience numbness in their feet (81%), with dizziness affecting 73% of this population. Individuals experiencing a deficiency in vitamin B12 may exhibit significant discomfort stemming from peripheral neuropathy, which impacts the lower limbs, as well as optic atrophy that can lead to visual impairments [9]. A significant 86% of individuals with folate deficiency exhibited symptoms of numbness in the feet and dizziness, underscoring findings from other studies. The neurological manifestations associated with folate deficiency share similarities with those of vitamin B12 deficiency, encompassing cognitive impairment, dementia, depression, and, less frequently, peripheral neuropathy and subacute combined degeneration of the spinal cord. In both deficiency states, one frequently observes a disconnection between the neuropsychiatric and hematologic complications [10]. In the study, 73% of the participants consumed a mixed diet, while the remaining 27% adhered to a vegetarian diet. Notably, all individuals in the control group were on a mixed food regimen. Individuals following plant-based diets face a heightened likelihood of experiencing nutritional deficiencies, particularly with regard to vitamin B12 levels. Individuals following a vegetarian diet often exhibit a notable deficiency in vitamin B12 levels when compared to those who consume animal products. The findings underscore the necessity for dietary strategies aimed at mitigating the risk of nutritional deficiencies in plant-based diets, including the potential for fortification or supplementation with vitamin B12 [11].

In the analysis, 44% of cases presented with hypotension, 38% exhibited normal blood pressure, while 18% were classified as hypertensive. Instances of hypotension linked to delirium have been documented in older individuals adhering to a vegetarian diet. Instances of orthostatic hypotension have been documented in individuals with vitamin B12 deficiency, occurring even when neurological and hematological symptoms are not present. To the best of our knowledge, the relationship between vitamin B12 deficiency and hypotension has not been previously documented in a young patient [12].

In the study, it was observed that 18% of cases presented with diabetes mellitus, with a notable 94% of those (17 out of 18) receiving metformin treatment. In comparison, the control group exhibited a 22% prevalence of diabetes mellitus, with only 18%

(4 out of 22) undergoing metformin therapy. The prolonged use of metformin is notably linked to vitamin B12 deficiency, which can lead to megaloblastic anemia. It appears that metformin may play a significant role in the development of this deficiency, while the concurrent intake of multivitamins might offer a protective effect against it [13]. The use of metformin leads to a decrease in the absorption of vitamin B12, thereby increasing the risk of vitamin B12 deficiency. Additionally, it may cause a decline in folic acid levels, which can result in megaloblastic anemia [14]. Approximately 14% of cases were identified as hypothyroidism, and it is frequently observed that vitamin B12 deficiency coexists in patients diagnosed with this condition. The connection between a deficiency in vitamin B12 and thyroid disorders primarily arises from the concurrent existence of other autoimmune conditions such as atrophic gastritis or pernicious anemia, which both result in hindered absorption of vitamin B12. The prevalence of vitamin B12 deficiency among individuals with hypothyroidism tends to rise as they age. In conclusion, this study reveals that the prevalence of B12 deficiency surpasses that of folate deficiency. In the majority of patients with megaloblastic anemia, neurological manifestations were frequently evident. Individuals experiencing a deficiency in vitamin B12 may exhibit symptoms of peripheral neuropathy, predominantly impacting the lower limbs. The prolonged use of metformin is notably linked to a deficiency in B12, which can lead to megaloblastic anemia; consequently, vitamin supplementation might serve as a safeguard against this deficiency.

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