

Subclinical Vitamin B12 Deficiency Presenting with Isolated Red Cell Distribution Width (RDW) Elevation Without Anemia In 20 Years Old Female: A Rare Hematological Presentation: Case Study

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Abstract

Megaloblastic anemia and neurological symptoms are common signs of vitamin B12 deficiency. However, the lack of traditional clinical and hematological findings may cause the condition to go undiagnosed in its early or subclinical stage. Before anemia develops, subtle changes in red cell indices, especially red cell distribution width (RDW), may act as early markers of compromised erythropoiesis.

This case study details a 20-year-old female patient who had mild, nonspecific fatigue and a rare presentation of subclinical vitamin B12 deficiency. Except for a single elevation in RDW, routine hematological analysis showed normal hemoglobin concentration, mean corpuscular volume, and other red cell parameters. Mild anisocytosis was revealed by peripheral smear analysis. Iron tests and other biochemical parameters were within normal ranges, but additional testing revealed decreased serum vitamin B12 levels.

Early detection of vitamin B12 deficiency allowed for the timely start of supplementation, which stopped the development of neurological issues and overt anemia. The diagnostic value of isolated RDW elevation as an early hematological indicator of subclinical vitamin B12 deficiency is demonstrated by this case.

Keywords: Vitamin B12, Red Cell Distribution Width (RDW), Megaloblastic anemia, Anisocytosis, Erythropoiesis.

Background

Macrocytic anemia and neurological symptoms are typical signs of vitamin B12 deficiency. However, in the absence of obvious anemia or notable clinical symptoms, early or subclinical stages might go unnoticed. An early hematological indicator of anisocytosis, Red Cell Distribution Width (RDW) may rise prior to changes in hemoglobin or mean corpuscular volume (MCV). This case demonstrates an uncommon and underappreciated manifestation of subclinical vitamin B12 deficiency in a young female patient that was only identified by isolated RDW elevation.

Epidemiology

Worldwide, vitamin B12 deficiency is common, especially in developing nations. Dietary practices, veg-

etarianism, menstrual blood loss, and increased nutritional demands put young women at higher risk. Because routine screening primarily concentrates on hemoglobin levels rather than subtle red cell indices, subclinical deficiency is frequently disregarded.

Disease Description

Inadequate intake, poor absorption, or elevated physiological demand are the causes of vitamin B12 deficiency. Early on, mild erythropoietic disruptions brought on by compromised DNA synthesis result in variations in red blood cell size without affecting total hemoglobin levels. This leads to increased RDW without obvious anemia.

Prevalence

About 15–40% of people worldwide suffer from vitamin B12 deficiency, which is particularly prevalent in developing nations. Two important contributing factors are inadequate dietary intake and restricted consumption of foods derived from animals.

Subclinical vitamin B12 insufficiency is common in young people, especially girls between the ages of 18 and 25. Research indicates that between 10–20% of young or clinical signs.

Overt megaloblastic anemia is less common than subclinical vitamin B12 insufficiency. Hemoglobin levels may stay normal in the early stages, and routine screening may miss modest hematological alterations.

One uncommon and underreported sign of vitamin B12 insufficiency is isolated increase of RDW without anemia. Such early cases are frequently overlooked due to ordinary practice's scant attention to RDW, which delays diagnosis.

Diagnosis

- Complete Blood Count (CBC) with RBC indices is used to diagnose subclinical vitamin B12 insufficiency.
- High RDW with normal MCV, MCH, and hemoglobin levels
- Serum vitamin B12 levels are lower; iron deficiency and other anisocytosis causes are ruled out.

Differential Diagnosis

- **Early Iron Deficiency:** Prior to a drop in hemoglobin or MCV, early iron deficiency may manifest as elevated RDW. Nonetheless, iron insufficiency is ruled out as the reason of isolated RDW rise by normal serum ferritin and iron tests.
- **Folate insufficiency:** Similar to vitamin B12 insufficiency, folate deficiency can result in megaloblastic alterations. In this instance, the absence of macrocytosis and normal folate levels aid in distinguishing it from asymptomatic vitamin B12 insufficiency.
 1. **Mixed Nutritional Deficiency:** Combined deficiency of iron and vitamin B12 can lead to variable red cell size and elevated RDW. Normal iron parameters and isolated low vitamin B12 levels rule out mixed nutritional deficiency.
 2. **Chronic Inflammatory Conditions:** Chronic infections or inflammatory diseases may cause alterations in red cell indices. Absence of clinical symptoms, normal inflammatory markers, and a healthy medical history exclude this condition.

3. **Liver Disease:** RDW increase and altered red blood cell shape can result from liver diseases. This is ruled out by normal liver function tests and the absence of clinical liver disease symptoms.
4. **Hemoglobinopathies:** Disorders like thalassemia trait can result in elevated RDW and aberrant red cell indices. Hemoglobinopathies are unlikely if there is no family history and normal RBC indices.
5. **Thyroid Conditions:** Anemia and macrocytosis may be linked to hypothyroidism. Thyroid-related causes are ruled out by normal thyroid function tests and the lack of clinical symptoms.

Presentation of a Case

A 20-year-old woman arrived at the outpatient clinic for a standard medical assessment. She denied experiencing symptoms like breathlessness, palpitations, dizziness, weight loss, or neurological complaints like numbness, tingling, or abnormal gait, but she did report mild, sporadic fatigue over the previous few months. There was no prior hospitalization, gastrointestinal issues, fever, or chronic illness. The patient did not have a history of blood loss, excessive menstrual bleeding, or drug use known to impact hematopoiesis. Her dietary history showed a mostly vegetarian pattern and sporadic consumption of foods derived from animals. Anemia, hemoglobinopathies, or autoimmune diseases did not run in the family.

As part of the screening process, standard laboratory tests were conducted. Hemoglobin of 12.8 g/dL, red blood cell count of 4.4 million/ μ L, mean corpuscular volume of 88 fL, and mean corpuscular hemoglobin of 29 pg. were all within normal reference ranges according to the complete blood count. On the other hand, anisocytosis was indicated by an increased red cell distribution width (RDW) of 15.8%. Both the platelet and white blood cell counts were within normal limits.

Peripheral blood smear analysis revealed normocytic, normochromic red blood cells with a slight variation in size and no aberrant platelet or leukocyte morphology. Iron deficiency anemia was ruled out because iron tests, including serum ferritin, were within normal ranges. Folate levels in the serum were normal. Subclinical vitamin B12 deficiency was confirmed by additional testing, which showed a lower serum vitamin B12 level of 165 pg/mL (reference range: 200–900 pg/mL). Thyroid profile and liver function tests were both normal.

The patient was diagnosed with subclinical vitamin B12 deficiency based on isolated RDW elevation with low serum vitamin B12 levels and lack of anemia. Dietary counseling was given, and oral vitamin B12 supplementation was started. The patient reported less fatigue at follow-up, underscoring the significance of early detection and intervention.

Assessment (Tabular Form)

Parameter	Observed Value	Reference Range	Interpretation
Hemoglobin	12.8 g/dL	12–15 g/dL	Normal
RBC Count	4.4 million/ μ L	4.0–5.2	Normal
MCV	88 fL	80–100 fL	Normal
MCH	29 pg	27–33 pg	Normal
RDW	15.8%	11.5–14.5%	Elevated
Serum Vitamin B12	165 pg/mL	200–900 pg/mL	Low
Serum Ferritin	Normal	—	Normal
Peripheral Smear	Mild anisocytosis	—	Suggestive

Uniqueness of the study

Because it describes subclinical vitamin B12 deficiency without anemia or macrocytosis, which makes the condition challenging to identify during routine investigations, this study is unique. The case emphasizes RDW as an early and sensitive indicator of vitamin B12 deficiency by highlighting isolated RDW elevation as the sole hematological abnormality.

The patient's young age (a female 20-year-old) adds uniqueness because early deficiencies in this age group are frequently disregarded.

In this instance, early detection through routine screening helped stop the development of overt anemia and neurological complications, highlighting the study's preventive value.

Result

The patient was diagnosed with subclinical vitamin B12 deficiency based on isolated RDW elevation and reduced serum vitamin B12 levels. Early intervention prevented progression to megaloblastic anemia.

Conclusion

This instance shows that isolated RDW elevation can be a sensitive and early indicator of subclinical vitamin B12 deficiency. Even in non-anemic people, routine RDW evaluation can help with early diagnosis and prompt treatment, especially in young girls who are at nutritional risk.

Study Limitations

- Single-Patient Case Study: The results of this study can't be applied to a broader population or to other age groups because it is based on a single patient.
- Lack of Advanced Biomarkers
- Serum methylmalonic acid and homocysteine levels, two metabolic markers that could have supported the diagnosis of subclinical vitamin B12 deficiency, were not measured.
- Short Follow-Up Period • No long-term follow-up was carried out to assess the course of the disease or the long-term effects of vitamin B12 supplementation

Limitations of Dietary Assessment

- The lack of a thorough quantitative dietary analysis limited the accuracy of the relationship between vitamin B12 deficiency and dietary intake.
- The absence of a comparative control group
- A control group with normal RDW and vitamin B12 levels is absent from the study, which limits comparative analysis.
- Potential Impact of Unknown Factors
- Despite standard routine investigations, other subclinical conditions affecting RDW might not have been fully ruled out.

Future Study Scope

- Extensive Population Research
- The true prevalence of subclinical vitamin B12 deficiency presenting with isolated RDW elevation may be ascertained by future studies with larger sample sizes.

Advanced Diagnostic Marker Utilization

- Inclusion of metabolic markers such as methylmalonic acid and homocysteine can improve early and accurate diagnosis of vitamin B12 deficiency.
- RDW as a Screening Tool
- Further studies can evaluate the role of RDW as a cost-effective and routine screening parameter for early vitamin B12 deficiency, especially in young and asymptomatic individuals.

Long-Term Follow-Up Studies

- Longitudinal studies can assess disease progression, response to supplementation, and prevention of neurological or hematological complications.
- Nutritional and Dietary Intervention Studies
- Research focusing on dietary habits, supplementation strategies, and nutritional education can help prevent vitamin B12 deficiency in high-risk groups such as young women.
- Development of Clinical Guidelines
- Findings from future studies may contribute to the development of screening and management guidelines for early detection of subclinical vitamin B12 deficiency.

References

1. Allen, L. H. (2009). Causes of vitamin B12 and folate deficiency. *Food and Nutrition Bulletin*, 30(2), S20–S34. <https://doi.org/10.1177/15648265090302S103>
2. Baik, H. W., & Russell, R. M. (1999). Vitamin B12 deficiency in the elderly. *Annual Review of Nutrition*, 19, 357–377. <https://doi.org/10.1146/annurev.nutr.19.1.357>
3. Carmel, R. (2011). Subclinical cobalamin deficiency. *Current Opinion in Gastroenterology*, 27(2), 151–158. <https://doi.org/10.1097/MOG.0b013e3283438c2b>
4. Carmel, R., Green, R., Jacobsen, D. W., Qian, G. D., & Stabler, S. P. (1996). Serum cobalamin, homocysteine, and methylmalonic acid concentrations in a multiethnic elderly population. *The American Journal of Clinical Nutrition*, 64(3), 388–394. <https://doi.org/10.1093/ajcn/64.3.388>
5. Ginde, A. A., Liu, M. C., & Camargo, C. A. (2012). Demographic differences and trends of vitamin B12 deficiency in the United States. *The American Journal of Medicine*, 125(6), 536–542. <https://doi.org/10.1016/j.amjmed.2011.10.030>
6. Green, R., Allen, L. H., Bjørke-Monsen, A. L., Brito, A., Guéant, J. L., Miller, J. W., Molloy, A. M., Nexø, E., Stabler, S., Toh, B. H., Ueland, P. M., & Yajnik, C. S. (2017). Vitamin B12 deficiency. *Nature Reviews Disease Primers*, 3, 17040. <https://doi.org/10.1038/nrdp.2017.40>
7. Hoffbrand, A. V., Moss, P. A. H., & Pettit, J. E. (2019). *Essential haematology* (7th ed.). Wiley-Blackwell.
8. Hoffman, R., Benz, E. J., Silberstein, L. E., Heslop, H., Weitz, J., & Anastasi, J. (2018). *Hematology: Basic principles and practice* (7th ed.). Elsevier.
9. Kassebaum, N. J. (2016). The global burden of anemia. *Hematology/Oncology Clinics of North America*, 30(2), 247–308. <https://doi.org/10.1016/j.hoc.2015.11.002>
10. Lindenbaum, J., Healton, E. B., Savage, D. G., Brust, J. C., Garrett, T. J., Podell, E. R., Marcell, P. D., Stabler, S. P., & Allen, R. H. (1988). Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *The New England Journal of Medicine*, 318(26), 1720–1728. <https://doi.org/10.1056/NEJM198806303182604>

10. O’Leary, F., & Samman, S. (2010). Vitamin B12 in health and disease. *Nutrients*, 2(3), 299–316. <https://doi.org/10.3390/nu2030299>
11. Patel, K. V., Ferrucci, L., Ershler, W. B., Longo, D. L., & Guralnik, J. M. (2009). Red blood cell distribution width and the risk of death in middle-aged and older adults. *Archives of Internal Medicine*, 169(5), 515–523. <https://doi.org/10.1001/archinternmed.2009.11>
12. Perumal, V., & Veerasamy, S. (2020). Nutritional anemia among young women: A growing concern. *Journal of Family Medicine and Primary Care*, 9(9), 4561–4566. https://doi.org/10.4103/jfmpe.jfmpe_713_20
13. Savage, D. G., Lindenbaum, J., Stabler, S. P., & Allen, R. H. (1994). Sensitivity of serum methylmalonic acid and total homocysteine determinations for diagnosing cobalamin and folate deficiencies. *The American Journal of Medicine*, 96(3), 239–246. [https://doi.org/10.1016/0002-9343\(94\)90143-0](https://doi.org/10.1016/0002-9343(94)90143-0)
14. Stabler, S. P. (2013). Vitamin B12 deficiency. *The New England Journal of Medicine*, 368(2), 149–160. <https://doi.org/10.1056/NEJMcp1113996>
15. Tefferi, A. (2003). Anemia in adults: A contemporary approach to diagnosis. *Mayo Clinic Proceedings*, 78(10), 1274–1280. <https://doi.org/10.4065/78.10.1274>
16. World Health Organization. (2008). *Worldwide prevalence of anaemia 1993–2005*. WHO Press.
17. Yajnik, C. S., Deshpande, S. S., Jackson, A. A., Refsum, H., Rao, S., Fisher, D. J., Bhat, D. S., Naik, S. S., Coyaji, K. J., & Joglekar, C. V. (2006). Vitamin B12 and folate concentrations during pregnancy and insulin resistance in the offspring. *Diabetologia*, 49(1), 29–38. <https://doi.org/10.1007/s00125-005-0089-z>