RESEARCH PAPER

Vitamin B12 Deficiency Presenting as Pancytopenia with Megaloblastic Bone Marrow Changes in a Patient with Type 2 Diabetes Mellitus: A Case Report

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Abstract

Background: Vitamin B12 deficiency is an important hematological disorder resulting from impaired DNA synthesis in rapidly dividing cells, leading to ineffective hematopoiesis and megaloblastic anemia. Although anemia is the most common manifestation, severe deficiency may occasionally present with pancytopenia, posing a diagnostic challenge. Early identification is essential because the condition is reversible with appropriate treatment.

Case Presentation: We report the case of a 55-year-old female with a known history of type 2 diabetes mellitus and hypertension who presented with complaints of giddiness for 20 days, palpitations and intermittent fever for two weeks, and cough with expectoration for one week. Clinical examination revealed pallor with stable vital parameters. Laboratory investigations demonstrated pancytopenia with severe anemia. Serial hematological evaluation showed hemoglobin levels ranging from 5.5–7.8 g/dL, platelet counts from 19,000–37,000/µL, and total leukocyte counts from 1,500–3,600/µL. Bone marrow aspiration and biopsy revealed normocellular marrow with marked erythroid hyperplasia, megaloblastic maturation, binucleated erythroid precursors, and altered myeloid-to-erythroid ratio, consistent with ineffective hematopoiesis due to nutritional deficiency. No dysplastic cells, blasts, or marrow fibrosis were identified. These findings supported the diagnosis of vitamin B12 deficiency– associated megaloblastic anemia presenting as pancytopenia. The patient showed gradual hematological improvement on follow-up evaluation.

Conclusion: Vitamin B12 deficiency should be considered in the differential diagnosis of unexplained pancytopenia. Bone marrow examination plays a crucial role in identifying characteristic megaloblastic changes and excluding other hematological disorders. Early recognition and timely treatment can lead to significant hematological recovery and prevent potential complications.

MeSH Keywords:

Vitamin B12 Deficiency; Pancytopenia; Megaloblastic Anemia; Bone Marrow Examination; Erythroid Hyperplasia; Diabetes Mellitus, Type 2; Hematologic Diseases.

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Introduction

Vitamin B12 deficiency is a clinically significant hematological disorder characterized by impaired DNA synthesis in rapidly dividing cells, particularly within the hematopoietic system, leading to ineffective hematopoiesis and the development of megaloblastic anemia. Vitamin B12, also known as cobalamin, is an essential water-soluble vitamin that plays a critical role in nucleic acid synthesis, methylation reactions, and normal neurological function. Adequate levels of vitamin B12 are necessary for the conversion of homocysteine to methionine and the metabolism of methylmalonic acid, processes that are fundamental for cellular replication and maturation. When vitamin B12 levels are deficient, nuclear maturation of hematopoietic precursor cells becomes defective while cytoplasmic maturation continues, resulting in a phenomenon known as nuclear-cytoplasmic asynchrony. This abnormal maturation produces enlarged erythroid precursors with immature nuclei in the bone marrow, a hallmark feature of megaloblastic anemia [1].

According to the hematology reference text *Hematology: Basic Principles and Practice* by Hoffman and colleagues, vitamin B12 deficiency leads to ineffective erythropoiesis, intramedullary destruction of developing blood cells, and morphological abnormalities across multiple hematopoietic lineages. These changes may manifest as anemia, leukopenia, thrombocytopenia, or in more

severe cases, pancytopenia. Bone marrow examination typically reveals erythroid hyperplasia, megaloblastic maturation, giant metamyelocytes, and dysplastic features within megakaryocytes and granulocytic precursors. These hematological abnormalities reflect defective DNA synthesis and impaired cell division within hematopoietic progenitor cells, ultimately leading to reduced peripheral blood cell counts [1].

Vitamin B12 deficiency may arise from a variety of etiological factors including nutritional deficiency, malabsorption syndromes, pernicious anemia, gastrointestinal disorders, and medication-related interference with vitamin absorption. The National Institutes of Health Office of Dietary Supplements describes vitamin B12 deficiency as a condition resulting from inadequate intake, impaired absorption in the gastrointestinal tract, or increased physiological demand. In adults, long-term use of medications such as metformin and proton pump inhibitors has been recognized as an important contributor to reduced vitamin B12 absorption. Chronic diseases such as diabetes mellitus may further predispose individuals to deficiency through prolonged pharmacological therapy and metabolic alterations that affect nutrient absorption and utilization [2].

From a global health perspective, anemia remains a major public health concern, particularly among women and older adults. The World Health Organization has identified anemia as a widespread condition affecting millions of individuals worldwide, with nutritional deficiencies—including vitamin B12 deficiency—contributing significantly to its burden. Although iron deficiency remains the most common cause of anemia globally, deficiencies of vitamin B12 and folate represent important yet frequently underrecognized etiologies of megaloblastic anemia. These nutritional deficiencies are particularly relevant in populations where dietary intake of animal-derived foods is limited or where chronic medical conditions influence nutrient absorption and metabolism [3].

Recognition of vitamin B12 deficiency is clinically important because the condition is readily treatable when identified early. However, delayed diagnosis may lead to progressive hematological abnormalities and neurological complications. Bone marrow examination plays an important diagnostic role in patients presenting with unexplained cytopenias or pancytopenia, as the characteristic megaloblastic changes can provide important clues to the underlying etiology. Understanding the hematological manifestations of vitamin B12 deficiency is therefore essential for clinicians when evaluating patients with unexplained anemia or multilineage cytopenias.

Case Presentation

A 55-year-old female presented to the outpatient department with complaints of giddiness for the past 20 days, palpitations for two weeks, intermittent fever for two weeks, and cough with expectoration for one week. The patient reported that she had been in her usual state of health until approximately twenty days prior to presentation, when she developed persistent episodes of giddiness that were not related to positional changes. The dizziness was continuous and gradually progressive in nature. Over the following two weeks, she also experienced intermittent episodes of fever associated with palpitations. The febrile episodes were not associated with chills or rigors. One week prior to presentation, the patient developed cough with expectoration.

There was no associated history of headache, vomiting, loose stools, upper respiratory symptoms, loss of consciousness, or shortness of breath. The patient also denied any history of bleeding manifestations, including epistaxis, gum bleeding, hematuria, or melena.

The patient had a known history of type 2 diabetes mellitus and systemic hypertension for the past ten years and was on regular medical treatment. There was no past history suggestive of bronchial asthma, tuberculosis, or coronary artery disease. Her personal history revealed normal appetite, adequate sleep, and normal bowel and bladder habits. The family history was non-contributory, with no known hematological disorders or chronic systemic illnesses among first-degree relatives.

On general physical examination, the patient was conscious, cooperative, and well oriented to time, place, and person. Her vital signs were stable at presentation. The blood pressure was 110/70 mmHg measured in the right arm in the supine position, pulse rate was 78 beats per minute, and oxygen saturation was 100% on room air. On general examination, pallor was noted, while icterus, clubbing, lymphadenopathy, and pedal edema were absent.

Systemic examination was performed. Cardiovascular examination revealed normal first and second heart sounds (S1 and S2) without murmurs or additional sounds. Respiratory system examination demonstrated bilateral equal air entry with normal vesicular breath sounds, and no adventitious sounds were appreciated. Per abdominal examination revealed a soft and non-tender

abdomen without hepatosplenomegaly, and bowel sounds were present and normal. Neurological examination did not reveal any focal neurological deficits.

Based on the presenting symptoms and initial laboratory findings suggestive of cytopenia, a provisional diagnosis of acute febrile illness with pancytopenia was considered. To further evaluate the underlying hematological abnormality, a bone marrow aspiration was performed from the posterior superior iliac spine under aseptic precautions.

Microscopic examination of the bone marrow aspirate demonstrated normocellular marrow with marked erythroid hyperplasia. The erythroid lineage showed predominantly normoblastic maturation admixed with occasional micronormoblastic and megaloblastic forms. Dysplastic features were also noted, including the presence of binucleated erythroid precursors.

Evaluation of the myeloid series revealed suppressed myelopoiesis with mild eosinophilic predominance. Certain myeloid precursors exhibited megaloblastic maturation with sieve-like nuclear chromatin, and giant metamyelocytes were also observed.

The megakaryocytic lineage appeared increased in number, with dysplastic forms including hypolobated and hyperlobated megakaryocytes. The lymphoid series and plasma cells were within normal limits in both number and maturation. Careful examination of the smears did not reveal any atypical or malignant cells, and no hemoparasites were identified.

The myeloid-to-erythroid (M:E) ratio was markedly altered at 0.22:1, indicating significant erythroid expansion relative to the myeloid series.

Based on the morphological findings, the bone marrow examination was interpreted as normocellular marrow with erythroid hyperplasia, increased megakaryopoiesis, and altered M:E ratio, along with features suggestive of megaloblastic hematopoiesis. In the appropriate clinical context, these findings were consistent with vitamin B12 deficiency–related megaloblastic anemia presenting with pancytopenia.

Table 1: Serial hematological parameters of the patient during hospitalization demonstrating persistent pancytopenia with gradual improvement in hemoglobin and leukocyte counts during follow-up.

Parameter	18/01/2025	19/01/2025	21/01/2025	22/01/2025	23/01/2025	24/01/2025	25/01/2025	27/01/2025	29/01/2025
Hemoglobin (g/dL)	6.0	6.0	6.0	6.2	5.5	5.6	5.7	6.5	7.8
Platelet Count (/µL)	37,000	34,000	34,000	34,000	23,000	26,000	19,000	25,000	29,000
Total Leukocyte Count (/µL)	2,500	2,300	1,850	2,010	1,500	1,880	2,520	3,600	3,440
Neutrophils (%)	44	44	47	53	52	49	79	79	75
Lymphocytes (%)	34	38	35	29	32	35	13	16	4
Eosinophils (%)	11	5	6	5	5	4	8	5	0
Basophils (%)	11	13	12	13	11	11	0	0	0
Mean Corpuscular Volume (fL)	85	84	85	84	83	84	84	82	84
Mean Corpuscular Hemoglobin (pg)	23	23	24	22	23	24	22	22	24

Table 2: Bone marrow biopsy findings demonstrating normocellular marrow with erythroid hyperplasia and megaloblastic changes suggestive of nutritional deficiency.

Parameter	Findings
Biopsy number	45/25
Clinical diagnosis	Acute febrile illness with pancytopenia
Nature of specimen	Bone marrow biopsy
Gross description	Single linear core of grey-white to grey-brown soft tissue measuring approximately **2 × 0.8 × 0.3 cm**
Cellularity	Overall cellularity appears **normocellular**
Marrow composition	Bone marrow shows **bony fragments and cellular components** including RBC, WBC, and platelet lineages
Distribution of cells	Predominantly **cell clusters with intervening fat spaces**
Hypocellular areas	Few focal areas appear **hypocellular**
Hematopoietic cell lines	All three hematopoietic lineages are present in focal areas
Blasts / immature cells	**Not identified**
Dysplasia	**No dysplastic cells identified**
Fibrosis	**Absent**
Myeloid–erythroid ratio	Altered (**2.6 : 1**)
Erythroid lineage	Erythroid series shows **erythroid hyperplasia with occasional megaloblasts**
Chromatin pattern	Megaloblasts show **large open "sieve-like" chromatin pattern**
Other erythroid forms	Presence of **micronormoblastic cells**
Final impression	Findings suggest **nutritional deficiency–related marrow changes with erythroid hyperplasia**
Recommendation	Clinical correlation and further investigations to identify cause of pancytopenia

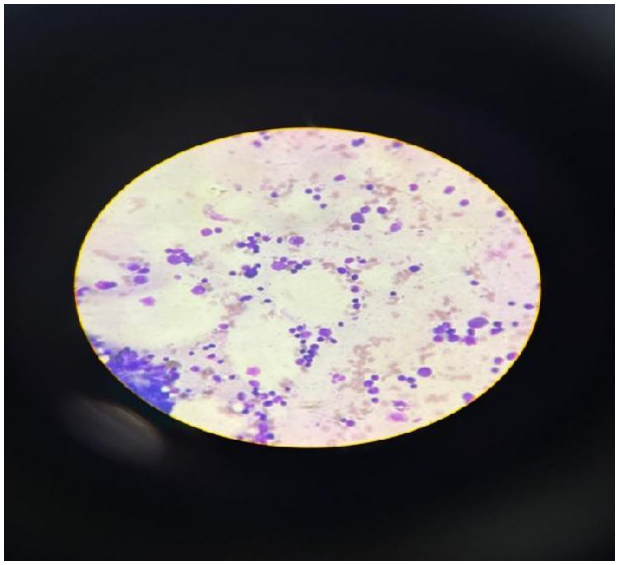

Figure 1. Bone Marrow Aspirate Smear Showing Megaloblastic Erythropoiesis Legend:

Bone marrow aspirate smear demonstrating marked erythroid hyperplasia with megaloblastic maturation. Several erythroid precursor cells exhibit enlarged nuclei with open chromatin pattern, reflecting defective DNA synthesis characteristic of vitamin B12 deficiency–related megaloblastic anemia. The background shows numerous erythroid lineage cells consistent with ineffective hematopoiesis and erythroid predominance.

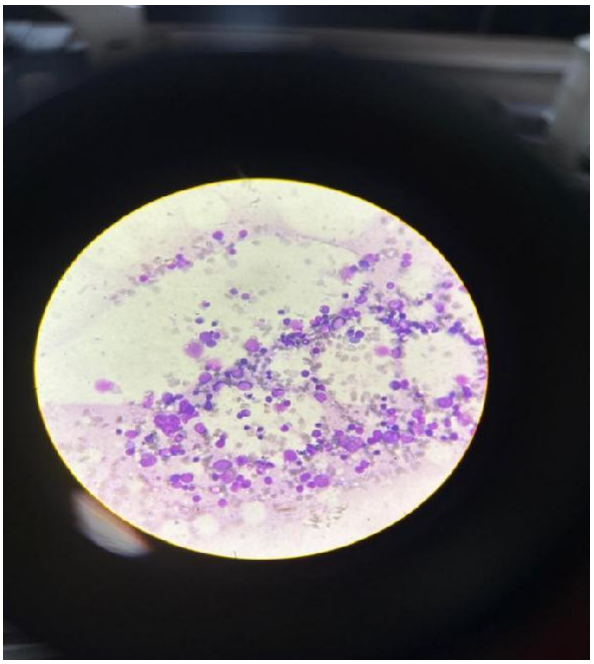

Figure 2. Bone Marrow Aspirate Showing Erythroid Hyperplasia

Legend:

Microscopic image of bone marrow aspirate revealing increased erythroid precursors with scattered normoblastic and megaloblastic forms. The erythroid cells demonstrate nuclear–cytoplasmic asynchrony, a hallmark feature of megaloblastic hematopoiesis. These findings correlate with the altered myeloid-to-erythroid ratio observed in the present case.

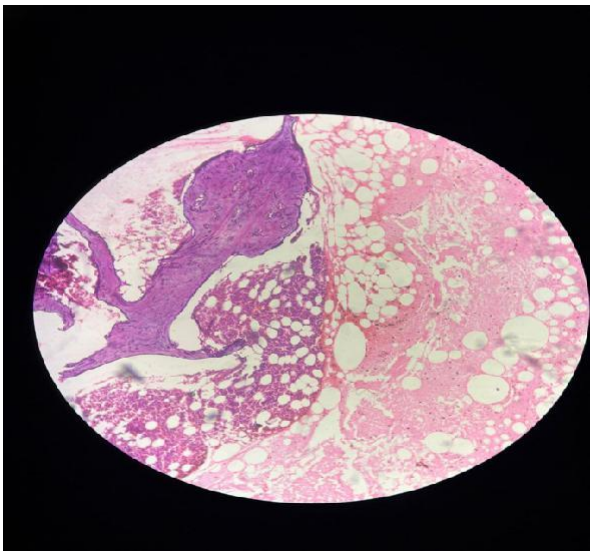

Figure 3. Bone Marrow Biopsy Showing Erythroid Hyperplasia with Megaloblastic Changes Legend:

Histopathological section of bone marrow biopsy demonstrating normocellular marrow with prominent erythroid hyperplasia. Numerous erythroid precursor cells with megaloblastic maturation and nuclear–cytoplasmic asynchrony are visible. The marrow spaces show clusters of hematopoietic cells interspersed with fat spaces and bony trabeculae, consistent with ineffective hematopoiesis. These findings support the diagnosis of megaloblastic anemia secondary to vitamin B12 deficiency presenting with pancytopenia. The morphological features correlate with the altered myeloid-to-erythroid ratio and erythroid predominance described in the case.

Discussion

Vitamin B12 deficiency is an important cause of hematological abnormalities and may present with a spectrum of manifestations ranging from isolated anemia to pancytopenia. The deficiency results in impaired DNA synthesis within rapidly proliferating hematopoietic cells, producing ineffective hematopoiesis and characteristic megaloblastic changes in the bone marrow. In the present case, the patient presented with clinical features including giddiness, palpitations, and intermittent fever, and laboratory evaluation revealed pancytopenia with severe anemia and thrombocytopenia. Serial hematological monitoring showed that hemoglobin levels ranged from 5.5 g/dL to 7.8 g/dL, platelet counts varied between 19,000/µL and 37,000/µL, and total leukocyte counts ranged from 1,500/µL to 3,600/µL, confirming significant suppression of all three hematopoietic lineages. These findings reflect ineffective hematopoiesis commonly seen in megaloblastic anemia secondary to vitamin B12 deficiency.

A recent case report by Akinola et al. described a rare presentation of severe vitamin B12 deficiency in which patients developed profound cytopenias. In their report, patients presented with hemoglobin levels as low as 4.8 g/dL, platelet counts of approximately 28,000/µL, and leukocyte counts around 2,000/µL, demonstrating the potential severity of hematological involvement in vitamin B12 deficiency. In comparison, the present patient demonstrated hemoglobin levels between 5.5–6.0 g/dL during the early phase of hospitalization, which is comparable to the severe anemia described by Akinola et al.. Similarly, the platelet count in our patient dropped to 19,000/µL, which is even lower than the platelet levels reported in their case. The leukocyte count in the present study reached a nadir of 1,500/µL, again reflecting severe bone marrow suppression similar to the cytopenias described by Akinola et al. [4].

The pathophysiological mechanism of vitamin B12 deficiency has been extensively explained by Green et al., who reported that defective DNA synthesis leads to the formation of megaloblasts within the bone marrow and results in ineffective erythropoiesis. Their work emphasized that the marrow in vitamin B12 deficiency typically demonstrates erythroid hyperplasia with megaloblastic changes and abnormal maturation of myeloid precursors. In the present case, bone marrow aspiration demonstrated erythroid hyperplasia with megaloblastic maturation and binucleated erythroid precursors, consistent with the morphological features described by Green et al.. Additionally, the myeloid-to-erythroid ratio in the present case was 0.22:1 in aspiration, indicating marked erythroid expansion, while the biopsy showed an erythroid to myeloid ratio of approximately 2.6:1, supporting the presence of erythroid hyperplasia typical of megaloblastic anemia [5].

According to Ankar and Kumar, vitamin B12 deficiency may manifest clinically with hematological abnormalities including macrocytic anemia, leukopenia, and thrombocytopenia due to ineffective hematopoiesis. They reported that patients often present with symptoms such as fatigue, dizziness, and palpitations associated with severe anemia. In the present case, the patient experienced persistent giddiness and palpitations, which correspond to symptoms resulting from reduced oxygen-carrying capacity due to low hemoglobin levels. Furthermore, mean corpuscular volume values in our patient ranged between 82–85 fL, which remained within the normocytic range despite severe anemia. Such findings have been described in early or mixed nutritional deficiency states, as highlighted by Ankar and Kumar, where classical macrocytosis may not always be evident in the initial stages of deficiency [6].

Pancytopenia is defined as a reduction in all three major blood cell lines—erythrocytes, leukocytes, and platelets. Chiravuri and De Jesus emphasized that nutritional deficiencies such as vitamin B12 deficiency represent an important reversible cause of pancytopenia. They reported that patients with pancytopenia may have leukocyte counts often below 4,000/µL and platelet counts below 150,000/µL, depending on the severity of marrow suppression. In the present case, the patient's total leukocyte count decreased to 1,500/µL, which is significantly below the lower reference limit, and the platelet count reached 19,000/µL, indicating severe thrombocytopenia. These findings are consistent with the hematological manifestations described by Chiravuri and De Jesus, supporting vitamin B12 deficiency as a reversible cause of pancytopenia [7].

Studies from India have also documented the clinical profile of vitamin B12 deficiency in tertiary care settings. Singh et al. conducted a study in northern India and reported that vitamin B12 deficiency is frequently associated with anemia and constitutional symptoms such as fatigue and dizziness. Their study found that many patients had hemoglobin levels below 8 g/dL, indicating moderate to severe anemia. In the present case, the hemoglobin level ranged from 5.5–7.8 g/dL, which is comparable to the severe anemia reported in the study by Singh et al., highlighting the clinical burden of vitamin B12 deficiency in the Indian population [8].

Similarly, Patel and Prajapati evaluated the spectrum of pancytopenia in adults attending a hematology department in western India and reported that megaloblastic anemia accounted for a significant proportion of pancytopenia cases. Their study demonstrated that nutritional deficiencies remain among the most common etiologies of pancytopenia in developing countries. The hematological findings observed in the present case, including severe anemia, leukopenia, thrombocytopenia, and erythroid hyperplasia in bone marrow, are consistent with the patterns described by Patel and Prajapati, supporting the diagnosis of nutritional deficiency–related pancytopenia [9].

Further evidence was provided by Shilpy et al., who investigated clinical and hematological correlations in vitamin B12 deficiency. Their study demonstrated that severe vitamin B12 deficiency may produce multiple cytopenias and significant morphological abnormalities within the bone marrow. The authors also noted that early recognition and treatment can lead to substantial hematological recovery. In the present case, serial monitoring of hematological parameters demonstrated gradual improvement in hemoglobin levels from 6.0 g/dL to 7.8 g/dL and improvement in leukocyte counts from 1,500/µL to 3,440/µL, suggesting a positive response to clinical management and supportive care. These findings are in line with the hematological recovery described by Shilpy et al., reinforcing the importance of timely diagnosis and treatment [10].

Conclusion :

Overall, the present case highlights that vitamin B12 deficiency can present as severe pancytopenia with characteristic bone marrow findings of erythroid hyperplasia and megaloblastic maturation. Careful evaluation of clinical presentation, peripheral blood

parameters, and bone marrow morphology is essential for establishing the diagnosis. Recognition of vitamin B12 deficiency is particularly important because it represents a treatable and reversible cause of pancytopenia, and early intervention can result in significant hematological recovery.

Reference :

1. Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weitz J, Anastasi J. Hematology: Basic Principles and Practice. 8th ed. Philadelphia: Elsevier; 2023.
2. National Institutes of Health Office of Dietary Supplements. Vitamin B12 Fact Sheet for Health Professionals. Bethesda (MD): NIH; 2023. Available from: https://ods.od.nih.gov/factsheets/VitaminB12 - HealthProfessional/
3. World Health Organization. Anaemia in women and children: global health estimates. Geneva: WHO; 2021. Available from: https://www.who.int
4. Akinola OO, Mandapati A, Douthit N. Unveiling the Pernicious Truth: A Case Report on the Rare Presentation of Severe Vitamin B12 Deficiency. Cureus. 2026 Jan 19;18(1):e101860. doi: 10.7759/cureus.101860. PMID: 41717155; PMCID: PMC12916071.
5. Green R, Allen LH, Bjørke-Monsen AL, Brito A, Guéant JL, Miller JW, Molloy AM, Nexo E, Stabler S, Toh BH, Ueland PM, Yajnik C. Vitamin B_{12} deficiency. Nat Rev Dis Primers. 2017Jun29;3:17040.doi: 10.1038/nrdp.2017.40. Erratum in: Nat Rev Dis Primers. 2017 Jul 20;3:17054. doi: 10.1038/nrdp.2017.54. PMID: 28660890.
6. Ankar A, Kumar A. Vitamin B12 Deficiency. [Updated 2024 Sep 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441923/
7. Chiravuri S, De Jesus O. Pancytopenia. [Updated 2023 Aug 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563146/
8. Singh J, Dinkar A, Gupta P, Atam V. Vitamin B12 deficiency in northern India tertiary care: Prevalence, risk factors and clinical characteristics. J Family Med Prim Care. 2022 Jun;11(6):2381-2388. doi: 10.4103/jfmpc.jfmpc_650_21. Epub 2022 Jun 30. PMID: 36119310; PMCID: PMC9480660.
9. Patel GR, Prajapati GR. Spectrum of Pancytopenia in Adults Attending a Clinical Hematology Department: A Four-Year Experience From a Tertiary Care Center of Western India. Cureus. 2022 May 12;14(5):e24933. doi: 10.7759/cureus.24933. PMID: 35706755; PMCID: PMC9188290.
10. Shilpy, Mishra M, Saha SS, Kumar A. Clinical and Hematological Parameters and Their Correlation With the Severity of Vitamin B12 Deficiency: A Hospital-Based Study. Cureus. 2025 Sep 9;17(9):e91907. doi: 10.7759/cureus.91907. PMID: 41080292; PMCID: PMC12512221.