B12 Before Iron - A Case - Based Protocol for Treating Severe Dimorphic Anaemia

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Introduction

Anaemia is a global public health crisis of staggering proportions, affecting over two billion people worldwide. India stands at the epicenter of this challenge, with a particularly high prevalence among women of reproductive age and pregnant women. The National Family Health Survey (NFHS-5, 2019-21) alarmingly reports that 57% of women aged 15-49 in India are anaemic. While iron deficiency has long been recognized as the primary culprit, a growing body of evidence highlights the complexity of nutritional anaemias in the Indian subcontinent. A significant portion of these cases are not due to a single nutrient deficiency but a combination of factors.

Among these complex conditions, dimorphic anaemia represents a significant diagnostic and therapeutic challenge. It is a type of anaemia characterized by the simultaneous deficiency of at least two key haematopoietic nutrients, most commonly iron and either vitamin B12 or folic acid. This dual deficiency results in the presence of two distinct populations of red blood cells in the circulation: the microcytic, hypochromic cells typical of iron deficiency, and the macrocytic cells characteristic of megaloblastic anaemia. The coexistence of these opposing morphological features can confound standard laboratory indices and mask the underlying severity of each deficiency.

For the practicing clinician, particularly in the field of obstetrics and gynaecology where anaemia management is a daily imperative, recognizing and appropriately managing dimorphic anaemia is critical. Misdiagnosis or improper sequential treatment can lead to suboptimal response, persistent anaemia, and, in the case of vitamin B12 deficiency, the precipitation of irreversible neurological damage. This article aims to provide a comprehensive analysis of dimorphic anaemia, elucidated through a detailed clinical case study from Faridabad, to offer a practical framework for its diagnosis and management.

Aim

The aim of this article is to comprehensively analyze the etiology, pathophysiology, clinical presentation, diagnosis, and management of dimorphic anaemia, utilizing a representative case study to bridge theoretical knowledge with practical clinical application in a high-prevalence setting.

Objective

To achieve the stated aim, this article will pursue the following objectives:

1. To define dimorphic anaemia and describe its underlying pathophysiology resulting from dual nutrient deficiencies.

2. To outline the key clinical and laboratory features, with a special emphasis on the pathognomonic peripheral blood smear findings.

3. To present a detailed, illustrative case study of severe dimorphic anaemia in a pregnant woman, reflecting a common clinical scenario in North India.

4. To discuss the step-by-step diagnostic reasoning, including the interpretation of conflicting haematological indices and the selection of confirmatory tests.

5. To analyze the nuanced, sequential management plan for dimorphic anaemia and the rationale behind it.

6. To highlight the potential pitfalls in diagnosis and treatment and provide evidence-based recommendations for monitoring therapeutic response.

Methodology

This article combines a comprehensive review of current medical literature with a descriptive, illustrative case study. The literature search was conducted using electronic databases including PubMed, Google Scholar, and the Cochrane Library. Guidelines and publications from authoritative bodies such as the World Health Organization (WHO), the Federation of Obstetric and Gynaecological Societies of India (FOGSI), the Indian Council of Medical Research (ICMR), and the American College of Obstetricians and Gynecologists (ACOG) were extensively reviewed.

Search keywords included: "dimorphic anaemia," "dual deficiency anemia," "iron deficiency anemia in pregnancy," "megaloblastic anemia," "peripheral smear dimorphism," "nutritional anemia in India," "vitamin B12 deficiency neuropathy," and "management of anemia in pregnancy."

The case study presented is a hypothetical but realistic composite, constructed based on years of clinical experience managing similar cases at Anjali Nursing Home in Faridabad, Haryana. It is designed to be representative of the demographic, dietary patterns, and clinical presentations commonly encountered in this region, thereby providing a tangible and educational context for the discussion.

Discussion

The complexity of dimorphic anaemia is best understood by walking through a real-world clinical scenario. The following case study will serve as the foundation for our analysis.

Part 1: The Case Presentation

Mrs. S.K., a 28-year-old female, gravida 2, para 1, presented to the outpatient department at 26 weeks of gestation with complaints of progressive and severe fatigue for the last two months. She reported feeling breathless on minimal exertion, such as walking a short distance within her home, and experienced frequent episodes of dizziness. She also noted a painful, "beefy-red" tongue and a persistent "pins and needles" sensation in both her feet.

• Socio-demographic and Dietary History: The patient resides in a semi-urban locality of Faridabad. Her family's diet is predominantly lacto-vegetarian. Her intake of green leafy vegetables, fruits, and dairy products was reported to be infrequent and inadequate, largely consisting of wheat-based bread (roti) and rice with lentils (dal) or potatoes.

• Clinical Examination: On examination, she appeared listless and exhibited marked conjunctival and palmar pallor. A faint icteric tinge was noted in her sclera. Her tongue was smooth, red, and devoid of papillae (atrophic glossitis). Her pulse was 110 beats/minute (tachycardia), and a soft systolic flow murmur was audible over the precordium. Neurological examination revealed diminished vibration and position sense in her lower limbs, with sluggish ankle reflexes. Her blood pressure was 110/70 mmHg, and her uterus size corresponded to her gestational age.

This clinical picture, with symptoms of severe anaemia (fatigue, breathlessness), glossitis (suggesting B12/folate deficiency), and peripheral neuropathy (highly suggestive of B12 deficiency), immediately raised suspicion of a complex nutritional anaemia beyond simple iron deficiency.

Part 2: The Diagnostic Workup – Unmasking the Dual Nature

The initial step was a complete blood count (CBC) and peripheral blood smear examination.
• Complete Blood Count (CBC):
◦ Haemoglobin (Hb): 5.2 g/dL (Severe Anaemia)
◦ Total Red Blood Cell (RBC) Count: 1.8 million/µL (Low)
◦ Mean Corpuscular Volume (MCV): 88 fL (Normal)

◦ Mean Corpuscular Haemoglobin (MCH): 29 pg (Normal)
◦ Red Cell Distribution Width (RDW-CV): 25% (High)

The CBC results were initially perplexing. Despite the severe anaemia, the MCV was in the normal range. This is a classic pitfall in dimorphic anaemia, where the averaging of microcytic and macrocytic cell populations by the automated analyzer produces a deceptively "normal" MCV. The most critical clue from the CBC was the high RDW, indicating a high degree of variation in red cell size (anisocytosis).

• Peripheral Blood Smear (The Key to Diagnosis): The peripheral smear was pathognomonic. It revealed a dimorphic picture with a striking dual population of red cells. There were numerous microcytic, hypochromic RBCs (small, pale cells) interspersed with large, oval-shaped red cells (macro-ovalocytes). Significant anisopoikilocytosis was present. Critically, several hypersegmented neutrophils (neutrophils with six or more nuclear lobes) were identified. The presence of hypersegmented neutrophils is a hallmark of megaloblastic change. This smear confirmed the co-existence of iron deficiency and megaloblastic anaemia.

• Confirmatory Biochemical Tests: To confirm the specific nutrient deficiencies, a panel of biochemical tests was ordered:

◦ Iron Studies:
▪ Serum Ferritin: 5 ng/mL (Markedly low; normal >30)
▪ Serum Iron: 20 µg/dL (Low; normal 60-170)
▪ Total Iron Binding Capacity (TIBC): 480 µg/dL (High; normal 240-450) This profile conclusively confirmed severe iron deficiency.
◦ Vitamin Assays:
▪ Serum Vitamin B12: 95 pg/mL (Markedly low; normal 200-900)
▪ Serum Folate: 4.5 ng/mL (Borderline low; normal >4.0) This confirmed a severe vitamin B12 deficiency, which was the primary driver of the megaloblastic component and the patient's neurological symptoms.

Diagnosis: Severe Dimorphic Anaemia (Iron and Vitamin B12 Deficiency) in Pregnancy.

Part 3: The Structured Management Plan

The management of dimorphic anaemia is nuanced and must follow a specific sequence to be safe and effective.

• The Treatment Dilemma: Treating a patient with severe B12 deficiency with iron alone can be dangerous. Iron can stimulate a burst of erythropoiesis, rapidly consuming the already scarce B12 reserves and potentially precipitating or worsening the neurological damage (subacute combined degeneration of the spinal cord). Therefore, the cardinal rule is to replete Vitamin B12 and Folate first.

• Step 1: Correcting the Megaloblastic Component (Weeks 1-2): The patient was immediately started on parenteral Vitamin B12 therapy to bypass any potential malabsorption and rapidly restore levels.

◦ Injection Hydroxocobalamin 1000 mcg intramuscularly, administered on alternate days for six doses.

◦ Oral Folic Acid 5 mg once daily.

• Step 2: Iron Repletion (Initiated after 2-3 days of B12 therapy): Given the severity of the anaemia (Hb 5.2 g/dL) and the need for a rapid response in the second trimester of pregnancy, parenteral iron therapy was chosen over oral iron, which can be slow and poorly tolerated.

◦ Intravenous Iron Sucrose was administered. The total dose was calculated using the Ganzoni formula: Total Iron Deficit (mg) = Body Weight (kg) x (Target Hb - Actual Hb) x 2.4 + Iron Stores (500 mg).

◦ The calculated dose was administered in divided doses of 200 mg over several sessions as per standard protocol, ensuring close monitoring for any adverse reactions.

• Step 3: Supportive Care and Counseling:

◦ Nutritional Counseling: The patient and her family were extensively counseled on incorporating iron-rich foods (green leafy vegetables, legumes), vitamin B12 sources (dairy products), and vitamin C-rich foods (citrus fruits) to enhance iron absorption.

◦ Blood Transfusion: A packed red blood cell (PRBC) transfusion was kept on standby but was not required as the patient remained hemodynamically stable and responded well to the initial therapy. Transfusion is reserved for cases with cardiac decompensation, fetal distress, or profound symptomatic anaemia unresponsive to initial treatment.

Part 4: Monitoring the Therapeutic Response

• Reticulocyte Count: A reticulocyte count was measured 7-10 days after initiating B12 therapy, which showed a robust peak of 15%. This "reticulocyte response" is the earliest indicator of effective treatment for megaloblastic anaemia.

• Haemoglobin and Follow-up: The patient’s Hb level was monitored weekly. It rose to 7.5 g/dL after two weeks and to 10.5 g/dL by four weeks post-treatment initiation. Her neurological symptoms began to improve within the first week.

• Long-term Maintenance: Following the completion of parenteral therapy, she was discharged on oral maintenance therapy consisting of ferrous ascorbate, folic acid, and methylcobalamin, which she was advised to continue throughout her pregnancy and for at least three months postpartum.

Conclusion

Dimorphic anaemia is a complex and frequently encountered clinical entity in India, masquerading as simple iron deficiency if not diligently investigated. As illustrated by this case, it represents a convergence of nutritional gaps prevalent in our communities. The deceptively normal MCV on automated counters can be a significant diagnostic pitfall, making the careful examination of a peripheral blood smear an indispensable skill for every clinician. A high RDW should always prompt a smear review.

The successful management of dimorphic anaemia hinges on two core principles: accurate diagnosis of the dual deficiencies and a correctly sequenced therapeutic plan. The treatment mantra—"B12 before Iron"—cannot be overemphasized, especially when neurological symptoms are present. By combining a high index of suspicion with a structured approach to diagnosis and management, we can effectively treat this complex condition, prevent irreversible neurological harm, and significantly improve maternal and fetal outcomes. Ultimately, tackling the root causes through robust public health initiatives focused on dietary diversification and nutritional education remains the cornerstone of preventing such severe deficiencies in our population.

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