



(CASE REPORT)



## Anemia and depression: A report of two clinical cases

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International Journal of Science and Research Archive, 2025, 17(02), 403-405

Publication history: Received on 25 September 2025; revised on 08 November 2025; accepted on 12 November 2025

Article DOI: <https://doi.org/10.30574/ijrsra.2025.17.2.3046>

### Abstract

This clinical study addresses the association between depression and anemia through two case presentations. Both instances initially exhibited as treatment-resistant depression but were later identified as having underlying iron deficiency anemia.

Case 1: A 5-year follow-up of a postpartum woman exhibiting depressive symptoms unresponsive to various antidepressants (maprotiline, escitalopram, sertraline). Laboratory tests showed that the person had iron deficiency anemia because they had thalassemia mild. Iron supplementation led to significant symptomatic enhancement.

Case 2: A 4-year follow-up of a patient with depression and significant somatoform symptoms, who was treated ineffectively with maprotiline and fluoxetine. A physical checkup and blood testing showed that the person had iron deficiency anemia. The combination of psychiatric and hematological treatment led to significant improvement.

The paper stresses that somatic comorbidities, especially anemia, go unreported in over half of psychiatric patients, even though they have an impact on clinical outcomes in 50–70% of cases. Iron deficiency may directly induce depression by inhibiting serotonin synthesis. The authors conclude that seemingly treatment-resistant depression may be sustained by underlying anemia, and early detection using basic laboratory screening can significantly improve therapy response.

**Keywords:** Depression; Anemia; Treatment-Resistant Depression; Iron Deficiency; Thalassemia; Somatic Comorbidity; Psychiatric Symptoms; Iron Deficiency Syndrome; Pernicious Anemia; Neuropsychiatric Manifestations

### 1. Introduction

The relationship between depression and anemia has been extensively documented in the literature. The symptom overlap identified in both conditions—including asthenia, cephalalgia, heightened irritability, and fatigue—may, at first, lead patients to pursue psychiatric evaluation. Medical practitioners often arrive at a diagnosis of a major depressive disorder, which subsequently exhibits persistence notwithstanding sufficient compliance with antidepressant treatment. Consequently, a diagnosis of treatment-resistant depression is likely to be rendered. This is well illustrated by our two clinical cases. Re-examination of these patients revealed anemia and corrected the diagnosis of treatment-resistant depression.

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## 2. Clinical Cases

### 2.1. Case 1

Mrs. B.H., a married homemaker and mother of three children, had been receiving outpatient psychiatric care for depression over a five-year period. Her initial presentation was characterized by rapidly progressive onset (occurring two months postpartum following her third delivery) of complete insomnia accompanied by depressed mood, anhedonia, psychomotor retardation, irritability, and diffuse somatic complaints (headaches, polyarthralgia, and epigastric pain). She underwent several consultations with general practitioners without improvement. Initially, she was prescribed maprotiline at a dosage of 75 mg. Notwithstanding several months of effectively managed therapeutic interventions, which necessitated a transition to escitalopram at 10 mg and subsequently to Nodop (sertraline) at 50 mg, her condition persisted without resolution. Following a two-year duration of treatment and in consideration of the continual physical symptoms despite appropriate therapeutic strategies, laboratory investigations revealed the existence of iron deficiency anemia. Further hematological evaluations produced no evidence of external hemorrhage, diarrhea, or epigastric disorders. Supplementary hemoglobin electrophoresis identified thalassemia minor. Following three months of iron supplementation, psychiatric reassessment demonstrated substantial symptomatic improvement.

### 2.2. Case 2

Mrs. T.A., a married homemaker and mother of four children. She has been followed for four years for depression: insomnia, low mood, and anhedonia, with somatoform symptoms as the primary symptom (headaches, abdominal pain, and arthralgia). Initially prescribed maprotiline 75 mg, then fluoxetine 20 mg. A follow-up consultation revealed a slight improvement in insomnia but persistent low mood and somatoform symptoms. Physical examination showed pallor of the skin and mucous membranes, and blood tests revealed iron deficiency anemia.

The patient was subsequently treated simultaneously in psychiatry (starting sertraline 50 mg) and hematology (correction of the anemia) over several months, producing remarkable improvement in psychiatric symptomatology, with resolution of somatoform symptoms, normalization of sleep patterns, and mood stabilization. During follow-up evaluations, the possibility of a previous hypomanic episode could not be definitively excluded.

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## 3. Discussion

Treatment-resistant depression is conventionally defined as an absent or insufficient response to two antidepressants with distinct mechanisms of action, administered at adequate dosages for a sufficient duration of six weeks, in the absence of underlying somatic pathology or interfering medication [1].

Somatic comorbidities accompanying psychiatric disorders are identified in 30-60% of hospitalized patients and influence clinical outcomes in 50-70% of cases. However, these comorbidities remain undetected in nearly half of all cases [2].

In both clinical cases presented, depression was the sole diagnosis established. When confronted with persistent symptoms including fatigue, asthenia, and irritability, clinicians rapidly considered treatment-resistant depression. The diagnostic challenge arises when underlying organic pathology is present. The most frequently encountered medical comorbidities include infectious diseases such as HIV and endocrine disorders, including hypothyroidism or hypothalamic-pituitary-adrenal axis dysregulation. Additional significant medical comorbidities comprise cardiovascular diseases and diabetes [3].

In a study of hospitalized patients, 7.4% presented with normochromic normocytic anemia, and 1.9% with hypochromic microcytic anemia. Extended laboratory evaluation (iron and ferritin assays) revealed iron deficiency in 1.6% of these patients. Additionally, 1.4% were identified as having microcytic pseudopolycythemia, indicating thalassemia minor [2].

Further investigations implicate iron deficiency itself as a causative factor in depression. Iron deficiency appears to limit serotonin production. Evidence demonstrates that iron deficiency can lead not only to iron deficiency anemia but also, years preceding its manifestation, to the development of health disturbances and depression [4].

Indeed, Iron Deficiency Syndrome (IDS) without anemia was initially described in 2006. IDS is characterized primarily by sleep disturbances, exhaustion, concentration difficulties, vertigo, neck stiffness, headaches, hair loss, and brittle nails. One year later, its existence was confirmed through multicenter data collection [4].

In other forms of anemia, such as pernicious anemia (Biermer's disease), depressive symptomatology represents the most frequent psychiatric manifestation [5]. It may occur in isolation or as part of a psychotic or anxiety presentation. This depressive symptomatology may predominate clinically. During inaugural neuro-Biermer's disease, macrocytic anemia and vitamin B12 deficiency may be absent, underscoring the importance of meticulous clinical examination and simple laboratory tests (complete blood count and vitamin B12 assay) when evaluating atypical neuropsychiatric presentations or at-risk patients [5].

Regarding thalassemia and depressive mood, genetic studies have identified a genetic susceptibility factor for bipolar disorders on the short arm of chromosome 16, in proximity to alpha-globin genes implicated in alpha-thalassemias [6].

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#### **4. Conclusion**

Absence of significant response following adequately conducted treatment does not invariably indicate resistance. Depressive episodes deemed treatment-resistant may be perpetuated or caused by underlying somatic pathology such as anemia. Consequently, early identification and management can substantially enhance response to antidepressant treatment.

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#### **Compliance with ethical standards**

##### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

##### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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