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101.RED CELLS AND ERYTHROPOIESIS, EXCLUDING IRON

Vitamin B12 Deficiency and Hemolytic Anemia Presenting As Pseudo Thrombotic Microangiopathy: A Systematic Review

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Introduction:
Vitamin B12 deficiency is a common nutritional issue associated with mild anemia and neurological deficits. While rare, hemolytic anemia and low platelet count can be complications of this deficiency, often misdiagnosed as thrombotic microangiopathy (TMA), specifically thrombotic thrombocytopenic purpura (TTP). Pseudo TMA features can occur with B12 deficiency and can be effectively treated with vitamin B12 supplementation. In contrast, true TMA requires plasmapheresis. This systematic review aims to differentiate between pseudo TMA and TMA cases through an analysis of published case reports, providing valuable insights to avoid unnecessary treatments.

Methods:
We performed systematic review from Pubmed, Web of Science, and Scopus database. Twin independent reviewers (SY and BL) performed the screening using Covidence. Search keywords included "((hemolytic anemia) AND (vitamin B12 deficiency)) OR ((cobalamin deficiency) AND (hemolytic anemia)) Filters: English" for Pubmed, "(((ALL=(Cobalamin deficiency)) OR ALL=(vitamin B12 Deficiency))) AND ALL=(hemolytic anemia) Filter: English" for Web of Science and "(vitamin AND b12 AND deficiency OR cobalamin AND deficiency) AND hemolytic AND anemia AND (LIMIT-TO (LANGUAGE , "English"))" from Scopus. Only case reports in English with full-text availability and adult subjects were selected. Cases without final clinical outcome after treatment were excluded. After a comprehensive review, we identified 43 case reports and series with a total 53 patients that fulfilled our criteria. The details of selection process is illustrated in the prisma diagram (Figure 1).

Results:
The majority of cases involved males with low hemoglobin and platelet counts upon admission. Evidence of hemolysis was observed, indicated by increased lactate dehydrogenase (LDH), undetectable haptoglobin, and elevated or normal total and direct bilirubin levels. Peripheral blood films confirmed the presence of hemolytic anemia. Due to the co-occurrence of thrombocytopenia and hemolytic anemia, some cases were initially diagnosed as TTP, leading to the initiation of plasmapheresis. In 16 out of 53 reported case reports/series, patient received plasmapheresis. However, low reticulocyte index and normal ADAMTS 13 suggested an alternative diagnosis. Once ADAMTS 13 levels were normal, plasmapheresis was discontinued as TTP was ruled out. Diagnosis of B12 deficiency was confirmed by low B12 levels and elevated methylmalonic acid (MMA) levels. Leading cause for B12 deficiency were pernicious anemia in 28/53 cases, followed by dietary deficiency, and malabsorption due to surgery. Some patients also exhibiting concurrent iron deficiency anemia and folate deficiency. Treatment with subcutaneous B12 injections showed improvement in hemolysis as early as one week.

Conclusion:
Many cases of Vitamin B12 deficiency presenting with hemolytic anemia and thrombocytopenia are mistakenly diagnosed as TTP, leading to unnecessary and expensive plasmapheresis. Routine B12 level checks should be performed in all patients with hemolytic anemia, as B12 deficiency can be rapidly diagnosed and effectively treated, avoiding misdiagnoses and unnecessary interventions associated with TTP. The short turnover time for B12 levels (hours) compared to ADAMTS 13 activity (1-2 days) further supports the importance of routine B12 assessment in these patients.

Disclosures No relevant conflicts of interest to declare.

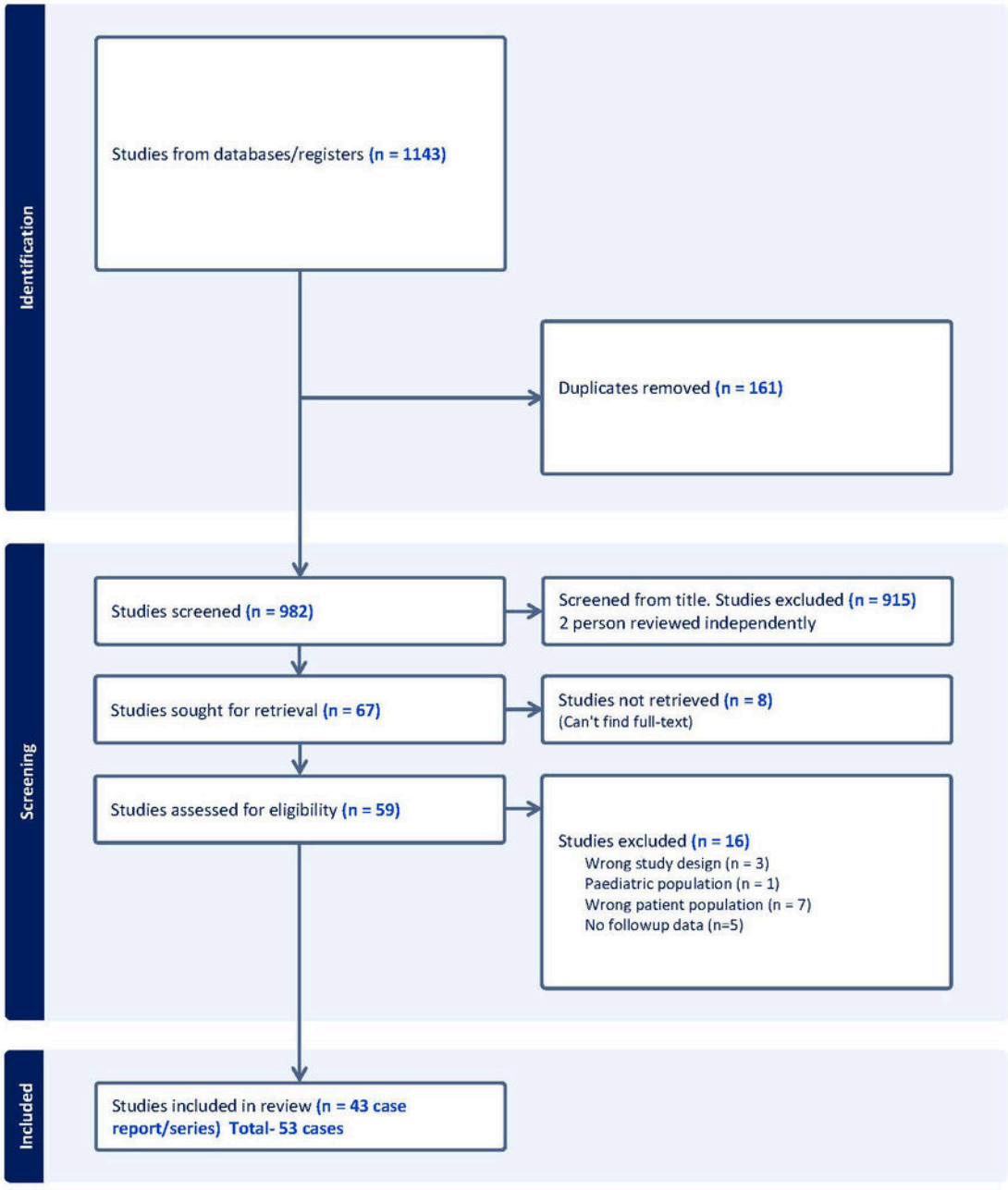

Figure 1: Prisma diagram of patient selection.

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Figure 1

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