AG Salud. 2025; 3:120
doi: 10.62486/agsalud2025120

CASE REPORT

Immune thrombocytopenia a key piece of the puzzle for the diagnosis of atypical systemic lupus erythematosus in critically ill patients. Case report

Trombocitopenia inmunitaria, una pieza clave en el diagnóstico de Lupus Eritematoso Sistémico atípico en pacientes críticos. Reporte de caso

Paul Cardozo Gil[1], Fernando Peralta[2], Jhossmar Cristians Auza-Santivañez[3], Mariela Marpartida Vildoso[2], Eduardo Ustarez[2], José Bismarck Ortiz Baptista[2], Franz Quiroz Carrasco[2], Freddy Ednildon Bautista-Vanegas[4]

[1]Hospital Obrero Nro. 3, Caja Nacional de Salud. Clínica de las Américas Santa Cruz Bolivia .
[2]Hospital Obrero Nro. 3, Caja Nacional de Salud. Santa Cruz Bolivia.
[3]Ministerio de Salud y Deportes. Instituto Académico Científico Quispe-Cornejo. La Paz, Bolivia.
[4]Kliniken Beelitz GmbH - Brandenburg Deutschland. Germany.

Cite as: Cardozo Gil P, Peralta F, Auza-Santivañez JC, Marpartida Vildoso M, Ustarez E, Bismarck Ortiz Baptista J, et al. Immune thrombocytopenia a key piece of the puzzle for the diagnosis of atypical systemic lupus erythematosus in critically ill patients. Case report. AG Salud. 2025; 3:120. https://doi.org/10.62486/agsalud2025120

Submitted: 03-02-2024 **Revised:** 12-08-2024 **Accepted:** 22-01-2025 **Published:** 23-01-2025

Editor: Dr. Telmo Raúl Aveiro-Róbalo

Corresponding author: Paul Cardozo Gil

ABSTRACT

Introduction: immune thrombocytopenia (ITP) is an autoimmune disorder characterized by autoantibody-mediated destruction of platelets, resulting in low platelet count and increased risk of bleeding, and may be an initial manifestation of systemic lupus erythematosus (SLE), especially in patients with findings suggestive of autoimmunity.
Clinical Case: a 52-year-old male presented with fever, hematuria, generalized petechiae (including mucous membranes), myalgia, mucosal bleeding, oliguria progressive to anuria, and severe arterial hypertension. Initial studies revealed severe anemia, severe thrombocytopenia, and acute kidney injury, which led to his admission to the Intensive Care Unit (ICU). Complementary studies showed positive ANA, low complement (C3, C4), and positive anti-Ro, while anti-dsDNA antibodies, ANCA, and markers of antiphospholipid syndrome were negative. Imaging revealed pulmonary edema with mild alveolar hemorrhage and renal ultrasound findings consistent with active lupus nephritis. These findings raised the possibility that severe thrombocytopenia was a prelude to SLE. After initial treatment refractory, the patient was escalated to rituximab, with a favorable response without complications, which allowed discharge from the ICU.
Conclusions: this case highlights the importance of considering SLE in patients with refractory thrombocytopenia without apparent cause, even in men, and underlines the need for a multidisciplinary approach for timely diagnosis and treatment, thus preventing serious complications.

Keywords: Atypical Systemic Lupus Erythematosus; Immune Thrombocytopenia; Lupus Nephritis; Rituximab; Severe Thrombocytopenia.

RESUMEN

Introducción: la trombocitopenia inmunitaria (PTI), es un trastorno autoinmune caracterizado por la destrucción mediada por autoanticuerpos de las plaquetas, lo que resulta en un recuento plaquetario bajo y un mayor riesgo de sangrado, pudiendo ser una manifestación inicial del lupus eritematoso sistémico (LES), especialmente en pacientes con hallazgos sugestivos de autoinmunidad.
Caso Clínico: varón de 52 años, con cuadro de fiebre, hematuria, petequias generalizadas (incluyendo mucosas),

mialgias, sangrado por mucosas, oliguria progresiva a anuria e hipertensión arterial severa. Los estudios iniciales revelaron anemia severa, trombocitopenia severa y lesión renal aguda, lo que motivó su ingreso a la unidad de Terapia Intensiva (UTI). Los estudios complementarios mostraron ANA positivo, complemento bajo (C3, C4) y anti-Ro positivo, mientras que los anticuerpos anti-dsDNA, ANCA y marcadores de síndrome antifosfolípido resultaron negativos. Las imágenes revelaron edema pulmonar con hemorragia alveolar leve y hallazgos ecográficos renales compatibles con nefritis lúpica activa. Estos hallazgos plantearon la posibilidad de que la trombocitopenia severa fuera un preludio de LES. Tras la refractariedad al tratamiento inicial, se escaló a rituximab, con respuesta favorable, sin complicaciones, que permitió el alta de la UTI.
Conclusiones: este caso resalta la importancia de considerar el LES en pacientes con trombocitopenia refractaria sin causa aparente, incluso en varones, y subraya la necesidad de un abordaje multidisciplinario para un diagnóstico y tratamiento oportuno, así prevenir complicaciones graves.

Palabras Clave: Lupus Eritematoso Sistémico Atípico; Trombocitopenia Inmunitaria; Nefritis Lúpica; Rituximab; Trombocitopenia Severa.

INTRODUCTION

Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is an autoimmune disorder characterized by autoantibody-mediated destruction of platelets, resulting in a low platelet count (<100 000/µL) and an increased risk of bleeding.[1,2] ITP can be classified as primary when no underlying cause is identified or secondary when it is associated with autoimmune diseases, infections, or neoplasms.[3] SLE is a chronic, multisystemic autoimmune disorder that predominantly affects women of childbearing age. However, it can also occur in men, with clinical manifestations ranging from mild forms to severe and potentially fatal complications.[4] Thrombocytopenia is a common manifestation of SLE, present in approximately 20-40 % of cases, and can be the first manifestation of the disease, representing a diagnostic and therapeutic challenge.[5]

ITP associated with SLE can present acutely, chronically, or refractory, and its management requires a multidisciplinary approach combining immunosuppression, antimalarials, and, in severe cases, biological therapies such as rituximab.[5] This clinical case describes a 52-year-old male with severe ITP as the initial manifestation of SLE, highlighting the importance of considering systemic autoimmune diseases in patients with thrombocytopenia of no apparent cause. In addition, the pathophysiological mechanisms, clinical impact, and current therapeutic strategies for managing this condition are discussed.

CLINICAL CASE

A 52-year-old male with no relevant medical or family history went to the emergency department with symptoms of one week's evolution, manifesting fever, gross hematuria, generalized petechiae (including mucous membranes), myalgia, arthralgia and bleeding from the mucous membranes (epistaxis and gingival bleeding). In addition, he presented progressive oliguria to anuria and severe arterial hypertension (200/110 mmHg). On admission, the patient was conscious and oriented (Glasgow Scale 15/15), including refractory metabolic acidosis, which led to his transfer to the intensive care unit (ICU).

Initial studies revealed hemoglobin (Hb) 6 g/dL (severe anemia), platelets 1 000-3 000/µL (severe thrombocytopenia), confirmed with peripheral blood smear, sternal manubrium aspiration myelogram (figure 1A-1B, figure 2A-2B), ruling out primary and central blood diseases, negative Coombs test with no apparent signs of hemolysis, thus ruling out hemolytic uremic syndrome (HUS), among others; acute kidney injury (creatinine: 14 mg/dL, urea: 200-300 mg/dL) and nephrotic range proteinuria (3 553 mg/24 h). Mild hyperkalemia (potassium: 5 mEq/L) and metabolic acidosis (pH: 7,18, HCO3: 12 mEq/L) were also observed. Serology for HIV, hepatitis B and C, leptospirosis, hantavirus (IgM ELISA), and hemorrhagic fever were all negative.

Imaging studies, such as a chest CT (figure 3) and renal ultrasound, were requested. Source: The author's renal, slightly enlarged kidneys increased cortical echogenicity and decreased corticomedullary differentiation, which is compatible with glomerular involvement without alterations in intrarenal flow. These findings, together with nephrotic-range proteinuria and renal dysfunction, were highly suggestive of active lupus nephritis. In the ICU, aggressive management was started with intravenous sodium nitroprusside to control the hypertensive emergency, achieving an adequate reduction in blood pressure without complications. Daily red blood cell and platelet transfusions were administered to manage active bleeding, and refractory metabolic acidosis was corrected with the initiation of renal replacement therapy (RRT).

There were no complications during treatment, such as thrombosis or opportunistic infections. The renal biopsy, initially considered to confirm the diagnosis of lupus nephritis, was postponed due to severe thrombocytopenia, which made it impossible to perform in the acute context—the favorable response to treatment and the absence of complications allowed for discharge from the ICU.

https://doi.org/10.62486/agsalud2025120

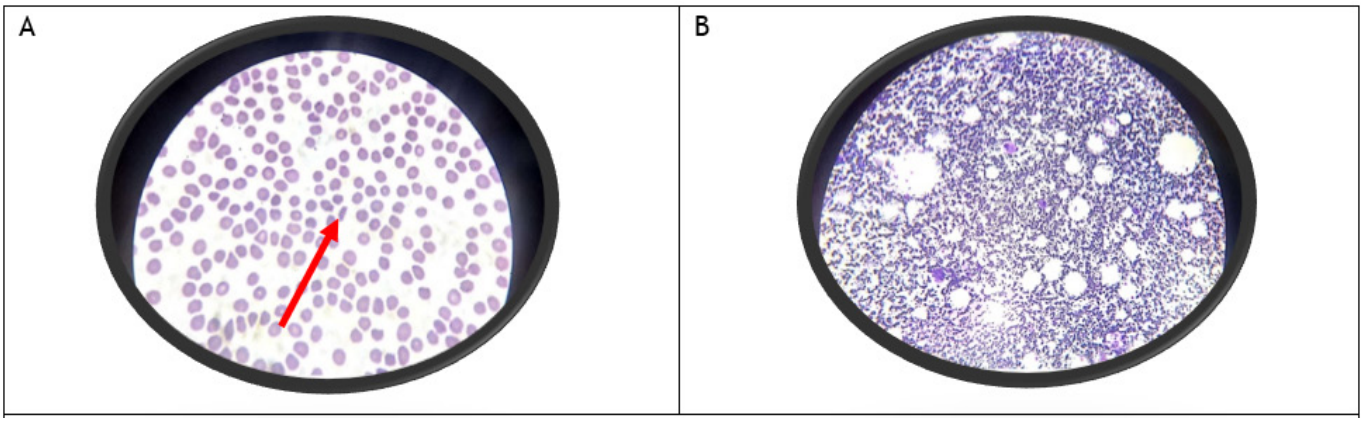

Figure 1. A: peripheral blood smear: few schistocytes are observed, with no marked alterations in the red series, which does not suggest evident microangiopathic hemolysis. **B:** sternal manubrium aspirate; shows hypercellularity with probable proliferation of hematopoietic lines. Clear spaces suggestive of megakaryocytic activity are observed

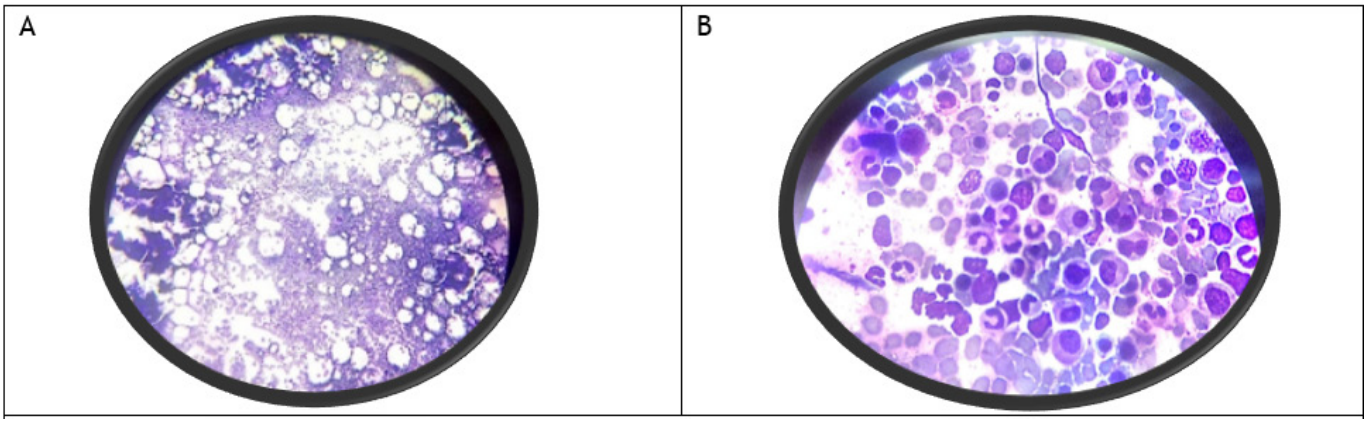

Figure 2. A: Marrow aspirate: shows hypocellular marrow with prominent adipose tissue (fat spaces). This pattern suggests suppression or insufficiency of the bone marrow. **B:** Megakaryocytic hyperplasia, with increased numbers and size of megakaryocytes. This is characteristic of a compensatory response to peripheral thrombocytopenia

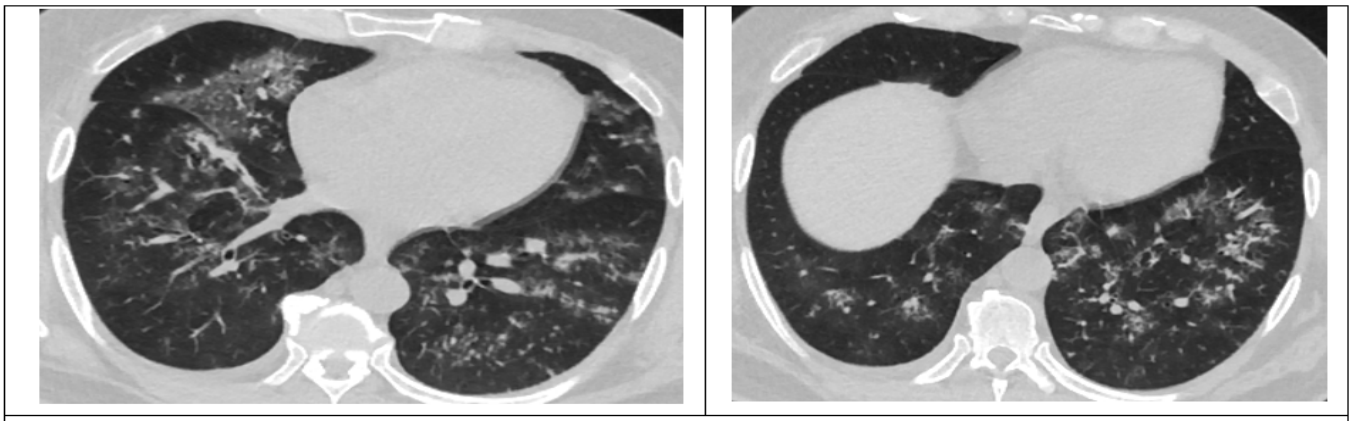

Figure 3. Ground glass opacities with bilateral perihilar consolidations, septal thickening and gravitational distribution in the lower lobes, suggestive of pulmonary edema, together with focal lesions compatible with mild alveolar hemorrhage

Given the presence of thrombocytopenia with autoimmune characteristics and the impossibility of completely ruling out thrombotic thrombocytopenic purpura (TTP) due to the presence of scarce schistocytes in the blood smear and the lack of availability in our environment to perform tests such as ADAMTS-13 (A disintegrin and metalloproteinase with thrombospondin type 1 repeats, member 13) and haptoglobin, immunosuppressive treatment was prioritized; methylprednisolone (1 g intravenously for 3 days) to control lupus activity, intravenous immunoglobulins (IVIG) for 5 days to raise the platelet count. However, the patient showed resistance to the initial treatment, with persistent severe thrombocytopenia and clinical deterioration. Subsequently, the immunological results were received, which showed antinuclear antibodies (ANA) 2,53 U (positive), low complements (C3: 81 mg/dL, C4: 16 mg/dL) and anti-Ro 2,821 U (positive), while anti-dsDNA,

https://doi.org/10.62486/agsalud2025120

ANCA and markers for antiphospholipid syndrome were negative.

Although it was not possible to measure haptoglobin or ADAMTS-13 due to limitations in our environment, these findings, together with the clinical picture, supported the diagnosis of Systemic Lupus Erythematosus (SLE) with severe manifestations, including lupus nephritis, secondary ITP, and pulmonary involvement. Given the refractoriness of the initial treatment, it was decided to escalate to induction therapy with rituximab (RTX). After the first week of treatment, a favorable response was observed, with an increase in the platelet count to 35 000/μL and general clinical improvement.

DISCUSSION

ITP may be the first piece of the puzzle as an early manifestation of SLE due to shared immunopathogenic mechanisms and overlapping clinical features, which highlights the importance of considering systemic autoimmune diseases in patients with thrombocytopenia of no apparent cause. Patients with ITP have a significantly higher risk of developing SLE compared to the general population. A population-based cohort study showed that patients with ITP have a 26-fold increased risk of developing SLE, with an adjusted hazard ratio indicating a markedly increased incidence.[6]

The pathophysiological link between immune thrombocytopenic purpura (ITP) and systemic lupus erythematosus (SLE) can be explained by the presence of autoantibodies (ANA), which are common in both conditions. A systematic meta-analysis confirmed that ANA positivity is a significant risk factor for developing SLE in patients with ITP.[7] In this case, ANA positivity was key in orienting the diagnosis towards SLE. In addition, factors such as young age, mucosal bleeding, and high ANA titers have been identified as predictors of progression from ITP to SLE,[8] all present in our patients, reinforcing their relevance in the early identification of systemic autoimmune diseases.

Autoimmune thrombocytopenia (<100×10⁹/L) is reported in 20 %–40 % of patients with SLE, and in 5–16 % of cases, it may be the initial manifestation of the disease.[9] Although the exact relationship between ITP and SLE is not fully defined, retrospective studies, such as that of Zhu et al., have shown that ITP can precede the diagnosis of SLE, especially in women.[6] However, this case highlights that males can also present this association, underlining the need to monitor all patients with ITP, regardless of sex.

ITP in the context of SLE is associated with a worse prognosis, higher mortality, and serious complications, such as renal involvement, neuropsychiatric disorders, and antiphospholipid syndrome. In this case, the patient presented with acute kidney injury (creatinine: 6 mg/dL) and proteinuria in the nephrotic range (>3,500 mg/day), findings highly suggestive of lupus nephritis, one of the most serious manifestations of SLE, which occurs in 40-60 % of patients. These findings were interpreted as proliferative lupus nephritis (class III or IV according to the ISN/RPS classification), supported by massive proteinuria, rapid deterioration of renal function, and low levels of complement (C3 and C4), which reflect immunological activity. Furthermore, anti-Ro positive (despite anti-dsDNA and anti-Smith negativity) does not rule out a diagnosis of SLE, as these antibodies are also associated with the disease. The severe thrombocytopenia and anemia (hemoglobin: 6 g/dL) may be secondary to lupus activity, either due to SLE-associated ITP or anemia of chronic disease.[6]

A meta-analysis by Pamuk et al. revealed that almost 2 % of patients with primary ITP develop SLE, especially those with positive ANA titers, who represent a high-risk group.[7] This risk increases over time, reinforcing the importance of close follow-up in these patients.[10]

In the case presented, a male with ITP developed SLE concomitantly, highlighting the need for rigorous clinical and laboratory follow-up in patients with ITP and positive ANA. Earlier diagnosis and treatment could have avoided complications such as the active bleeding that led to his admission to the ICU. This case highlights the importance of a comprehensive diagnostic approach and multidisciplinary management in patients with ITP, especially when findings suggest systemic autoimmune diseases.

In the case of thrombocytopenia refractory to conventional treatments, using rituximab (RTX), an anti-CD20 monoclonal antibody, was considered. This is effective and safe in patients with SLE and refractory thrombocytopenia.

Recent studies support that RTX induces remission in many cases, reducing dependence on glucocorticoids and immunoglobulins.[11] Therefore, induction therapy with RTX was chosen, followed by antimalarials such as hydroxychloroquine, to maintain long-term remission. This approach controls lupus activity, reduces the risk of relapses, and avoids complications associated with the prolonged use of glucocorticoids.[12] The favorable response observed in this case supports the usefulness of RTX in the comprehensive management of patients with SLE and refractory ITP.

CONCLUSIONS

ITP may be the first piece of the puzzle as a manifestation of SLE, underlining the importance of a comprehensive clinical approach in patients with thrombocytopenia of no apparent cause. Although SLE is more common in women, this case shows that men can also develop it, with ITP as the initial manifestation,

even before specific symptoms appear. Careful evaluation is crucial to differentiate between SLE-associated ITP, lupus nephritis, and thrombotic microangiopathies, entities with very different therapeutic and prognostic implications. Management required a multidisciplinary approach, integrating hematologists, nephrologists, rheumatologists, and intensivists, allowing control of lupus activity and preventing irreversible organ damage. Early detection of SLE in patients with ITP and positive ANA is key to improving prognosis and avoiding serious complications such as lupus nephritis. This case reinforces the need to perform a complete autoimmune profile in patients with ITP, facilitating timely diagnosis and treatment.

REFERENCES

1. Ye QD, Jiang H, Liao XL, Chen K, Li SS. Identification and validation of gene expression pattern and signature in patients with immune thrombocytopenia. SLAS Discov. 2017;22(2):187-95. https://doi.org/10.1177/1087057116664029

2. Rodeghiero F, Stasi R, Gernsheimer T. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009 Mar 12;113(11):2386-93. https://doi.org/10.1182/blood-2008-07-162503

3. Tsokos GC. Autoimmunity and organ damage in systemic lupus erythematosus. Nat Immunol. 2020;21(6):605 614. https://doi.org/10.1038/s41590-020-0677-6

4. Yen EY, Singh RR. Brief report: lupus-an unrecognized leading cause of death in young females: a population-based study using nationwide death certificates, 2000-2015. Arthritis Rheumatol. 2018;70(8):1251 1255. https://doi.org/10.1002/art.40512

5. Zitek T, Weber L, Pinzon D, Warren N. Assessment and Management of Immune Thrombocytopenia (ITP) in the Emergency Department: Current Perspectives. Open Access Emerg Med. 2022; 14:25-34.

6. Zhu FX, Huang JY, Ye Z, Wen QQ. Risk of Systemic Lupus Erythematosus in Patients with Idiopathic Thrombocytopenic Purpura: A Population-Based Cohort Study. Annals of the Rheumatic Diseases. 2020;79(6):793-799. https://doi.org/10.1136/annrheumdis-2020-217013.

7. Pamuk ON, Ali SM, Hasni S. Development of Systemic Lupus Erythematosus in Patients with Immune Thrombocytopenic Purpura: A Systematic Meta-Analysis. Autoimmunity Reviews. 2023;22(4):103297.

8. Ahn SM, Choi EJ, Oh JS. Prognostic Factors for the Development of Systemic Lupus Erythematosus in Patients with Immune Thrombocytopenia. Arthritis Research & Therapy. 2022;24(1):213. https://doi.org/10.1186/s13075-022-02901-y

9. Fanouriakis A, Bertsias G, Boumpas DT. Population-based studies in systemic lupus erythematosus: immune thrombocytopenic purpura or 'blood-dominant' lupus? Ann Rheum Dis. 2020 Jun;79(6):683-684. https://doi.org/10.1136/annrheumdis-2020-217356

10. Pamuk ON. Thrombocytopenia in Patients with Systemic Lupus Erythematosus. Eur J Rheumatol. 2023 oct;10(4):159-162. https://doi.org/10.5152/eurjrheum.2023.23069

11. Zeynep Toker Dincer, Beste Acar, Yagmur Ersoy, et al. Rituximab intervention in management of thrombocytopenia in patients with systemic lupus erythematosus: A single centre experience. 2025 Feb 11, https://doi.org/10.1177/09612033251319395

12. Erik Cimé-Aké, Ana Barrera-Vargas, Roberta Demichelis-Gómez, et al. Description of therapeutic strategies in severe systemic lupus erythematosus-associated immune thrombocytopenia: a retrospective cohort study of response and relapse. Clin Rheumatol, 2024 Aug;43(8):2521-2532. https://doi.org/10.1007/s10067-024-07031-1

CONSENT

The patient's consent was obtained for the realization of this work.

FINANCING

The authors did not receive funding for the implementation of this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONTRIBUTION OF AUTHORSHIP

Conceptualization: Paul Cardozo Gil, Jhossmar Cristians Auza-Santivañez.

Research: Paul Cardozo Gil, Fernando Peralta.

Methodology: José Bismarck Ortiz Baptista.

Visualization: Mariela Marpartida Vilsoso.

Original draft: Paul Cardozo Gil, Fernando Peralta, Eduardo Ustarez, Mariela Marpartida Vilsoso, José Bismarck Ortiz Baptista, Franz Quiroz Carrasco.

Writing-revision and editing: Paul Cardozo Gil, Fernando Peralta, Jhossmar Cristians Auza-Santivañez, Mariela Marpartida Vilsoso Eduardo Ustarez, José Bismarck Ortiz Baptista, Franz Quiroz Carrasco, Freddy Ednildon Bautista-Vanegas.

https://doi.org/10.62486/agsalud2025120