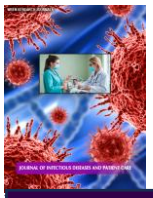

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Mini-Review

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Usefulness of Mean Platelet Volume as a Predictor of Activity and Severity in Patients with Syphilis: An Applied Study in Cuba

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Abstract

Background: Syphilis is a persistent sexually transmitted infection with diagnostic limitations in low-resource settings. The need for accessible biomarkers that complement clinical-laboratory diagnosis has promoted interest in Mean Platelet Volume (MPV) as a relevant hematological parameter.

Objective: To evaluate the usefulness of Mean Platelet Volume (MPV) as a marker of activity and severity in syphilis after treatment.

Methods: Applied prospective study (July 2024-May 2025) in 88 patients with confirmed syphilis. MPV, Platelet Distribution Width (PDW), platelet count and VDRL titers were measured at diagnosis and 30 days after benzathine penicillin treatment. Descriptive statistics, Pearson's correlation, Student's t-test and ROC analysis were used.

Results: MPV significantly increased post-treatment (6.9 ± 1.1 fL *vs.* 8.8 ± 1.0 fL; $p<0.001$). There was an inverse correlation with VDRL titers ($r=-0.57$; $p<0.01$). ROC curve showed an AUC of 0.83 (95% CI: 0.74–0.91), with 81% sensitivity and 76% specificity for an MPV cut-off <7.5 fL.

Conclusion: MPV is a practical, accessible and effective biomarker for monitoring syphilis activity and treatment response in resource-limited settings, compatible with primary care practice.

Keywords: Syphilis; Mean platelet volume; Biomarkers; Inflammation; Hematologic diagnosis; Infectious disease monitoring

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Introduction

Syphilis is one of the most devastating sexually transmitted infections, surpassed only by HIV/AIDS and continues to be a significant public health issue. It may also be transmitted congenitally through the placenta, *via* contaminated blood transfusions or accidental direct inoculation. Treponema pallidum is sexually transmitted (oral, vaginal or anal) with an estimated infectivity rate of ~30%. Vertical transmission during the first four years post-infection can result in a fetal mortality rate exceeding 30%-40%. Untreated, it progresses through multiple phases and is classified as early or late based on time from infection to diagnosis [1].

Between 2007 and 2017, over 260,000 confirmed syphilis cases were reported in 30 European countries. Despite a slight decline from 2007 to 2010, cases rose again to over 33,000 by 2017. The WHO aims to reduce syphilis incidence by 90% between 2018 and 2030. In countries with fragile health systems, STI registration and treatment are often lacking, resulting in uncontrolled infections [2].

In Latin America, WHO data indicate that over 1 million individuals aged 15-49 contract a curable STI daily, totaling over 376 million new annual cases, including syphilis. For instance, in Chile, syphilis cases rose by 65% between 2010

and 2019 [3]. In Cuba, syphilis incidence increased, reaching 7,428 cases and a rate of 67.0 per 100,000 people in 2022, with a higher incidence in men (75.5) than women (58.7). Diagnosis varies by clinical stage and relies on clinicalepidemiological findings combined with lab confirmation. Serological tests are most common but have low sensitivity in early stages, where molecular methods like PCR are more valuable [4].

Two diagnostic paths exist: indirect and direct. Indirect diagnosis uses serological tests, divided into non-treponemal and treponemal. Non-treponemal tests (*e.g.,* VDRL, RPR) detect antibodies against damaged cell lipids and are useful for initial screening due to low cost and ease of quantification. Treponemal tests (*e.g.,* FTA-ABS, TPHA, TP-PA, TP-EIA, CLIA) use specific antigens and detect long-lasting antibodies. IgM antibodies are detected about two weeks after exposure, followed by IgG. IgM levels drop after treatment, while IgG may persist for years regardless of therapy. To improve diagnostic capacity with accessible biomarkers, Mean Platelet Volume (MPV) a standard hematology parameter has emerged as a promising marker. MPV reflects the geometric size of platelets, whose morphology and function are defined during megakaryocyte fragmentation and influenced by cytokines like thrombopoietin and IL-6 [5].

Inflammatory conditions increase pro-inflammatory cytokines (especially IL-6), stimulating platelet production. IL-6 increases megakaryocyte ploidy and cytoplasmic volume, leading to larger platelets. These macroplatelets migrate to inflammation sites and are rapidly consumed, causing MPV to fall in acute inflammation. In contrast, in chronic stable inflammation, MPV may rise [6,7].

Platelets express Toll-Like Receptors (TLRs), which recognize pathogen-associated molecular patterns and stimulate pro-inflammatory cytokine production. MPV tends to decrease with intense inflammation and increase during chronic, stable phases. These MPV shifts have been observed in infections, sepsis, appendicitis, lupus, rheumatoid arthritis, inflammatory bowel disease and Behçet's disease [8,9].

A 2015 study at Shanghai Dermatology Hospital found significant platelet changes in primary and secondary syphilis but no other stages. Elevated IL-6, TNF and IL-1 levels in early syphilis may influence MPV and PDW through increased macroplatelet consumption. IL-6, IL-1, TNF, M-CSF and G-CSF are known to modulate platelet size in inflammatory diseases. This highlights the potential role of MPV in the inflammatory response and syphilis pathogenesis [10].

Justification

Early detection and timely treatment of syphilis reduce complications. However, in Cuba, access to bacterial infection markers is limited due to cost. No national studies have assessed MPV as a marker in syphilis. A need exists for accessible, low-cost bacterial infection markers to evaluate disease activity and treatment response. Platelet indices can help clinicians monitor infection without invasive bone marrow aspiration.

Hypothesis

Mean platelet volume is an indicator of syphilitic activity.

Study contributions

Proposes an accessible hematologic tool for dynamic syphilis activity monitoring.

Encourages platelet markers in settings with limited specialized testing.

Promotes interdisciplinary collaboration in hematology, infectious diseases and microbiology.

Enables primary care and hospital protocol development in Cuba and similar settings.

General objective

To evaluate the usefulness of MPV as a predictor of disease activity and severity in confirmed syphilis cases.

Methodology

Study type

Observational, descriptive, longitudinal study assessing MPV as a hematologic biomarker in confirmed syphilis cases pre- and post-treatment.

Population and sample

Population: Patients at Iván Portuondo Teaching Hospital with suspected syphilis.

Sample: 88 TPHA-positive patients, non-probabilistic sampling.

Inclusion criteria

Age ≥ 18 years;

Positive TPHA result and;

Signed informed consent.

Exclusion criteria

Pregnancy;

Active chronic infections or diseases and;

Recent antibiotic use (past 4 weeks), smoking or alcohol consumption.

Variables

Age, sex, TPHA result, VDRL titers, MPV, PDW, platelet count, peripheral smear description.

Instruments

Sysmex XS 1000i automated hematology analyzer VDRL Plus (Cromatest), TPHA (Centis) kits Giemsa-stained peripheral smear microscopy.

Procedure: Collection of clinical and sociodemographic data;

Blood sampling for serology and baseline hematology;

Repeat hematology 1-month post-treatment and;

Statistical analysis using SPSS v22.0.

Results

Cohort profile

Mean age: 34.7 ± 10.1 years 62% male;

Syphilis stage: 25% primary, 63% secondary, 12% latent, 11.3% HIV co-infection.

Hematologic changes

MPV: 6.9 ± 1.1 fL → 8.8 ± 1.0 fL ($p < 0.001$);

PDW: 13.4 ± 2.7% → 16.1 ± 2.2% ($p < 0.01$);

Platelet count: 264 ± 77 $\times 10^9$/L → 248 ± 71 $\times 10^9$/L ($p = 0.065$);

VDRL titer: Median 1:32 → 1:4 ($p < 0.001$).

Correlations

MPV ↔ VDRL: $r=-0.57$; $p<0.01$;

MPV ↔ PDW: $r=0.46$; $p < 0.01$ MPV ↔ platelet count: $r=-0.42$; $p<0.05$.

ROC curve

AUC: 0.83 (95% CI: 0.74–0.91);

MPV <7.5 fL → Sensitivity: 81%, Specificity: 76%.

Discussion

The study confirms MPV significantly decreases during active syphilis and normalizes posttreatment, supporting its role as an inflammatory biomarker. These findings align with global evidence showing MPV's sensitivity in chronic infectious and inflammatory conditions. IL-6 appears key in modulating megakaryocyte activity and platelet size. MPV inversely correlated with VDRL titers ($r=-0.57$; $p<0.01$), reflecting both inflammation and immune response magnitude. Prior studies found similar trends [11].

MPV <7.5 fL showed good sensitivity/specificity and is widely available *via* routine hematology, unlike costlier tests like PCR or Western Blot. The moderate correlation with PDW suggests platelet anisocytosis also plays a role but requires further study [12]. MPV may also aid short-term monitoring, as serological titers can take months to decline. The main study limitations were single-center design and moderate sample size. Systemic co-infections were excluded to reduce confounding [13].

Despite limitations, MPV may significantly aid syphilis management, especially in primary care, rural hospitals and low-resource clinics. The applied research model emphasizes translating scientific findings into practical tools for physicians and public health professionals [14].

Conclusion

MPV is a practical, reliable and low-cost marker for monitoring syphilis activity and severity. Its inclusion in clinical guidelines is recommended, particularly in primary healthcare.

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Conflict of Interest

The authors declare no conflicts of interest.

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