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Hematological changes associated with Covid-19 and their diagnostic implications.

Hematological alterations associated with COVID-19 and their diagnostic implications

Nathalia Cassimiro Pessoa

nathalia.csmr@gmail.com

Thais Santana de Oliveira

thais.santana@iesb.br

SUMMARY

Infection with the SARS-CoV-2 virus triggers a complex interaction between the inflammatory and hemostatic systems, making laboratory monitoring a key component in the management of COVID-19. This study aimed to investigate the profile of hematological alterations in infected patients and evaluate the effectiveness of biomarkers as predictors of clinical prognosis. To this end, a descriptive literature review with a qualitative approach was conducted, based on the analysis of secondary data collected from the SciELO and Google Scholar databases, covering the period from 2020 to 2026. The results indicated that severe lymphocytopenia and subsequent neutrophilia are classic indicators of severity, reflecting the state of immune exhaustion and the development of a cytokine storm.

Hematimetric ratios and indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR) and the Systemic Immune Inflammation Index (SII), have been found to have high accuracy in predicting severe outcomes, ICU admission, and the need for mechanical ventilation.

Additionally, the exponential increase in D-dimer and consumptive thrombocytopenia highlighted the critical role of immunothrombosis and coagulopathy in the pathogenesis of the disease.

It is concluded that the complete blood count, when combined with the stratified interpretation of inflammatory indices and hemostatic markers, constitutes a low-cost tool with significant prognostic utility for hospital screening, allowing for the optimization of bed management and more assertive clinical care.

Keywords: COVID-19. Blood count. Lymphocytopenia. Biomarkers. Prognosis.

ABSTRACT

Infection with SARS-CoV-2 triggers a complex interaction between the inflammatory and hemostatic systems, making laboratory monitoring a key component of COVID-19 management. This study aimed to investigate the profile of hematological changes in patients with infection and to evaluate the efficacy of biomarkers as predictors of clinical prognosis. To this end, a descriptive and qualitative literature review was conducted, based on the analysis of secondary data collected from SciELO and Google Scholar databases, covering the period from 2020 to 2026. The results indicated that severe lymphocytopenia and subsequent neutrophilia are classic indicators of disease severity, reflecting immune exhaustion and the development of a cytokine storm. It was found that hematimetric ratios and indices, such as the Neutrophil-to-Lymphocyte Ratio (NLR) and the Systemic Immune-Inflammation Index (SII), show high accuracy in predicting severe outcomes, ICU admission, and the need for mechanical ventilation. Additionally, the exponential rise in D-dimer and the occurrence of consumption thrombocytopenia evidenced the critical role of immunothrombosis and coagulopathy in the pathogenesis of the disease. In conclusion, the complete blood count, when combined with the stratified interpretation of inflammatory indices and hemostatic markers, constitutes a low-cost tool with significant prognostic utility for hospital screening, enabling optimization in hospital bed management and more assertive clinical care.

Keywords: COVID-19. Complete Blood Count. Lymphocytopenia. Biomarkers. Prognosis.

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1. INTRODUCTION

The COVID-19 pandemic, triggered by the SARS-CoV-2 virus, took place as one of the greatest health and scientific challenges of the 21st century. Taxonomically, the The pathogen belongs to the order *Nidovirales,* family *Coronaviridae* , and subfamily *Orthocoronavirinae,* being classified as SARS-CoV-2 (coronavirus of the syndrome). severe acute respiratory infection 2) (Xavier *et* al., 2020). Structurally, coronaviruses (CoVs) are characterized as enveloped viruses with a single-stranded, sense RNA genome positive (Schoeman; Fielding, 2020). Its morphology features pleomorphic capsids with superficial radial projections that resemble a crown, which justifies its nomenclature (Cascella, 2020). Although molecular detection by RT-PCR is the gold standard For diagnosis, understanding systemic manifestations has become vital for management. clinical (Al-Saadi; Abdulnabi, 2021).

Although initially described as a predominantly respiratory pathology, The evolution of COVID-19 revealed a complex systemic nature with involvement multiorgan, significantly affecting the hematopoietic system (Rahman, 2021). A The interaction between the virus and the host triggers an exacerbated inflammatory response. culminating in a hyperinflammatory state and oxidative damage that alters physiology. leukocyte count and global hematological parameters (Xavier *et* al., 2020; Pereira *et* al., 2021). This "cytokine storm" scenario promotes morphological and quantitative changes in blood cells, which reflects the severity of the infection (Bahadur *et* al., 2021).

In this context, the complete blood count stands out as an indispensable clinical tool. Low cost, fast and widely available. Monitoring of blood lines. It allows for risk stratification and outcome prediction, with parameters such as Leukopenia, lymphocytopenia, and the presence of immature forms aid in patient screening. with a greater potential for complications (Urbano *et* al., 2022; Al-Saadi; Abdulnabi, 2021). Recent studies reinforce that marked lymphocytopenia and neutrophilia are not only Common findings, but also critical biomarkers of poor prognosis and mortality. (Coelho *et* al., 2021; dos Santos Medeiros *et* al., 2024).

Additionally, hematological ratios and changes in platelet counts have demonstrated high sensitivity in identifying patients who may progress to critical states (Sadeghi-Nodoushan *et al.,* 2024). COVID-19 is also intrinsically linked to hemostasis disorders, in which there is excessive activation of the coagulation cascade and

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Reduced platelet counts increase the risk of thrombotic events and intravascular coagulation.
widespread (Karimi Shahri *et* al., 2020). Therefore, careful analysis of these biomarkers is necessary.
Laboratory tests are fundamental for defining accurate prognoses (Xavier *et* al., 2020).

Despite the abundance of data, the variability of hematological responses and the
There is still a need to consolidate accessible indicators for risk stratification.
They constitute a gap in optimized clinical management.

2. JUSTIFICATION

The relevance of this research is based on the need to understand the
systemic mechanisms of COVID-19 and the search for diagnostic methods that combine accuracy
and viability. Although the disease was initially cataloged as a syndrome
respiratory, the evidence points to a systemic pathology with a profound impact on
hematological homeostasis (Xavier *et* al., 2020). In this sense, the study is justified.
primarily due to the importance of establishing clear correlations between the cellular profile of
blood and the clinical evolution of patients.

From a scientific and academic point of view, the research contributes to the
Filling gaps in the characterization of the hematological profile in SARS-CoV infection.
CoV-2, highlighting how specific cellular imbalances and alterations in homeostasis occur.
They serve as indicators of disease progression (Pereira *et al.,* 2021). Systematizing these
These findings allow the academic community to have an updated theoretical framework.
that supports the effectiveness of inflammation and coagulation biomarkers in monitoring
of emerging viral diseases.

In the social context, this work is justified by its potential impact on management.
public health: validating the use of accessible laboratory indices as robust predictors of
With a better prognosis, it becomes possible to optimize the allocation of ICU beds and therapeutic resources.
in scenarios of high hospital demand. Thus, the study not only expands knowledge
scientific, but it also offers a practical contribution focused on the efficiency of care and to
Improving clinical outcomes in the healthcare system.

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3. OBJECTIVE

3.1 GENERAL OBJECTIVE

Analyze the main quantitative and qualitative variations of leukocyte lineages.
and platelet counts in patients with COVID-19 and describe how these hematological changes
They assist in the diagnosis and clinical screening of the disease.

3.2 SPECIFIC OBJECTIVES

- To describe the pathophysiology of COVID-19 and its impact on the hematological system;
- Identify quantitative and qualitative changes in the white blood cell count and platelet count.
of infected patients;
- To analyze the use of hematological indices as biomarkers of severity and
clinical prognosis.

4. METHODOLOGY

The research was conducted through a descriptive scoping review and
A qualitative approach, based on the analysis of secondary data. The study sought
to investigate the scientific publications that discussed the hematological profile of patients with
COVID-19, using the BVS database and Google as the main sources of information.
Academic. Data collection was carried out through a literature review.
structured, employing standardized descriptors in the Portuguese language and their respective
English equivalents: "COVID-19", "Blood Count", "Changes"
(Changes), "Biomarkers" and "Diagnosis", which were
combined to refine the search.

In this sense, the investigation is guided by the following guiding question: what are
The main leukocyte and hemostasis alterations described in the literature and how they occur.
These biomarkers act as clinical prognostic indicators in patients with
COVID-19? In order to answer this question, the following were selected, as
Inclusion criteria: scientific articles published between 2020 and 2026, written in Portuguese.

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or English, which presented relevant data on quantitative and qualitative variations.
of leukocyte and platelet lineages, as well as hemostasis markers. In
Conversely, incomplete texts, event summaries, and paid files were excluded.
editorials and studies that did not establish a direct relationship between laboratory changes and the
Clinical prognosis of SARS-CoV-2 infection. For the organization and management of
References found were analyzed using digital filtering and storage tools.
ensuring the systematization of sources.

5. RESULTS AND DISCUSSION

The data analysis was performed using documentary and bibliographic techniques.
structured in four consecutive screening stages. In the first analysis, the search for
The keyword search resulted in the identification of 174 articles. In the second stage, after evaluation...
After considering the titles and excluding those that deviated from the main proposed theme, the amount was...
refined to 29 publications. The third analysis consisted of screening the abstracts, in which
Articles that did not present quantitative results were excluded, reducing the corpus.
23 papers. Subsequently, in the fourth stage, the selected articles were submitted to a
a complete analytical reading, excluding incomplete and/or paid texts, which resulted in
final selection of 12 studies that comprised the scope of this research. The entire process of
The refinement process and exclusion criteria applied at each stage are systematized in a
flowchart, as shown in Figure 1.

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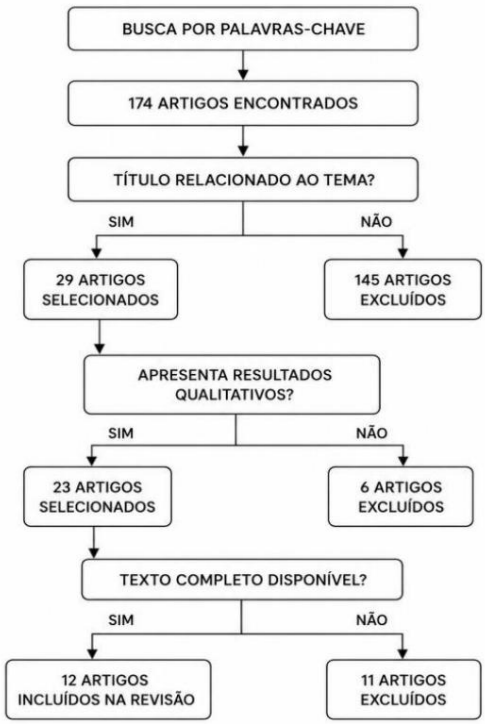
FIGURE 1: Selection and screening process for scientific articles



Source: author's own.

In order to answer the guiding question and contextualize the scientific debate, the essential characteristics of these articles, as well as the counterpoint evidence used in The critical discussions were mapped and summarized in Table 1 below.

TABLE 1: Evidence Matrix

Author(s) and Year	Article Title	Study Objectives	Main Results Presented
AL-SAADI & ABDULNABI (2021)	*Hematological changes in cell counts associated with COVID-19 infection.*	To assess the variations in Blood types associated with the severity of the infection.	It consolidates the use of PLR and NPR relationships to identify the transition from the viral phase to the hyperinflammatory phase of the disease.
BAHADUR *et al.* (2021)	*Changes in peripheral blood in SARS COV-2 patients and their clinical-pathological correlation...*	To correlate changes in peripheral blood with the clinical and pathological status of patients.	It associates severe lymphocytopenia with an unfavorable prognosis and identifies the presence of giant platelets as a compensatory bone marrow response.

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BUONACERA *et al.* (2022)	Investigating the influence of the NLR/SII *lymphocyte ratio: Confirms that the NLR/SII lymphocyte ratio is an emerging marker of* diabetes and lacks specificity. *between systemic inflammation and cardiovascular risk* and cardiovascular risk in etiological baseline fluctuations of the NLR.		factors, presenting *relationships* chronic elevations arising from pre-existing comorbidities or age-related factors, which masks the isolated real impact of COVID-19.
DOS SANTOS MEDEIROS *et al.* (2024)	Identifying *predictive* biomarkers of mortality *in patients* with *severe COVID-19 hospitalized in the* ICU. *intensive care unit*		The of Systemic Immunoinflammation (SII) index showed the highest accuracy in predicting death, surpassing the counts. isolated.
GUMANOVA *et al.* (2023)	*Effects of COVID-19 Infection* virus on oxygen transport parameters, coagulation and inflammation markers, and *biomarkers of oxygen function and* coagulation cascade dysregulation . Demonstrates the impact of *infection in healthy subjects on cardiac* function and inflammation. phase *of Transport, Blood . Coagulation, and Inflammation*	Investigate the effects of infection on	the systemic impact of the Inflammatory even after the acute
MANAÇAS *et al.* (2024)	*Evaluation of* hematological *changes . immune response* biomarkers correlated with *COVID-19.*	Assess the changes in the neutrophil-hematological ratio and such as the Lymphocyte-Lymphocyte Prognostic factors in low monocyte (LMR) *in* critically ill patients.	Elevated lymphocyte (NLR) *and* Ratio . *critical patients* are strongly associated with immune exhaustion and death *from* in the ICU.
BIRTH *and al.* (2020)	*COVID-19 and the State of Hypercoagulability: Perspective* and Proposing Damage-Mediated Approaches *hypercoagulability:* coagulopathy due to COVID-19	Hypercoagulability: Discussing the mechanisms of the state of hemostatic monitoring.	Hypercoagulability: *A New* endothelial and *therapeutic* storm of cytokines, which justifies the elevation of D-dimer.
PEREIRA *et al.* (2021)	*Hematological changes in patients with COVID-19: a systematic review*	To systematically gather and analyze the evidence regarding the main hematological changes of the disease.	It summarizes the global occurrence of lymphopenia, prolonged prothrombin time (PT), and anemia associated with chronic inflammation.
RAHMAN *et al.* (2021)	*Hematological Abnormalities*	Reviewing the abnormalities: Detailing the mechanism of hematological changes in COVID-19: A *narrative review* of neutrophil-mediated NETs by COVID-19 and its pathophysiological basis.	immunothrombosis, the formation resulting peripheral thrombocytopenia due to consumption.

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SALAME *et al.* **(2022)**	*Utility of hematological analysis and inflammatory* biomarkers *biomarkers in* hematological prediction *recovery in* patient recovery. *COVID-19* decline.	*:* Analyze the utility of D-dimer levels > 1.0 critics.	µg/mL at admission: predict the need for *predicting* ICU. The absence of a *critical* in NLR/PLR *patients* after day 5 This indicates a worse prognosis.
SIEVING *et al.* **(2022)**	*Corticosteroid therapy:* Assess the impact of therapy. Corticosteroid therapy *as a confounding factor in the prognostic value* of corticosteroids (dexamethasone) inducing *the neutrophil-to-* neutrophil-to-pharmacological relationship. *Lymphocyte ratio in* neutrophil-to-lymphocyte (NLR) that result in false *severe COVID-19* in severe cases.	with	It demonstrates that the increases in NLR and SII, regardless of viral activity.
URBANO *et al.* **(2022)**	*Hematological changes :* Analyzing general hematological changes *in SARS-CoV-2 positive patients.* patients with SARS-CoV-2.		The increase is confirmed. prevalence of lymphocytopenia severe as the event central to virus-induced immunosuppression.

Source: author's own.

Based on the synthesis of the evidence, it can be observed that the characterization of the profile The hematological investigation in COVID-19 is marked by significant quantitative changes in the series. leukocyte counts, which cease to be seen merely as consequences of infection and become... to indicate the course of clinical severity. Severe lymphocytopenia is the most common alteration and Early onset, being considered a classic sign of severity. As pointed out by Al-Saadi and Abdulnabi (2021), this reduction results from direct viral infection, from apoptosis induced by cytokines and cellular exhaustion.

Urbano *et al.* (2022) corroborate this evidence by reporting lymphocytopenia in 81% from their cohort, associating values below 1,000 cells/µL with the risk of ICU admission. and mechanical ventilation. Alongside this decrease in lymphocytes, monocytopenia and... Marked eosinopenia at the first clinical contact acts as a crucial indicator for early screening. As explained by Rahman *et al.* (2021), the abrupt drop in Peripheral monocyte counts reflect the massive recruitment of these cells to the lung parenchyma, where they differentiate into inflammatory macrophages that worsen the lesion. local tissue.

In contrast, neutrophilia notably appears in advanced stages and is intrinsically associated with the phenomenon of the "cytokine storm". This state Acute hyperinflammation results from the unregulated and massive release of soluble mediators. in the bloodstream, with particular emphasis on interleukins IL-6, IL-2 and Necrosis Factor.

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Tumor Alpha (TNF-alpha), triggered by an exacerbated host immune response to SARS-CoV-2 (Xavier *et al.,* 2020; Nascimento *et al.,* 2020).

This systemic inflammatory influx acts directly on the bone marrow microenvironment. bone, dramatically accelerating granulopoiesis and forcing mobilization and release. accelerated levels of mature and immature neutrophils in the peripheral circulation, as an attempt to contain tissue damage (Bahadur *et al.,* 2021). From a pathophysiological perspective, the Hyperactivated neutrophils migrate en masse to target tissues (such as parenchyma). pulmonary), perpetuating local oxidative damage and, in later stages of hospitalization, this An elevated count often signals the development of bacterial infections. secondary, constituting a clinical marker that distinguishes patients who progress to death (Rahman *et al.,* 2021; Coelho *et al.,* 2021).

Based on these isolated cellular fluctuations, the literature advanced in hematology. From descriptive to predictive, through the integration of these counts into mathematical models, known as hematological ratios. Among these indicators, the Neutrophil-Lymphocyte (NLR) stands out as the gold standard. According to Manaças *et al.* (2024), the elevation The NLR simultaneously expresses the expansion of immature neutrophils and apoptosis of T lymphocytes. From an evolutionary perspective of pathology, studies by Salame *et al.* (2022) They reinforce that the dynamic trajectory of this index is crucial, highlighting that the absence A drop in NLR after the fifth day of hospitalization serves as a predictor of mortality. since this time period usually coincides with the critical transition between the phase of viral replication and the peak of the hyperinflammatory phase of the disease (Meng *et al.,* 2020).

Thus, the persistence of a high NLR after this time threshold signals that The inability of the immune system to restore homeostasis, indicating the maintenance of a vicious cycle of neutrophil recruitment and profound lymphocyte exhaustion (LI *et al.,* 2020). Clinically, this stagnant inflection reflects the patient's resistance to anti-inflammatory therapies. initial inflammatory processes and the consolidation of irreversible systemic tissue damage, which justifies its prognostic robustness (Ciculini *et al.,* 2021; Salame *et al.,* 2022).

Despite the reported consistency in the use of these biomarkers in screening In hospitals, in-depth analysis of the data reveals methodological limitations and discrepancies. in the literature that prevent the establishment of static cutoff values. One of the main Confounding factors lie in the impact of standardized corticosteroid therapy in the management of COVID-19. severe. Sieving *et al.* (2022) introduce a counterpoint to this prognostic linearity by to demonstrate that corticosteroids, such as dexamethasone, induce neutrophilia via pathways

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strictly pharmacological. This interference artificially raises the NLR.
regardless of viral activity, which can generate false alarms of clinical worsening and
limiting the reliability of these indices in patients already medicated. Furthermore, Buonacera *et al.*
(2022) argue that the NLR exhibits significant baseline fluctuations due to
biological aging and pre-existing chronic comorbidities. This overlap
It makes it difficult to isolate the true impact of viral load on low-grade chronic inflammation.
degree or of a secondary bacterial co-infection, requiring that these predictors
Hematological results should be interpreted in an individualized, serial, and contextualized manner.

Despite methodological reservations, the incorporation of other indicators, such as the
Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) help
significantly in identifying the transition from the viral phase to the hyperinflammatory phase, highlighting
peripheral platelet consumption (Bahadur *et al.,* 2021; Pereira *et al.,* 2021). It is in this scenario of cellular
integration that the Systemic Immune Inflammation Index (SII)
It is becoming established in the literature as a marker with predictive potential. As demonstrated
According to dos Santos Medeiros *et al.* (2024), the SII presents diagnostic accuracy for predicting death.
in the Intensive Care Unit (ICU), precisely because it holistically encompasses the triad of
"Hyperinflation-thrombosis-immunosuppression." Finally, it is important to highlight that normalization
Early detection of these mathematical parameters precedes visible clinical improvement, giving the
Clinical analysis laboratories play a proactive and strategic role in bed management.
hospitals.

Beyond the predictive utility of these mathematical models, immune dysregulation
The information expressed by these indices is directly linked to platelet activation and disorders.
Hemostatic agents through the immunothrombosis mechanism. The invasion of SARS-CoV-2 into
Endothelial cells generate severe endotheliitis that exposes collagen and releases tissue factor.
recruiting neutrophils that form extracellular traps (NETs). These networks serve
as scaffolding for microvascular fibrin deposition and intense platelet aggregation.

According to Nascimento *et al.* (2020), this state of hypercoagulability
Systemic damage, mediated by endothelial injury, justifies the triggering of microthrombi.
capillaries. This phenomenon results in peripheral consumptive thrombocytopenia, although
Bahadur *et al.* (2021) identify the presence of giant platelets as an attempt to
compensatory medullary response.

The most critical laboratory reflection of this process is the exponential increase in D-
dimer; Salame *et al.* (2022) and Pereira *et al.* (2021) emphasize that levels above 1.0

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Admission levels in µg/mL strongly predict the risk of venous thromboembolism and heart failure. Multiple organs, which positions the biomarker as a byproduct of regulatory failure.
between the immune system and the endothelium.

From a molecular perspective, this pathological convergence is consolidated through a vicious cycle, in which the local generation of thrombin stimulates receptors activated by protease (PAR) in inflammatory cells, inducing them to release even more cytokines. (Nascimento *et al.,* 2020). Simultaneously, the deposited fibrin networks interact with the Toll-like receptors (TLR4) on macrophages, keeping the immune system in hyperactivity; this continuous stimulus blocks physiological fibrinolysis, which perpetuates the microvascular obstruction and solidifies the systemic pro-thrombotic state (Pereira *et al.,* 2021).

In summary, the data discussed show that the hematological profile in COVID-19 This directly reflects the biological evolution of the disease. The patient's clinical progression begins... with leukocyte imbalance and elevated mathematical indices, which act as early indicators of severity. This process evolves into endothelial injury and... immunothrombosis, characterized by platelet consumption, elevated D-dimer, and Continuous fibrin deposition in the microvasculature. Therefore, monitoring Serial and contextualized hematological analysis functions as a reflection of systemic severity. allowing tracking from the initial immune response to thrombotic complications in microcirculation.

CONCLUSION

This study fulfilled its fundamental objective by investigating and systematizing the scientific publications on the hematological profile of patients affected by COVID-19, demonstrating that the blood count transcends its basic diagnostic function and becomes a a predictive tool of significant clinical utility. The synthesis of the findings demonstrates that the SARS-CoV-2 infection leaves a characteristic biological signature in the blood. peripheral, characterized by a combination of severe lymphocytopenia and subsequent neutrophilia. These results confirm that the drastic drop in lymphocyte count upon admission is a An early and sensitive indicator of severity, while neutrophilia acts as a marker. reliable indicator of cytokine storm and progression to critical conditions.

In-depth analysis also revealed the clinical relevance of monitoring. The hematological aspect lies, above all, in the interpretation of hematimetric relationships and of

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Hemostasis markers. The Systemic Immune Inflammation Index (SII) and the Ratio Neutrophil-to-lymphocyte (NLR) ratios have established themselves as high-potential predictors for the Need for mechanical ventilation and mortality in an Intensive Care Unit setting. Intensive Care Unit (ICU). Additionally, the correlation between consumptive thrombocytopenia and levels Elevated D-dimer levels served as the basis for understanding the hypercoagulable state and immunothrombosis, which characterizes severe forms of the disease. Such evidence indicates that An imbalance between the inflammatory and thrombotic systems can be detected and monitored. In an effective way, through accessible laboratory parameters. However, the investigation also highlighted important limitations and confounding factors in the literature, demonstrating that the The predictive accuracy of these inflammatory indices can be artificially altered by the use of... prior use of corticosteroid therapy or the presence of chronic comorbidities in patients.

In terms of applicability, the study demonstrates that the integration of these indices into Hospital triage protocols have a direct impact on optimizing healthcare resources. public, provided that its reading is done in a strictly serial, individualized and contextualized. In high-demand scenarios, the rapid identification of patients with profiles Identifying high-risk hematological conditions allows for a more targeted allocation of beds and therapeutic support. early. It is concluded, therefore, that constant and critical monitoring of bloodlines and The use of coagulation biomarkers not only enriches academic knowledge about viral diseases emerging, but also offers a practical and low-cost contribution to improvement. of clinical outcomes and the efficiency of hospital care in the face of pandemic challenges.

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