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Clinical Performance of Hematological Indices as Predictors of Mortality in Patients with Severe Acute Pancreatitis of Biliary Origin in the General Hospital of Zone No. 3, of Aguascalientes, México

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ABSTRACT

Background: Acute pancreatitis is a common disease with a potentially high mortality rate, making early risk assessment essential for optimizing treatment.

Objective: To evaluate the clinical performance of hematological indices as predictors of mortality in patients with severe acute biliary pancreatitis admitted to General Hospital Zone No. 3 in Aguascalientes.

Material and methods: An instrumental, retrospective, and observational study was conducted at General Hospital Zone No. 3 in Aguascalientes, Mexico, from January 1, 2023, to March 31, 2024. The study included 25 patients over 18 years of age diagnosed with severe acute biliary pancreatitis. Clinical and demographic data were extracted from medical records. The performance of each index was assessed using ROC curves, with sensitivity, specificity, and predictive values calculated at various cutoff points. Fagan's nomograms were used to interpret pre-test and post-test probabilities of mortality.

Results: Among the 25 patients evaluated, 36% died. The neutrophil-to-lymphocyte ratio (NLR) demonstrated the best performance as a mortality predictor, with an area under the curve (AUC) of 0.823. The optimal cutoff point was 15.1, with a sensitivity of 78% and a specificity of 88%, confirming its ability to distinguish between patients who died and those who survived. The red cell distribution width (RDW) had an AUC of 0.747, with high sensitivity (89%) but lower specificity (56%) at a cutoff of 15.0, making it a moderately effective predictor. Conversely, the platelet-to-lymphocyte ratio (PLR) performed poorly, with an AUC of 0.451, indicating low predictive value for mortality.

Conclusions: The neutrophil-to-lymphocyte ratio (NLR) emerged as the most effective predictor of mortality in this population of patients with severe acute biliary pancreatitis, followed by the red cell distribution width (RDW), which also showed moderate capability in predicting adverse outcomes.

KEYWORDS: Acute pancreatitis, Mortality, Hematological indices.

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INTRODUCTION

Acute pancreatitis (AP) is one of the most common gastrointestinal diseases, characterized by rapid inflammation of the pancreas that potentially affects surrounding tissues and distant organs or systems. Each year, 270,000 patients are hospitalized due to AP in the United States, with inpatient treatment costs exceeding US$ 2.5 billion annually. (1) Severe acute biliary pancreatitis is a critical condition that poses a significant clinical challenge due to its high morbidity and mortality. Statistics suggest that 10-20% of patients develop severe pancreatitis, leading to a mortality rate of up to 30-50%. (2)

Despite advancements in diagnostic and therapeutic methods, the early prediction of prognosis in these patients remains an area of significant interest and need in medical practice. Currently, the timely identification of patients at risk of death is crucial to improving their clinical management, optimizing decision-making, and reducing mortality associated with this condition. However, despite the availability of various prognostic tools, such as the Acute Physiology And Chronic Health Evaluation II (APACHE II), Ranson, and the Bedside Index of Severity in Acute Pancreatitis (BISAP) scores, their use requires complex data, which is often not readily available at the time of admission. (2) In this context, hematological indices, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width (RDW), have emerged as potential accessible, rapid, and cost-effective predictors of mortality, as they are derived from routine tests like the complete blood count. These indices reflect the inflammatory status and immune response of the body, which are key factors in the development and progression of severe acute pancreatitis. (3) However, despite their promise as predictive tools, the evidence regarding their performance in predicting mortality in patients with severe acute biliary pancreatitis is limited and fragmented. Although some preliminary studies have suggested their usefulness, the lack of specific research in this population and in hospital settings like those in Mexico highlights the need for further studies to validate their accuracy and clinical applicability.

This project aims to address this knowledge gap by evaluating the clinical performance of hematological indices as predictors of mortality in patients with severe acute biliary pancreatitis at General Hospital Zone No. 3 in Aguascalientes. Given the potential impact of these indices on clinical practice, this study could provide an additional and accessible tool for risk stratification, facilitating the early identification of high-risk patients and improving clinical outcomes.

MATERIALS AND METHODS

Participants

An observational, retrospective, and instrumental study was conducted at General Hospital Zone No. 3 in Aguascalientes, Mexico. Twenty-five patients over 18 years of age with a diagnosis of severe acute biliary pancreatitis were included, with data collected from January 1, 2023, to March 31, 2024. All included patients were followed until hospital discharge or death. Clinical information, prognostic data (survival or death), and demographic data were obtained from medical records. The diagnosis of acute pancreatitis (AP) was based on the revised Atlanta criteria of 2012, which require two of the following three features: (a) prolonged abdominal pain characteristic of AP, (b) serum amylase and/or lipase levels elevated three times above the normal range, and (c) characteristic findings of AP on abdominal ultrasound and/or CT scan. Severe acute pancreatitis (SAP) was defined as persistent organ failure lasting more than 48 hours. (4) Patients were excluded from this study if they met any of the following criteria: under 18 years of age, known Child-Pugh C cirrhosis, previously diagnosed hematological disease, cancer, pregnancy, chronic pancreatitis, immunosuppressive therapy, or immunosuppressive pathology.

Sample Size

The sample size was calculated using the SELECT STATISTICAL SERVICE calculator (5) for finite populations, with a 95% confidence level and a 5% margin of error, resulting in a sample size of 25 patients.

Data collection

Data were collected using a data collection instrument, and recorded in a Microsoft 365 Excel consisted of the following parts: Registration number, patient name and social security number, clinical and demographic aspects, Hematological index values, inclusion or elimination criteria and disease outcome (death). Laboratory data were obtained from the electronic record, NLR, PLR and RDW were calculated at admission (NLR = neutrophil count/lymphocyte count, PLR = platelet count/lymphocyte count and RDW included in the hematologic biometry). The accuracy and correct entry of the data were then verified.

Ethics statement

Our study was approved by the Local Committee for Health Research and Ethics with the following registration number R- 2024- 101 – 072 in Aguascalientes, México. The study was conducted in accordance with the ethical principles contained within the Declaration of Helsinki.

Statistical analyses

The data obtained from the registration forms were entered into an Excel database and subsequently processed using SPSS v.25 for Mac. For descriptive analysis, absolute frequencies and percentages were used for qualitative variables such as gender and comorbidities, while means and standard deviations were calculated for quantitative variables such as age and body mass index. The prevalence of mortality and the clinical performance of hematological indices as predictors of mortality were calculated through ROC (Receiver Operating Characteristic) curve analysis. These curves allowed for the evaluation of the discriminatory capacity of indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width (RDW). The area under the curve (AUC) for each index was determined from the ROC curves, which enabled the measurement of their overall performance as mortality predictors. For each index, the optimal cutoff point was identified to maximize both sensitivity and specificity using the Youden index. Sensitivity and specificity for these cutoff points were then calculated, along with positive predictive value (PPV) and negative predictive value (NPV).

Additionally, likelihood ratios (LR+ and LR-) were calculated, and Fagan's nomograms were used to interpret the change in pre-test and post-test mortality probabilities when applying the cutoff points of the hematological indices (NLR, PLR, and RDW).

RESULTS

Patient characteristics

Applying the inclusion criteria, the clinical records (both physical and electronic) of 26 patients were evaluated. One patient was excluded due to a diagnosis of malignancy, resulting in a final study population of 25 patients.

Figure 1 shows the gender distribution in the study population. Of the total 25 patients, 56% were male, with 14 cases, while the remaining 44% were female, with 11 cases. On average, the age of male patients was 64.36 years, while female patients had an average age of 64.82 years. Regarding body mass index (BMI), there was a tendency toward overweight, with male patients having an average BMI of 28.90, whereas females had an average of 30.46. In terms of comorbidities, hypertension was the most common, affecting 76% of patients (19 cases), highlighting its high prevalence in this population. This was followed by type II diabetes mellitus, which was present in 48% of patients (12 cases). Additionally, heart disease affected 12% of the patients (3 cases).

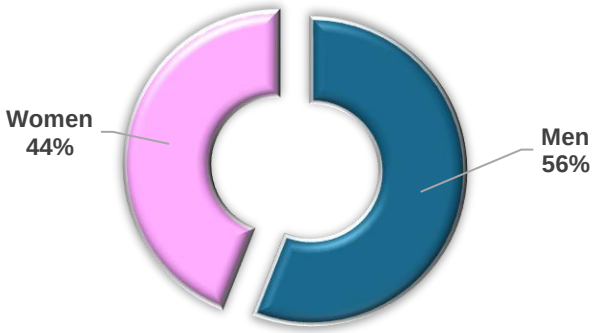

Figure 1. Gender Distribution

Respecting to mortality, **Figure 2** presents the distribution of mortality in the patients analyzed in the study. Of the 25 patients included in the analysis, 9 died, representing a 36% mortality rate, while 16 patients (equivalent to 64%) survived. These data suggest a significant mortality rate in this patient sample, highlighting the severity of the condition evaluated.

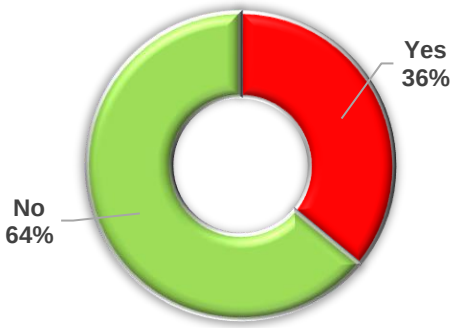

Figure 2. Mortality

Table 1 presents the results of the area under the curve (AUC) analysis for the different hematological indices used as predictors of mortality in patients with severe acute biliary pancreatitis. The table shows that the neutrophil-to-lymphocyte ratio (NLR) has an AUC of 0.823, with a standard error of 0.103 and an asymptotic significance of 0.008, indicating a high discriminatory power to predict mortality in this group of patients. The 95% confidence interval for this index ranges from 0.621 to 1.000, further supporting its utility as a diagnostic tool. In contrast, the platelet-to-lymphocyte ratio (PLR) has an AUC of 0.451, with a standard error of 0.136 and an asymptotic significance of 0.692, suggesting that its predictive capacity is no better than chance, as its confidence interval, ranging from 0.185 to

0.717, includes a value of 0.5. Lastly, the red cell distribution width (RDW) shows an AUC of 0.747, with a standard error of 0.114 and an asymptotic significance of 0.044, indicating moderate discriminatory capacity. Its confidence interval, ranging from 0.522 to 0.971, reflects an acceptable level of certainty, though lower than that of the neutrophil-to-lymphocyte ratio.

Table 1. Areas under the curve (AUC)

Variables resulting from contrast	AUC	Standard error	Asymptotic significance	Asymptotic confidence interval at 95%	
				Lower limit	Upper limit
Neutrophil-lymphocyte ratio	.823	.103	.008	.621	1.000
Platelet-lymphocyte ratio	.451	.136	.692	.185	.717
Red blood cell distribution width	.747	.114	.044	.522	.971

Figure 3 presents the ROC (Receiver Operating Characteristic) curves for the hematological indices evaluated as predictors of mortality in the study. The neutrophil-to-lymphocyte ratio, represented in blue, shows a curve considerably closer to the upper left corner of the graph, indicating superior performance compared to the other indices. This suggests a high ability to distinguish between patients who survived and those who died, corroborating its high area under the curve (AUC) of 0.823 described in **Table 1**. On the other hand, the platelet-to-lymphocyte ratio, represented in green, shows a curve closer to the diagonal reference line, indicating poor discriminatory capacity, nearly equivalent to chance, as also evidenced in **Table 1** with an AUC of 0.451. Its initial nearly horizontal trajectory and gradual ascent suggest that it is not a good predictor for this clinical context. The red cell distribution width (RDW), represented in gold, shows intermediate behavior, with a curve that rises more steeply compared to the platelet-to-lymphocyte ratio, but does not reach the effectiveness of the neutrophil-to-lymphocyte ratio. This supports its AUC of 0.747, suggesting moderate performance in predicting mortality.

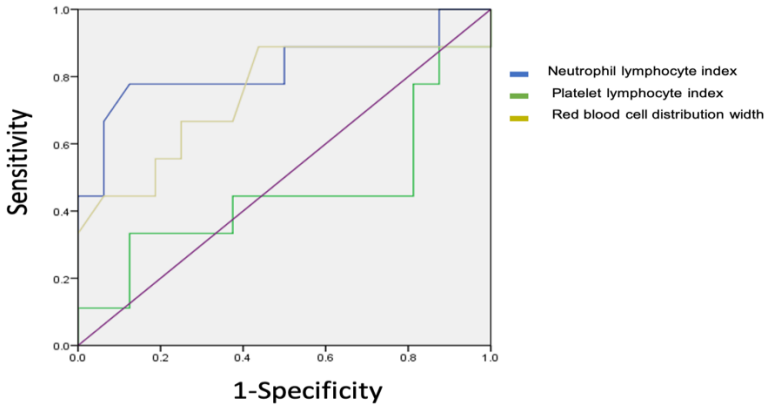

Figure 3. ROC curve

Table 2 below presents the area under the curve (AUC), the ideal cutoff value determined by the Youden test, sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (+LR), negative likelihood ratio (-LR), pretest probability, posttest probability (+) and posttest probability (-) for each prognostic variable used to predict mortality.

Table 2. Hematological indices as predictors of mortality

	AUC	Cut off value	SE	SP	PPV	NPV	LR+	LR-	Pretest probability	Post-test probability +	Post-test probability -
NLR	0.823	>15.1	78%	88%	78%	88%	6.5	0.25	36%	79%	14%

PLR	0.451	>345.3	33%	88%	60%	70%	2.75	0.76	36%	61%	33%
RDW	0.747	>15.0	89%	56%	53%	90%	2.02	0.20	36%	53%	12%

Table 2 presents the different cutoff points. It is important to note that the values for NLR (15.1), PLR (345.3), and RDW (15) are the most appropriate for predicting mortality, as these points achieve a favorable balance between sensitivity and specificity. This indicates that these thresholds maximize the ability of these hematological indices to differentiate between patients who survive and those who die.

Neutrophil-to-Lymphocyte Ratio (NLR)

The neutrophil-to-lymphocyte ratio (NLR) showed the best specificity, at 88%, indicating a high capacity to correctly identify patients who did not die. The sensitivity was 78%, reflecting a strong ability to correctly detect patients who died. Regarding predictive values, the positive predictive value (PPV) was 78%, and the negative predictive value (NPV) was 88%. This means that out of 100 patients with an NLR greater than 15.10, the test was able to identify 78 cases of mortality, leaving some false positives. Similarly, for every 100 patients with an NLR below 15.09, 88 patients will not die, leaving few false negatives. These results suggest that the test is reliable for predicting both mortality and survival in this patient sample.

An important aspect in interpreting these data is its application in ruling out a clinical process. To do this, it is essential to calculate the likelihood ratio, which indicates how much more likely it is to find a positive result in a patient who died compared to one who survived (LR+), and the negative likelihood ratio, which shows how much more likely it is to find a negative result in a patient who survived than in one who died (LR-). In our results, we found a positive likelihood ratio (LR+) of 6.5. This value means that a patient with an NLR greater than 15.10 is 6.5 times more likely to die compared to one who survives. On the other hand, the negative likelihood ratio (LR-) was 0.25, indicating that if the NLR is below the threshold of 15.09, the likelihood of the patient dying is reduced to a quarter.

Figure 4 presents a Fagan nomogram that illustrates the relationship between pre-test probability, likelihood ratio, and post-test probability using the neutrophil-to-lymphocyte ratio (NLR) as a mortality predictor in patients with severe acute pancreatitis of biliary origin. This tool integrates pre-test probability information with diagnostic test results (positive and negative likelihood ratios) to adjust the final probability of the clinical event, in this case, mortality. The green line represents the scenario of a positive test. Starting with a pre-test probability of 36% (the mortality rate in our population), the nomogram calculates a post-test positive probability close to 80%. This means that if a patient has an elevated NLR, the probability of death increases significantly, confirming the value of this marker as a good predictor of mortality.

Conversely, the red line shows the behavior in a negative test scenario. Starting again from the same pre-test probability of 36%, the post-test probability drops to 14%, when the test is negative, that is, when the NLR is low. This reflects that the probability of death is significantly reduced in patients who do not have an elevated NLR, reinforcing the usefulness of the test in ruling out mortality in these cases.

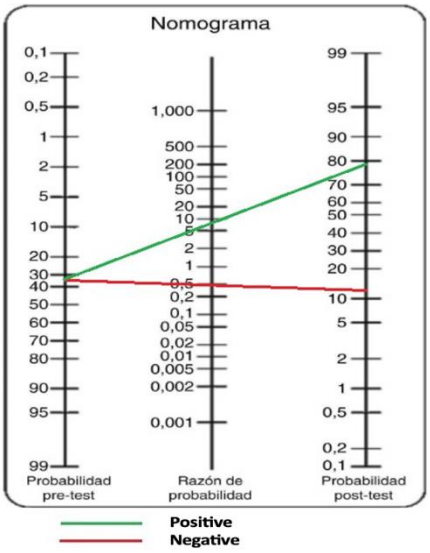

Figure 4. Fagan normogram for NLR

Platelet-lymphocyte ratio (PLR)

Similar to the Neutrophil-Lymphocyte Ratio (NLR), the specificity was 88%, indicating a high ability to correctly identify patients who did not die. However, the sensitivity was 33%, suggesting that the index has a low capacity to accurately detect those patients who did die, which limits its utility as a primary predictor. The positive predictive value (PPV) was 60%, implying that in this case, a positive result (high PLR) has moderate accuracy in predicting mortality. On the other hand, the negative predictive value (NPV) was 70%, indicating that a low PLR is relatively reliable in predicting survival. **Figure 5** shows that the pre-test probability was 36%, reflecting the prevalence of mortality before applying the test. Subsequently, the post-test positive probability was 61%, meaning that if a patient has a high PLR, their probability of death increases to more than 60%. In the case of a negative result, the post-test probability drops to 33%, suggesting that a negative result does not provide enough certainty to rule out mortality in these patients.

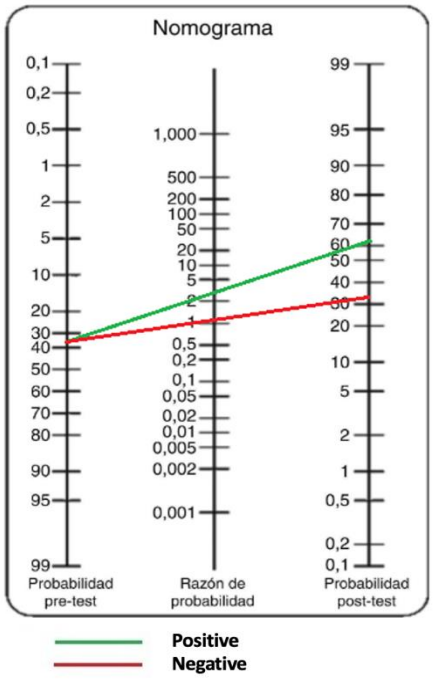

Figure 5. Fagan normogram for PLR

Red cell distribution width (RDW)

With a cutoff point of 15.0, it shows the best sensitivity of 88.9%, but its specificity is only 56%, suggesting a moderate ability to correctly identify those patients who did not die. The positive predictive value (PPV) is 53%, meaning that out of 100 people with a RDW greater than or equal to 15.00, it can detect 53 cases of death. This indicates that a high RDW result predicts mortality in just over half of the cases. On the other hand, the negative predictive value (NPV) is 90%, which reinforces the utility of this index for predicting survival, as a low RDW is associated with a high probability that the patient will survive. In contrast, the negative likelihood ratio (LR-) is 0.20, indicating that if the RDW is below 14.99, the probability of the patient dying is reduced by one-fifth. This value is lower than the other indices, which strengthens the role of RDW as a reliable marker for ruling out the risk of mortality. Using Fagan's nomogram for RDW, as shown in **Figure 6**, starting from a pretest probability of 36%, the post-test positive probability rises to 53%. Conversely, the post-test negative probability, or the probability of the patient dying after obtaining a low RDW, is 12%, demonstrating that a low RDW is the best indicator of survival.

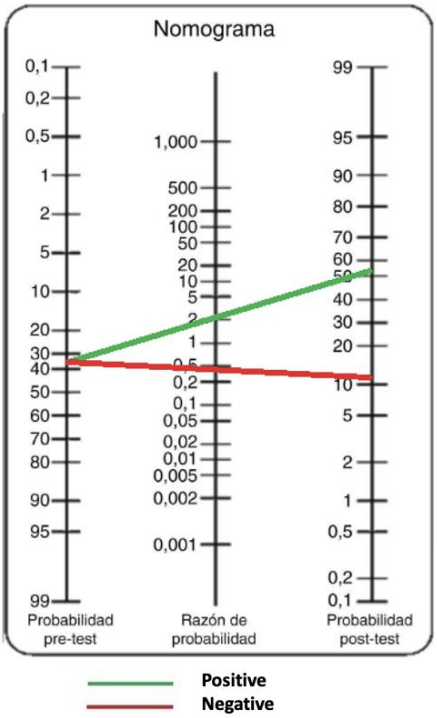

Figure 6. Fagan normogram for RDW

DISCUSSION

In our setting, as reported in the global literature, severe acute pancreatitis of biliary origin is associated with a high mortality rate. Therefore, early identification is crucial to rapidly initiate supportive treatment and refer the patient to a critical care unit for follow-up, aiming to limit the spread and progression of the disease, ultimately improving the prognosis for these patients.

Regarding the clinical-demographic characteristics of the study population, it was observed that 56% of the patients were male and 44% female, suggesting a slight male predominance in this population. This contrasts with national data, which reported a higher prevalence in females (6). These findings align with those reported by Marín Rios (2019) and Jinno (2020) (7,8). However, a review by Petrov (2019) showed that sex does not influence the severity of the condition (9). The average age was 64.56 years, which is similar to international reports by Jinno (2020) (8) and national data from González (2012), who noted that older age is associated with a higher risk of severity and mortality (10). Regarding body mass index (BMI), the average was 29.59, indicating a prevalence of overweight in this sample. A study by Dalma D. (2019) found that a BMI greater than 25 triples the risk of severe pancreatitis, and a BMI greater than 30 triples the risk of mortality, due to its association with an elevated systemic inflammatory response from pro-inflammatory cytokines released by adipose tissue (11). When analyzing comorbidities, hypertension was the most common, affecting 76% of the patients, followed by type II diabetes mellitus, present in 48% of the cases. These cardiovascular and metabolic diseases play a crucial role in the health profile of these patients, which is related to the high prevalence of obesity in our population.

The observed mortality rate was 36%, with 9 deaths, highlighting the severity of severe acute pancreatitis of biliary origin in this specific population, similar to what has been reported in the international literature (12,13). On the national level, there is no updated prevalence data, so this study represents an important epidemiological finding for our population.

Various studies have explored the use of hematological indices as early predictors of mortality to guide a faster and more targeted approach. However, discrepancies have been observed regarding the cut-off points for predicting mortality (1,14,15,16). For example, a study by Zhou et al. (2019) (14) established a cut-off of 12.1 for predicting mortality at 28 days in patients with severe acute pancreatitis, achieving a sensitivity of 85.7% and specificity of 84.2%. Similarly, in a study by Junare et al. (2021) (15), they found that the neutrophil-lymphocyte ratio (NLR) had a cut-off of 16.5, with a sensitivity of 83% and specificity of 87%. On the other hand, Gezer et al. (2020) (16) proposed a cut-off of 11.91, with a sensitivity of 76.5% and specificity of 94.1%.

Regarding the platelet-lymphocyte ratio (PLR), a study by Zhou et al. (2019) (14) demonstrated that for a cut-off ≥ 148.80, the sensitivity and specificity were 85% and 47%, respectively. Junare et al. (2021) (15) established that PLR is a good predictor of mortality with a cut-off > 208, achieving a sensitivity of 100% and specificity of 69%.

Finally, concerning the red cell distribution width (RDW), a study by Goyal et al. (2017) (17) established a cut-off of 13.55% at admission for predicting mortality, with a

sensitivity of 88.2% and specificity of 91.8%. Jain et al. (2023) established cut-offs of 14.75% and 15% on days 1 and 3 to predict mortality (18). The methodology used in the studies mentioned above was similar, but the main difference observed was the study population, which is based on Bayes' Theorem. Based on this, we decided to investigate our own population.

The results of this study have shown that the neutrophil-lymphocyte ratio (NLR), the platelet-lymphocyte ratio (PLR), and the red cell distribution width (RDW) have varying levels of utility as predictors of mortality in patients with severe acute biliary pancreatitis. The NLR, with an area under the curve (AUC) of 0.823 and an optimal cut-off point of 15.1, demonstrated high discriminative ability to identify patients at risk of mortality, with a sensitivity of 77.8% and a specificity of 87.5%, a positive predictive value (PPV) of 78%, a negative predictive value (NPV) of 88%, a positive likelihood ratio (LR+) of 6.5, and a negative likelihood ratio (LR-) of 0.25. Subsequently, the Fagan nomogram was used to establish the post-test cut-off value. Starting from a pre-test probability of 36%, the nomogram calculates a post-test positive probability of 79%. This means that if a patient presents with a high NLR, the probability of death increases significantly, confirming the value of this marker as a good predictor of mortality. On the other hand, in a negative test scenario, the post-test probability decreases to 14% when the test is negative, that is, when the NLR is low, the probability of death significantly decreases, reinforcing the utility of the test for ruling out mortality in these cases.

On the other hand, the performance of the PLR was more limited, with an AUC of 0.451 and a cut-off point of 345.3, achieving a sensitivity of 33.3% and a specificity of 87.5%, a PPV of 60%, an NPV of 70%, a positive likelihood ratio (LR+) of 2.75, and a negative likelihood ratio (LR-) of 0.76. A high PLR was associated with a post-test mortality probability of 61%, while a low PLR reduced this risk to 33%, suggesting that the PLR has limited ability to conclusively rule in or rule out mortality. However, the relatively high specificity suggests that the PLR could be useful in conjunction with other clinical markers or scales to identify patients at lower risk of mortality, although it should not be used as a standalone predictor.

Regarding RDW, this index showed a moderate ability to predict mortality with an AUC of 0.747. With an optimal cut-off point of 15.0, it achieved a sensitivity of 88.9%, a specificity of 56.3%, a positive predictive value (PPV) of 53%, a negative predictive value (NPV) of 90%, a positive likelihood ratio (LR+) of 2.02, and a negative likelihood ratio (LR-) of 0.2. A high RDW was associated with a post-test mortality probability of 53%, while a low RDW significantly reduced this risk to 12%. This index stood out as the most appropriate marker for excluding death, significantly reducing the probability of mortality in these patients.

CONCLUSIONS

The clinical performance of hematological indices was determined, finding that the neutrophil-lymphocyte ratio (NLR) demonstrated the best overall performance with an area under the curve (AUC) of 0.823, positioning it as the best predictor of mortality in patients with severe acute biliary pancreatitis in our population. This was followed by the red cell distribution width (RDW) with an AUC of 0.747, which also showed a moderate ability to predict mortality but proved to be the most appropriate marker for excluding death. Finally, the performance of the platelet-lymphocyte ratio (PLR), with an AUC of 0.451, showed a limited capacity to conclusively predict mortality. Therefore, it is recommended to use hematological indices (NLR and RDW) at the time of diagnosis, as they are simple, rapid, and available markers to establish early therapeutic strategies that improve the prognosis of patients.

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