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Red blood cell distribution width to platelet ratio in neonatal foals with sepsis

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Abstract

Background: Rapid and accurate markers to aid diagnosis of sepsis are needed in neonatal foals. The CBC variable red blood cell distribution width (RDW) to platelet ratio (RPR) is associated with inflammatory response and linked to poor outcomes of sepsis in human patients.

Hypothesis: Explore the correlation of RPR with sepsis in neonatal foals and evaluate RPR predictive and prognostic value.

Animals: Three hundred seventeen hospitalized neonatal foals ≤7 days of age that had a CBC and physical exam performed at admission between 2012 and 2021.

Methods: Retrospective case-control study. Clinical records were used to calculate sepsis scores and define groups. Red blood cell distribution width to platelet ratio was calculated and compared between groups (septic vs nonseptic) based on Kruskal-Wallis and Wilcoxon signed-rank tests. A multivariate logistic regression model to predict sepsis was created. The cutoff for RPR was obtained based on the maximal Youden Index. The Kaplan-Meier method and the log-rank test were used to estimate survival curves and compare survival rates based on RPR.

Results: Red blood cell distribution width to platelet ratio was significantly higher in septic foals (Median = 0.099, confidence interval [CI] [0.093; 0.108]) than in sick nonseptic (0.085, CI [0.083; 0.089]) and healthy foals (0.081, CI [0.077; 0.086]; $P < .0001$). Red blood cell distribution width to platelet ratio was able to predict sepsis with high accuracy (AUC = 82.1%). The optimal RPR cutoff for sepsis was 0.09.

Conclusions and Clinical Importance: Red blood cell distribution width to platelet ratio calculation is practical, inexpensive, and based on CBC-derived data. Calculation of RPR along with CBC can aid in the diagnosis of sepsis and estimation of outcome.

Abbreviations: CBC, complete blood cell count; MCV, mean corpuscular volume; RDW, red blood cell distribution width; RPR, red blood cell distribution width to platelet ratio; SNS, sick nonseptic; WBC, white blood cell count.

Rebeca Scalco and Gabriela Novo de Oliveira had equal contribution as first authors.

KEYWORDS
equine neonatology, foal sepsis, RDW, RDW to platelet ratio, RPR

1 | INTRODUCTION

Sepsis is the primary cause of death in neonatal foals.[1,2] Clinical signs of sepsis are nonspecific and untreated foals deteriorate rapidly; thus, early detection of disease is essential.[3,4] Empirical use of broad-spectrum antibiotics remains the cornerstone of treatment as it reduces death and improves outcomes.[5] Blood culture is the gold standard for diagnosis of sepsis.[3,6] However, delay in reporting bacterial growth and poor sensitivity limit the diagnostic value of blood culture.[6] Therefore, negative results alone cannot exclude a septic process.[6] Exposure of foals to antibiotics during the peripartum also affects the sensitivity of blood cultures.[1] Additional markers used to evaluate the clinical status of a foal and aid in referral and treatment decision-making are white blood cell count (WBC) and plasma fibrinogen concentration.[7-9] Serum amyloid A and lactate are markers also linked to perinatal diseases and sepsis risk in foals.[9-11] However, these tests can be imprecise, nonspecific; emphasizing the importance of leveraging more accessible markers.

Red blood cell distribution width (RDW), calculated multiplying the SD of mean corpuscular volume (MCV) by 100 to yield a percentage value, indicates erythrocyte size variability and can aid in characterizing anemias in humans and animals.[12,13] Increasing evidence suggests that high RDW values indicate systemic inflammation and aid in determining prognosis for multiple inflammatory and infectious conditions in humans.[14-17] Red blood cell distribution width can indicate poor prognosis in septic human patients, as high values on admission are linked with death.[18,19] Elevated RDW values occur in dogs, cats, and horses with systemic processes (eg, cardiomyopathies, infection).[20-22] Moreover, RDW to platelet ratio (RPR) is a novel, inexpensive, noninvasive index calculated dividing RDW by platelet count, 2 variables included in a standard CBC.[23] Because RPR is calculated from RDW and platelet count, RPR is going to be affected by the degree of anisocytosis reflected by RDW and low platelet count as often seen in sepsis.[24,25] Elevated RPR is effective in human medicine for assessing and predicting degree of fibrosis and inflammation in various conditions, including hepatic cirrhosis, acute pancreatitis, severe burns, and acute kidney injury.[23,26-28] High RPR is proposed to correlate with sepsis diagnosis and prognosis in adult and neonatal human patients.[24,25] Across all studies, nonsurvivors had greater RPR values than survivors.[28]

In a recent study, RPR was evaluated as a tool to aid in diagnosing perinatal disease in neonatal Thoroughbred foals, finding that foals at risk of developing systemic disease had higher RPR values.[29] In the present study, we investigated the predictive and prognostic values of RPR for sepsis in neonatal foals. We utilized records for foals admitted to a referral center over an 11-year period to examine the association between RPR and a modified sepsis score. We hypothesized that septic foals have greater RPR upon admission than sick nonseptic and healthy ones. We also expected nonsurvivor foals to have higher RPR than survivors.

2 | MATERIALS AND METHODS

2.1 | Animals and study design

For this retrospective case-control study, we searched the electronic medical database of the William R. Pritchard Veterinary Medical Teaching Hospital at the University of California Davis for all foals admitted by the Large Animal Clinic between the years of 2012 to 2021. We included foals ranging from 0 to 7 days of age and that have had a CBC (Advia 2120i Hematology System; SIEMENS Healthineers, Cary, NC) and physical exam performed by a board-certified veterinary specialist or veterinary specialist in-training at admission; exclusion criteria included equid foals other than horses (*Equus ferus caballus*, ie, mules, donkeys) and foals with CBCs reporting any degree of platelet clumping. Institutional animal care and use committee (IACUC) approval was not necessary for this retrospective analysis of clinical data. A flowchart of the study sample can be seen in Figure 1. The STROBE guidelines were used to guide reporting of this study.[30]

Data recorded included patient (mare and foal) signalment, gestational age, history, total days of hospitalization, physical examination findings at presentation, clinical diagnosis, discharge status (alive vs euthanized vs died), and results of clinicopathologic testing performed, including CBC, differential nucleated cell count, total protein, and plasma fibrinogen concentration. Blood culture was carried out using routine clinical methods, and results were recorded when performed. Clinical biochemistry analysis results recorded included serum glucose, lactate, creatinine, and immunoglobulin G concentration. Because of the study's retrospective nature, all diagnostic testing choices were based on the clinicians' discretion; therefore, not all information was available for every patient. The same hematologic analyzer was used during the whole study period. Differential cell counts and cell morphology were performed by clinical pathology board-certified veterinary specialist or veterinary specialist in-training.

Based on the collected data, a modified sepsis score was applied, as previously reported[4]: Foals with physical examination, CBC, and serum biochemistry profile within the normal range, serum immunoglobulin G >800 mg/dL, and modified sepsis score <4 were classified as healthy. Healthy foals were identified as part of a routine health-check examination for all foals born or presented at our institution and research herd, and those clinically normal accompanying their dams to the hospital. Sick foals presented to the hospital and that had a positive blood culture, a modified sepsis score ≥12, or a combination of these were considered septic, whereas foals who presented for illnesses other than sepsis (eg, laceration, orthopedic conditions,

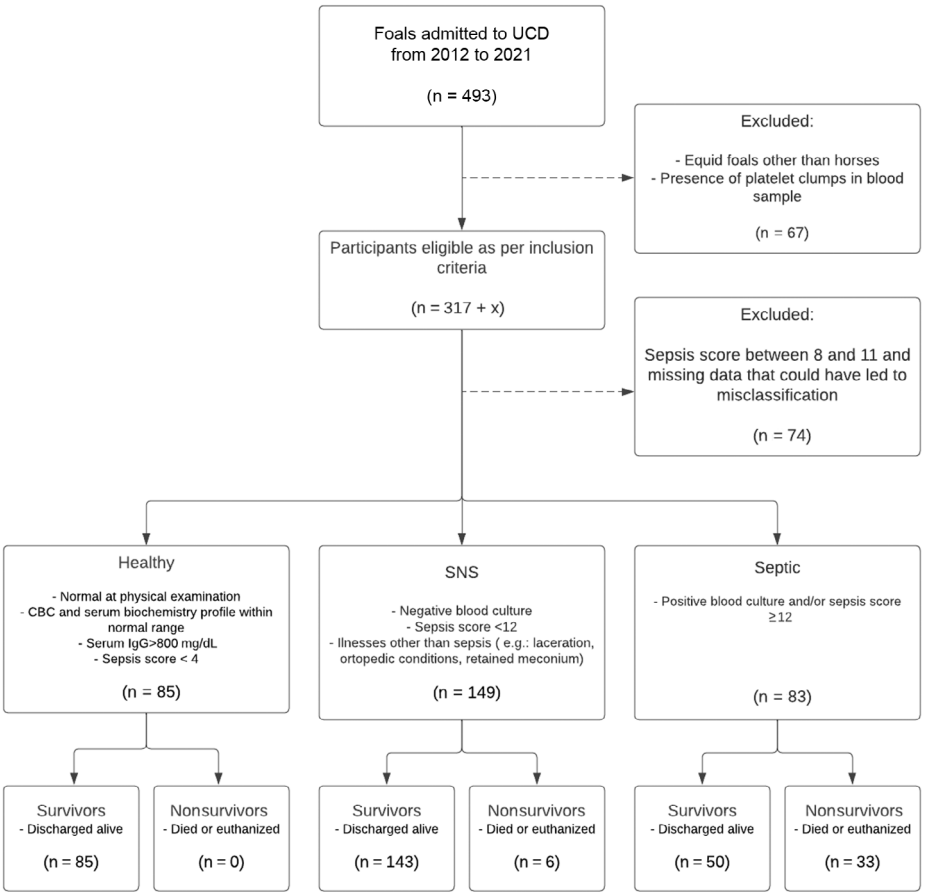

FIGURE 1 Flowchart of the study sample. [Correction added on 26 June 2023, after first online publication. Figure 1 has been updated.]

retained meconium, umbilical infection), negative blood cultures, and modified sepsis score <12 were classified as sick nonseptic (SNS). Foals in the SNS group with scores between 8 and 11 and that had missing data which could have led to their potential misclassification in the septic group were excluded from the study. Foals were also classified as survivors or nonsurvivors based on their discharge status. Survivors were foals discharged alive, whereas nonsurvivors died or were euthanized because of a poor medical prognosis. The calculation of RPR was performed as reported,[23] using the formula RPR = RDW (%)/platelet count (10^9/L).

2.2 | Statistical analysis

Extracted data were assessed for normality using histograms, *Q-Q* plots, and the Shapiro-Wilk test for normality. Kruskal-Wallis and Wilcoxon signed-rank tests were used to evaluate significant differences between the medians of grouped variables. Statistical significance was set at *P* value <.05. Associations were evaluated between RDW and RPR among the total dataset and data subdivisions (previously described). For continuous variables, the Spearman test was used to assess for correlation with RDW and RPR. Continuous variables are presented as medians with 95% confidence intervals (CIs), whereas categorical variables are presented as frequencies and percentages. For median RPR values identified as significantly different between groups, box plots were created for ease of visualization. Scatter plots were likewise created for significantly varying continuous variables. The data were assessed for multicollinearity (defined as absolute Pearson correlation between covariates >0.7), and univariate analyses were performed for each variable of interest as predictors for sepsis. Variables were evaluated individually across the entire dataset as well as 2 subsets (SNS only and septic only). We created a multivariate logistic regression model for sepsis that included all variables identified as significant in the univariate analyses and that had a correlation coefficient <0.7. We performed stepwise backward model selection based on Akaike's information criterion (AIC) for our full model using the *stepAIC* function from the *MASS* package in R (statisical sofware R version 2022.07.1).[31] Receiving operating characteristic (ROC) curves were plotted for each significant covariate in the final model. The optimal cutoff value for RPR in neonatal foals was then calculated by identifying the maximal Youden Index (sensitivity + specificity − 1).[32] We used the Kaplan-Meier method to estimate survival curves based on values of RPR (above and below the optimal threshold) and the log-rank test to compare the survival rates in both groups. Animals euthanized because of financial constraints were not included in the survival analysis to avoid bias.

3 | RESULTS

During the study period, 493 foals were evaluated at our hospital. A total of 317 foals met the inclusion criteria, and their medical records and diagnostic test results were reviewed. There were more colts

TABLE 1 Demographic characteristics of the neonatal foals included in the study sample.

	Healthy		SNS		Septic		
Variable	**n**	**Percent (%)**	**n**	**Percent (%)**	**n**	**Percent (%)**	**Total**
Sex							
Female	44	51.77	72	48.32	34	40.96	150
Male	41	48.23	77	51.68	49	59.04	167
Survival status							
Survivor	85	100	143	95.97	50	60.24	278
Nonsurvivor	0	0	6	4.03	33	39.76	39
Blood culture performed							
Yes	0	0	36	24.16	55	66.26	91
No	85	100	113	75.83	28	33.74	226
Total foals	85		149		83		317

Abbreviations: n, number of foals; SNS, sick nonseptic.

(n = 167; 52.7%) than fillies (n = 150; 47.3%) included in this study. Foals had a median age of 18 hours (range: 0-168) at admission. Healthy foals represented 26.8% (n = 85) of the cohort, those being 44 fillies and 41 colts. Sick animals represented 73.2% of the cohort (n = 232). Data were then divided into subsets for analysis: 149 foals (47% of the cohort) had sepsis scores between 4 and 11 and were categorized in the SNS group (72 fillies and 77 colts), of which 143 (96%) were discharged alive and 6 (4%) did not survive; 83 foals (26.2% of the cohort) had positive blood culture and/or sepsis score ≥12 and were classified in the septic group (34 fillies and 49 colts), of which 50 (60.2%) survived and 33 (39.8%) did not survive. Demographic characteristics of the study cohort are shown in Table 1. Among the sick animals, 39.2% (91/232) had a blood culture performed and 23.1% were reported to have bacterial growth on cultures (21/91) with 38 bacterial isolates identified (Table S1).

Horse breeds represented in our study were 110 (34.7%) Quarter Horses and related breeds (Paints and Appaloosas), 62 (19.6%) Thoroughbreds, 39 (12.3%) Warmbloods, 27 (8.5%). Horses of other breeds included 26 (8.2%) Arabians, 21 (6.6%) draft breeds, 21 (6.6%) mixed breed horses, and 10 (3.2%) pony/miniature breeds. Breed was not available in 1 case. The survival rate was 83.2%, with 193/232 sick foals (SNS and septic) discharged alive. Nonsurvivors (n = 36) included foals that died (n = 8) or were subjected to euthanasia for poor prognosis determined by the clinician (n = 28). Days of hospitalization ranged from 0 to 153 days with a median of 2 days.

Univariate analysis of the total study sample showed that RPR was significantly greater for foals in the septic group (Mdn = 0.099, CI [0.093; 0.108]) than in SNS (Mdn = 0.085, CI [0.083; 0.089]) and healthy groups (Mdn = 0.081, CI [0.077; 0.086]; $P < .0001$). This was also true for nonsurvivors (Mdn = 0.099, CI [0.083; 0.119]) relative to survivors (Mdn = 0.085, CI [0.083; 0.088]; $P = .02$). Red blood cell distribution width to platelet ratio values were higher in males (Mdn = 0.092, CI [0.086; 0.097]) versus females (Mdn = 0.082, CI [0.079; 0.086]) among all foals ($P < .01$), possibly because of higher platelet counts that were observed in colts (Mdn = 199, CI [191; 208]), compared with fillies (Mdn = 221; CI [212; 230]). A comparison of platelet count, RDW and RPR by foal group subset is shown in Table 2.

A significant, though weak correlation was observed between RPR and sepsis score among all foals ($r = .2110$; $P < .001$), and sick animals (SNS + Septic groups; $r = .2108$; $P < .01$). Additionally, RPR was correlated to days of hospitalization among the whole cohort ($r = .1454$; $P < .01$) and sick animals (SNS + Septic groups; $r = .1413$; $P = .03$). Red blood cell distribution width to platelet ratio had a significant correlation with age of foals in all subsets: general cohort ($r = .2108$; $P < .001$), SNS animals ($r = .2383$; $P < .001$) and septic animals ($r = .3602$; $P < .001$). Red blood cell distribution width was weakly correlated to the septic foals' sepsis score ($r = .2355$; $P = .03$). Red blood cell distribution width values were not significantly different between groups for any of the group subsets (healthy foals, SNS foals, septic foals). Figure 2 contains box plots for group subsets where significant differences in median RPR values were identified. Results of Kruskal-Wallis, Wilcox, and Spearman tests are summarized in Table S2.

All covariates that were significant in the univariate analysis for sepsis and had an absolute Pearson correlation coefficient lower than 0.7 were retained in the model. The optimal reduced model selected based on AIC yielded an area under the curve (AUC) of 82.1% and included the following predictors: RPR, WBC, neutrophils, lymphocytes, monocytes, basophils, platelets, and creatinine. The calculated Youden Index threshold for RPR was 0.0928, with a sensitivity of 62.7% and specificity of 66.2%, resulting in 52 true positives, 31 false negatives, 79 false positives, and 155 true negatives results for sepsis. A comparison of hematological variables for the entire study sample and for subsets of foals based on the RPR cutoff is shown in Table 3. The ROC curve combining all individual predictors as well as the final model can be seen in Figure 3. Survival curves and survival rates by day of hospitalization compared across groups can be seen in Figure 4 and Table 4, respectively.

TABLE 2 Comparison of platelet count, RDW, and RPR by foal group.

Variables	Healthy group (n = 85), median (95% CI)	SNS group (n = 149), median (95% CI)	Septic group (n = 83), median (95% CI)	Kruskal-Wallis, *P*-value
Platelet count (10^3/μL)	221 (208; 235)	214 (206; 224)	191 (165; 199)	**<.001**
RDW (%)	18.1 (18.0; 18.4)	18.3 (18.2; 18.6)	18.3 (18.1; 18.5)	.1680
RPR	0.08 (0.078; 0.086)	0.085 (0.083; 0.089)	0.099 (0.093; 0.108)	**<.001**

Note: Bold signifies *P* values. *P* = .0005153, could leave as .0005. *P* = .0006497, could leave as .0006.
Abbreviations: n, number of foals; SNS, sick nonseptic.

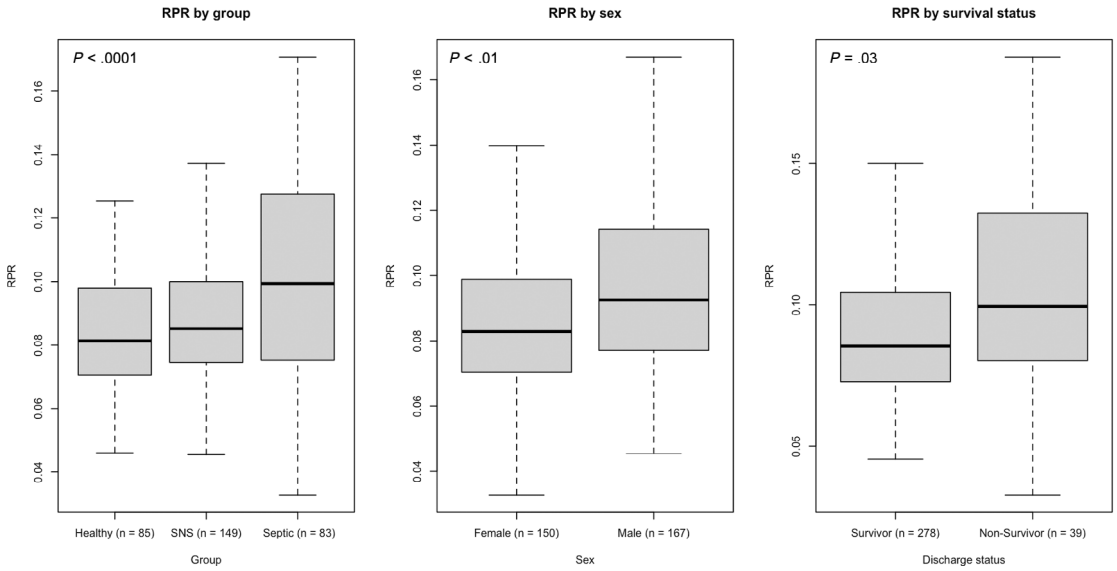

FIGURE 2 Box-and-whisker plots of RPR values for different groups of neonatal foals. Interquartile range and median are represented by horizontal lines. Whiskers represent minimum and maximum values within the range.

4 | DISCUSSION

Our results aligned with our hypothesis that high RPR values at admission significantly correlate with sepsis in neonatal foals, indicating that this ratio can be a supportive tool for diagnosing sepsis. Moreover, our multivariate logistic regression model demonstrates that RPR enhances the CBC's diagnostic value upon septic foals' admission. Although not significant in the log-rank tests (Chi-square = 2.5, *P* = .1), the Kaplan-Meier method showed that neonatal foals with RPR ≥0.0928 at admission had lower chances of survival during the first 3 days of hospitalization, validating RPR prognostic potential. However, as with most biomarkers, there is considerable overlap in RPR values between survivors and nonsurvivors and therefore RPR should not be solely relied upon to prognosticate in individual foals. This study evaluated the relationship between RPR, sepsis, and outcomes in hospitalized foals up to 7 days of age.

In recent years, RPR has been increasingly studied as a novel indicator of systemic inflammation in human patients with sepsis. Evaluation of RPR values in newborn infants admitted to the ICU indicates significant differences between healthy neonates and infants with suspected or proven early onset of sepsis.[24] Similarly, our study showed that foals in the septic group had higher RPR values at admission than those in the healthy and SNS groups (*P* = .0001). Species-specific variation could potentially account for differences in RPR values across studies. Additionally, in a preceding study in Thoroughbred foals <24 hours of age, higher values of RPR were found in foals considered at-risk for developing systemic perinatal disease (mean = 0.073 ± SD 0.018) than in healthy ones (mean = 0.068 ± 0.014; *P* = .01).[29] In the present study, we found that values of RPR for septic and SNS foals were even higher than those we had previously encountered for at-risk and healthy foals,[29] which suggests RPR might be a strong indicator of the severity of inflammatory processes. Furthermore, RPR on admission was higher in nonsurvivors than in foals with a favorable outcome (discharged alive from the hospital), therefore, demonstrating its association with inflammation severity and organ damage.[28] In human studies, a high RPR is consistently associated with a poorer prognosis, regardless of the medical condition evaluated.[23,26-28] Based on these results, RPR might be a valuable prognostic tool used in conjunction with physical exam and other diagnostic findings for infirm neonatal foals.

The retention of RPR as a significant variable among other hematological and clinical variables in our multivariate model to predict sepsis was another noteworthy result of our study. The model that derived from clinicopathologic variables routinely evaluated in the

TABLE 3 Comparison of evaluated blood values and clinical variables for the entire study sample of foals and for groups based on RPR values (above and below the optimal cutoff of 0.0928).

	All (n = 317)			RPR <0.0928 (n = 131)			RPR ≥0.0928 (n = 186)			
Variables	Median	Lower 95% CI	Upper 95% CI	Median	Lower 95% CI	Upper 95% CI	Median	Lower 95% CI	Upper 95% CI	Wilcoxon *P* value
Basophil count (cells/μL)	11	8	13	11	9	16	9	4	13	.3668
Creatinine (mg/dL)	1.7	1.5	1.8	1.7	1.5	1.9	1.6	1.4	1.9	.7757
CRT (s)	1.5	1.2	1.5	1,2	1	1.5	2	1.5	2	**<.001**
Eosinophil count (cells/μL)	10	8	12	10	8	12	9	5	13	.9172
Glucose (mg/dL)	132	124	140	135	123	145	129	118	144	.5584
Heart rate (bpm)	108	104	114	107	100	112	110	104	120	.1022
Hematocrit (%)	39.5	38.4	40.2	40.6	40.1	41.2	36.2	34.9	38.5	**<.0001**
Hemoglobin (g/dL)	13.7	13.3	13.8	13.9	13.7	14.3	12.8	12.3	13.3	**<.0001**
Lactate (mmol/L)	3.0	2.7	3.6	2.9	2.6	3.4	3.3	2.6	4.4	.5123
Lymphocyte count (cells/μL)	1262	1140	1350	1268	1138	1363	1179	1092	1391	.5594
MCH (g/dL)	14.0	13.9	14.2	14.0	13.9	14.2	14.2	13.8	14.3	.8802
MCHC (g/dL)	34.7	34.4	34.9	34.5	34.2	34.8	35.1	34.4	35.4	**.0174**
MCV (fL)	40.6	40.1	41.0	40.6	40.1	41.0	40.2	39.2	41.0	.0649
Monocyte count (cells/μL)	143	130	162	146	125	172	140	111	168	.8592
Neutrophil count (cells/μL)	5823	5437	6418	6500	5748	6969	4910	4133	5742	**<.0001**
Platelet count (10^3/μL)	209	203	218	236	230	250	164	155	171	**<.0001**
RBC (10^6/μL)	9.56	9.37	9.82	9.96	9.72	10.15	9.20	8.90	9.43	**<.0001**
RDW (%)	18.3	18.2	18.4	18.1	18.0	18.3	18.5	18.4	18.7	**<.0001**
Respiratory rate (bpm)	40	40	44	40	40	48	40	38	44	.9061
RPR	0.086	0.084	0.090	0.076	0.073	0.079	0.113	0.107	0.119	**<.0001**
Sepsis score	4	4	5	4	3	4	7	5	8	**<.0001**
Temperature (°F)	100.7	100.5	100.9	100.7	100.5	101.0	100.6	100.2	100.9	.2273
WBC count (cells/μL)	7380	6960	8160	8170	7350	8660	6640	6170	7360	<.0001

Note: Bold numbers = statistically significant.

Abbreviations: CRT, capillary refill time; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red cell distribution width; RPR, red cell distribution width to platelet ratio; WBC, white blood cell.

CBC with the addition of RPR values yielded an AUC of 82.1%, demonstrating the importance of performing hematological evaluations in the triage of neonatal foals. The AUC is the summary of the entire ROC curve and, as an index, represents the overall diagnostic accuracy of a test.[33] The AUC for RPR alone was 63.2%, which might be considered a modest value. However, the values encountered for RPR are similar to the AUC index of other hematological markers retained in the model and commonly evaluated in septic foals, such as lymphocytes and creatinine, although slightly lower than total white blood cell, neutrophil, and basophil counts.[34] Red blood cell distribution width to platelet ratio had a statistically significant correlation with sepsis in the univariate analysis ($P \leq .001$) and was retained in the optimal model for sepsis prediction. This emphasizes that incorporating RPR in the CBC alongside the hematological variables typically analyzed can aid in the early recognition of sepsis, especially considering the ease and practicality of calculating this ratio. Hematological evaluation of neonatal foals is considered a standard of care and is generally performed around 12 hours of life to evaluate passive transfer status or earlier if clinically indicated.[1,34] In this study, an RPR ≥0.09 was associated with lower survival rates, highlighting the value of RPR as a diagnostic tool to aid treatment and referral decisions.

Because clinical signs of sepsis are nonspecific, early diagnosis challenges veterinarians. The recognition of sepsis onset in neonatal foals is crucial not only to improve outcome, but also to prevent

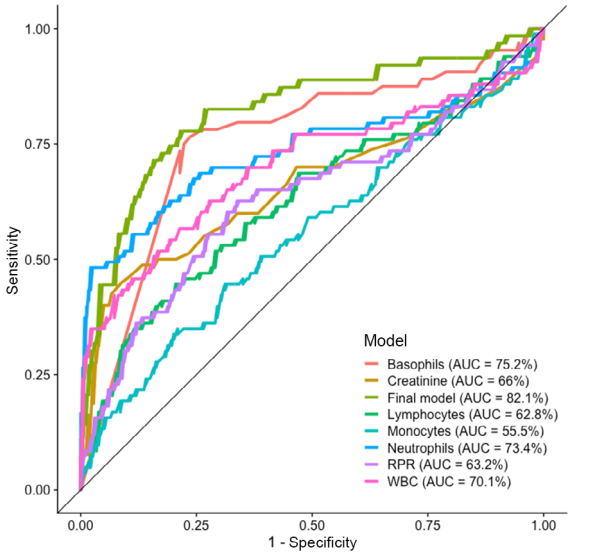

FIGURE 3 ROC curves for the final model and significant individual predictors for sepsis.

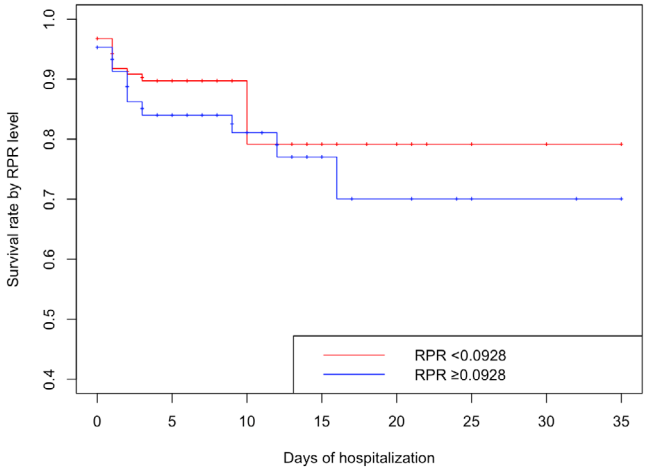

FIGURE 4 Kaplan-Meier survival plot based on RPR levels (below and above the optimal cutoff of 0.0928).

sequelae, especially those compromising the musculoskeletal, neurological, and respiratory systems.[1] Many equine farms now have access to automated hematologic analyzers available on site; moreover, field veterinarians often have access to laboratories, supporting the feasibility of adopting this ratio. Variation in RPR values might be affected not only by different analyzers because of the cell count method (impedance vs laser) and different reagents but also because of iatrogenic causes, such as blood collection method and sample preservation. In addition, platelet clumping might result in inaccurate platelet counts and can interfere with the value of RPR.

Inflammatory mediators have a crucial role in the pathogenesis of sepsis, influencing hemostasis and leading to coagulation abnormalities.[8] Increasing evidence indicates that RDW is closely related to several disease processes in humans and small animals. Red blood cell distribution width correlates with cardiovascular conditions in dogs and cats.[21,35] In human neonates, RDW has been correlated with prematurity and was prognostic for sepsis.[18,36] Red blood cell distribution width was not significantly correlated with neither nonsurvival nor sepsis across groups in our study. In our study, platelet count remained within reported reference ranges in all groups.[34] However, we also chose not to include foals with samples that reported platelet clumping to avoid false thrombocytopenia that would influence the calculation of RPR. We speculate that the higher values of RPR encountered in septic foals might represent a disparity between RDW and platelet counts in response to the inflammatory onset of sepsis, without necessarily affecting the total values or cell counts, respectively.

The limitations of this study should be considered when interpreting the results. First, all data were collected retrospectively from a single center, potentially creating bias and inaccuracy; in some instances, historical and physical examination information can be missing or incorrectly recorded. Furthermore, blood cultures have been considered the gold standard for defining sepsis. However, because of the relatively low sensitivity of blood culture and the low number of tests performed in our study, the use of the modified sepsis score to create group subsets might have led to the misclassification of some foals. Another limitation is the definition of sepsis and the lack of a gold-

TABLE 4 Comparison of log-rank test results for foals with RPR values below and equal or above the optimal cutoff of 0.0928.

Day of hospitalization	Foals at risk	Number of deaths	Survival rate	Lower 95% CI	Upper 95% CI
RPR <0.0928					
0	186	6	0.968	0.943	0.993
1	116	6	0.918	0.873	0.965
2	100	1	0.909	0.861	0.959
3	80	1	0.897	0.846	0.952
RPR ≥0.0928					
0	128	6	0.953	0.917	0.990
1	95	4	0.913	0.862	0.967
2	90	5	0.862	0.799	0.930
3	77	2	0.840	0.772	0.914

standard definition in foals. Therefore, the definition used in this study was based on published data from other studies, making groups of foals similar among many studies.[37,38] Lastly, the continuous fluctuation of RPR values during hospitalization was not evaluated, which could have been useful in determining foal evolution and response to therapy, and, therefore, necessary to formulate a more thorough conclusion. Despite these limitations, RPR should be considered as a diagnostic and prognostic aid in foals with sepsis.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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