Neonatal Foals Admitted to a Veterinary Teaching Hospital in Israel: Diagnosis, Mortality Rates and Risk Factors

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ABSTRACT

In horses, the risk of death is greatest during the first days of life. The objectives of this study were 1) to describe the distribution of diagnoses and the case fatality rates among neonatal foals; and 2) to identify potential risk factors for mortality within the septic foal population. Two hundred cases were included in the study. The median age at admission for foals in the general population was 72 hours, and the Arabian was the most common breed (82.4%). The general mortality rate was 24.5%, (95% Confidence Interval (CI): 18.7-31.1), and the top three diagnoses and their respective mortality rates at admission were sepsis (22.5%; 31.8% (95% CI: 18.6-47.5)), diarrhea (20.5%; 9.8% (95% CI: 2.7-23.1)) and omphalitis (17%; 8.8% (95% CI: 1.9-23.7)). Of the entire population of foals, 43% (95% CI: 36-50.2) were classified as septic using the definition in this study. The median age of septic foals at admission was 96 hours, with the most common breed being Arabian (82.6%). The mortality rate among septic foals was 30.2% (95% CI: 20.8-41.1), and a foal that was diagnosed with sepsis at admission was 4.1 (95% CI: 1.2-13.4) times more likely to die or be euthanized compared to a foal that was not. Furthermore, although outcomes in veterinary medicine are confounded by euthanasia, in this cohort, a relatively small percentage of the non-survivor foals were euthanized, possibly due to cultural differences, in local religion or beliefs.

Keywords: Horse; Foals; Sepsis; Mortality rates.

INTRODUCTION

Treating a neonatal foal in an intensive care unit is labor intensive, relatively expensive and often stressful for the owners (1). Prognosis for survival has improved over time, as reported in a large-scale study from the USA. The adjusted odds of survival for foals admitted in the 2000's were approximately 3.4 times higher than that in the 1980's (2). Still, despite considerable progress in the care of hospitalized foals, mortality rates remain notable in this population, with a recent study from Belgium reporting a fatality rate of 33.3% for hospitalized neonatal foals (3). It is important to mention, however, that outcomes in veterinary medicine are confounded by euthanasia (2). Poor prognosis and financial constraints are key reasons for which sick foals are subjected to euthanasia (2), creating challenges in assessing death percentages, as has been reported previously (3). Owners often request that veterinarians provide prognoses for these foals before referral, as well as during the early stages of hospitalization. Such decisions depend on signalment, case history, physical examination, clinicopathological data and knowledge provided by previously published data. To enable better decision-making, knowledge of the prognoses of specific pathologies is required, but this may vary over time and between countries and facilities. Specific studies might not be

applicable to other equine neonatal intensive care units due to differences in referral populations, case distribution and treatment protocols, as suggested by Giguère *et al.,* 2017 (2). The severity of the disease at the time of admission, which is dependent on both owners and referring veterinarians, also affects survival in these foals. The population characteristics of horses differ between countries, which affects the prevalence of different pathologies as well as their outcomes. Data regarding the prevalence of different pathologies among neonatal foals in our region are limited.

The objectives of this study were to describe the distribution of diagnoses and the case mortality rates among neonatal foals admitted to the Koret School of Veterinary Medicine, Veterinary Teaching Hospital (KSVM-VTH), Israel, from birth to 14 days of age, and to identify potential risk factors for mortality in the septic foal population on admission to the hospital.

MATERIALS AND METHODS

This retrospective cohort study involved all cases of neonatal foals from birth to 14 days of age admitted to the KSVM-VTH between the years 2018 and 2020. Data collected included history, physical examination findings and blood parameter results. This information was extracted from the hospital digital medical records program (Chameleon, Elad Software) and arranged in an Excel file (version 1.5, © 1985-2003 Adobe Systems Incorporated).

Diagnoses at admission (possibly more than one) were routinely documented by the receiving clinicians at the hospital following a basic diagnostic workup (clinical signs, blood test and ultrasound) and clinical assessment within the first two hours after admission. Blood was collected from a catheter, placed immediately upon admission before the administration of any treatment. Quantitative values recorded as descriptive parameters in the files (e.g., low, normal, high) were categorized into predefined numerical ranges. Specifically, heart rate values were categorized as follows: <80 beats per minute (bpm) was defined as low, 80–120 bpm was normal and >120 bpm was high. The respiratory rate was categorized as low at <20 breaths per minute, normal at 20–40 breaths per minute and tachypneic at >40 breaths per minute. These thresholds were defined based on previously published criteria (4). Foal age at presentation was categorized into the following groups: ≤12 hours, 13–24 hours, 25–48 hours, 49–72 hours and >73 hours. Gestational age was categorized, based on the original Sepsis Score-related criteria (4), into the following ranges: 300–310 days, 311–330 days and >330 days (considered within the normal range) (5). Since the association between neutrophil counts and sepsis is non-linear, neutrophil counts were categorized (0-3) as per the definitions of the original Sepsis Score (5). Neutrophil toxicity was subjectively evaluated. Band neutrophil count was assessed qualitatively rather than quantitatively, and hypoglycemia was defined as 50 mg/dL. Attitude was classified as normal or abnormal (e.g., hypotonia, coma, depression or seizures). Foals diagnosed with sepsis were defined according to the criteria outlined below, and analyses of risk factors for mortality were conducted exclusively in this defined population.

The study was approved by the Hebrew University Ethics Committee (HU-NER-2020-033-A).

Septic foal classification

Based on Wong's classification of sepsis (6) and on the equine neonatal Systemic Inflammatory Response Syndrome (SIRS) criteria, and adapted to the variables examined at KSVM-VTH, sepsis was defined as follows.

Adapted from Wong's classification of sepsis (6): The presence of more than one of the following criteria: infected joints, omphalitis (based on ultrasound morphological appearance or positive umbilical culture) and signs of diarrhea (loose, watery stools).

Adapted from SIRS criteria: The presence of at least three of the following five criteria: heart rate >120 bpm, respiratory rate >30 breaths per minute, glucose <50 mg/dL and abnormal temperature (T>38.8°C or T<37.7°C) or white blood cells (WBC<4.3x10^3/μL or WBC>14.8x10^3/μL). At least one of the latter two criteria was required.

Statistical analysis

The entire population of foals admitted to the KSVM-VTH, as well as the subset classified as septic, were summarized and characterized through descriptive statistics. The distribution of continuous variables was assessed for normality using the Shapiro–Wilk normality test and is reported as medians and quartiles. Frequencies were reported as percentages and 95% confidence intervals. Short-term mortality was defined as death occurring during hospitalization. Foals identified as septic based on the study's previously defined criteria were included in the analysis of risk factors for short-term

Table 1. Distribution of common diagnoses assigned by clinicians at hospital admission (n=200) and case fatality rates for each diagnosis. Multiple diagnoses could be assigned per foal. [FPT—failure of passive transfer; NMS—neonatal maladjustment syndrome].

Diagnosis	Percentage (n; %; 95% CI*)	Case Fatality (n; %; 95% CI*)
Sepsis	44; 22.5 (16.5-28.4)	14; 31.8 (18.6-47.6)
Diarrhea	41; 20.5 (15.1-26.8)	4; 9.8 (2.7-23.1)
Omphalitis	34; 17 (12.1-22.9)	3; 8.8 (1.9-23.7)
FPT	25; 12.5 (8.3-17.9)	2; 8.0 (1.0-26)
NMS	16; 8 (4.6-12.7)	3; 18.8 (4.1-45.7)

* CI=Confidence Intervals.

mortality. The Mann–Whitney U test was used for univariable analyses of continuous variables, and odds ratios were therefore not available. Categorical variables were analyzed using either the chi-square test or Fisher's exact test, with the latter being applied when expected cell counts in one or more cells were <5. Clinical and laboratory parameters at admission that demonstrated a statistically significant association with short term mortality ($p<0.05$) in the univariable logistic regression analysis for the population of septic foals were further assessed using a multivariable logistic regression model. To reduce multicollinearity, variables with strong intercorrelations (Spearman's rho>0.9) or significant associations based on Fisher's exact test ($p<0.01$) were excluded from the multivariable model by choosing to exclude those with less significant p-values. Only first-order factors were evaluated. A receiver operating characteristic (ROC) curve was used to assess the ability of potassium to predict mortality in septic foals. The final multivariable logistic regression model was constructed using a forward stepwise likelihood ratio selection procedure. IBM SPSS versions 27 and 31 and WinPEPI Describe A (version 3.18) were used to calculate 95% confidence intervals (CIs) for descriptive proportions.

RESULTS

General population description

Two hundred cases were included in the study, with the study population comprising 132 females (66%) and 68 (34%) males. The foal age distribution (n=199) was as follows: ≤12 hours (n=43, 21.6%), 13–24 hours (n=29, 14.6%), 25–48 hours (n=25, 12.6%), 49–72 hours (n=23, 11.6%) and >73 hours (n=79, 39.7%). The gestational age distribution (n=119) was 300–310 days (n=1, 0.8%), 311–330 days (n=21, 17.6%) and >330 days (n=97, 81.5%). Heart rate at admission (n=195) was distributed as follows: <80 bpm (n=12, 6.2%), 80–120 bpm (n=136, 69.7%) and >120 bpm (n=47, 24.1%). The respiratory rate distribution (n=189) was <20 breaths per minute (n=5, 2.6%), 20–40 breaths per minute (n=145, 76.7%) and >40 breaths per minute (n=39, 20.6%). Arabian was the most common breed (82.4%). Of the 200 foals, 151 were discharged alive (75.5%, 95% CI: 0.69-0.81), 36 died (18%) and 13 were euthanized (6.5%). Due to the retrospective nature of this study, data were not available for all parameters that were collected.

Distribution of diagnoses

In the entire foal population, the frequency of the most common diagnoses assigned by clinicians at hospital admission (based on their clinical judgment) and the case fatality rates are presented in Table 1 (multiple diagnoses per foal were recorded). The most frequent diagnoses at admission were sepsis (22.5%), diarrhea (20.5%) and omphalitis (17%). Other less common diagnoses that are not included in the tables were laryngeal/pharyngeal weakness, congenital patellar luxation, uroperitoneum, aspiration pneumonia, small intestinal intussusception, meconium impaction, angular limb deformity (carpal valgus), prematurity/dysmaturity, weakness, seizures and foal rejection by the mare.

The retrospectively classified septic population description (n=86)

The retrospectively classified septic foal population represented 86 of the 200 cases (43%), with 56 (65.1%) females and 30 (34.9%) males. The foal age distribution (n=85) was as follows: ≤12 hours (n=12, 14.1%), 13–24 hours (n=9, 10.6%), 25–48 hours (n=8, 9.4%), 49–72 hours (n=15, 17.6%) and >73 hours (n=41, 48.2%). The gestational age distribution (n=49) was 300–310 days (n=0, 0%), 311–330

Table 2. Medians (quartiles) of clinical findings and blood values in retrospectively classified septic foals (n=86). The number of foals included for each parameter (n) is presented.

Parameter	Median (Quartiles)	Number of foals (n)
Clinical parameters		
Body temperature (°C)	38.2 (37.7, 38.9)	82
CBC		
Hematocrit (%)	41.4 (36.5, 46.6)	76
Platelets ($X10^3/\mu L$)	137.5 (86.2, 180.7)	76
WBC ($X10^3/\mu L$)	5.6 (3, 9.6)	83
Neutrophils ($X10^3/\mu L$)	4.4 (2.3, 8.2)	76
Biochemistry		
Sodium (mmol/L)	137.9 (136, 142.2)	79
Potassium (mmol/L)	3.6 (3.2, 4.0)	79
Chloride (mmol/L)	99 (96.5, 102.4)	79
Glucose (mg/dL)	86 (42.2, 119.7)	60
Urea (mg/dL)	45.3 (23.6, 62.4)	22
Creatinine (mg/dL)	1.3 (1.0, 2.1)	75

days (n=8, 16.3%) and >330 days (n=41, 83.7%). Heart rate at admission (n=85) was distributed as follows: <80 bpm (n=5, 5.9%), 80–120 bpm (n=44, 51.8%) and >120 bpm (n=36, 42.4%). The respiratory rate distribution (n=83) was <20 breaths per minute (n=1, 1.2%), 20–40 breaths per minute (n=58, 69.9%) and >40 breaths per minute (n=24, 28.9%). The most common breed among the septic foals was Arabian (n=71, 82.6%). A description of the clinical findings and blood values is presented in Table 2. Neutrophil toxicity was described as normal (19.4%), mild toxicity (16.4%), moderate toxicity (29.9%) and severe toxicity (34.3%). A left shift in neutrophils was recorded as normal (63.6%), slight left shift (13.6%) and marked left shift (22.7%). Among septic foals, 60 foals were discharged alive (69.8%), 22 died (25.6%) and four were euthanized (4.6%). Due to the retrospective nature of this study, data were not available for all parameters that were collected (Table 1, Supplementary Materials).

Parameters associated with death among the retrospectively classified septic foals by univariable analysis

Clinical findings, blood values and diagnoses assigned by clinicians at hospital admission (based on their clinical judgment) that were associated with death are presented in Table 3. All subsequent analyses were based on the 26 foals that died (22 spontaneously, 4 euthanized).

Multivariable analysis of factors associated with death among septic foals

Included in the model were the following: the neutrophil count in categories (Category 3 vs. 0–2), sodium (mmol/L), potassium (mmol/L), glucose (mg/dL) and attitude (normal vs. abnormal). WBC was not included, as it was found to be strongly associated with neutrophil counts (rho=0.98). The neutrophil count was included as it had a lower p-value than WBC in the univariable analysis of the association with short-term mortality. The capillary refill time (CRT) and mucous membrane color were strongly associated with attitude ($p<0.03$) and were therefore not included in the multivariable model. Attitude was chosen due to its lower p-value in association with short-term mortality ($p=0.00006$). The final multivariable regression model had a Nagelkerke R-square of 0.45 and improved the prediction of the model from 70% to 86%. The results of this analysis are presented in Table 4. In the multivariable analysis of septic foals (n=86), which included only the two diagnoses at presentation associated with short-term death among the septic foals in the univariable analysis, those diagnosed as septic at admission retained a statistically significant association with death, with an odds ratio of 4.1 (95% CI: 1.2-13.4).

Table 3. Clinical findings, blood values and diagnoses of cases retrospectively classified as septic (n=86) assigned by clinicians at hospital admission associated with death by univariable analysis (Mann–Whitney or X^2) (p-value) and the direction of change associated with death for significant parameters. Of the significant parameters, the number (percentage) of cases that died out of those with the finding, shown in parentheses, and the odds ratio and 95% confidence interval (95% CI) are available only for categorical parameters.

	p-value	N (%) died; odds ratio (95% CI)
Clinical parameters		
Age	0.514	--
Gestation age	0.898	--
Breed	0.764	--
Sex	1.0	--
Heart rate	0.628	--
Respiratory rate	0.378	--
Capillary Refill Time (CRT) (prolonged)	0.005	7/12 (58.3%); 7.6 (1.9-30.9)
Mucous membranes (abnormal)	0.002	15/31 (48.4%); 5.1 (1.7-14.8)
Attitude (abnormal)	0.00001	19/33 (57.6%); 8.9 (3.1-25.6)
Blood parameters		
WBC ($X10^3/mm^3$) (Decrease)	0.032	*
Platelets ($X10^3/\mu L$) (Decrease)	0.016	*
Sodium (mmol/L) (Increase)	0.006	*
Potassium (mmol/L) (Increase)	0.029	*
Glucose (mg/dL) (Decrease)	0.0003	*
Monocytes ($X10^3/\mu L$)	0.651	--
Lymphocytes ($X10^3/\mu L$)	0.645	--
Neutrophil count category 3 (<2 $X10^3/mm^3$)	0.002	11/17 (64.7%); 36.7 (3.9-344.8)
RBC ($X10^6/mm^3$)	0.5	--
Hematocrit (%)	0.894	--
Hemoglobin (g/dL)	0.874	--
Creatinine (mg/dL)	0.151	--
Chloride (mmol/L)	0.2	--
Calcium (mmol/L)	0.634	--
Neutrophil toxicity	0.443	--
Diagnoses assigned by clinicians		
Sepsis	0.017	11/30 (36.7%); 4.1 (1.2-13.4)
Omphalitis	0.028	1/20 (5%); 0.12 (0.00-0.94)
Diarrhea	0.069	

* Not available from the Mann–Whitney U test.

Assessment of potassium for predicting death among septic foals

The ROC curve assessing potassium as a predictor of mortality in septic foals is presented in Graph 1. Area under the curve: 0.61 (95% CI 0.501-0.718).

DISCUSSION

In this study, we described the distribution of diagnoses for neonatal foals admitted to the KSVM-VTH. Currently, this is the only equine hospital in the country in which foals are hospitalized. Referring veterinarians should note that the

Graph 1. ROC curve assessing potassium as a predictor of mortality in septic foals.

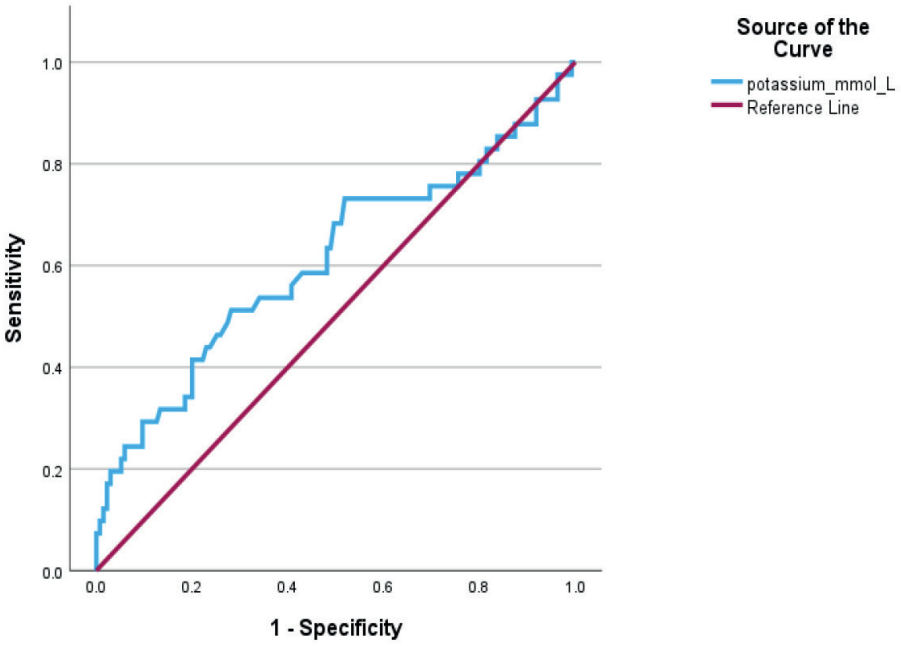

Table 4. Factors significantly associated with short-term death in multivariable analysis within the subset of foals diagnosed as septic. The p-value of the association, the odds ratio and the 95% Confidence Interval (95% CI). N=50.

Factors associated with death	p-value	Odds ratio (95% CI)
Attitude (abnormal vs. normal)	0.006	9.7[a] (1.9, 48.6)
Potassium (mmol/L)	0.02	6.5[b] (1.3, 32.5)

[a] Abnormal attitude increases odds of death by 9.7.
[b] For every unit increase in potassium, the odds of death increase by 6.5 times.

most common diagnoses made by the receiving clinicians at admission (potentially including more than one) were sepsis (22.5%), diarrhea (20.5%), omphalitis (17%), FPT (12.5%) and NMS (8%), and that diarrhea and omphalitis carried better prognoses than other diagnoses. This information regarding diagnoses, together with the prognoses for these conditions, contributed to the decision-making process when treating similar cases. It was also important to consider that the majority of the foals were assigned one or two diagnoses at the time of admission.

Consistent with previous reports (2), the observed sepsis prevalence of 43% (95% CI: 36–50.2%), based on the definition of sepsis in this study) was twice the rate recorded by clinicians upon admission (22.5%). A large animal hospital at the University of Florida categorized only 113 foals (10.6%) as septic in the primary diagnosis in the records, whereas 60.2% met the criteria for sepsis (positive blood culture and more than one site of infection) (2). Classifying sepsis is indeed challenging and differs between studies, which results in different prevalence rates; for example, while the prevalence of sepsis was 27% in a study from Denmark and Sweden (7), it was higher in studies from the USA (6) and Belgium (3) (46% and 43.9%, respectively). In a recently published large-scale study that included data on 1068 critically ill neonates from 16 veterinary referral hospitals in four countries, the authors reported that the ability to predict infection using history, signalment, physical examination findings, laboratory results and SIRS-related indices was poor to fair (8). Therefore, diagnosing sepsis at admission is complicated, and improved definitions for this stage of case management are required.

The rate of diarrhea as an initial presenting sign (20.5%; 95% CI:16.9-28.9) for the foals in this study is similar to the rate reported in one of two studies from the USA (25.7%) (2), but is significantly lower than the rate reported in the other (33.4%) (9) based on the 95% confidence interval. Enteritis was reported in 14% of foals in a recent study from Belgium (3). As the clinical sign of enteritis in a foal is diarrhea, and since it is probable that some of the foals for which diarrhea was written in the records as the primary diagnosis

were septic (3) comparisons between studies and populations are challenging.

The prevalence rate [8% (4.6-12.7)] and case fatality rate for NMS in this study [18.8% (4.1-45.7)] were not significantly different from the rates found for foals in Belgium (8.6%, with 26.3% case fatality) (3). However, in studies from the USA, the prevalence of NMS was significantly higher (14.6%), but with a similar case fatality rate in two studies: 20% (2) and 14.9% (9). Mortality in foals diagnosed with NMS depended on the onset of clinical signs; prognosis was good when signs appear 6-24 hours after delivery, but poor when present at birth. It depended on the presence of major complications, such as sepsis (10). The prognosis of the foals in this cohort could be considered relatively good, since all but one of the foals in this cohort were between 6 and 24 hours old. However, the age used in this study was the age the foals presented to the hospital and not the age at onset of signs.

The foal population in this study differs from others reported in the literature, in that they are predominantly Arabian fillies (82.4%). The Arabian is one of the oldest horse breeds in the history of humankind (11), with a high financial value. The fact that more females (66%) than males were admitted to the hospital might also be related to their higher financial value as future broodmares. This is in contrast to the foal population in two studies from the USA, in which the main breed was Thoroughbreds, with only a few Arabian horses, and colts being more prevalent than fillies (2, 9). This is also different from the populations in three studies from Europe, where Warmbloods were the common breed and colts were also more prevalent (3, 7, 12). Such differences between the populations may lead to different outcomes. Some pathologies in neonatal foals are more common in specific breeds or in a particular sex. For example, regarding breed, foal rejection is relatively common in the Arabian breed (13), possibly leading to FPT and sepsis and regarding sex, a ruptured bladder is more common in colts (14).

Short-term survival in our study was 75.5% (95% CI: 69-81), which was higher than previously reported survival rates: 66% in South Africa (15), 66.7% in Belgium (3) and 67% in the USA (16), but comparable to one study from the USA (72.8%) (2) and one from Denmark (71.6%) (12), and significantly lower than another study (82.1%) from the USA (9) and one from Denmark and Sweden (83%) (7). However, these differences, though significant, were very slight. The relatively good prognosis in this study was likely the result of increased awareness and early referrals by both owners and referring veterinarians in the country (17), as well as the internationally recognized specialization of the hospital clinicians.

Sepsis, defined as concurrent evidence of SIRS and the identified or suspected presence of microbial infection, is a common cause of morbidity and mortality in neonatal foals (8). In this study, 39 cases were classified as septic based on the presence of more than one of Wong's criteria, 36 were classified as septic based on Wong's SIRS criteria and 11 were septic by both classifications. The mortality rates among septic foals reported in the literature were highly variable but, in general, the outcome had improved significantly over time, likely due to early detection and the treatment of at-risk foals (17). In a recently published large-scale study, the mortality rate of septic foals was 23.8%, of which two-thirds were euthanized (8), similar to the findings in this study of 30.2% (26/86) (95% CI: 0.21-0.41), although only 15.4% (4/26) of those that died were euthanized. In a recent study from Belgium, a foal with sepsis was 1.9 times more likely to die than a foal without sepsis (3). This was not statistically significantly different from the results in our study [4.1 (95% CI: 1.2-13.4)].

In our study, attitude, defined as normal or abnormal (e.g., hypotonia, coma, depression or seizures), was found to be strongly associated with short-term mortality within the subset of foals diagnosed as septic. This finding was expected, as attitude (hypotonia, coma, depression, convulsions) is part of the Sepsis Score and provides 1-2 points depending on severity (4). Interestingly, in a previous study on 65 septicemic foals (18), attitude (normal, depressed, moribund or seizing) was reported for 57 foals, of which 50 were abnormal, but no difference was found in mortality. However, the authors concluded that it was possible that a larger study would have resulted in a significant difference (18).

The blood potassium level was also found to be associated with death in foals with sepsis in this study. The risk of death increased with every unit increase in potassium. Although this is the first study to report that an increase in potassium was significantly associated with death in septic foals within a multivariable analysis, the median potassium levels of both groups were within normal limits. In human medicine, critically ill patients with abnormal potassium levels (lower or higher than the reference values) had a higher incidence of

ventricular arrhythmia and death than patients with normal potassium levels (19). This finding should be evaluated in future research. ROC curve analysis yielded an AUC of 0.61 (95% CI: 0.50–0.70) for potassium concentration as a predictor of mortality in septic foals, reflecting its limited discriminatory power. This suggests that potassium levels alone are unlikely to serve as a reliable prognostic marker, and should be interpreted in conjunction with additional clinical parameters.

As opposed to a report from Belgium, in which omphalitis was associated with a higher risk of death (35%) (3), in this study and in a study from Tufts University, foals with omphalitis were more likely to survive (9). This finding was unexpected, since omphalitis is a clinical sign that characterizes sepsis, and foals with sepsis as a working diagnosis assigned by clinicians at admission were 4.1 times more likely to die (Table 3). This outcome may have associated with case management, since foals presenting with omphalitis in this hospital are routinely managed surgically quite successfully (20) by an innovative surgical technique (21). Therefore, the association observed between omphalitis at admission and improved survival may suggest differences in clinical management. Accordingly, any potential benefit of early omphalectomy cannot be inferred from the present data and warrants further evaluation in prospective studies.

Limitations: Our study had a number of limitations, primarily the reliance on retrospective recorded historical and physical examination information which, on occasion, may have missing data or been recorded inaccurately and/or subjectively (e.g., neutrophil toxicity) by multiple observers. The amount of missing data in the medical records may have resulted in the omission of variables (e.g., gestational age) pertinent to the search for risk factors associated with death among septic foals, and some important information may have been lost. Additionally, the missing data (e.g., glucose) limited the number of cases included in the final multivariable model (n=50).

Further research should be conducted to examine these additional parameters. Furthermore, mortality included natural death (n=36/49; 73.5%) and euthanasia (n=13/49; 26.5%) on ethical or economic grounds, which caused challenges in assessing death percentages, as reported previously (3). However, euthanasia was only performed in approximately one quarter of the non-survivors in this cohort study and only in 15.4% (4/22) of the septic foals, compared to 78.6% (228/290) in a study from the USA (2), which might be attributed to differences in local traditional or religious beliefs. Another limitation is that there were many potential risk factors in the univariable analysis but not enough mortality cases to produce a reliably stable logistic regression model (22), possibly resulting in overfitting.

We acknowledge that our final models resulted in an event per variable (EPV) of 6.5; therefore, the results should be interpreted with caution and validated in a larger cohort. Regarding sepsis definitions, the retrospective design resulted in an incomplete availability of clinical and laboratory data, which are used in standard sepsis scoring systems (e.g., fibrinogen, lactate, band neutrophils and IgG) and that were not consistently performed in all cases. Therefore, in retrospect, a modified definition of sepsis was used, which may have led to misclassification, particularly in cases with incomplete data. Given that the main analysis focused on septic foals, this limitation should be considered when interpreting the results. Any misclassification is likely to have biased the results. Our study did not rely on blood cultures for septic foal classification, as blood cultures were not routinely examined in this hospital and because a study from 2014 found that positive blood cultures may result from transient bacteremia and may occur in healthy foals early in the postnatal period (23). This may have also resulted in the misclassification of sick, non-septic foals as septic foals (or vice versa), which is an additional reason to interpret the results with caution. Foals that were classified retrospectively as septic may have had more than one diagnosis, which further complicates interpretation of the conclusions. Lastly, the unique population of foals in this study makes comparisons between studies difficult.

CONCLUSIONS

In conclusion, we found that our cohort was unique including mostly Arabian fillies, possibly due to their higher local financial value. Although sepsis was the most common diagnosis, only half of the foals that were determined as septic in retrospect by the authors were diagnosed as such by the clinician at admission, demonstrating the need for an accepted definition of sepsis in foals.

Institutional Review Board Statement: The study was approved by the Hebrew University Ethics Committee (HU-NER-2020-033-A).

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