

## Risk factors and diseases associated with failure of natural passive immunization in foals

[Fatores de risco e enfermidades associadas a falha na imunização passiva natural em potros]

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### ABSTRACT

This study aimed to report the prevalence of diseases in foals, patients at the Hospital Veterinário de Grandes Animais, Universidade Federal de Lavras (HVGA-UFLA), and its association with deaths and possible failures in the transfer of passive immunity (FTIP) via colostrum. Data were obtained from clinical records of horses aged between 0 and 3 months, admitted to the HVGA between January/2014 and December/2018. Descriptive analyzes of the diseases and organ systems affected were performed, as well as univariate analyzes with chi-square or Fisher's exact tests, identifying possible associations between FTIP, infectious diseases and other factors. No significant relationships were found between FTIP and infectious disease, meconium retention, sepsis, or death. However, it was shown that animals weighing between 10 and 30kg were 29.333 times more likely (95% confidence interval 1.734 – 505.951) to die than those weighing between 30.1 and 130kg. Therefore, it can be concluded that low weight is a very relevant risk factor, which may be related to the failure of postural reflexes and, consequently, to the inability to ingest colostrum, impairing the ability to respond to infectious agents.

Keywords: immunity, colostrum, infectious diseases

### RESUMO

*Este trabalho objetivou relatar a prevalência de enfermidades em potros, pacientes do Hospital Veterinário de Grandes Animais da Universidade Federal de Lavras (HVGA-UFLA), e sua associação com óbitos e possíveis falhas na transferência de imunidade passiva (FTIP) via colostro. Os dados foram obtidos pelas fichas clínicas de equinos com idade entre 0 e 6 meses, internados no HVGA entre janeiro/2014 e dezembro/2018. Foram realizadas análises descritivas das enfermidades e os sistemas orgânicos acometidos, além de análises univariadas, com testes de qui-quadrado ou exato de Fisher, identificando possíveis associações entre FTIP, enfermidades infecciosas e outros fatores, com p menor que 0,05 e intervalo de confiança (IC) de 95%. Não foram encontradas relações significativas entre FTIP e enfermidades infecciosas, retenção de mecônio, sepsse ou morte. No entanto, foi demonstrado que animais com peso entre 10 e 30kg tiveram 29,333 vezes (IC 95% 1,734 - 505,951) mais chance de virem a óbito que aqueles com peso entre 30,1 e 130kg. Portanto, pode-se concluir que o baixo peso é um fator de risco bastante relevante, que pode estar relacionado à falha de reflexos posturais e conseqüentemente, à incapacidade de ingerir colostro, prejudicando a capacidade de resposta a agentes infecciosos.*

*Palavras-chave: imunidade, colostro, doenças infecciosas*

### INTRODUCTION

Horse farming in Brazil is a profitable activity, with a national troop composed of 5,557,539 animals in 2016 (Lima and Cintra, 2016), which moves 16.5 billion reais annually, generates 610,000 direct jobs and more than 2 million

indirect jobs (Santos *et al.*, 2018). In addition to their economic importance, horses have a close relationship with humans, being used in agricultural and livestock activities. There are also equestrian events aiming to present the qualities of examples of relevant national breeds such as Mangalarga Marchador, Campolina, Jumento Pêga and Crioulo (Vieira *et al.*, 2015).

The success of equestrian activity depends mostly on good management practices, which must be implemented from birth, when the transfer of natural passive immunity via colostrum is necessary. Colostrum is the first substance secreted by the mammary glands after the foal birth, composed of large amounts of proteins, fatty acids, vitamins, minerals, substances with laxative effects and by cells and immunoglobulins, essential for temporary protection against various infectious diseases and for the maturation of the newborn's immune system (Csapó-Kiss *et al.*, 1995). However, it is possible that the transfer of passive immunity via colostrum is inefficient and may occur due to inadequate composition or failure to administer colostrum to the animal within the first 12 hours of life, intestinal disorders, prematurity, among others, as already presented by Jeffcott (1974).

The failure in natural passive immunization, as well as the individual's age, mother's age, birth conditions, among others, can be a predisposing factor to many diseases of infectious etiology (Rizzoni and Miyauchi, 2012). Not ingesting colostrum commonly predisposes foals to diseases such as diarrhea, sepsis, meconium retention, polyarthritis and omphalopathies (Taylor, 2015; Rizzoni and Miyauchi, 2012). The construction of a solid immunity is necessary for the survival and satisfactory development of the animal, directly influencing public health, since horses, in general, can participate in the dissemination of zoonoses such as rabies, influenza, glanders, among others (Sack *et al.*, 2020).

Thus, it is essential to determine the relationship between the main diseases caused by pathogenic microorganisms, the inadequate transfer of passive immunity via colostrum in foals and death, so that, later, effective ways to prevent these diseases and appropriate therapies for the animals that fit can be established under these conditions. Therefore, the aim of this study was to report the prevalence of diseases in foals, patients at the Hospital Veterinário de Grandes Animais (HVGA) of Universidade Federal de Lavras (UFLA) and to associate them with possible failures in the transfer of passive immunity (FTIP) via colostrum and deaths.

## MATERIAL AND METHODS

The study was conducted using data from clinical records containing age, sex, breed, weight, physiological parameters, clinical suspicion, and diagnosis, adopted therapies and complementary tests, from horses hospitalized at the HVGA-UFLA in Lavras, Minas Gerais, Brazil, between January 2014 and December 2018. According to Normative Resolution No. 30, of February 2, 2016 - DBCA, item 6.1.10, this project does not require analysis and approval by the ethics committee on the use of animals (Comitê de Ética para o Uso de Animais - CEUA), as it falls under the class of studies retrospective and did not use live animals.

Hospitalizations of equine animals, aged from 0 to 90 days, hospitalized at the HVGA - UFLA between January 2014 and December 2018 were included in the statistical analyses. The absence of data, such as clinical signs and diagnosis of the illnesses that affected the patient, was used as a criterion for the exclusion of individuals from the study. Animals born at term, without a history of infectious diseases or rejection by the mother, who received adequate colostrum or presented serum levels of Immunoglobulin G (IgG) greater than 800mg/dL in an immunochromatographic test, had passive immunization via colostrum considered adequate. Foals with a clinical history of rejection by the mother, infectious diseases, prematurity, and orphans who did not receive colostrum in sufficient quantity or quality or had serum IgG levels lower than 400 mg/dL, because of the immunochromatographic test, had natural passive immunization via colostrum considered inadequate, as well as animals with serum IgG levels between 400mg/dL and 800 mg/dL (concentrations that reflect partial failure of passive immunity transfer). These criteria and serum IgG concentrations were defined following recommendations from the company VetAll laboratories®, manufacturer of the immunochromatographic test. Data regarding hospitalizations were collected from clinical records of the HVGA - UFLA and tabulated in spreadsheets in a computer program (Microsoft Excel®, Microsoft, USA). Of the total number of hospitalizations, 34 were included in the

analyzes and categorized by sex, weight (between 10 and 30kg and between 30.1 and 130kg), diagnosis of infectious disease or other etiology, affected organic system and transfer of adequate or inefficient passive immunity.

Descriptive analyzes were performed to define the proportion between females and males among the animals included in the research, the percentages corresponding to each organic system affected by various diseases, the ratio between infectious diseases and non-infectious, as well as the number of deaths from infections and among patients with failed colostrum and submitted to plasma administration.

To determine the associations between passive immunity transfer failure and the presence of infectious disease or deaths, univariate analyzes were performed using the chi-square ( $\chi^2$ ) or Fisher's exact tests, with p value  $\leq 0.05$  adopted as significant. All statistical analyses and 95% confidence interval (CI) were performed in the EPI-Info™ 7.0 software (Dean, *et al.*, 1996).

## RESULTS AND DISCUSSION

Passive immunity transfer via colostrum is crucial for the survival of equine neonates, since the components of the mother's immune system that protect them from various environmental challenges do not cross placental barriers and therefore make them agammaglobulinemic and capable of acquiring potentially dangerous infectious agents (Baptista *et al.*, 2020). For this reason, studies are needed to determine the main diseases associated with failure to transfer passive immunity or deaths in foals, therefore it is possible to prevent their occurrence or minimize their consequences to the animal.

For this purpose, data from 34 admissions that occurred between 2014 and 2018 at the HVGA-UFLA were used, which included animals hospitalized only once and animals that needed hospital care repeatedly at certain time intervals. Of these, two male foals were hospitalized two times during their first three months of life, both with recurrent history of diarrhea on all admissions and pneumonia one of them.

Age from 0 to 90 days was used as an inclusion criterion, considering that in the first months of life, the animals' immune system still does not

provide satisfactory protection in a timely manner against pathogens in the external environment of the mother's uterus, which makes them very dependent on the immunity provided via colostrum (Spindola *et al.*, 2017). However, this immunity does not last longer than some months and, therefore, it is considered that infectious diseases acquired after three months of age are less related to failure to transfer passive immunity (Jeffcott, 1974), which justifies the maximum age defined in the study.

Female foals accounted for 41.18% [18/34] of total admissions, while male foals accounted for 58.82% [20/34]. At admission, 14.71% [5/34] of animals weighed between 10 and 30kg, 73.52% [25/34] were between 30.1 and 130kg and 11.76% [4/34] of admissions had no information described for the category. This majority of animals weighing between 30.1 and 130kg was expected, considering the fact that the breeds most attended by the HVGA are usually large breeds, from which healthy foals must be born weighing more than 30kg, e.g. Mangalarga Marchador breed (Siqueira *et al.*, 2018) and Campolina breed (Oliveira, 2017). For this reason, animals weighing less than 30 kg were considered low weight. This is an important factor to be considered, as it can characterize animals with signs of immaturity, which may have problems with postural reflexes and sucking, which directly interfere with their ability to ingest colostrum and, thereby with their ability to survive. Indeed, this could be seen in the present study, in which 100% of animals weighing between 10 and 30kg present fail of passive immunity, presenting 29.333 times (95% CI 1.734 - 505.951) more likely to die than those weighing between 30.1 and 130kg.

After characterizing the population, the main illnesses that resulted in hospitalizations were infectious diseases, representing 52.94% [18/34] of diagnoses, with septicemia present in 8.82% [3/34] of admissions. Septicemic shock is the leading cause of mortality in neonates up to 30 days of age that are affected in intrauterine life or soon after delivery, being closely related to failure to transfer passive immunity (Taylor, 2015), as shown in this research, since septicemic conditions were not present in patients who received adequate colostrum.

The most affected organic system was the gastrointestinal system reaching 26.47% [9/34] of the cases. Of the hospitalizations caused by changes in this system, 17.65% [6/34] exhibited diarrhea, which only affected patients who failed to transfer passive immunity. This clinical sign can be caused by agents such as rotavirus, *Clostridium perfringens*, *Salmonella* spp., *Clostridium difficile*, among others, more frequently during the first 3 months of life (Ayala and Espinosa, 2015). Moreover, 11.76% [4/34] of the cases showed meconium retention, which was only reported in animals with failed colostrum, in which there was no laxative effect of colostrum, essential for the expulsion of

meconium in the first 12 hours of life (Rizzoni and Miyauchi, 2012). 82% [3/34] of hospitalizations equivalent to foals born from dystocic births or complicated pregnancies had proven immunity failure. The failure of transference in passive immunity is quite associated with disturbances in pregnancy or parturition (premature, premature and dystocic births) and malnutrition, as animals often have difficulties in sucking or do not get up to nurse (Wonhlfender, 2009). Some patients had more than one diagnosis, in which all the animals in these groups showed failed natural passive immunization. The proportions equivalent to the other affected systems is shown in Figure 1.

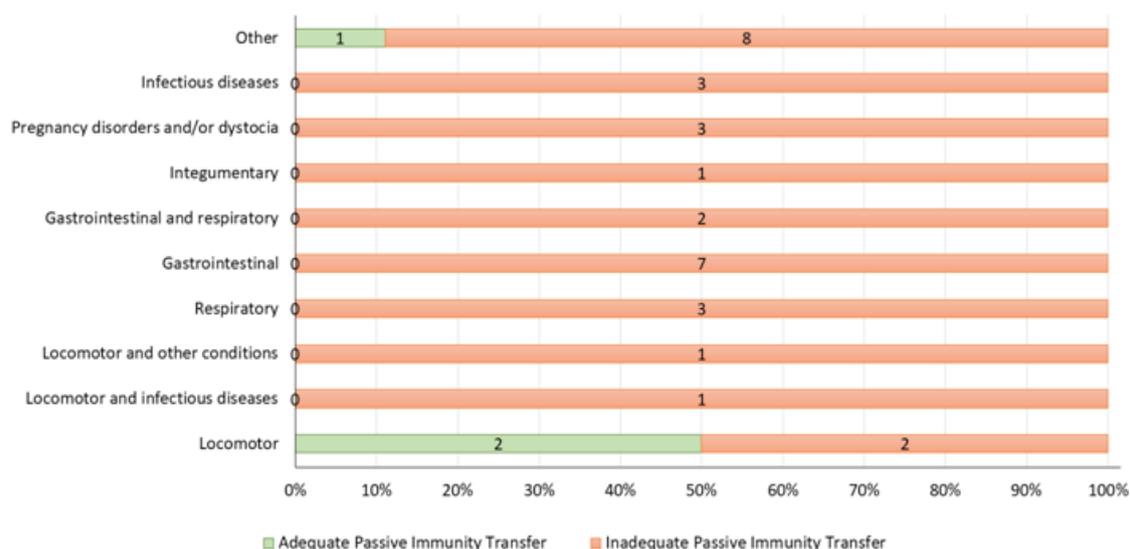


Figure 1. Proportion of disease distribution between adequate and inadequate passive immunity transfer considering the main systems affected in foals (0–90 days) of different breeds, admitted to the Hospital Veterinário de Grandes Animais, Universidade Federal de Lavras, 2014 – 2018.

All diseases observed among the animal admitted in HVGA interfere in the foals' survival and development rates, which may explain the fact that mortality in animals with proven transfer failure in HVGA was higher compared with others with adequate immunity. Of the admissions in which inadequate passive immunity transfer was found, 20.59% [7/34] died, whereas of patients with adequate transfer, only 2.94% [1/34] died (Table 1).

Table 1. Distribution of deaths that occurred during the hospitalization of foals from 0 to 90 days of age at the Hospital Veterinário de Grandes Animais, Universidade Federal de Lavras, 2014–2018 according to adequate or inadequate transfer of passive immunity

Death	Adequate passive immune transfer	Inadequate passive immune transfer	Total
Yes	1 (2.94%)	7 (20.59%)	8 (23.53%)
No	2 (5.88%)	24 (70.59%)	26 (76.47%)
Total	3 (8.82%)	31 (91.18%)	34 (100%)

### Risk factors and diseases...

The treatment of failure of passive immunization via colostrum must be done as soon as possible. Colostrum should be given during the first 6 hours of life, as, after this period, the capacity to absorb antibodies is gradually reduced as the intestinal epithelial cells suffer modifications (Dias *et al.*, 2015). If it is not possible to manage the colostrum, animals older than 12 hours of life can receive intravenous equine plasma in ideal volume and quality to establish adequate serum levels of immunoglobulin G (IgG) (Curcio and Nogueira, 2012), which justifies the administration of plasma equine as additional therapy performed in 8.82% [7/34] of the visits at the HVGA included in the study.

In the present study, univariate analyzes were performed to verify the relationship between foal mortality, failure of passive immunity, and the incidence of infectious diseases (Table 2). However, no significant associations were found between these variables. The same occurred with the analysis between the failure of passive immunity transfer and cases of sepsis, meconium retention, and infectious diseases. This can be attributed to the limited sample size, as several other studies demonstrate the significant relationship between the failure of passive immunity transfer and the emergence of infectious diseases and other problems that can lead to death (Felippe, 2013).

Table 2. Results of the univariate analysis of obits in foals from 0 to 90 days of age treated in the Hospital Veterinário de Grandes Animais, Universidade Federal de Lavras, 2014 – 2018

Exposure		Death	Survival	OR	IC 95%	p
Inadequate passive immune transfer	Yes	7	24	NT‡	NT‡	1.00
	No	1	2			
Plasma administration in foals that did not suckle colostrum	Yes	2	5	NT‡	NT‡	0.64
	No	5	19			
Infectious diseases	Yes	4	14	NT‡	NT‡	1.00
	No	4	12			
Weight (kg)	10 – 30	4	1	29.33	1.73 - 505.95	0.01*
	30.1 – 130	3	22			

\* =  $p \leq 0,05$ ; NT‡ = Not tested

### CONCLUSIONS

In conclusion, most of the conditions that affected the foals admitted to the HVGA-UFLA were of infectious origin and, as already proven in the literature. This can be attributed to the failure of passive immunity transfer that occurred with most animals affected by these pathologies. However, it was not possible to establish significant associations between colostrum failure and the onset of infectious diseases, deaths, or other variables tested in this work due to the limited sample size. Despite this, a significant relationship between weight and mortality has been identified and may be associated with transfer failure in passive immunity.

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