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Diseases with neurological manifestations diagnosed in cattle in the hospital routine: a retrospective epidemiological study (2009-2019)

Enfermidades com manifestações neurológicas diagnosticadas em bovinos na rotina hospitalar: estudo epidemiológico retrospectivo (2009-2019)

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Abstract
Neurological disorders in cattle comprise a group of economically relevant diseases with high occurrence and mortality. In this way, the objective was to carry out an epidemiological study of the diseases with neurological manifestations in cattle admitted (alive or dead) to the Garanhuns Bovine Clinic/Federal Rural University of Pernambuco (CBG/UFRPE) from January 2009 to December 2019. Epidemiological information was collected from the clinical records regarding the age group, rearing system, time of year, and area of origin of the animals. The diseases were grouped into categories according to their origin: toxic or toxi-infectious, viral, traumatic/physical, parasitic, metabolic degenerative, bacterial, neoplastic, and others. A total of 6103 cattle were treated during the study period, of which 604 (10.1%) were diagnosed with diseases that had neurological manifestations. Of these, 331 cases were of single occurrence, and 231 cases occurred as outbreaks in the herd. Death was the outcome in almost 80% of the cases (465/596). The frequencies of the different categories were toxic or toxi-infectious (25.2%), viral (21.5%), traumatic/physical (13.6%), parasitic (9.8%), metabolic (9.3%), degenerative (2.3%), bacterial (2.2%), neoplastic (1.2%), and others (1.2%). It was found that almost half of the animals were older than 24 months (229/475), almost 80% were females, more than 60% were submitted to a semi-intensive to intensive rearing system, and the occurrence of disease was higher during the dry period of the year (363/614). The three most frequent neurological diseases in this study were rabies, trauma, and botulism.
Keywords: diseases of viral origin; epidemiological study; hospital routine; neurological diseases; retrospective study

Resumo
Os distúrbios neurológicos em bovinos abrangem um grupo de enfermidades economicamente relevantes de elevada ocorrência e mortalidade. Desta forma, objetivou-se realizar um estudo epidemiológico das enfermidades que cursaram com manifestações neurológicas que deram entrada (vivos ou mortos) na Clínica de Bovinos de Garanhuns/Universidade Federal Rural de Pernambuco no período de janeiro de 2009 a dezembro de 2019. Nos prontuários clínicos, foram coletadas informaçõe epidemiológicas referentes ao sexo; a faixa etária; ao sistema de criação, época do ano e a área de procedência dos animais. As doenças foram agrupadas em categorias de acordo com sua origem: tóxica ou toxi-infecciosa, viral, traumática, parasitária, degenerativa, metabólica, bacteriana, neoplásica e outras. Um total de 6103 bovinos foram atendidos no período estudado, dos quais 604 (10,1 %) foram diagnosticados com enfermidades que cursaram com manifestações neurológicas. Destes, 331 casos foram de ocorrência individual, 231 casos cursaram como surtos no rebanho. Quase 80% dos casos (465/596) teve o óbito como desfecho. As frequências das distintas categoria foram tóxica ou toxi-infecciosa (25,2%), viral (21,5%), traumática/física (13,6%), parasitária (9,8%), metabólica (9,3%, degenerativa (2,3%), bacteriana (2,2%), neoplásica (1,2%), outras (1,2%). Verificou-se que quase metade dos animais apresentavam idade superior a 24 meses (229/475), quase 80% eram fêmeas, mais de 60% eram submetidos a um sistema de criação de semi-intensivo a intensivo e a ocorrência foi maior durante o período seco do ano (363/614). As três enfermidades com manifestações neurológicas de maior ocorrência neste estudo foram a raiva, os traumatismos e o botulismo.
Palavras-chave: doenças de origem viral; enfermidades neurológicas; estudo epidemiológico; estudo retrospectivo; rotina hospitalar

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1. Introduction

Neurological disorders in cattle comprise a group of economically relevant diseases with high occurrence and mortality[1,2]. Two important aspects are involved in bovine neuropathies: the frequency of occurrence and the difficulty of diagnosis, the latter of which is focused on the variability in the clinical presentation of the same disease, as well as the close similarity between some of them[3]. The origin of these diseases can be infectious, toxic, physical, metabolic, congenital, or neoplastic[4].

The study of neurological diseases increased after the epidemiological surveillance program for Bovine Spongiform Encephalitis (BSE) emerged[5]. Active search in the program is based on capturing samples from slaughter establishments, whereas passive search focuses mainly on obtaining samples from the Herbivore Rabies Control Program (PNCRH), which establishes that all tested samples with a negative result for rabies must be sent for the differential histological diagnosis of BSE in official laboratories accredited by the Ministry of Agriculture, Livestock, and Supply (MAPA). Thus, the search for differential diagnoses in negative cases for rabies generates important information about the diseases that affect the nervous system of cattle[2].

A vast number of diseases with neurological manifestations were diagnosed in the first four decades of operation of the Bovine Clinic of Garanhuns/Rural Federal University of Pernambuco (CBG/UFRPE). However, a systematic study of the occurrence of these different diseases has not yet been performed. In this way, the objective of the current work was to carry out an epidemiological study of the diseases with neurological manifestations diagnosed in bovines in a period of 11 years.

2. Material and methods

Initially, screening was carried out in the general registry book of patients diagnosed with diseases that caused neurological symptoms, admitted (alive or dead) to CBG/UFRPE from January 2009 to December 2019. Subsequently, clinical records, necropsy reports, and complementary *post-mortem* examinations were retrieved. In the clinical records, epidemiological information was collected regarding sex (female or male), age group (0 to 12 months, 12 to 24 months, and over 24 months), rearing system (semi-intensive, intensive, or extensive), season of the year (seasonality), and area of origin of the animal (state, municipality, and geographic region).

Drug therapy was instituted when the clinical diagnosis suggested the possibility of treating the disease, with poor to good prognosis. Sick animals were monitored daily and, depending on the clinical evolution/severity of the disease, it could progress to hospital discharge, natural death, or euthanasia (with prior authorization from the owner)[6]. In cases of death, the animals underwent anatomopathological examination[7]. Tissue fragments of the organs were collected, fixed in 10% buffered formalin, and a histopathological examination was performed[8], using hematoxylin-eosin staining (HE).

Suspected cases of rabies were referred to the Pernambuco State Agricultural Defense and Inspection Agency (ADAGRO) for laboratory diagnosis (direct immunofluorescence and biological test in mice)[9]. The histopathological analysis was performed at CBG/UFRPE and at the pathological anatomy section of UFCG, in Patos Campus - PB. The diagnosis of trauma cases was based on clinical and anatomopathological findings and, in some cases, on the response to the established therapeutic protocol. For the diagnosis of botulism, the main criteria adopted were the characteristic clinical and epidemiological findings of botulism (existence of a source of toxins such as carcasses in the pasture or dams, silage, poultry litter, straw, etc.), the absence of macro and microscopic lesions that would justify the clinical signs observed, and the identification of botulinum toxins in biological samples when possible, in addition to the negative result for rabies. The diagnosis of cerebral babesiosis was made by direct examination of blood smears or imprinting of organs at necropsy[4]. With respect to the diagnosis of metabolic diseases, in the case of ketosis, this was established by determining the blood concentration of β-hydroxybutyrate (BHB) or checking for the presence of ketone bodies in the urine, as well as the response to drug treatment. In cases of intoxication by plants or chemical products, information from the visualization of plant grazing and evidence that they had been ingested, or the use of the chemical product in question were considered, in addition to clinical, laboratory, and anatomopathological findings.

The clinical diagnosis of hypocalcemia was based on anamnesis, clinical findings, determination of ionizable calcium in the blood (Device: Roche - 9180), and the response to drug treatment. The diagnosis of malignant catarrhal fever was based on epidemiology as well as clinical and anatomopathological findings. The diagnosis of tetanus was established by anamnesis, clinical examination, and the absence of necroscopic findings. Cases of polioencephalomalacia (PEM), caused by thiamine deficiency, were diagnosed based on clinical findings and therapeutic diagnosis; in animals that died, it was obtained through histopathological examination. Trypanosomiasis was diagnosed by direct examination of *T. vivax* in blood smears, associated with clinical and epidemiological findings. Confirmation of the diagnosis of meningoencephalitis due to BoHV-5 or BoHV-1 was based on histopathology and polymerase chain reaction

(PCR)[10].

The information obtained from the clinical records was entered into a database created using the Microsoft Excel 2010® computer program and divided into epidemiological, clinical, laboratory, and anatomo-histopathological data, direct immunofluorescence (DIF), inoculation in mice, and PCR for herpes virus.

For the study of seasonality, the dry period was considered the months from September to March, with average monthly precipitation below 75 mm (min. 10.3 mm - Nov./max. 70.4 mm - Mar.) and the rainy period the months of April to August with average monthly precipitation greater than 75 mm (min. 78.1 mm - Apr./max. 157.2 mm - Jun.). This criterion was defined according to the evaluation of precipitation in the region, over the course of 20 years studied, using the database of the National Institute of Meteorology (INMET), experimental station 82893 Garanhuns-PE[11].

The diseases were grouped, according to Galiza et al.[12] and Terra et al.[13], into categories based on their origin: toxic or toxi-infectious, viral, traumatic, parasitic, metabolic, degenerative, bacterial, neoplastic, and others. The inconclusive cases formed a single group and consisted of diseases with neurological manifestations, for which it was not possible to establish the etiology.

For data analysis, a descriptive statistical model was used, observing the distribution of data through the relative and absolute frequencies of diseases, as well as the epidemiological characteristics[14].

3. Results

A total of 6103 cattle were treated during the studied period, of which 604 (10%) were diagnosed with diseases that had neurological manifestations. Of these, 331 cases were of individual occurrence, 231 cases occurred as outbreaks in the herd, and for 42 this information was not available. Approximately 80% of the cases (465/596) progressed to death. Table 1 shows the frequencies of occurrence (relative and absolute) of the different diseases, distributed by category.

In the case of total diseases with neurological manifestations, it was found that almost half of the animals were older than 24 months (229/475), almost 80% were female, more than 60% underwent a semi-intensive to intensive rearing system, and the occurrence was higher during the dry period of the year (363/604). It should be noted that the lethality was 80.2% (478/596). Table 2 describes the epidemiological information (age, sex, and rearing system) observed in the different diseases.

The animals originated from 64 municipalities in the state of Pernambuco that made up the mesoregions of the state, as well as the states of Alagoas, Sergipe, and Maranhão (Fig. 1).

4. Discussion

In the current study, the frequency of 10% obtained for diseases that were diagnosed with neurological manifestations in cattle demonstrates that these are important causes of mortality in these animals in the region, being responsible for significant economic losses in the state of Pernambuco. Similar results were found in studies carried out in Rio Grande do Sul, where neurological diseases accounted for 10% of the diseases diagnosed in cattle[1,15]. Ribas et al.[2] and Galiza et al.[12] reported higher frequencies of 33.81% and 53.45% in Mato Grosso do Sul and in the semi-arid Northeast, respectively.

Rabies stood out as the most prevalent among the diseases that present clinical neurological manifestations in cattle. This condition was also observed by Borges et al.[16], in a systematic review of the main neurological diseases of cattle in the country, which shows that the other variations in frequencies may be related to regional, state, and local particularities that determine specific differences in the occurrence of certain diseases.

Inconclusive cases totaled 10.1%, which is lower than other studies carried out in cattle, in which the percentages were 26.6%[1], 46.2%[2], and 26.5%[12]. In general, the illnesses of bovines presenting with clinical neurological manifestations affect predominantly females of reproductive age reared in a semi-intensive system. These epidemiological characteristics are mainly because the studied animals come from municipalities that make up the largest dairy center in the state, where there is a predominance of females with aptitude for milk production, in the productive phase, due to the productive characteristics of the region, and where the predominant rearing system is semi-intensive.

4.1 Rabies

Rabies stood out as the most prevalent among the diseases that affect cattle with clinical neurological manifestations, a condition also observed by Borges et al.[16]. The frequency of reported cases of rabies is similar to that reported by Lemos[17] and Ribas et al.[2] in the Center-West and Southeast regions of Brazil, respectively. However, the frequency was lower than that reported in other states such as PB (48.7%), RS (41.0%), and PR (30.6%)[12,18,19]. In addition to local particularities, the lower occurrence found in this study can be justified by the fact that this survey was carried out by analyzing cases seen and clinically followed up including all the diseases of bovines with neurological manifestations that were admitted to the hospital and not through the results of analysis of brain samples sent for evaluation in a diagnostic laboratory, when a previous screening is already part of the referral for diagnoses.

Table 1. Differential diagnosis of neurological diseases with neurological manifestations in cattle (n=604) diagnosed at the Bovine Clinic of Garanhuns/UFRPE between 2009 and 2019.

Origin	Disease	Total	Relative value of neurological diseases	Relative internal value of the source category
Toxic or toxi-infectious		n=152	25.2%	
	Botulism	78	12.9%	51.3%
	Plant poisoning	28	4.6%	18.4%
	Chemical poisoning	27	4.5%	17.8%
	Tetanus	17	2.8%	11.2%
	Mycotoxicosis	2	0.3%	1.3%
Viral		n=130	21.5%	
	Rabies	101	16.7%	77.7%
	Malignant catarrhal fever	19	3.1%	14.6%
	Bovine herpesvirus-1 meningoencephalitis	6	1.0%	4.6%
	Bovine herpesvirus-5 meningoencephalitis	4	0.7%	3.1%
Traumatic		n=82	13.6%	
	Trauma to the spinal cord	43	7.1%	52.4%
	Trauma to peripheral nerves	21	3.5%	25.6%
	Encephalic trauma	18	3.0%	22.0%
Parasitic		n=59	9.8%	
	Cerebral babesiosis	43	7.1%	72.9%
	Trypanosomiasis	14	2.3%	23.7%
	Nervous eimeriosis	1	0.2%	1.7%
	Parasitic otitis	1	0.2%	1.7%
Metabolic		n=56	9.3%	
	Clinical ketosis	36	6.0%	64.3%
	Hypocalcemia	20	3.3%	35.7%
Degenerative	Polioencephalomalacia	14	2.3%	100%
Bacterial		n=13	2.2%	
	Brain and spinal cord abscesses	9	1.5%	69.2%
	Tuberculosis	3	0.5%	23.1%
	Bacterial meningitis	1	0.2%	7.7%
Neoplastic		n=7	1.2%	
	Bovine Enzootic Leukosis	6	1.0%	85.7%
	Medulloblastoma	1	0.2%	14.3%
Others		n=30	1.2%	
	Metabolic acidosis	1	0.2%	3.3%
	Pituitary cyst	1	0.2%	3.3%
	Spinal cord compression by post-vaccination granuloma	3	0.5%	10.0%
	Electrocution	1	0.2%	3.3%
	Non-suppurative encephalitis	9	1.5%	30.0%
	Hepatic encephalopathy	4	0.7%	13.3%
	Enterotoxemia	2	0.3%	6.7%
	Nonspecific liver disease	2	0.3%	6.7%
	Non-suppurative leptomeningitis	1	0.2%	3.3%
	Non-suppurative meningoencephalitis	2	0.3%	6.7%
	Suppurative meningoencephalitis	2	0.3%	6.7%
	Posterior paramyoclonus	1	0.2%	3.3%
	Vestibular syndrome	1	0.2%	3.3%
Inconclusive	Inconclusive	n= 61	10.1%	100%
Total		604	100.0%	

Table 2. Distribution by sex, age group, and rearing regime of the different diseases that occurred with neurological manifestations in bovines (n=604) admitted to CBG/UFRPE from January 2009 to December 2019.

Disease	n	Sex		Age group			Rearing regime		
		Female	Male	≤ 12 months	> 12 to ≤ 24 months	> 24 months	Semi-Intensive	Intensive	Extensivo
Rabies	101	81 (80.2%)	20 (19.8%)	37(42.0%)	26 (29.5%)	25 (28.4%)	32 (33.0%)	16 (16.5%)	49 (50.5%)
Trauma (spinal, peripheral, encephalic)	82	67 (81.7%)	15 (18.3%)	29(40.3%)	7 (9.7%)	36 (50%)	40 (51.9%)	14 (18.2%)	23 (29.9%)
Botulism	78	63 (81.8%)	14 (18.2%)	4 (7.1%)	8 (14.3%)	44 (78.6%)	33 (55.0%)	8 (13.3%)	19 (31.7%)
Cerebral babiosis	43	31 (73.8%)	11 (26.2%)	12(32.4%)	5 (13.5%)	20 (54.1%)	25 (64.1%)	6 (15.4%)	8 (20.5%)
Clinical ketosis	36	36 (100.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	24 (96.0%)	19 (52.8%)	11 (30.6%)	6 (16.7%)
Plant poisoning	28	22 (78.6%)	6 (21.4%)	5 (25.0%)	7 (35.0%)	8 (40.0%)	11 (44.0%)	2 (8.0%)	12 (48.0%)
Chemical poisoning	27	16 (59.3%)	11 (40.7%)	15(78.9%)	0 (0.0%)	4 (21.1%)	16 (59.3%)	3 (11.1%)	8 (29.6%)
Hypocalcemia	20	20 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13(100.0%)	9 (47.4%)	1 (5.3%)	9 (47.4%)
Malignant catarrhal fever	19	15 (78.9%)	4 (21.1%)	5 (29.4%)	3 (17.6%)	9 (52.9%)	10 (55.6%)	5 (27.8%)	3 (16.7%)
Tetanus	17	14 (82.4%)	3 (17.6%)	2 (22.2%)	2 (22.2%)	5 (55.6%)	11 (64.7%)	4 (23.5%)	2 (11.8%)
Polioencefalomalacia	14	7 (50.0%)	7 (50.0%)	6 (54.5%)	3 (27.3%)	2 (18.2%)	5 (35.7%)	3 (21.4%)	6 (42.9%)
Trypanosomiasis	14	13 (100.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	6 (85.7%)	6 (50.0%)	6 (50.0%)	0 (0.0%)
Herpetic meningoencephalitis	10	4 (40.0%)	6 (60.0%)	4 (50.0%)	3 (37.5%)	1 (12.5%)	3 (30.0%)	0 (0.0%)	7 (70.0%)
Inconclusive	61	41 (67.2%)	20 (32.8%)	22(44.9%)	10 (20.4%)	17 (34.7%)	21 (37.5%)	7 (12.5%)	28 (50.0%)
Disease with frequency of < 10 cases	54	40 (74.1%)	14 (25.9%)	19(43.2%)	10 (22.7%)	15 (34.1%)	27 (50.9%)	6 (11.3%)	20 (37.7%)
Total	604	470 (78.2%)	131 (21.8%)	161 (33.9%)	85 (17.9%)	229 (48.2%)	268 (47.9%)	92 (16.4%)	200 (35.7%)

* Forty-four records did not contain information about the rearing regimen; sixty-nine did not contain information about age; and three about sex.

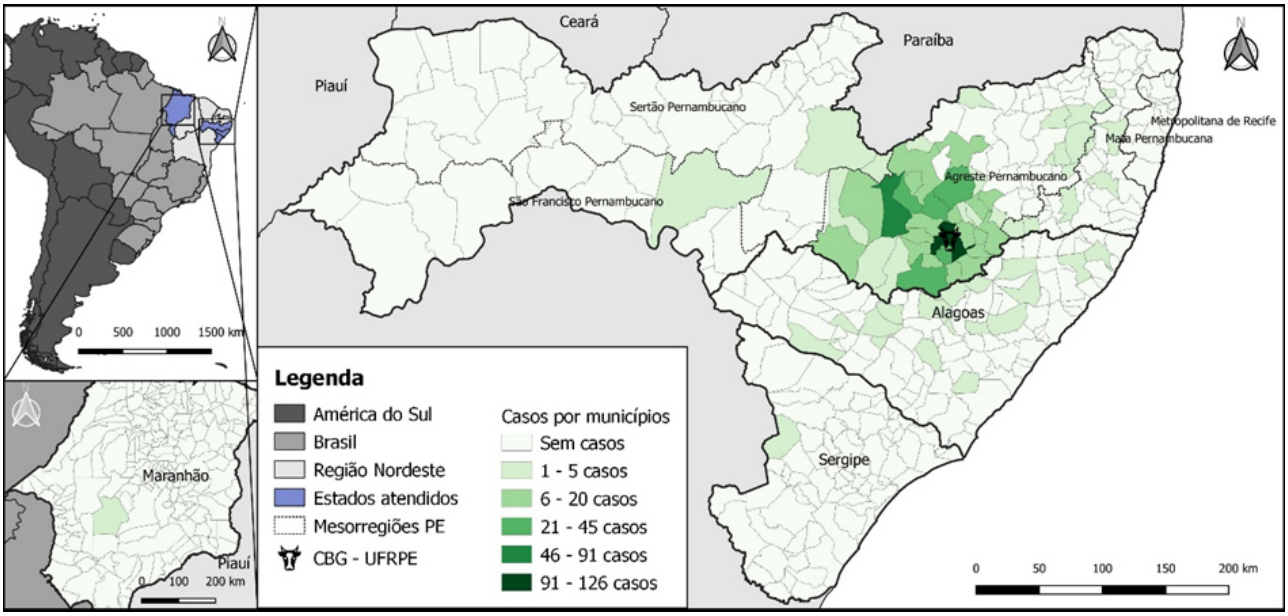

Figure 1. Spatial distribution of the municipalities of origin of clinical cases of neurological diseases diagnosed in cattle (n=604) treated at the Bovine Clinic of Garanhuns, Federal Rural University of Pernambuco, from January 2009 to December 2019.

The high frequency of rabies cases in this study draws attention because the disease is one of the most important zoonoses in Public Health, not only because of its drastic and lethal evolution, but also because of its high social and economic cost to the state. Studies based on surveys carried out in different regions of the country demonstrate the importance of rabies as a cause of mortality in cattle and that despite the presence of cases of the disease throughout the country, there are regional variations in the proportion of cases of positive cattle[20].

The data obtained in the present study reinforce that vaccination needs to be expanded in the region, since less than 50% of the properties had a history of vaccination, and there were reports of bat attacks on

animals present in about 16% of the cases. These facts underpin the observations made by Ribas et al.[2], who characterized the presence of hematophagous bats on the property as the main risk factor for rabies in herbivores, associated with non-vaccination of cattle.

The highest numbers of outbreaks occurred in the years 2010/2011, which declined in the following years and rose again in the years 2018/2019. A similar cyclicity every five or seven years was found in the states of Pernambuco[12], São Paulo[21], and Mato Grosso do Sul[2]. According to Barros et al.[4], this is because there is an apparently cyclical characteristic of outbreaks of rabies in herbivores in South America, with a periodicity of 3-7 years. In this situation, peaks in the number of cases are associated with the greater number of infected bats, which then die, leading to a period of decline, and as the growth of the colonies is slow, this period is then necessary for their reinfection. A greater apparent cyclicity every 18 years has been suggested in Paraná[19]. The paralytic form characterized by ascending paresis was the most frequent in this study, with 95.05% (96/101), corroborating the literature[22, 23].

Despite the continuous occurrence of cases throughout the year, there was a higher frequency in the local dry period (September to March). It is believed that the greater number of cases that occurred during this period may be related to the negligence of the breeders with regard to sanitary measures, prioritizing the food issue, coupled with the fact that the animals are more grouped together to receive supplementation, and the climatic conditions are favorable to the movement of bats. Corroborating these results, Teixeira et al.[24] report a predominance of this disease in the regional dry season in the state of Goiás. In Paraíba, according to Lima et al.[25], the highest frequency of rabies cases coincides with the second half of the rainy season and the first months of the dry season. In Mato Grosso do Sul Ribas et al.[2] attributed the highest occurrence in the rainy season to the greater susceptibility of calves, due to the decline in colostral immunity antibodies since the calving season is concentrated in the months from August to November, although, in another retrospective study of 36 years in Paraná, there was no seasonal pattern[19].

Although the occurrence in animals of all ages has been recorded, a greater number of cases of rabies was observed in cattle younger than two years (71.60%). This same situation was observed in other areas of the Northeast region[25], in Rio Grande do Sul[17,22], Mato Grosso do Sul[2], and Goiás[13]. As cited by Ribas et al.[2], this fact may be related to the lower immunity of young animals, due to failure to carry out the booster dose after the first immunization dose, or to a delay in the age of primary vaccination, which must be carried out between the first three to four months of age since anti-rabies vaccination is performed annually and with advancing age there is a greater frequency of immunization of animals[5]. In this study, the occurrence of nine cases in calves aged four months or less is highlighted. This fact may be related to the inadequate transfer of passive immunity through colostrum, due to an inadequate vaccination schedule of the mothers.

The average duration of illness was four days, ranging from one to 16 days, and this epidemiological information is consistent with reports by other authors[12,23,25,26]. In this survey, 97% of the positive cases in direct immunofluorescence (DIF) were also positive in the histopathological examination, when this was performed. Meanwhile, in a study identifying the distribution of lesions in the nervous system in cases of rabies in cattle in the northeast region, Lima et al.[25] reported the presence of intracytoplasmic inclusion bodies in 87%. The frequency found in the current study suggests that the period of evolution after the infection was sufficient for the development of the Negri bodies, because, according to Langohr et al.[22], these are found in only 30% of cases and the non-visualization of them in some cases of rabies can be directly associated with the animal's survival time after infection.

4.2 Traumas

Together, spinal, peripheral, and encephalic traumas corresponded to the second highest occurrence among diseases that present with neurological manifestations. The percentage of occurrence was higher than that reported in the semi-arid northeast region (4.5% -5/111) by Galicia et al.[12]; in the southern region of the country by Lemos et al.[17], Sanches et al.[1], and Queiroz et al.[26]; and in Goiás by Terra et al.[13]. This high occurrence is justified by the greater involvement of animals kept in predominantly semi-intensive and intensive rearing systems, which leads to greater animal handling, as well as the adoption of few conscious management measures, in opposition to studies that have highlighted the positive impact of adopting good management practices on the welfare and performance of beef and dairy cattle, taking into account that the welfare of cattle also adds ethical value to milk and meat[27].

The predominance of traumas in females of reproductive age is probably because these animals are subjected to handling in which they are more manipulated than males, especially in the dry period, a time that requires greater intensification in food management in semi-intensive or intensive rearing systems, which prevail in the studied region. In addition, due to the productive characteristics of the region, there is a greater predominance of females on the properties.

The higher prevalence of spinal cord trauma corroborates the statement made by Thomas[28] that acute spinal cord injuries in cattle are commonly associated with fracture or dislocation of the spine during handling.

Among the peripheral neuropathies, radial nerve injury stands out, which is related to the superficial projection of the nerve on the lateral face of the elbow joint, leaving it vulnerable to compressive injuries, mainly due to prolonged lateral decubitus or inadequate limb protection. This survey corroborates the study by Poulton et al.[29], who evaluated the influence of secondary injuries of recumbency, regardless of the primary cause, on the recovery of 218 dairy cows, and found that secondary injuries were responsible for the lack of recovery in 72% of cows after prostration.

According to Zachary[30], peripheral nerve injuries are relatively common in animals and may result from stretching, lacerations, contusions, and compressions, as well as from compressive injuries resulting from decubitus for more than six hours. It should be noted that our survey found a recovery of 50% for these cases, while Moreira et al.[31] attained values of 100%.

Obturator nerve injury was also observed among peripheral traumas. This condition usually occurs at the time of calving, where the calf with distortion, fetal pelvic disproportion, and excessive or prolonged traction during restraint can cause compression of this nerve that runs along the inner part of the pelvis[32,33].

Traumas occurred mainly in isolation, and the vast majority of cases resulted in euthanasia or the indication for slaughter. Compression of peripheral nerves are important secondary causes of decubitus in ruminants, and often render maintaining the animal unfeasible. Therefore, although they frequently occur as isolated cases, this category of diseases entails enormous financial losses due to the low survival rate of the affected animals[31].

Encephalic trauma was the least frequent in this survey, in contrast to a study carried out in the state of Paraná, which found that out of nine traumas in cattle, five were cranioencephalic[26]. In most cases reported in this study, there was a history of falls or fights between the animals, in agreement with the literature, which reports external trauma, stretching, or violent flexion of the head or neck as the main causes[34].

4.3 Botulism

Botulism was the disease of toxic origin with the highest occurrence, representing 51.3% of the diseases in this category, a frequency higher than the 16.7% reported by Borges et al.[16] in a study which gathered the occurrence of the main neurological diseases of bovines described in several states. Other retrospective studies of neurological diseases in cattle also described significant occurrences of botulism in the country[2,12,13]. Characteristics linked to sanitary management, observed in the clinical records of the animals, such as lack of vaccination, predilection for the use of polyvalent vaccines in relation to those specific for botulism, lack of adequate practices for the destruction of carcasses on the properties, and easy access and acquisition of poultry litter, are among the factors that may be related to the high frequency of botulism observed in this study. In addition to these factors peculiar to food management, the contamination of water reservoirs, such as dams or drinking troughs, with the carcasses of rodents, small birds, wild animals, or even cattle, as well as sugarcane bagasse and silage contaminated with animal carcasses can also be considered as possible sources of poisoning for cattle in the field or stabled since botulism outbreaks are linked to the ingestion of toxins pre-formed in cadavers[35, 36].

The absence or inadequate mineral supplementation of the animals found in almost half of the cases is another factor that must be taken into account for the occurrence of botulism, considering that the phosphorus levels in the soil of the region are considered insufficient, at only 2 mg/dm^3[37]. According to Mehlich[38], levels below 11 mg/dm^3 are inadequate to meet animal demand. It is also noteworthy that even though vaccine protection is the most relevant prophylactic measure against botulism, vaccinated animals can develop the disease when exposed to large amounts of toxin[39].

Difficulties in detecting botulinum toxins are mentioned in the literature and are related to several factors. According to Lobato et al.[40], despite the high sensitivity and specificity of the serum neutralization test in mice, it is not always possible to detect the presence of toxins in the analyzed material due to the low concentrations present in the substrate and the speed with which the material needs to be collected *post-mortem* or after euthanasia of the animals in a pre-agonic state. This can generate false-negative results, as evidenced in the 27 samples tested in this study, among which only two tested positive.

In the current study, the evolution of the disease occurred predominantly in the subacute form, with an average of 3.4 days, a period compatible with that reported by some authors[35,37] and greater than the average duration of six to twelve hours reported by Costa et al.[41] and the 24 to 48-h average reported by Lobato et al.[39]. The onset, severity of clinical signs, incubation period, and course of the disease are directly related to the amount of toxin ingested[4].

Lethality was 100%, as mentioned in the literature[35,41]. Of the 27 samples of the ruminal and intestinal contents of necropsied cattle that were performed in the bioassay test in mice, only two results were positive one with toxin “C” and the other with toxin “D”. This finding can be justified by the fact that cattle are extremely sensitive to small amounts of botulinum toxin, making laboratory diagnosis extremely difficult[42].

In this study, the presence of subepicardial and

subendocardial hemorrhages (15/78) was nonspecifically observed, as cited by Barros et al.[4], Veloso Neto et al.[37], and Constable et al.[32]. The presence of mucohemorrhagic enteritis and petechiae was also evidenced in 24/78 of the necropsied animals, as also observed by Veloso Neto et al.[37]. Less frequently, hepatomegaly, splenomegaly, dark kidneys, and lumpy bile were observed.

4.4 Cerebral Babesiosis

Cerebral babesiosis, caused by *Babesia bovis*, was the main disease of parasitic origin causing neurological manifestations in cattle. The state of Pernambuco exhibits favorable conditions for the development of the babesiosis vector, the *Rhipicephalus* (*Boophilus*) *microplus* tick; however, in regions with intense periods of drought, such as the 'sertão' of the state, the evolutionary cycle of the tick can be interrupted[43]. The frequency of this disease was slightly higher than the average prevalence (3.5%) found by Borges et al.[16] in a survey of pooled Brazilian studies. Nonetheless, several prevalence studies report great variation in the frequency with which this disease occurs in different regions of the country[2,12,13,15,44].

The higher occurrence of cerebral babesiosis in adult cattle, observed in this study, can be justified by the habit of moving animals from the sertão to the 'agreste' biomes of the state, considering that the prolonged periods of drought characteristic of the northeastern sertão make it an area of enzootic instability, while the agreste is considered an area of stability, which is endemic for the disease[45]. Added to this fact, the indiscriminate use of drugs based on pyrethroids and their associations, combined with the lack of information regarding strategic control programs on the part of producers in relation to control measures in populations of *Rhipicephalus* (*Boophilus*) *microplus* in the dairy region of Garanhuns, have induced the emergence of populations of resistant ticks[46].

In the current work, outbreaks of cerebral babesiosis occurred mainly at the end of the rainy season and beginning of the dry season, probably explained by the instability in the driest areas, where *Rhipicephalus* (*Boophilus*) *microplus* does not survive during the dry season[47]. Cases that occur at the beginning of the rainy season can be supported by the introduction of animals from areas of instability, which are more prone to infection. In areas of enzootic instability, cerebral babesiosis is described as the most frequent disease in the summer and fall months[44].

Although the presence of the tick is constant in the Zona da Mata and agreste region of Pernambuco, favored by the conditions of humidity and milder temperatures, the lethality rate of babesiosis (86%) was higher than the 33.4% reported by Câmara et al.[48]. The high lethality can be justified by the inefficiency in maintaining immunity in the animals due to the inconstancy of the *R. microplus* population, reinfesting the animals with advancing age, and the transfer of animals from areas of instability or tick-free areas to others where the epidemiological situation is stable[47,49].

Of the 43 cases of babesiosis, four were diagnosed in newborn calves aged between one and 12 days and all died, constituting cases of transplacental transmission since, according to Bracarense et al.[50], the incubation period for *Babesia bovis* is approximately 12 days. Although reports exist, outbreaks of cerebral babesiosis due to *B. bovis* in newborn calves are uncommon[51,52].

Other cases are supported by the observation that in conditions of high tick infestation, even in the period of protection by maternal antibodies, high morbidity and mortality may occur[53].

4.5 Clinical Ketosis

Clinical ketosis was the most relevant disease among those of metabolic origin, representing 6.0% of the total surveyed disorders, similar to the prevalence found by Audor and Spinosa[54]. Clinical cases reached 7% in studies carried out by González and Silva[55], and even higher rates were found in Paraná, by Massuqueto et al.[56], who identified occurrences of 11.11% in high-producing cows.

In the current study, 83% of cases occurred during the first and second postpartum months, a percentage close to the 90% found in the same period by Rutherford et al.[57]. This is also in agreement with Duffield[58] and Schein[59], who claim that the highest risk of the disease varies from the first two to the ninth postpartum weeks. This high occurrence is due to the natural metabolic response to increased energy demand in early lactation[54,60].

Most cases occurred in second- and third-lactation animals, disagreeing with the reports of Audor and Spinosa[54], who mentioned that the disease was more prevalent in cows in their third or further lactations. Two cases were also found in animals with more than five lactations, similar to what was reported by Barbosa et al.[60].

Regarding the rearing system, the highest frequency of occurrence was in intensive and semi-intensive rearing systems, as mentioned by Constable et al.[32] and Schein[59]. However, Barbosa et al.[60] and Schneider et al.[61] reported that ketosis was more prevalent in animals raised in a pasture system.

The highest number of cases occurred in the dry period of the region, probably suggesting that the animals experienced a greater energy deficit in this period due to a greater scarcity of food. There was a favorable outcome in 86% of cases in our study, confirming that mortality is low[32].

4.6 Plant and Chemical Intoxication

Poisoning by plants and chemicals had a similar frequency of cases and occurred mainly in the form of outbreaks. Intoxications by *Cestrum laevigatum* and *Prosopis juliflora* were the most prevalent among plant poisoning cases, while poisoning by abamectin and urea were the most prevalent among poisoning by chemical products. Although *P. juliflora* is a plant with wide distribution in the northeast region, there are few reports of natural intoxication by this plant[62]. The scarcity of forage combined with the characteristic of *C. laevigatum* of remaining green and flowering in the dry season, standing out among the other forage options, is a factor considered for the occurrence of natural intoxication by this plant, given that it is not a palatable plant. Another important factor linked to the ingestion of this plant is the lack of knowledge when transporting animals from areas where it does not occur to places where it is present[63].

Intoxication by *P. juliflora* is often related to the ingestion of pods in large quantities for prolonged periods[48]. The prognosis of poisoning by *P. juliflora* is considered poor; in the present study, for instance, it progressed to death in 100% of affected animals. Clinical and pathological findings are compatible with dysfunction of the cranial nerves (trigeminal, hypoglossal, vagus, and glossopharyngeal), which culminates in nutritional deficiency due to difficulty in prehending, chewing, and swallowing food[48,64].

Urea poisoning mainly affected adult females in semi-intensive rearing regimens. These factors are related to the productive characteristics of the region and the frequent use of urea as a source of nitrogen in the cattle diet. This study corroborates Barros et al.[4], who stated that cases of urea poisoning occurred mainly in the rainy season and the affected animals were adequately adapted to urea, but had access to higher doses of this substance.

Abamectin poisoning cases occurred both in extensive and semi-intensive rearing, affecting mainly young animals aged less than 12 months. Poisoning by this substance is often related to inadequate use in young calves and the administration of overdoses when these are estimated or standardized to facilitate the handling of animals in batches[65].

4.7 Hypocalcemia

Within the category of metabolic origin, hypocalcemia had a lower occurrence than clinical ketosis, reaching an occurrence of 3.3% (20/604) among the diseases studied, also being lower than the 10% found in Minas Gerais by Schafhäuser Junior and Casarin[66]. However, it is close to the frequency observed in herds of Holstein and Girolando cows in Rio Grande do Sul (1.9%)[67], as well as the incidences of puerperal hypocalcemia in dairy cows in the US (3.45%), Europe (6.17%), and Australia (3.5%) described in retrospective studies conducted between 1977 and 2009[68].

In the current study, the disease occurred mostly in cows in the third or fourth lactations, corroborating Lean et al.[69]. According to Oetzel[70], older cows are more susceptible to the disease as a consequence of the decrease in the number of parathyroid hormone receptors in osteoblasts, with a consequent decrease in calcium reserve, bone remodeling capacity, and intestinal absorption. Thus, the mean concentration of calcium in the blood decreases more significantly in cows with two or more lactations, with lower values being observed around 12-24 h after parturition. The disease manifested predominantly between 24 and 48 h, as reported by Floss et al.[71]. A positive response to treatment occurred in 75% of the cases, close to the 85% observed in the field[32].

4.8 Malignant Catarrhal Fever

Malignant catarrhal fever (MCF) was the second most frequent among viral diseases. Its frequency (3.1%) was similar to those reported by Sanches et al.[1] and Macêdo et al.[72] in the south of the country and in the state of Paraíba, respectively.

Terra et al.[13] and Del Fava et al.[73] found lower frequencies in the states of Goiás and São Paulo, respectively. In the current study, approximately 53% of the positive animals were raised simultaneously with sheep. According to Macêdo et al.[72], the greater occurrences of the disease in the Northeast and South regions can be explained by the greater number of sheep farms in these two regions and by the difficulty in avoiding contact between bovine and ovine species. Ovine herpesvirus type 2 (OvHV-2) is thought to be responsible for sheep-associated MCF. In this case, domestic sheep (*Ovis aries*) are natural hosts, manifesting subclinical infection and being capable of transmitting the virus to susceptible species[74,75]. It was also observed that 78.9% of cases diagnosed as malignant catarrhal fever occurred in female animals, 52.9% aged over 24 months, and 83.4% were kept in intensive and semi-intensive regimes, which is justified by the fact that the study was conducted in a dairy region. The lethality of 100% is similar to that cited by Mendonça et al.[76].

4.9 Tetanus

The frequency of tetanus cases (2.8%) was close to those described by Galiza et al.[12] and Barros[15]. However, a lower frequency was described by Ribas et al.[2]. The higher occurrence of tetanus in animals over 24 months of age differs from that reported by Leite Filho[77], who found no predilection in relation to age, and by Galicia et al.[12], who diagnosed the disease in animals aged 30 days or less.

As for the rearing regime, the vast majority of animals were raised intensively or semi-intensively,

differing from the 24 outbreaks in beef cattle raised under an extensive regime described in the south of Rio Grande do Sul by Quevedo et al.[78]. Furthermore, in the current study, most cases occurred individually, and although the disease usually occurs sporadically in ruminants, outbreaks have occurred after neglected animal husbandry practices, as described by Quevedo et al.[78] and Barbosa et al.[79]. The lethality observed here was 100%, agreeing with Raymundo[80], but it should be noted that isolated cases of recovery in ruminants have been cited[79].

4.10 Polioencephalomalacia

Polioencephalomalacia represented 2.3% of the illnesses, less than the 4.4% reported in Mato Grosso do Sul[81], 4.78% of cases of bovine diseases diagnosed at the Laboratory of Pathological Anatomy at UFMS[82], 8.05% in Mato Grosso do Sul[2], and 17.06% in Goiás[13]. However, this occurrence was greater than the 0.1% of diagnoses made in cattle in Rio Grande do Sul[1] and 1.8% in the northeastern semi-arid region[12].

No differences in the occurrence of polioencephalomalacia between sexes were found in this study, and 57.1% of the positive cases were reared in an intensive or semi-intensive system. Considering age, 81.8% of the animals belonged to the age group of less than 24 months, similar to the cases reported in the semi-arid northeast region[12]. As cited by Assis et al.[83], several nutritional etiologies are implicated in the appearance of the disease. In the current study, it was observed that the animals' diet was varied, but in more than 50% of the cases corn silage and mash feed were provided, which may be related to disturbances in the ruminal and intestinal ecosystem in intensive rearing regimens with an abundant supply of carbohydrates[84], a fact reinforced by the greater occurrence precisely in the period of greatest food scarcity in the region.

In 64% of the cases, polioencephalomalacia occurred in the form of isolated cases, as mentioned in the literature[82,85]. According to Gonçalves et al.[86], the course of this disease can be chronic for up to 22 days, a period compatible with what was found in the current study. In this survey, lethality was 21.4%, which is lower than the rate of 48.5-100% described by Nakazato et al.[82] and 50-100% by Ribas et al.[2]. This fact can be explained by the early diagnosis and treatment.

4.11 Trypanosomiasis

In the current study, the occurrence of trypanosomiasis was predominantly in cows reared in a semi-intensive or intensive system, as mentioned by Frange[87], also associated with the fact that the study region is located in a dairy basin. Considering age, the vast majority of animals belonged to the age group above 24 months, a fact attributed to older animals being subjected to longer exposure to vectors, and agreeing with Angwech et al.[88]. In addition, it is known that in calves, passive immunity (maternal) contributes to the maintenance of low parasitemia[88]. However, the national literature reports cases of trypanosomiasis in animals of different ages, such as calves in Maranhão[89], cows in Paraíba[90], and both age groups in Pernambuco[91] and Goiás[92].

In the current study, the disease progressed to mortality in 64% of the cases, while in Paraíba, Batista et al.[90] described two outbreaks of trypanosomiasis caused by *T. vivax* in cattle, with 28.6% of the diseased animals dying in the first and 70% of those affected dying in the second outbreak. Vieira et al.[93] reported a percentage of 20% of deaths in those affected by an outbreak in Sergipe. The elevated mortality rate documented in this study can be ascribed to a prevailing trend in Brazil, where cattle herds lacking prior exposure to *T. vivax* tend to experience heightened mortality rates[94]. These herds do not possess resistance to the parasite and, consequently, face challenges in mounting effective responses to the parasite when it infiltrates the central nervous system[90].

The highest occurrence of trypanosomiasis was in the dry period of the year, when there are fewer flies. Allied to this fact, the reports of the producers about the sharing of needles for the application of oxytocin during milking suggest that this was an important factor in the spread of the disease in the studied cases. As in this study, Bastos et al.[95] placed greater emphasis on iatrogenic transmission. The acquisition of adult animals from endemic regions justifies the higher occurrence of this disease in this category. This condition may have contributed both to the entry of the parasite into local properties and to the dissemination of the parasite between animals of the same herd, as already widely mentioned in the literature[91,92,96]. However, in Paraiba, outbreaks of the disease in cattle coincided with an increase in the number of vectors[90,94]. In an outbreak reported by Pimentel et al.[91], the high density of hematophagous flies in the coastal region of the state of Pernambuco during the rainy season may have facilitated the spread of the parasite in that region.

4.12 Herpetic meningoencephalitis

In the current study, among diseases of viral etiology, herpetic meningoencephalitis had a frequency of 7.7%. This value was lower than those of rabies and malignant catarrhal fever, as reported in other regions in the semi-arid northeast region[12], and disagrees with several retrospective studies of diseases affecting the central nervous system that have been carried out in different regions of Brazil in recent years, according to which the highest occurrences were predominantly attributed to rabies, followed by meningoencephalitis due to herpesvirus[1,2,16,17]. Differences in incidence can be explained by the type of management frequently used in

the northeast region, which promotes greater contact between sheep and cattle[72].

The literature reports occurrence predominantly in young cattle under two years of age[18,97]. In the current work, although there was a predominance of cases in animals aged less than 12 months, cases were also observed in cattle aged between seven and 10 years, as well as no seasonal variation, with this disease occurring in practically every month of the year, corroborating Blume et al.[97]. In addition, animals of both sexes were affected and the lethality found here was 100%, similar to the data observed by Rissi et al.[98].

Noteworthy low-frequency diseases were leukosis and tuberculosis. Cases of leukosis with neurological symptoms were observed in animals whose manifestations were associated with compressive lesions in the spinal cord in the lumbosacral region. In the cases of tuberculosis, the clinical signs and the anatomo-histopathological lesions were encephalic, highlighting an animal in which tuberculosis and leukosis were diagnosed simultaneously.

5. Conclusions

The three diseases with the most frequent neurological manifestations in the current study were rabies, trauma, and botulism. The increase in the occurrence of rabies cases in recent years and its occurrence in animals younger than four months confirm the importance of anti-rabies vaccination in the region, including younger animals. It is important to sensitize people who deal with animals with regard to management practices appropriate to animal welfare, in view of the high occurrence of injuries caused by human action. When addressing botulism, the significance of adhering to sound food management practices becomes paramount. This entails avoiding poultry waste utilization and the presence of carcasses in grazing areas, alongside the implementation of vaccination measures. It is recommended that the diagnosis of meningoencephalitis due to herpesvirus be included in the differential diagnosis of diseases with neurological manifestations in cattle in the region. The cases of MCF that occurred in the absence of sheep on the properties suggest the need to expand research into wider possibilities of transmission of the etiological agent of this disease.

Conflict of interests

The authors declare no conflict of interest.

Author contributions

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