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Study of Correlations between Pedal Bone Lesions Diagnosed through Radiographic Examine with Body Weight, Thoracic Circumference, Bone Mineral Densitometry, Clinical Chemistry, Osteocalcin, Ruminal PH and White Blood Cells of Nelore Bovine

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Abstract: The purpose of this study was to know the occurrence and type and degree of pathological bone changes in Nelore bovine females phalangies, species *Bos indicus*, without clinical signs diagnosed through radiographic. The 656 radiographs were got of 82 Nelore cows from Center National of Research of Beef Bovine, cnpgc-Embrapa, city Campo Grande-MS, Brazil. These animals were living on extensive system pasture of *Brachiaria decumbens*. The radiographic bone lesions were correlated with body weigth, thoracic circumference, bone mineral density, protein total serum, creatine phosphokinase, gama-glutamiltransferase, albumin, globulin, aspartate aminotransferase, calcium, phosphorus, magnesium, zinc, alkaline phosphatase, osteocalcin, counting of white blood cells and ruminal pH. The claws of fore and hind limbs of cows were radiographed in dorso-palmar, dorso-plantar and latero-medial views, and the bone metacarpus was radiographed in dorso-palmar view to evaluation densitometric. The bone lesions were exostosis, bone reabsorption, osteonecrosis, podotrocleosis, osteocondrosis in the distal phalanx, and periostitis in the proximal and intermedium phalangies. The statistical analyses with SAS did not occur correlation between samples obtained and pedal bone lesions ($p < 0.05$), only occurred correlation with age and pedal exostosis. There were 87.81% of cows with pedal bone exostosis, and 93.91% with bone reabsorption in the distal phalangies. The radiographic examine is an important recourse diagnosis to bovine subclinic laminitis, mainly for bovines that have pigmented claws.

Key words: bovine, laminitis, phalanx, podology, radiology

1. Implications

The podal disease has a great impact on economic and welfare damage on dairy cattle, and on beef cattle too, but the most part of research has been done in dairy cattle and in the species *Bos taurus*. Bovine laminitis is a insidious disease, so, the development is subclinic, and when the laminitis becomes clinic, this fase is grave, and usually others animals of the flock are suffering subclinically without visible lesions on the claw, consequently, the flock production begins in down. This work was done with a breed that have not been received studies in relation to podal lesions, this work shows other reality about "the *Bos indicus* can be as sensible as *Bos Taurus*", owing to high incidence of subclinic lesions found.

2. Introduction

The studies in Europe have informed the podal

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disease like the third disease more important on dairy cattle, after mastitis and reproductive problems [1-3]. 18% of the highest performance beef bulls were eliminated for reasons involving feet and legs during the winter at the Saskatoon Record of Performance Bull Test Station, Canada [4]. The lame cows had reduced fertility rate, during the winter housing period [1]. The three bulls that had affections in limbs, from Semen Frozen Center, did not produce good quality semen for freezing and it resulted in economic loss during a period over one year [5]. Nowadays, farmers have included the bovine footcare in the control production system, or organization chart, for reducing damage production [6]. The bovine laminitis is an insideous diseases, causing a great problem to herd, for welfare and to production, resulting on economic damage.

Laminitis is the damage of the sensitive laminae of the hoof, the subclinical form is the most common [7]. Histological examination shows marked changes in the microvasculature of the dermal laminae resulting in adjacent epidermal laminae resulting in oedema and distension and subsequent necrosis of adjacent epidermal laminae [8-12].

Many reasons may be given for justifying a study of radiology of the bovine foot, the site of most lameness in cattle. The veterinarian must then be in a position to make an accurate diagnosis and prognosis, both of which may be aided by radiography [13].

The bone lesions should be regarded as a secondary response inflammatory, and bone reaction, if any, are presented subclinically, chronic or recurrent superficial open lesions, these would be inactive and superficial; open lesions of the sole running a more ulcerative course are associated with more active changes of the pedal bone [14, 15]. The correlation between chronic subclinic laminitis and bone lesions in male bovines was positive, the prevalance of osteopathy in the distal phalanx of the calves is further evidence that laminitis ocurred [4]. Bone alterations as bone production, increased and decreased density, bone destruction and sequestration, exostosis, displacement of navicular bone, rotation of phalanges and deformity of bone can be diagnosed by radiographic exam [9, 16-18]. The subclinical bone lesions can be definitive and damage the animal performance, it can be found by radiographic examine.

Researchers are looking for know the laminitis physiopathology in several areas involving the bovine laminits, because it is a disease multifactorial and of great complexity, the radiology contribute for studying pedal bone alterations, since the observation related by Rusterholz (1920) [14]. And this work was realized with a breed that have not been received studies in relation to podal lesions, this work shows other reality about "the *Bos indicus* can be as sensible as *Bos Taurus*", because the majority of publications of bovine laminitis has been done in animals of species *Bos taurus*. We hypothesized if some pedal bone lesion could be cause some alterations on biochemicals and mineral values, counting white blood cells, or could be correlated with body weight, or thoracic circumference, and transversal rings of the claw.

3. Objectives

The purpose this work was to investigate the occurrence of phalangeal pathological osseus alterations without clinical signs through radiographic diagnosis and to correlate with body weight, thoracic circumference, transversal rings of the claw, serum concentrations of calcium (Ca), phosphorus (P), magnesium (Mg), zinc (Zn), alkaline phosphatase (ALP), total protein serum (TPS), creatinine phosphokinase (CPK), gama-glutamiltransferase (GGT), albumin (Alb), globulin (Glo), osteocalcin, aspartate aminotransferase (AST), and ruminal pH and bone mineral density (BMD).

4. Materials and Methods

The 82 bovine females of species *Bos indicus*, breed Nelore, were selected for this study, without lameness. The age average was 8.49±3.97 years old. These

animals were from Centro Nacional de Pesquisa de Gado de Corte (National Center of Beef Bovine Research) of EMBRAPA, city Campo Grande, State Mato Grosso do Sul, Brazil, located south latitude 20°28´´ and longitude 5.4°40´. The Nelore cows lived on pasturage, periodicly staied in corral to sanitary and reproductive management. The cows that showed claudication were excluded of this study. These animals were evaluated in the corral, after, each cow was binded in the stock's contention of corral, using ropes and pulley for elevating and standing the limb was realized the evaluation of each foot and cleanness of the sole, following a system for the Recording of Clinical Data as an aid in the diagnosis of Bovine Digital Disease second Greenough [19]; after, proceeded to examine radiographic. This examine consisted of views dorsopalmar, dorsoplantar and 30º oblique lateromedial of distal phalanges of forelimbs and hindlimbs. The portable equipment was the Ray X machine of 95 KVp and 25 mA type jockey, Kodak radiographic film size 18×24 cm (Kodak medical X-ray film general purpose green Carestream Health, Inc USA), in cassette with screens (Kodak), the development of film was manual kind (developer and fixer Kodak, Carestream Health, Rochester, NY, USA), realized on farm, in room adapted for laboratory. Plumbiferum aprons, gloves, glasses were used to protection against radiation (Fig. 1). Each radiograph of each foot was evaluated in the radiology room. The exostosis length was measured with a caliper and each bone reabsorption area was measured in the long axis. The blood sample was got from jugular vein for blood count, put in tube vacutainer of 5 mL with EDTA, and put in two tubes of 10 mL (Shandong Welgao Group Medical Polymer Co.) for biochemical analysis. The thoracic circunference was got with tape measure, and the body weight in corral weighing-machine. The rumenal fluid was got with 5mL seryng and needle 30×8 (21G) for measuring pH with tape (pH box of

Fig. 1 Getting the radiography.

Emerk), after punction. The densitometric radiographic examine was made from right 3th metacarpo bone of each cow, on dorsopalmar view, with radiographic film and chassis size 24×30 cm, and beside 5 cm of metacarpo was used an aluminum scale with 25 degrees, each degree had 1 mm of thickness, the radiographic technique was 70 kVp and 2 mAs with 70 cm focus-film distance. Each radiograph was scanned with Scanner HP Scanjet6C (Hewlett Packard System INC) and stored in computer, using software (ATHENA Sistema de Inteligência Avançada, São José dos Campos-SP Brazil), the digital radiographs were evaluated to obtain the Bone Mineral Density of 3th metacarpus bone, in the distal space below interdigital artery forame and values were converted to milimeter of aluminum (mmAl), theses samples were studied in the Department of Veterinary Radiology of Veterinary Medicine and Animal Science School (FMVZ) UNESP, campus of Botucatu. The biochemical samples were meseared using technics to each variable: Ca-Cresolftalein (catalog .248), P-Phosphomobilato (catalog .242), Mg-Magon Sulfanado (catalog 250), Alb-Bromocresol green (catalog 219), Totals protein-Biureto (catalog 218), theses with colorimetric methods; and with cinetic methods CK-UV method (DGKC and SSCC article n. 490), GGT-Sodium nitrito, AST UV method (IFCC article n 1666), AP-Dietanolamin (DGKC and SSCC article n 1674) made with Analisa Kits (GoldAnalisa

Diagnóstica Ltda, Belo Horizonte, Brazil) done on the Veterinary Pathology Laboratory of FMVZ UNESP Botucatu-SP. The Zn with spectrofotometry method by atomic absorption of wave length 213.9 and sensibility 0.008 μg/mL it made in the CEATOX, UNESP Botucatu-SP. The osteocalcin was dosed by radioimmunoassay (Human Osteocalcin 100kit-catalog 40-2248, Nichols Institute Diagnostics, California, USA), IRMA machine (Kineticount 48, Vitek Systems, Missouri, USA) meseared on Department Veterinary Radiology FMVZ UNESP Botucatu-SP.

5. Statistical Analysis

The Correlation Analysis was used between the samples obtained with phalanx's bone lesions of forelimb and hindlimb by Statiscal Analysis System Program (SAS) of Pearson Correlation Coefficient.

6. Results and Discussion

In this study were got 656 radiographs of 328 feet of total 82 Nelore cows. The lesions observed were bone reabsorption, exostosis, osteocondrosis, osteoarthritis, bone degeneration, bone necrosis, podotrocleosis with formation osseous bridge, periostitis, difuse osteitis pedal, same related for authors [9, 14-18]. The length of exostosis ranged of 2 to 26 mm. For statistical analysis of correlation was counted the presence of lesions, independent on length or size.

The samples values are on Table 1 (X, sd), and Positive Correlation with bone image and samples is on Table 2.

The statistical analysis of Pearson correlation coefficient showed the results with positive correlation ($p < 0.05$), in this study in relation to radiograph image did not occur correlation with variables. There was correlation between exostosis with bone reabsorption in the same variable bone.

The pH rumenal was 7 and 8, these animals were living only on pasture, they did not receive supplement, only mineral mixture.

Table 1 Average and standard deviation of samples from Nelore cows.

Samples	Mean	Sd (±)
Age (years)	8.49	3.97
Body Weight (Kg)	408.42	69.13
Thoracic circunference	178.57	10.89
White cell blood /μL	10.461	5.245
Alk. Phosphatase (UI/L)	171.21	86.55
GGT (UI/L)	9.17	3.7
AST (UI/L)	50.37	17.24
CPK (UI/L)	80.05	85.98
Total Protein Serum(g/dL)	6.49	0.73
Alb (g/dL)	2.71	0.34
Ca (mg/dL)	8.18	1.00
P (mg/dL)	4.87	1.04
Zn (μg/dL)	0.35802	0.22518
Mg (mg/dL)	2.64	0.35
Osteocalcin (ηg/mL)	66.1366	32.1451
BMD (mmAl)	17.55	2.92
Glob (g/dL)	3.77	0.66

Table 2 Positive Correlation with bone image and samples of Nelore cows ($p < 0.05$).

Exostosis × Bone reabsorption
Age × Exostosis
BMD (bone mineral density) × Thoracic circumference
BMD × body weight

The objective of this study was to find correlation between pedal bone lesions and with variables obtained, we used the criterion of Zetterholm (1972) [20] that consider like normal phalanx with smooth surface, without alterations. We observed many pedal bone alterations similar to several authors [9, 13-18, 21], but exostosis and bone reabsorption were more frequent. There were 87.81% of cows with pedal exostosis (2 to 26 mm) and 93.91% with bone reabsorption more frequent on distal phalanx, this caused lower bone density. But there was not correlation between pedal bone lesions with variables obtained of this study, only with age and exostosis. The aetiology of laminitis is multifactorial and the researchers believe there are a lenght association of several factors interdependents. The nutritional management, rumenal acidosis,

hormonal changes, infections diseases, systemic diseases, genetics, age, calving, conformation, behaviour, growth, season and housing are important factors predisposing that yet are known [3, 7, 12, 13, 15, 22-24]. The bone physiopathology have several inflammatory factors involved, the bone radiographic alterations appear some days after the action of this substances,

Histologically, hyperaemia, oedema, thrombi, haemorrhages and accumulations of lymphocytos, histiocytes and fibroblasts are seen in the corium. In chronic laminitis the pathological process in the laminar and solar regions is still dominated vascular change [9], accumulations of mononuclear cells, chronic granulation tissue with marked proliferation of capillaries and heavy fibrosis in the corium; in the lamellae coriales vessels appeared in increased numbers; dilation of capillaries and veins, changes in arteries and arterioles, including intimal proliferation, hypertrophy of the tunica media and fibrosis of the tunica adventitia; also local moderate to advanced arteriolosclerosis and arteriosclerosis were findings, particularly in the solar corium [9, 12]. In the histopathology of chronic bovine laminitis was observed that the number of arterial-venous shunts increased as age increased; in the digital cushion area, more severe abnormalities occured with respect to arteriosclerosis, arterial-venous shunt and sole hemorrhages [21]. The site in the hoof of the primary attack has long been the subject of considerable debate. The histological changes in cases examined at a very early stage clearly suggest that the vascular changes are primary, and that the primary process in the hooves in accute laminitis may be summarized as a toxic influence on capillary walls causing an insufficient nutrient supply to the keratin-producing cells with a synthesis of structurally defective keratin, progressive circulatory changes may involve aggregation of erythrocytes and platelets with further loss of capillary integrity, which lead to the release of vasoactive substances that trigger mechanisms that cause degenerative changes in the hoof [9, 12, 21].

The subclinical laminitis can be slow, long and insidious process and depend on persistent stimulus of degree low. During the chronic phase of laminitis many alterations are associated with areas of claw, the corium tissue is disorganized and the claw's form is changed. The ridges on dorsal wall and fissures can be developed, these alterations were found in this study, that correspond with Nocek's conclusions (1997) about ulcerations solear and double sole continue being the major signal clinicals. Bovine with laminitis suffer a vasoconstriction on digital artery causing hypoperfusion sanguineous during chronic inflammatory process, clinical or subclinical [9, 21, 24]. This kind inflammatory process is like a compartment due structural corneum and sanguineous hypoperfusion causing little venous return of catabolics produced, and they keep in the claw. This fact may be a reason of neither alterations in biochemicals values of cows of this work. The same observations were made for others workers [25, 26], the WBC, biochemical serum and rumenal fluid analysis do not reveal systemic alterations, characterizing a local inflammatory process and which the pedal lesions do not cause systemic alterations that can be determined by biochemicals examines, and because the number of arterial-venous shunts increased as age increased [21]. If microscopically, the changes in the corium in the chronic cases are local, moderate to advanced arteriolosclerosis and arteriosclerosis, especially in the solar corium, these lesions cause occlusion of vascular lumen, occasionally the arterial walls are totally destroyed, can form chronic thrombi, chronic granulation tissue and heavy perivascular accumulations of macrophages, and a combination of chronic a acute lesions can occur with hyperaemia, oedema, focal infiltration of neutrophils, local fibrinous thrombi, local fibrinous exudation and haemorrhages; the thrombi are present predominantly in the outer most part of the wall, pericapillary

accumulations of cells, predominantly macrophages, in the epidermis there are degenerative changes especially close to the sites of the thrombi [12] and produced locally stimulation of osteoclastic bone resorption [27]. Histamine is a mediator of inflammation and allergic response. The presence of histamine has been suggested in the lesions of laminitis [28]. Many groups have reported that histidine decarboxylase, a histamine-synthesizing enzyme, is induced by Lipopolisacharides, cytokines, and lymphocyte mitogen in macrophages [29], T lymphocytes [30], and in peripheral tissues [31, 32]. Osteoclasts are responsible for bone resorption [33, 34], and this depent on the Receptor activator Nuclear factor-kappa B (RANK) ligand (RANKL)/Osteoclast differentiation factor (ODF) is a soluble molecule in the bone microenvironment. The ODF/RANKL binds to a receptor, which is present on T cells and bone marrow stromal cells called RANK [35]. The RANKL/ODF mRNA is induced by histamine during osteoclastogenesis supporting osteoblast and stromal cells and that RANKL/ODF produced locally because of histamine stimulation plays a functional role in osteoclastic bone resorption [27]. Osteoblasts express RANKL in response to bone resorbing factors such as PTH, interleukin-1 (IL-1), and prostaglandin E2 (PGE2), and interact with osteoclast precursors. The PGE2 is produced in bone mainly by osteoblasts and stimulates bone resorption [36]. The Tumor necrosis factor-α (TNF-α) is one member of a large family of inflammatory cytokines; and it has a central role in bone pathophysiology. TNF is necessary for stimulation of osteoclastogenesis along with the receptor of Nf-$_k$B. The TNF also stimulates in a manner that hinders their bone-formative action, suppresses recruitment of osteoblasts from progenitor cells, inhibits the expression of matrix protein genes, and stimulates expression of genes that amplify osteoclastogenesis. TNF damage the bone at many levels [37]. The IL7 suppresses the bone-forming osteoblast, stimulating formation and function of the osteoclast, the exclusive resorptive cell [38]. Bone pathophysiology involves a great number of factors in its inflammatory process, and these factors are important for studing the pathophysiology of the laminitis.

Probably, these observations about tissue damages can be a reason of large number of bone reabsorption area on distal phalanx found in this study, with 93.91% of cows, most frequency on this extremity of distal phalanx and the cause of its low bone density (Fig. 2). These physiopathologicals and haemodynamic alterations cause release of factors and enzym inflammatories (histamine, PG, cytokin, TNF-α, IL) that active the osteoclats and osteoblasts action, producing process of exostosis and bone reabsorption [27-31, 33-44], which can contribute to explain the pedal bone lesions observed on radiographs of this study. As there was correlation between exostosis with bone reabsorption, this corroborated the occurrence of bone inflammatory process localized in the distal falanx, like a compartmentelized process.

Usually, the bovine laminitis is associated with change in feeding regimens, especially feeding rations high in carbohydrates, a disturbed digestion in the rumen, or a toxic agent in the fodder are considered to be causative factors [9, 12, 22, 24], however, in this study we found considerables pedal lesions in Nelore cows keeping on extensive feeding of pasture

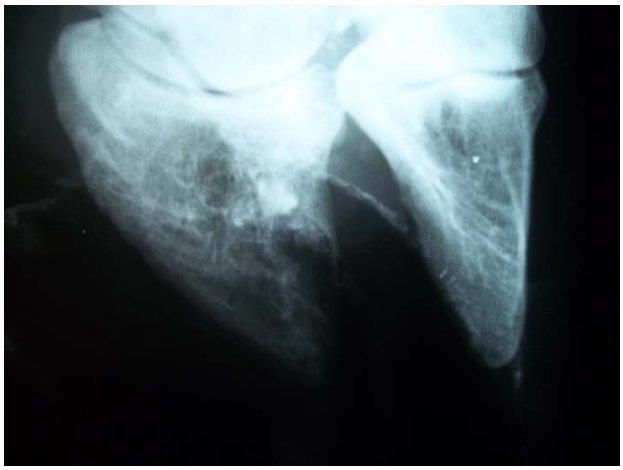

Fig. 2 This radiography shows extensive bone reabsorption areas in lateral distal phalanx.

Brachiaria decumbens, supplemented only with mineral mixture, having rumenal pH 7 to 8, this result differs totaly of others authors, most probable there are more factors involved in the pathogenesis of subclinical laminitis. The positive correlation was the exostosis with age, this can be related with a sequence of lesions that can occur month upon month, when the bone reaction is produced, it keep for long time, and bone neoformation can begin and increase itself size, like the periostitis [45]. Similar case was observed with shunt arterial-venous that increased in the older animals [21]. Probably this is an amount of circumstance of this inflammatory process.

The diagnosis of bovine subclinical laminitis begin with foot examine and of all aspect and health of herd cattle, we must do not underestimate some signal which can be found, independent on its length, the radiographic examine contribute for diagnosis and prevalence of disease, mainly of animals that have pigmented claws with bone lesions, this examine can be done on the farm. The inflammatory process in bovine laminitis is very complex, many factors are involved, for you get good preventive management, you could evaluate all factors that you can find, and evaluate the production system, thinking about economic damage of subclinical disease and before that the insidious rotation of the distal phalanx can result in permanent anatomical damage, dorsal wall concavity, fissure and ridging of the dorsal wall and damage of welfare animal [9, 24].

7. Conclusions

In this study, we observed none correlations between pedal bone lesions with biochemical values of Ca, P, Mg, Zn, ALP, TPS, Glob, CPK, GGT, Alb, AST, osteocalcin; and with body weight, thoracic circunference, WBC, BMD, and with lesions on claw's wall. There were correlations with age and phalangeal exostosis and with exostosis and bone reabsorption. We observed the importance of radiographic evaluation to assintomatic animals, mainly to high yield animals, and that have pigmented claw too, when the performance productive can be damage for subclinical podal bone lesions or to previous study of subclinic laminitis.

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