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A retrospective study of avascular necrosis of the femoral head in dogs in Delta State, Nigeria

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Abstract

The study evaluated the prevalence of avascular necrosis of the femoral head in dogs in Delta State, Nigeria. For ten years, data of cases presented to Veterinary Clinics in five government clinics in Delta state were evaluated and analysed. The breed of dog, sex, age on presentation, the limb affected and the radiographic appearance of the lesions on presentation were reviewed. The treatment and clinical management approaches were also reviewed and discussed. Of the cases of avascular necrosis of the femoral head recorded (N = 24) for the period under review, breed prevalence recorded 62.5% (Alsatians); 16.67% (Caucasians) and 20.83% (Mixed Breeds). Sex prevalence recorded 79.17% females and 20.83% males. According to age at the time of the first presentation, 83.83% of the affected dogs were 6-12month old, 12.5% were 13-24month old, and 4.16% were 25–36 month-old. Lameness was observed in 91.67%, while 8.33% of cases presented non-weight bearing lameness. Pain in the limbs during palpation of the hip joint was detected in 100% of the cases. Atrophy in the hind limb was identified in 41.66% of the patients, while 62.5% of the dogs showed different degrees of medial patellar luxation. In 91.6% of cases, the disease was unilateral, with 63.63% unilateral lesions in the right hind limb and 36.37% in the left hind limb. The study results showed a high prevalence of avascular necrosis of the femoral head in large breeds of dogs in the Delta state. The management of the disease is mainly conservative with poor follow-up. Cost of surgery and management may discourage owners from follow up. However, surgery remains the gold stand of care for managing avascular necrosis of the femoral head in dogs.

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Introduction

Osteonecrosis of the femoral head, often referred to clinically as avascular necrosis of the femoral head, is a pathological condition of the femoral head that causes a decrease in blood supply to the subchondral bone of the femoral head, which results in osteocyte death and collapse of the articular surface of the bone (Jones, 1985; DeCamp *et al.*, 2016). This condition and other pathologies such as Salter-Harris fractures

(fractures of the femoral head and neck in growing animals), acetabular fractures, coxofemoral joint luxation and hip dysplasia may compromise the integrity of the coxofemoral joint and result in lameness. The condition, often referred to as Legg-Calvé-Perthes disease (Jones, 1985; DeCamp *et al.*, 2016) is a developmental disease caused by ischemic necrosis, which is commonly seen in young dogs (Jones, 1985; Gambrardella, 1993; Demko & McLaughin, 2005; Cardoso, 2018). Several aetiology such as trauma, infection (Demko & McLaughin, 2005), hereditary (Gambardella, 1993), hormonal imbalance (Robinson, 1992), vascular abnormalities (Ginja *et al.*, 2010), metabolic imbalances (Towle & Beuer, 2012) and developmental anatomic deformities (Kim, 2011) have been reported. Findings reveal that there is a relationship between the onset of the disease with age and clinical presentation (Gambardella, 1993). Clinically, the disease presents a palpable pain in the hip, pain on abduction, extension or minimal movement of the affected hind limb. Crepitation and a limitation in the degree of extension have also been reported (Nebzydoski, 1982; Jones, 1985; Gambardella, 1993; DeCamp *et al.,* 2016). Typical clinical presentation is a shortening of the hind limb with a prominence of the greater trochanter and atrophy of the gluteal and quadriceps muscles (Nebzydoski, 1982: Jones, 1985; Gambardella, 1993; Demko & McLaughin, 2005; Madore *et al.*, 2007). Severe cases may compromise hind limb usage, locomotion and subsequent no weight bearing at all on the hind limb (Nebzydoski, 1982; Jones, 1985). The diagnosis is based on imaging such as radiography and magnetic resonance imaging (Nebzydoski, 1982; Jones, 1985; Bowlus *et al.*, 2008). Radiographic findings may reveal enlargement at early stages and a flattening or collapse of the femoral head at late stages. Hip dysplasia is often considered for the differential diagnosis in dogs (Ginja *et al.*, 2010; Kobayashi *et al.*, 2015). However, hip dysplasia may present a history of chronic onset with occasional micro-fracture, but there is no significant range of sub-chondral bone necrosis and degeneration (Ginja *et al.*, 2010; Kobayashi *et al.,* 2015).

This study reviewed the prevalence of avascular necrosis of the femoral head in dogs presented to veterinary clinics in Delta State to review the basic clinicopathological features presented by the disease and analyse the radiographic findings.

Materials and Methods

Data collection

Clinical and radiographic records of dogs presented, diagnosed and treated for avascular necrosis of the femoral head during the period from January 2009 to January 2019 in state government-owned clinics located in Warri, Sapele, Effurun, Agbor and Ughelli in Delta State were analysed. This was to determine the prevalence of the disease and radiographic findings reported. The breed of dog, sex, age on presentation, the affected limb and the significant radiographic features of the lesions seen on presentation were reviewed. The treatment and clinical management approaches were also reviewed. Breed of dog, age on presentation and sex prevalence were calculated and recorded. The affected limb, the radiographic evidence of necrosis of the femoral head, the history and clinical signs on presentation, the age and time of occurrence and the type of treatment and clinical management protocol applied were also evaluated. The lesions of the disease observed were subsequently classified based on the radiological appearance and stage of development of the lesions seen and graded from 1 to 5 as described in Table 1 (Kobayashi *et al.,* 2015; Cardoso *et al.,* 2016).

Radiographic changes seen in the clinical radiographs (Figure 1-6) were also recorded according to the lesion grades presented.

Statistical analysis

Data were analysed using Graph Pad Prism Version 7 for Windows. The simple linear regression analysis was used to quantify the relationship among lesion grades. The Spearman's correlation was subsequently used to analyse the association between lesion grade and other variables (gender, breed, and affected hind limb, unilateral or bilateral lesion). The differences were considered significant at $P < 0.05$. In addition, the data were analysed using descriptive statistics to feature the frequency of numerical variables.

Results

Twenty-four cases of avascular necrosis of the femoral head were identified in the present study. Breed prevalence showed 62.5% of the affected dogs were Alsatians (n = 15); 16.67% were Caucasians (n = 4) and 20.83% were mixed breeds (n = 5) (Figure 7).

Nineteen cases were females (79.17%), and 5 were males (20.83%) (Figure 8). According to the age group at the time of the first presentation, 20 dogs were within 6–12-month-old (83.83%), three dogs were within 13–24-month-old (12.5%), and one dog was 25–36-month-old (4.16%) (Figure 9).

Lameness of the affected hind limb was observed in 91.67% (n = 22) of the cases; 8.33% (n = 2) of the lame dogs presented non-weight bearing lameness.

Table 1: Grading of avascular necrosis of the femoral head in dogs

Lesion Grade	Clinical Presentations
Grade 1	Acetabulum and contour of the femoral head and of the femoral neck are apparently normal, and there is wide joint space, decreased density of the femoral head and of the femoral neck.
Grade 2	There is femoral head flattening and the presence of multiple density foci of decreased density, the acetabular rim may contain a small spur.
Grade 3	There is irregularity in the articular surface of the femoral head and the presence of multiple low-density foci, the spur is more prominent in the acetabular rim.
Grade 4	There is loss of the normal shape of the femoral head, increased prevalence of areas with decreased density.
Grade 5	There is fragmentation of the femoral head with discontinuity of the articular surface, and the acetabular changes are more pronounced than those observed in Grade 4.

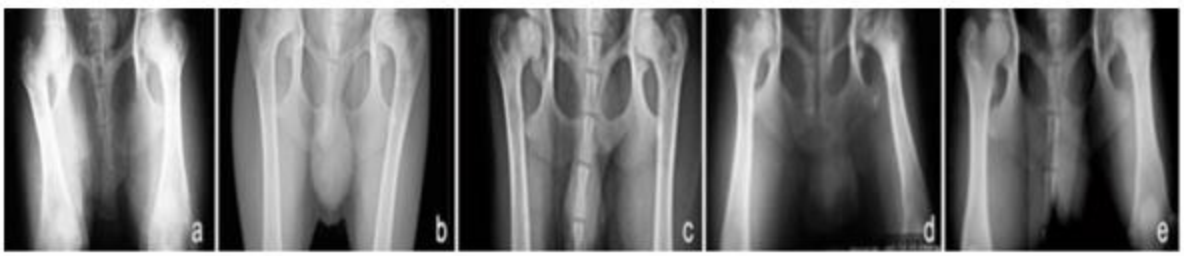

Figure 1. Ventrodorsal radiographic views of the hip joints in dogs with avascular necrosis of femoral head.
a- Grade 1: Decreased density of the femoral head;
b- Grade 2: Flattening of the femoral head and presence of density foci of decreased density;
c- Grade 3: Irregularity of the articular surface of the femoral head and presence of multiple low density foci, spur on the acetabular rim;

Pain in the limbs on palpation of the hip joint was detected in 100% (N = 24) of the cases. Atrophy in the hind limb was identified in 41.66% (n= 10) of the affected dogs, and 62.5% (n = 15) of the dogs showed different degrees of medial patellar luxation. In 21 dogs (91.6%), the disease was unilateral and in one dog, it was bilateral (4.16%). Also 63.63% (n= 14) of the unilateral lesions were located in the right hind limb and 36.37% (n = 8) in the left hind limb.

Figure 2: Radiograph of dog showing decreased bone density (Grade 1)

Figure 3: Radiograph of dog showing increased width of joint spaces (Grade 2)

The radiographic grades of the lesion were not significant ($p > 0.05$) in the present study in comparison to other variables in both the simple linear regression and the Spearman's correlation. Thus, the descriptive analysis was done based on the radiographs: 18.83% were Grade 1 (n = 2); 16.67%, Grade 2 (n = 4); 16.67%, Grade 3 (n = 4); 25%, Grade 4 (n = 6); and 37.5%, Grade 5 (n = 9) (Figure 10).

Surgical treatment was performed in 6 cases (25%), and conservative treatment was done in 18 (75%) cases. The owner did not return the dog for post-operative follow up in 50% (n = 3) of the surgical cases (n = 6).

Discussions

Young dogs have been reported to develop a debilitating hind limb condition, often resulting in lameness in which the femoral head degenerates and becomes necrotic due to ischemia. This condition, ischemic or avascular necrosis of the femoral head, also referred to clinically as Legg-Calvé-Perthes disease, generally appear between 3 and 13 months of life. The resulting lameness may be present for several weeks or may have a sudden onset (Gambardella, 1993). The present study reviewed 24 cases of dogs 6-36 months of age presented to be a result of avascular necrosis of the femoral head. Results showed that the syndrome was more prevalent in dogs between the ages of 13–24 month-old. At the time of clinical presentation, only one dog was 36-month-old. This correlate report that the disease is more prevalent in young dogs (Lika *et al.*, 2012). This may also be due to owners not presenting the dogs to the clinics at the onset of lameness or trying conservative management of observed lameness on their own before presentation to the clinics. More so, owners may not recognise the clinical signs early enough.

Figure 4: Radiograph of dog showing osteophyte Production (Grade 3)

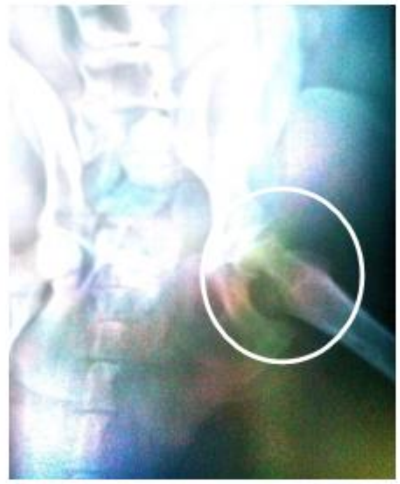

Figure 5: Radiograph of dog showing flattening of the articular Surfaces of the Femoral head (Grade 4)

Figure 6: Radiograph of the dog showing femoral Head Fragmentation (Grade 5)

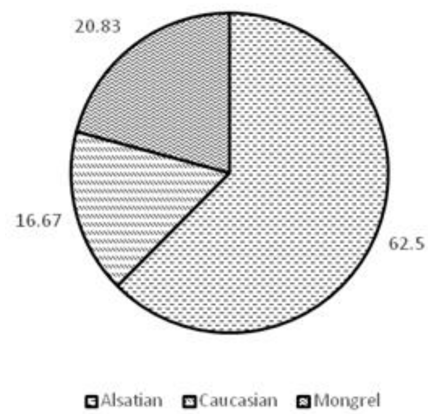

Figure 7: Breed distribution of lesions of Avascular Necrosis of the femoral head

Twenty-four cases of avascular necrosis of the femoral head were diagnosed. Sixty-two and a half (62.5%) of the different breeds of dogs recorded were Alsatians; 16.67% were Caucasians, and 20.83% were of mixed breeds.

More female dogs (79.17%) were presented than males (20.83%). In addition, the age at the time of the first presentation, younger (juvenile) dogs (83.83%) between 6–12 months old were presented as compared to adolescent (13–24-month-old) dogs (12.5%) and adults (25-36-month-old) dogs (4.16%).

Alsatian and Caucasian breeds observed to have a high prevalence in this study were large breeds of dogs; this is contrary to reports of the disease being more common in small breeds of dogs; however, this difference in breed predisposition can be due to the fact that the small breeds of dogs are not commonly kept by pet owners in the region under study as compared to the large breeds. Most dog owners in southern Nigeria keep dogs mostly for security purposes, and this may contribute to the low incidence of the disease in small breeds in the region (24 of 3215 cases presented to the clinics under review for a period of 10 years). Small breeds of dogs

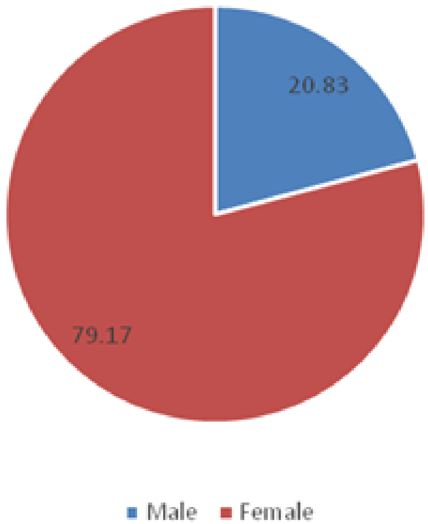

Figure 8: Prevalence of Avascular Necrosis of the femoral head based on sex

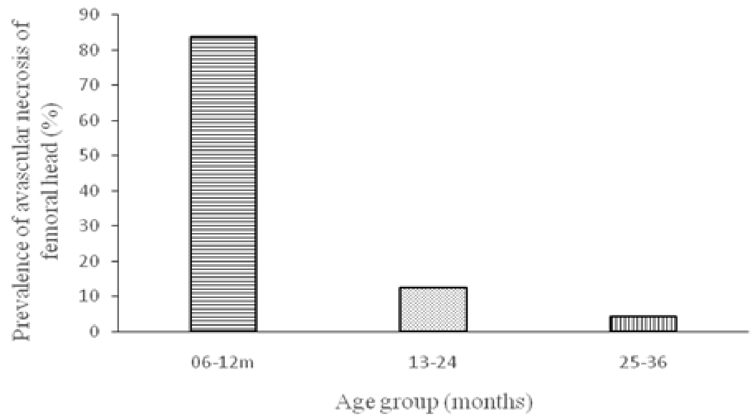

Figure 9: Age Distribution of Lesions

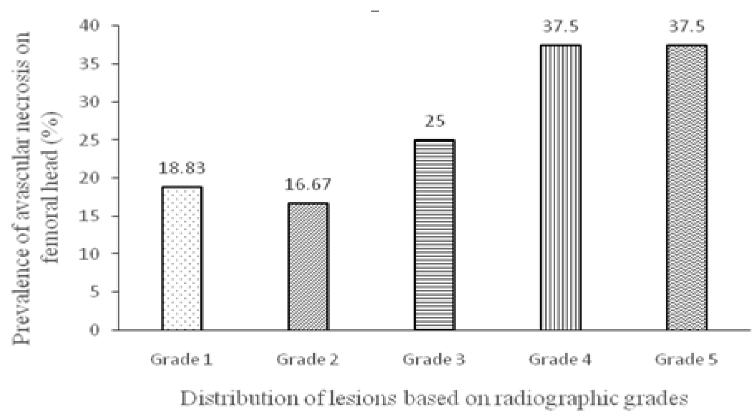

Figure 10: Age Distribution of lesions according to Radiographic Grading of Avascular Necrosis of the Femoral Head

such as the West Highland White Terrier, Cairn terrier and poodle have been reported amongst the breeds commonly affected (Harper, 2017). In an earlier study comprising 35 dogs, 60% were Yorkshire terriers (Millis, 2014). In another study comprising 14 dogs, the incidence of the disease was higher in Pekingese and Terrier breeds (Lika *et al.*, 2012). The differences observed in these studies may be associated with the different socio-economic and geographic regions and the breed preference of pet owners.

Studies have also reported a high prevalence of avascular necrosis of the femoral head in dogs, with an average mean body weight of 4-6 kg matches the small breeds of dogs (Demko & McLaughin, 2005; Towle & Beuer, 2012; Cardoso *et al.*, 2018). This study, however, did not compare the mean bodyweight of the dogs with the disease prevalence.

About seventy-nine percent (79.17%) of the total cases reviewed in this study were females, and 20.83% were males, supporting an earlier study that had also reported high sex prevalence for females (Lika *et al.*, 2012) while another study of 188 cases (Cardoso *et al.*, 2018) reported no sex prevalence for the disease.

Early clinical signs of non–weight-bearing lameness or an intermittent subtle lameness have been reported in avascular necrosis of the femoral head (Nebzydoski, 1982; Demko *et al.*, 2005). Complete physical and radiographic examinations must be conducted to eliminate the possibility of slipped upper femoral epiphyses, fracture of the femoral neck, hip dysplasia and patella luxation. Weight-bearing lameness of the affected hind limb was observed in 91.67% of the cases in this study, while 8.33% of cases presented non-weight bearing lameness. Pain in the limbs during palpation of the hip joint was detected in 100% of the cases; this has also been previously reported, and in general, the pain may get worse during hip joint abduction (Nebzydoski, 1982). Atrophy in the hind limb muscle was identified in 41.66% of the dogs, and 62.5% of the dogs showed different degrees of medial patellar luxation. In this study, 6.97% of the cases reviewed were bilateral and thus agreed with an earlier report that bilateral avascular necrosis of the femoral head is rare. (Towle & Beuer, 2012; Cardoso *et al.*, 2018),

Based on the clinical, radiographic appearance of the lesions, avascular necrosis of the femoral head has been classified into five grades (Madore *et al.*, 2007; Cardoso *et al.*, 2018). The common radiographic features includes: areas of decreased bone density close to the epiphyseal line in early cases; increased width of the joint space seen in the early course of the disease persists throughout the disease. An initial osteophyte production in the anterolateral aspect of the acetabulum becomes more pronounced as the condition persists. Also reported is the flattening of the articular surface of the femoral head ranging from the minimal loss of the articular contour of the anterodorsal aspect of the articular surface to a marked concave depression of the anterodorsal aspect to complete disruption with loss of contour of the articular surface and fragmentation of the femoral head (George, 1992; David *et al.*, 2012; Cardoso *et al.*, 2018)

The radiographic grade of the lesion was not significant in the present study; therefore, a descriptive analysis was done based on the radiographic classification: 18.83% were Grade 1, 16.67% Grade 2; 16.67% Grade 3; 25% Grade 4 and 37.5% Grade 5. Non-operative management and treatment of osteonecrosis involved the application of non-invasive methods to dissipate and reduce the force and load-bearing on the affected hip by the use of splints, bandages or a walker and cane, thus decreasing weight-bearing on the affected hind limb. Furthermore, a modification of the dogs' routine activities and, in some cases, exercise limitation and control, as well as physiotherapy, have been advocated (Cardoso *et al*., 2018). These methods, however, have not shown any significant impact in the treatment and management of osteonecrosis, especially at the late stages. More so, limited was recorded by the use of these methods in preventing disease progression even at the onset or very early stages of the disease (Cardoso *et al*., 2018). In this study, surgical treatment was performed in 6 cases (25%), and conservative treatment was applied in 18 cases (75%). However, the owners did not return the dogs for postoperative follow-up in up to 50% of the surgical cases. From the study, the stage 5 lesions of avascular necrosis of the femoral head were more frequent; the prognosis was poor to guarded. The high prevalence of Grade 5 lesions may be associated with chronic lameness resulting from late diagnosis and delay in the institution of care and management of the condition. Surgical management with intensive care is often required. In some cases, it has been reported that a second surgery may be needed to remove the remaining part of the femoral head in order to achieve total recovery (David *et al.*, 2012; Cardoso *et al*., 2018) and functional recovery of the affected hind limb may also require physiotherapy and rehabilitation.

A study comprising seven dogs with unilateral avascular necrosis of the femoral head found that the radiographic areas presenting decreased density in Grades 2 and 3 did not alter the global mineral content of the scanned regions in dual-energy X-ray absorptiometry scans (Isola *et al.*, 2005).

In assessing the treatment options and novel strategies in the management of avascular necrosis of the femoral head, it must be noted that vascular damage and resultant ischemia is a crucial factor in the pathogenesis of avascular osteonecrosis. Scientists have tried to experimentally simulate the injury by inducing vascular deprivation and ischemia clinically (Levin *et al.,* 1999; Vadasz *et al.*, 2004; Peled *et al.*, 2009; Terayama *et al.*, 2011). The usefulness of several novel therapies for osteonecrosis and the possible cellular and molecular mechanism that are involved in the pathology of the disease is being studied extensively using these models in the last few decades. The use of cellular therapies as a treatment option for osteonecrosis has also been considered. A recent study reported the use of CD34+ cells intending to take advantage of its vasculogenic and osteogenic potentials. CD34+ cells were harvested and transplanted after Granulocyte Colony Stimulating Factor (G-CSF) mobilization intravenously in a rat model to manage avascular necrosis. The study showed improved and promising results (Terayama *et al.*, 2011). It has equally been reported that Mesenchymal Stem Cell (MSC) proliferation is affected during osteonecrosis (Wang *et al.*, 2008). Thus, scientists have made several attempts to treat the disease condition by using MSC either by systemic intravenous administration or locally in the form of transplants/grafts in various animal models. Bone growth and regeneration have been linked to a myriad of cellular events involving growth factors and mediators such as the BMP, angiogenic growth factors, interleukins, and cytokines (Baltzer *et al.*, 2000; Southwood *et al.*, 2004; Roedersheimer *et al., 2*005; Uwagie-Ero *et al.*, 2017). It is thought that with the application of these growth factors and cellular agents alone and in their combination, coupled with a well-defined surgical technique, healing of avascular necrosis of the femoral head lesions can be enhanced (Houdek *et al.*, 2015; Ma *et al.*, 2015). Animal studies have also investigated the use of BMP for the treatment and management of osteonecrosis (Houdek *et al.*, 2015). The local administration of BMPs has been fraught with complications related to the high concentration needed to induce bone regeneration with resultant heterotopic bone formation (Govender *et al.*, 2002; Vandermeer *et al.*, 2011; Houdek *et al.*, 2015; Ma *et al.*, 2015). In addition to using BMP alone, BMPs has been used in combination with surgical modalities such as core decompression (Pan *et al.*, 2014; Sun *et al.*, 2014; Houdek *et al.*, 2015;) and "trapdoor" bone grafting (Gibson, 1990; Mont *et al.*, 2001) Osteonecrosis of the femoral head is a complex, multifactorial medical condition (Petek *et al.*, 2019; Atilla *et al.*, 2020) and the exact pathophysiology behind osteonecrosis is yet to be elucidated (Cardoso *et al.*, 2019; Atilla *et al.*, 2020). Currently, the use of ancillary growth factors for the treatment of this disease process attempts to treat osteonecrosis at a pathophysiological level (Atilla, 2020; Cardoso *et al*., 2018). Although promising reports have been observed in several animal models, the clinical use of adjuvant growth factors remains under investigation. (Cardoso *et al.*, 2018; Atilla *et al.*, 2020).

To date, conservative and surgical treatments are being used in the treatment of avascular necrosis (Demko & McLaughin, 2005; Lika *et al.*, 2012; Towle & Breuer, 2012; DeCamp *et al.*, 2016; Cardoso *et al.*, 2018). The conservative treatment includes rest, controlled exercise, analgesic and anti-inflammatory medication, external coaptation, and physiotherapy (Nebzydoski, 1982; Gambardella, 1993; Lika *et al.*, 2012). Chondroprotective medication and acupuncture; has also been reported to provide excellent outcomes. However, there are reports that only 25% of dogs recover from lameness after the conservative treatment (Gambardella, 2003; Demko & McLaughin, 2005; Kim, 2011). Thus, reports suggest that surgical intervention should be ideal if there is no improvement of clinical signs after four weeks of conservative management (Millis, 2014).

A femoral head and neck osteotomy is the surgical procedure of choice in avascular necrosis of the femoral head. The procedure not only provides pain relief for the dog but also reduces lameness resulting from the condition (Nebzydoski, 1982; Gambardella, 1993; Lika *et al.*, 2012; DeCamp *et al.*, 2016; Harper, 2017). Dogs have been reported to experience mild intermittent lameness after the procedures. The outcome, however, has thus far been reported to be excellent (Millis, 2014; Cardoso *et al.*, 2018). A major challenge to the management of avascular necrosis of the femoral head is the cost of surgery; most pet owners may not be able to afford the cost of initial surgery and may choose the option of euthanasia. Availability of suitable prosthetic devices is also a major challenge as they have to be ordered when needed, especially when all conservative management fails. This may account for the lack of follow-up of cases seen in this study. A major limitation to this study, however, was the challenge of poor record-keeping in a majority of the clinics assessed. The results obtained and reported in this study are therefore based on available records, this must be borne in mind in the interpretation and extrapolation of the results presented herein and should form part of policy recommendations in the management of and preservation of clinical data and records. Standardization of veterinary clinical data should be considered a priority.

The study showed a high prevalence of avascular necrosis of the femoral head in large breeds of dogs in Delta state. At the time of this study, management of the disease in the state is still largely conservative and follow up is relatively poor. Most pet owners see the condition as recalcitrant, and that may account for why they do not want to do a follow-up. Also, the cost of surgery and management may discourage owners from follow-up. However, surgery remains the gold standard for managing avascular necrosis of the femoral head in dogs.

Conflict of Interest

The authors declare that there is no conflict of interest.

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