

FUNAAB

INAUGURAL LECTURE SERIES __ 106 _____

**THE SILENT VOICES: RECOGNIZING AND RELIEVING PAIN IN
ANIMALS FOR BETTER WELFARE**

Protocols

The Vice Chancellor,
The Deputy Vice Chancellor (Academic),
The Deputy Vice Chancellor (Development),
The Registrar,
The Bursar,
The University Librarian,
The Dean, College of the Veterinary Medicine,
Other Deans and Directors,
The Head, Department of the Veterinary Surgery and Theriogenology,
Other Heads of Departments and Units,
Members of the University Senate,
All Academic and Non-teaching Staff,
All Special Guests and Friends of the University,
Members of my Immediate and Extended Family and Friends,
Gentlemen of the Press,
Distinguished Ladies and Gentlemen,
Great FUNAABITES!!!

PREAMBLE

1.0 INTRODUCTION

The *Veterinarian's Oath* is a pledge made by veterinarians at the point of induction into the Veterinary profession. It contains important components of professionalism in the daily routine practice of Veterinary Medicine. The oath for Nigerian Veterinarians states thus:

Being admitted to the Veterinary profession, I

Solemnly declare and promise to use my scientific knowledge and professional skills for the benefit of the society, through the protection of animal health, the relief of animal suffering, the conservation of livestock resources, the promotion of animal production and of public health and the advancement of veterinary knowledge. I will practice my profession conscientiously and with dignity, in keeping with the principles of veterinary ethics. I accept as a life-long obligation the continual improvement of my professional knowledge and competence.

The Vice Chancellor Sir, I took this oath on 30th June, 1998 at Trenchard Hall, University of Ibadan, and this has been a major driving force for my engagements in the noble profession of Veterinary Medicine till now. The Veterinary oath has five basic themes namely (1) protection of animal health, (2) relief of animal suffering, (3) conservation of livestock resources, (4) promotion of animal production, and (5) promotion of public health.

The first inaugural lecture from the College of Veterinary Medicine titled “Healthy Meat for Wealth” was delivered by my mentor and a former Deputy Vice Chancellor of the University, Professor Morenike Atinuke Dipeolu, on 23rd June, 2010, and was centered on the theme “Promotion of Public Health”. The second inaugural lecture from the College titled “The Magnum Opus of Reproductive Anatomy: The African Giant Rat and the Giant of Africa” was delivered by my brother and a former Dean of the College, Professor Adebayo Koyoum Akinloye on 6th March, 2024, and was centered on the theme “Promotion of Animal Production”. Today’s inaugural lecture titled, “The Silent Voices: Recognizing and Relieving Pain in Animals

for Better Welfare” is the third from the College of Veterinary Medicine and the first from the Department of Veterinary Surgery and Theriogenology. This lecture will focus on the theme ‘Relief of Animal Suffering’.

1.1.1 *Explanation of Concepts*

The ability to experience pain is universally shared by all mammals. Physiological and behavioural observations show that animals do not only experience the sensory aspect of pain but also the unpleasantness, averseness and negative emotions attached to pain experience. Animals have the capacity to feel both positive and negative emotions. This is observed as animals seek pleasure and avoid suffering. Animal sentience has been recognized in numerous countries and jurisdictions.

Veterinary professionals have both ethical and medical duty to manage pain in animals (Steagall *et al.*, 2021). The ethical duty relates to the fact that pain causes suffering. Veterinarians must therefore, prevent, diagnose and treat pain as part of their ethical responsibility. The medical aspect of pain management relates to the fact that pain is a medical problem leading to unwanted physiological consequences such as activation of the sympathetic nervous system, immunosuppression, altered metabolism, impaired healing, increased morbidity, and occasionally, death. Veterinarians, therefore, have the responsibility to make decisions free of external influences based on ethical and medical responsibilities to their patient, and abstain from causing unwanted injury or harm to animals through their interventions (elective tail docking or ear cropping). Ethics in pain management is the result of a complex interplay involving culture and societal norms, and the triad relationship between the Animal, the Veterinarian and the Client.

1.1.2 *Animal Sentience*

Animal Sentience is the capacity of an animal to experience both positive and negative emotions. Discussions on the abilities of animals to experience feelings such as pain, pleasure and suffering have been on for several decades. Philosophers such as Plutarch, Hippocrates, and Pythagoras were all advocates for humane treatment of animals. Their reason simply was based on the understanding that animals can experience pain and suffering, even if they cannot communicate it (*the silent voices*). Jeremy Bentham wrote in 1789, “The issue is not, whether they can reason, or talk, but whether they can suffer”.

Discussion on sentience in animals continued in to the 19th Century, a period marked by the works of Darwin who wrote about the ability of animals to feel pain, and the many similarities they shared with humans. He stated that animals were capable of many emotions and experiences, both similar to and different from humans (Proctor, 2012). Darwin proposed that some animals were capable of self-consciousness; a trait once generally assumed to be exclusive to humans. The early to mid-20th century was characterized by the behaviourist movement. In the 1960s, Ruth Harrison in her book *Animal Machine* exposed the realities of intensive farming at the UK farms, and the suffering of the animals within them (Harrison, 1966). In response to this, the UK Government set up the Brambell Committee in 1965 which looked specifically at the welfare of animals in farming systems (Proctor, 2012). The Committee understood the importance of sentience, and ensured that all assessments took in to account both the feelings and behaviour of the animals. Since then, there has been a notable increase in the number of publications concerned with animal welfare and the recognition of sentience (Duncan, 2006). However, despite this long history of thinking about animals as conscious beings, the science of animal sentience is still a developing subject.

Pain is a complex multi-dimensional experience involving sensory and emotional components. Pain in animals can be defined as “*an aversive sensory and emotional experience representing an awareness by the animal of damage or threat to the integrity of its tissues*” (Molony and Kent, 1997). This implies that the “inability to communicate pain does not remove the possibility of experiencing pain. Pain is a unique individual experience making it difficult for others to appreciate how it feels. The conscious experience of pain is a subjective emotion that can be experienced even in the absence of obvious noxious stimulation, and which can be modified by fear, anxiety, memory and stress. In non-verbal patients, including animals, behavioural patterns is used as the backbone for the recognition and assessment of pain.

1.1.3 *Pathophysiology of pain*

Perception of pain is the final product of a complex neurological information-processing system resulting from the interplay of facilitatory and inhibitory mechanisms throughout the peripheral and central nervous systems (CNS). The conscious experience of acute pain resulting from a noxious stimulus is mediated by a high-threshold nociceptive sensory system. Nociceptors are free nerve endings (primary afferent/sensory fibres) with their cell bodies located in the dorsal root and trigeminal ganglia. The primary afferent nerve fibres (Table 1) which carry information from these free nerve endings to their central location consist of two main types: C fibres and A δ fibres. Within these two broad categories are many sub-categories based on the precise receptors they express.

Table 1: Primary afferent fibres

Fibre	Description	Diameter (μm)	Conduction velocity (m/second)
A β	Large myelinated and rapidly conducting fibres involved in low threshold innocuous mechanical stimulation (e.g. touch)	More than 10	30 to 100
A δ	- Thinly myelinated and slowly conducting fibres primarily involved in nociceptive signalling - Contribute to the rapid "stab" of the acute pain response and functions primarily as a warning, resulting in rapid withdrawal from the stimulus (i.e. fast pain)	2.0 to 6.0	12 to 30
C	- Unmyelinated and very slowly conducting fibres primarily involved in nociceptive signalling - Activated by intense mechanical, chemical and thermal stimuli contributing to the "slow burn" sensation of pain (i.e. slow pain) - A population of C-fibres called "silent" nociceptors may become active during inflammation or tissue damage and reflects one of the changes in peripheral sensitisation	0.4 to 1.2	0.5 to 2.0

Adapted from Monteiro and Simon, 2022

Following tissue damage, changes in the properties of nociceptors can occur such that the A β fibres which normally are not associated with nociception may also transmit pain information (maladaptive pain). Continued noxious stimulation results in the C fibre activation, the extent of which is dependent on the severity of injury. Primary afferent fibres carrying sensory information from nociceptors synapse in the dorsal horn of the spinal cord onto second order neurons. From here, information (nociceptive message) is projected to various higher centres (Figures 1 and 2). Several brainstem-spinal pathways are activated simultaneously when a noxious stimulus occurs, providing widespread positive and negative feedback loops by which information relating to noxious stimulation can be amplified (pain facilitation) or diminished (pain inhibition).

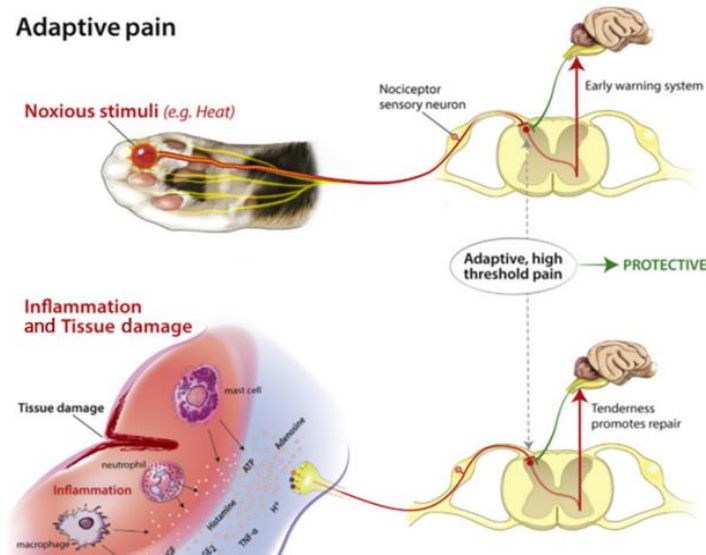


Figure 1: Schematic diagram of functional (adaptive pain) in cat. Source: Adrian *et al.*, 2017

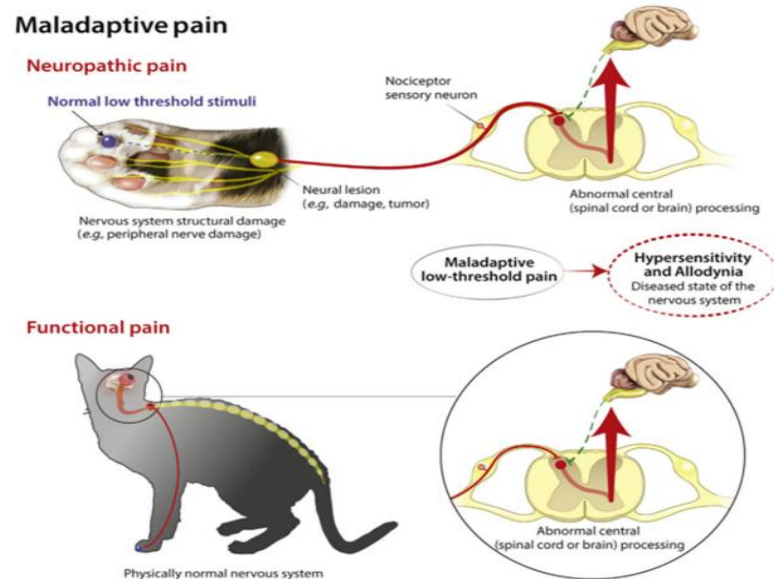


Figure 2: Schematic diagram of neuropathic pain in cat. Source: Adrian *et al.*, 2017

The cerebral cortex is the seat of conscious experience of pain (perception). It exerts top-down control (e.g. sending signals down to the spinal cord) modulating the sensation of pain. This is known as the descending noxious inhibitory control. In other words, the nociceptive input from the periphery to the spinal cord is modulated (amplified/facilitated or diminished/inhibited)

locally but also by signals coming from the cerebral cortex before information is sent to the cerebral cortex and perceived as “pain.”

Pain is considered to consist of three key components: a sensory-discriminatory component (temporal, spatial, and thermal/mechanical), an affective component (subjective and emotional, describing associated fear, tension, and autonomic responses) and an evaluative component, describing the magnitude of the quality (e.g. stabbing/ pounding; mild/severe). Undoubtedly, an animal’s pain experience has these three components, however, there is a tendency to focus only on pain intensity.

1.2 Classification of pain

Pain can be categorized according to duration (acute, chronic), anatomic location (superficial, deep, visceral, somatic, musculoskeletal), or underlying mechanism (nociceptive, inflammatory, neuropathic) (Guedes, 2017). Acute pain is a short-term pain with sudden onset of action usually caused by an injury, surgery, illness, or trauma (Table 2). It is a warning sign that something is damaging or could become damaging to the body. It is a normal physiologic (adaptive) response to noxious stimuli. Chronic pain is a long standing pain that persists beyond the usual recovery period or occurs along with a chronic health condition, such as arthritis, neuropathic disorders or cancer. Chronic pain may be on and off, or continuous and persists for more than 12 weeks.

Nociceptive pain is an adaptive alarm system that is activated in response to acute tissue damage or impending injury. It dominates attention and elicits a strong motivational drive with the goal of avoiding or limiting injury. Inflammatory pain is a type of nociceptive pain that results from the activation and sensitization of nociceptors by inflammatory mediators; encouraging a decrease in movement until the tissue heals. Neuropathic pain on the other hand results from

disease, damage, or dysfunction of the peripheral or central nervous system. Neuropathic pain is maladaptive in that it serves no discernible protective or reparative role (Guedes, 2017).

Table 2: Classifications of pain

	Adaptive (acute)	Maladaptive (chronic)
Characteristics	• Associated with potential or actual tissue damage • Purpose: to rapidly alter the animal's behaviour to avoid or minimise damage and optimise the conditions in which healing can take place • Varies in severity and is proportional to the degree of tissue damage • Self-limiting: diminishes with healing and ceases when healing is complete	• Persists beyond the expected course of the acute disease • Not associated with healing • No clear endpoint • Associated with recurrent or long-standing disease conditions • Can exist without a cause • Serves little to no biological purpose
Examples	• Surgical procedures • Trauma (cut, wound, fracture) • Acute onset diseases (e.g. pancreatitis)	• Osteoarthritis • Cancer • Periodontal disease
Comments	• Often considered to serve a protective purpose. However, in the context of controlled surgical or therapeutic interventions, this protective purpose is not needed • The mechanisms producing acute pain tend to reflect the normal physiological pain transmission system, and in general, acute pain is easier to manage than longer-standing (chronic) pain • Sometimes referred to as physiological pain and may involve inflammation	• Persistent postsurgical pain refers to acute surgical pain that becomes chronic • Patients with chronic pain can present with episodes of acute pain (i.e. "acute on chronic" or "breakthrough pain") • Sometimes referred to as pathological pain

Adapted from Monteiro *et al.*, (2022).

1.3 Pain recognition

The process by which pain is perceived is complex, incompletely understood and cannot be measured objectively. Accompanying unpleasant experiences are measurable physiological responses that are mediated primarily by the autonomic nervous system. Many of these responses are not unique to pain, they only reflect a physiological stress response. Therefore, the parameters used to identify and define pain often limit the understanding of its complexity and the ability to treat it effectively (Ugwu, 2020).

Behavioural expression of pain is species-specific and influenced by several factors such as age, breed, demeanour, type and duration of pain, clinical condition and the presence of additional stressors such as anxiety or fear (Monteiro *et al.*, 2022). Debilitating disease can dramatically reduce the range of behavioural indicators of pain that an animal would normally show.

Therefore, when assessing an animal for pain, a range of factors should be considered, including the type, anatomical location of trauma site, severity of injury and duration of traumatic events (Grant, 2019). Pain in trauma patient increase stress response with resultant increase in metabolic and energy demands, delayed wound healing, reduced immune function, weight loss, decreased mobility and prolonged recumbency.

1.4 Pain Assessment

Animals are non-verbal and cannot self-report the presence of pain, thus the burden of pain assumption, recognition, and assessment lies with the Veterinary professionals. It is now accepted that the most accurate method for evaluating pain in animals is not by physiological parameters but by observations of behavior (Alamrew & Fesseha, 2020). Pain assessment, should be a routine component of every physical examination, and a pain score should be considered the fourth vital sign, after temperature, pulse, and respiration in trauma patient (Monteiro *et al.*, 2022).

A systematic and holistic approach that considers the animal, as well as its environment, is essential to recognize changes in behavior and physiologic parameters. Behavioral signs of pain, including both loss of normal behavior and development of new and abnormal behaviors, may be subtle and easily overlooked by both the owners and the veterinary health care team (Epstein *et al.*, 2015). The expression of pain through behavior has many dimensions, including suppression of behavior as well as active indicators of pain. For example, terminal stages of some abdominal

disorders can produce severe depression with very few outward signs, and animals severely debilitated by major surgery may be the least able to express pain overtly. Changes in normal animal behavior are almost always associated with pain or discomfort. Knowledge of the animal's normal behavior is required to optimally characterize subtle abnormalities. Common behaviors displayed by animals in pain include anxiety, depression, inappetence, reluctance to move, reclusiveness (non-interactive), and irritability (aggressiveness).

1.5 Pain Management

Owing to the complex nature of pain in individuals, there is no single method for pain management, thus Veterinarians must individualize whichever method is adopted in order to provide optimal pain control. The “PLATTER” approach (Epstein *et al.*, 2015) provides individualized pain management for any patient and is devised not on a static basis, but according to a continuous cycle of plan-treat-evaluate based on the patient's response to treatment.

1.5.1 Emergency Management of Acute Pain

The goal of emergency pain management is to control pain as quick as possible and prevent acute pain from being transformed into chronic (maladaptive) pain (Rousseau-Blass *et al.*, 2020). This allows the practitioner to determine the patient's basal requirements before starting long-acting medications (Porter *et al.*, 2020). Administration of rapidly acting intravenous agents in small doses at frequent intervals until pain relief is achieved is recommended for emergency pain control (Ahmadi *et al.*, 2016). Although total elimination of pain is not practically attainable during the emergency period, multimodal pain management techniques (involving administration of two or more drugs with different mechanisms) can provide suitable analgesia (Harvin *et al.*, 2021). These drugs may be administered via the same route or by different routes.

1.5.2 General Management of Pain in Trauma Patients

Pain is best managed early and with a robust protocol in dogs and cats with traumatic injury. It is harder to treat pain once it is well-established. The goal in the management of pain is to abolish it or to reduce it to the barest minimum. Preventive analgesia refers to the administration of analgesics pre, intra, and post-operatively (Monteiro *et al.*, 2022). It considers factors in all perioperative moments that can contribute to peripheral and central sensitization and involves any perioperative analgesic techniques/drugs for pain relief (Dahl & Kehlet 2011). Drugs frequently used for preventive analgesia include non-steroidal anti-inflammatory drugs (NSAIDs), local anaesthetics, opioids, alpha-2-adrenoceptor agonists, N-methyl, D Aspartate (NMDA) antagonists (*e.g.* ketamine) and gabapentin (Clarke *et al.*, 2015). These therapies reduce the severity of perioperative pain and might contribute to a reduction in the prevalence of persistent postsurgical pain.

1.5.3 Multi-modal analgesia

Multimodal analgesia (MMA) is the use of multiple analgesics, regional analgesia, and non-pharmacologic interventions to modulate peripheral and/ or central nervous system loci in the pain pathway (Monteiro *et al.*, 2022). Concurrent administration of drugs and treatments that act at different sites of the nociceptive pathway can provide optimal analgesia. Because the drugs target different pain mechanisms, lower doses of each drug can be administered, minimizing the occurrence of adverse effects. Benefits of MMA include the potentiation of multiple medication effects and greater pain control without relying on any single class of medication or strategy. It also prevents dependency on any of the agents.

Successful MMA in dogs and cats with traumatic injury should include NSAIDs, opioids, adjuvant drugs, local and regional analgesia, cognitive modalities, and physical modalities

(Harvin *et al.*, 2021). Non-opioid analgesics (NSAIDs) should be administered on a scheduled basis rather than “as needed”. Agents such as ketamine and systemic lidocaine are safe and effective components of a MMA strategy in trauma patient. The choice of drug(s) used to treat pain will depend on the underlying cause of pain, its severity and duration. Knowledge of the drug pharmacology in each specie and in patients of different age and physical status is very important.

1.5.4 *Non-pharmacologic Management of Pain*

Non-pharmacologic treatment should be part of multimodal system for pain management in trauma patients (Monteiro *et al.*, 2022). Neuromodulating treatments aimed at stimulating the pain systems should be considered in the management of dogs and cats with traumatic injury (Martins *et al.*, 2021). Currently, several neuromodulation methods such as percutaneous nerve electrostimulation (TENS), peripheral nerve stimulation, acupuncture, and vibration are available (Gruen *et al.*, 2022; Monteiro *et al.*, 2022). Neuromodulation supports pain treatment methods by activating the pain inhibitory mechanisms, thus reducing pain and improving the quality of life of patients with chronic pain.

Physical rehabilitative methods of pain management are appropriate for many types of pain and are essential in patients with chronic pain. In addition to relieving pain, such methods can reduce fear and anxiety, improve physical function, and alter physiological responses to pain.

Thermotherapy (heat application), cryotherapy (cold application), counter-irritation, and electroanalgesia are other non-invasive physical remedies for pain (Millie *et al.*, 2023).

1.6 Myths and Misconceptions on Pain in Animals

Pain management can be complex and challenging in any setting, however Veterinarians and Para-Veterinarians have both medical and ethical responsibility to manage pain in animals. The

major barrier to good pain management are the myths and misconceptions that have persisted over the years around the physiology of pain, animal pain behavior, availability of safe and effective analgesic drugs and techniques, and owners' psychology (Ajadi, 2023). The misconception that animals don't feel pain as humans do, or at least don't express pain as humans has led to neglect in the recognition and treatment of animal pain. The misconception that animals tolerate pain than humans have led to under-treatment of pain in animals. There are also specie and breed misconceptions about pain in animals. Further misconception is that pain is beneficial in limiting a recovering animal's activity. Veterinarians and Para-Veterinarians therefore have a huge responsibility to correct these misconceptions.

2.0 CONTRIBUTION TO KNOWLEDGE

Mr. Vice Chancellor, Sir, as an academic Veterinary Surgeon, I have spent the last 25 years in teaching, research and offering surgical consultation to the community. I have carried out over 2000 surgeries in several species of animals including dogs, cats, cattle, horses, pigs, sheep, and goats, rabbits, several species of monkeys, lions, and several species of birds. I have carried out extensive research on different techniques of providing a conducive environment during surgery. My research focus has been under four broad themes namely:

- i) Management of acute pain in animals by developing anaesthetic techniques for the control of perioperative pain in surgical patients especially in a poor resource setting.
- ii) Understanding the pathophysiology of chronic pain especially in musculoskeletal diseases with special focus on osteoarthritis.
- iii) Application of diagnostic imaging techniques to understand the pathophysiology of musculoskeletal diseases in rapidly growing large breed dogs.

iv) Evaluation of animals' welfare during transportation, and the veterinarians' work-place welfare.

I shall discuss some of my important scientific contributions in these areas.

2. 1 Management of Acute Pain Management in Animals

Control of perioperative pain in veterinary surgical patients is a corner stone of modern anaesthetic practice. Perioperative pain management has direct impact on patient well-being, and prevention of the development of chronic and maladaptive pain states (Almeida *et al.*, 2023).

Acute postoperative pain is nociceptive in nature and is associated with tissue damage. It is caused by direct activation of peripheral nociceptors and by inflammation, with resultant slowing down of patient recovery (Cicirelli *et al.*, 2022).

There is no ideal anaesthetic or analgesic agents due to the differences in efficacy and side effects of different agents in different species, which is occasioned by the metabolism of each agent in a particular specie. For example, paracetamol a common analgesic in human will cause fatal adverse effects in cat. In the same vein tramadol which is reported to be effective in cats is reported to be less effective in dogs because of the pharmacokinetic disposition of its metabolites. Thus, the practice of anaesthesia have to be tailored to the needs and peculiarities of each animal species. With this understanding, I worked on a number of anaesthetic agents to determine their effectiveness for perioperative pain control in different species of animals

2. 1.1 Studies on ketamine

Ketamine is a rapid acting dissociative anaesthetic, and N, methyl, D- Aspartate (NMDA) receptor antagonist used for induction of anaesthesia, and long duration analgesia. Ketamine has

been widely used for anaesthesia, as well as provision of postoperative analgesia in many species, including humans, non-human primates, dogs, cats, horses, ruminants, pigs, laboratory rodents, wildlife, and birds (Ajadi *et al.*, 2007a; 2008a & b; 2009a & b). Advantages of ketamine include minimal cardiovascular depression and potential stimulation of cardiovascular function via the drug's sympathomimetic effect. Ketamine can be administered intramuscularly, subcutaneously, intrathecally, intraperitoneally, and intravenously which makes it practical for use even in animals in which venous access is difficult. It is perhaps the safest and most widely used anaesthetic agents in the world. However, its use can result in poor muscle relaxation, muscle tremors, myotonic contractions, opisthotonus, and rough recovery. Thus, ketamine is rarely used alone, but often paired with drugs such as alpha-adrenergic agonists, benzodiazepines, and propofol for chemical restraint and induction of anaesthesia.

2.1.1.1 *Ketamine anaesthesia in pigs*

No single anaesthetic agent has been found ideal in providing adequate anaesthesia for surgery in pigs. Thus two or more drugs are often combined for the purpose. Drug combinations that have been used for anaesthesia in swine include telazol-ketamine, telazol-xylazine, telazol-ketamine-xylazine, ketamine-xylazine-butorphanol and ketamine-medetomidine-butorphanol combinations. Most of these drug combinations are not available in a poor resource settings, while majority are not economically feasible for production animal surgery. In the light of the above, Ajadi *et al.*, (2008a) evaluated the safety and efficacy of ketamine-xylazine-midazolam combination in pigs, as well as the influence of increasing the dosage of ketamine on anaesthesia induced by these combination in pigs. It was observed that the lower dose of ketamine combination lacks analgesia (Table 3) and is only suitable for the induction of anaesthesia, while the higher dose of

ketamine combination is preferable for surgery of short duration in pigs (Ajadi *et al.*, 2008a).

Both combinations did not significantly affect the physiological parameters in the pigs (Fig. 3).

Table 3: Anaesthetic indices following administration of either 20mg/kg or 10mg/kg of ketamine in pigs sedated with xylazine and midazolam combination

Anaesthetic indices (min)	K ₂₀ XM (n = 10)	K ₁₀ XM (n = 10)
Onset of analgesia	2.2 ± 0.2	1.4 ± 0.2*
Duration of analgesia	41.4 ± 12.6	Nil*
Anaesthesia time	92.0 ± 13.6	55.4 ± 8.4*
Recovery time	18.6 ± 1.4	7.8 ± 2.2*

Source: Ajadi *et al.*, 2008a

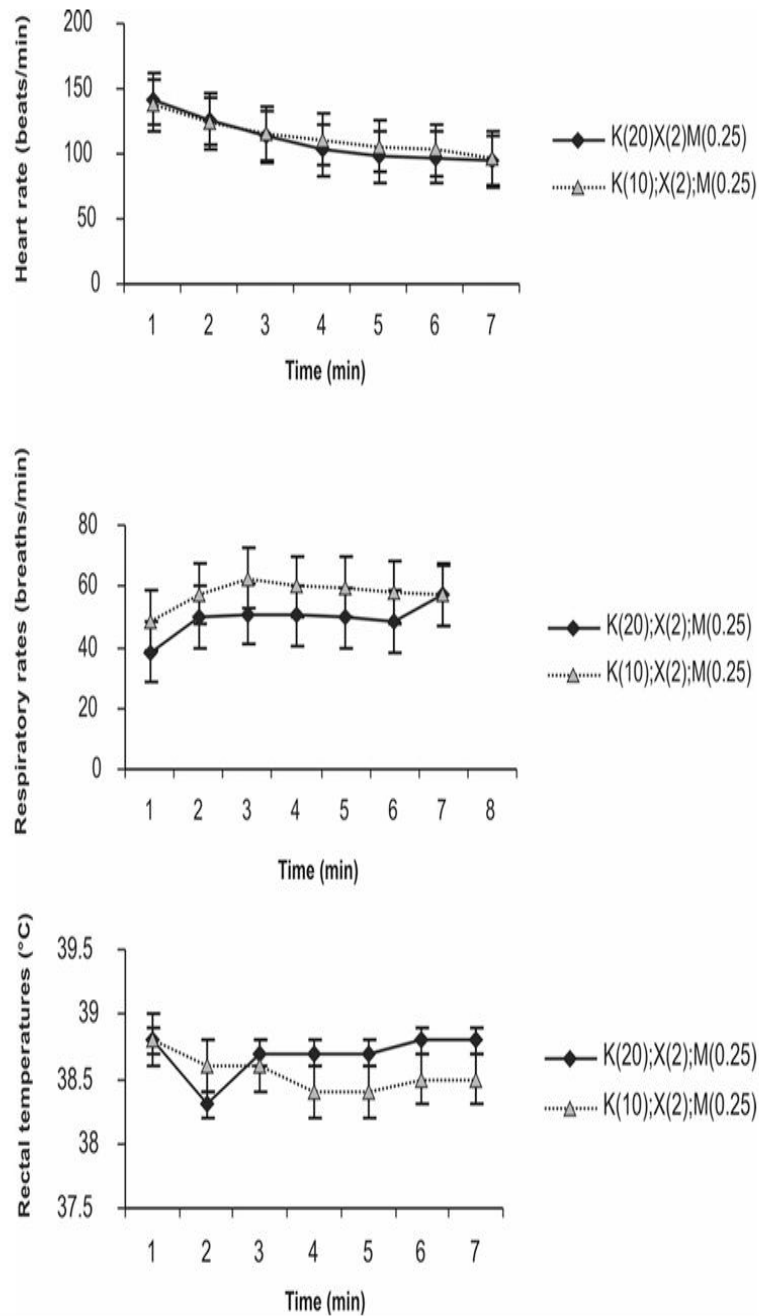


Figure 3: Changes in rectal temperatures, heart and respiratory rates following ketamine-xylazine-midazolam combination in pigs. Source: Ajadi *et al.*, 2008a

2.1.1.2 Ketamine anaesthesia in birds

Ketamine-xylazine combinations have been evaluated in several avian species, and are associated with increased blood pressure, decreased heart rate, and hypoxemia. A ketamine-midazolam combination assessed in mallard ducks (*Anas platyrhynchos*) was associated with moderate sedation and only produced anaesthesia and analgesia at very high dosages. Ajadi *et al.*, (2009b) evaluated the influence of midazolam on ketamine-xylazine combinations to determine if addition of midazolam would improve the quality of anesthesia in guinea fowls (Table 4 and Figure 4). It was observed that intramuscular administration of midazolam improved the anaesthetic quality of ketamine – xylazine combination in guinea fowls without adversely affecting safety (Ajadi *et al.*, 2009b) and thus recommend the combination for surgery of short duration in birds

Table 3. Comparison of anesthetic indices in guinea fowl after administration of ketamine-xylazine or ketamine-xylazine-midazolam combinations

Anesthetic indices	Group KX, min (n = 10)	Group KXM, min (n = 10)
Onset of anesthesia	3.2 ± 1.3	1.3 ± 0.15
Duration of analgesia	0	37.4 ± 4.8*
Duration of recumbency	56.4 ± 5.4	91.4 ± 7.6*
Recovery time	26.3 ± 8.9	18.6 ± 5.6

Source: Ajadi *et al.*, 2009b

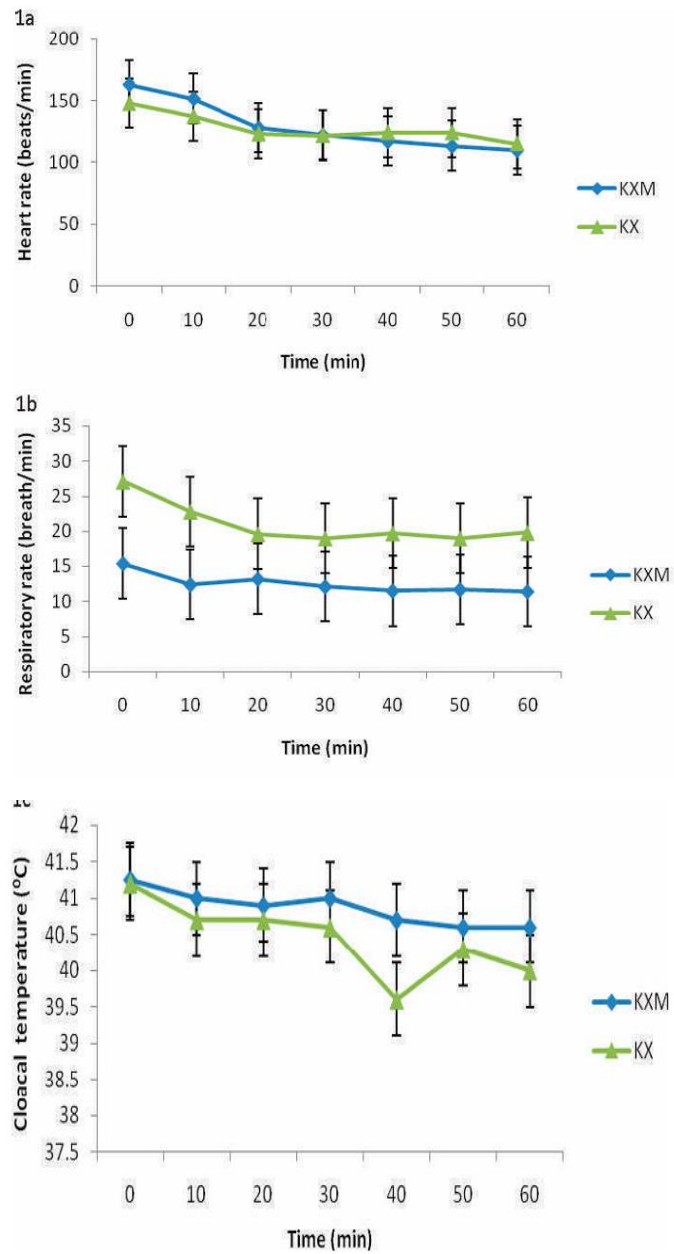


Figure 4: Changes in heart rate (a), respiratory rate (b), and cloaca temperature (c) after either ketamine and xylazine or ketamine-xylazine-midazolam combination in guinea fowl.

Source: Ajadi *et al.*, 2009b

2.1.2 *Studies on tramadol*

Tramadol is a dual-action analgesic drug with both opioid and non-opioid activity that is widely used for the control of acute and chronic pain in dogs and cats (Dominguez-Oliva *et al.*, 2021). It is a commonly prescribed opioid for dogs and cats in most of the countries of the world. The widespread administration of tramadol may be attributed to its low cost and less stringent regulatory restrictions compared to other opioids in many countries. Tramadol has been used as a premedicant to reduce the dose of induction and maintenance agents (Meunier *et al.*, 2019), postoperative pain management (Zhang *et al.*, 2017; Donati *et al.*, 2021), and treatment of acute and chronic pain (Oliva *et al.*, 2019; Trettene *et al.*, 2023) in dogs and cats; premedication in pigs (Ajadi *et al.*, 2009a) and perioperative analgesia for castration in goats (Ajadi *et al.*, 2012a), and sheep (Ajadi *et al.*, 2017).

2.1.2.1 *Tramadol evaluation in pigs*

Owing to the potentials of tramadol to provide perioperative analgesia, Ajadi *et al.*, (2009a) evaluated the influence of premedication with tramadol on xylazine–ketamine anaesthesia in young pigs. It was observed that tramadol premedication at 5mg/kg improved the quality of anaesthesia induction, and increased the duration of antinociception in xylazine–ketamine anaesthetized young pigs without increasing duration of recumbency, nor causing additional depression of the physiological parameters measured (Figure 5). This was the first study that evaluated the use of tramadol in combination with ketamine – xylazine in pigs. The article has been cited over 40 times.

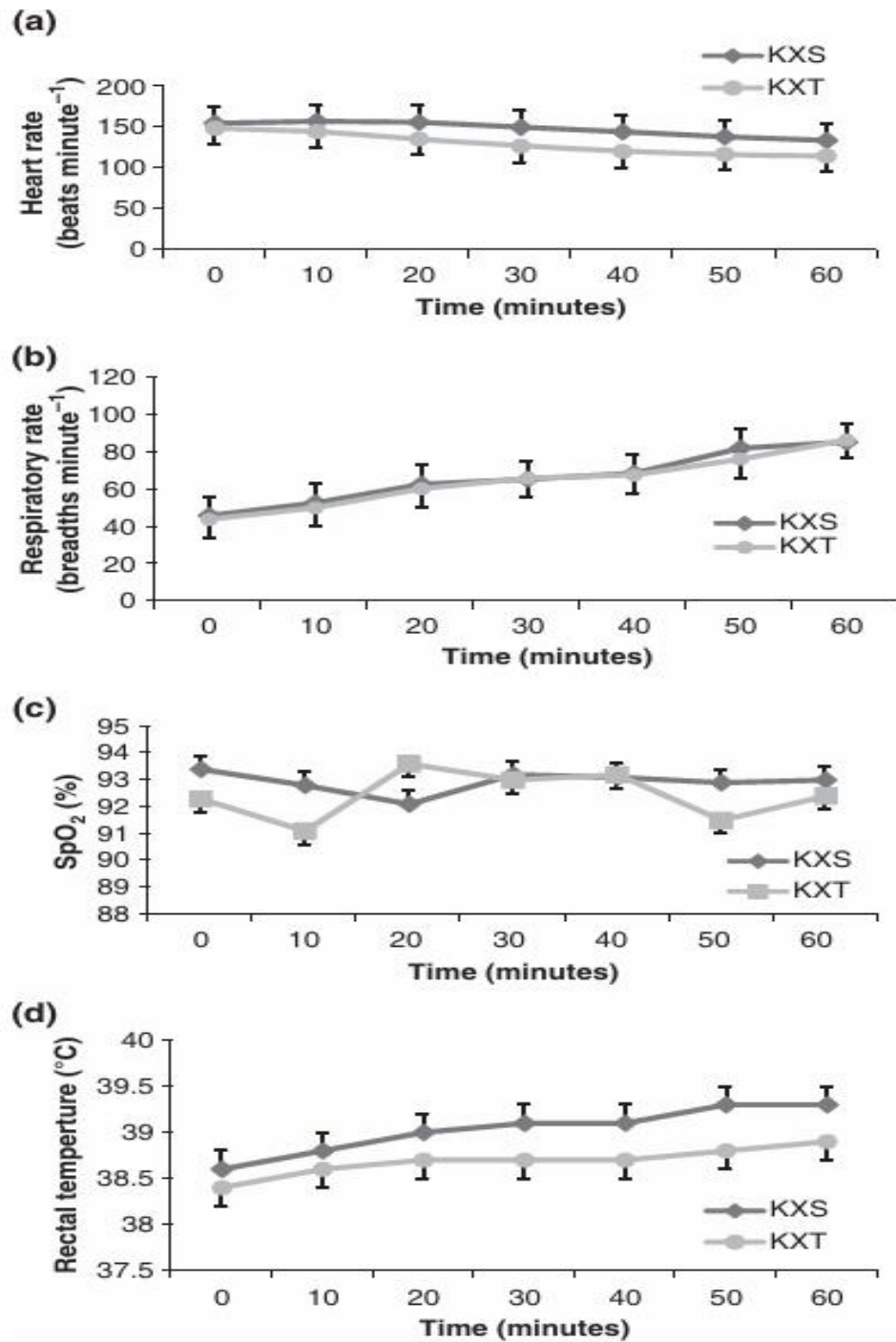


Figure 5: Changes in heart rate (a), respiratory rate (b), saturated oxygen pressure (c) and rectal temperature (d) following either ketamine-xylazine-tramadol or ketamine-xylazine-saline (KXS) combinations in growing pigs. Source: Ajadi *et al.*, 2009a

2.1.2.2 Evaluation of epidural tramadol in goats undergoing castration

Castration using rubber ring in lamb or kid is a common husbandry practice to improve meat quality. However, this practice has been associated with welfare concerns relating to pain. Owing to the potential perioperative analgesia of tramadol, Ajadi *et al.*, (2012a) evaluated the effect of a single epidural injection of tramadol on behavioural changes, anaesthetic indices, leucocyte parameters, erythrocyte sedimentation rates and plasma concentration of cortisol (Figure 6) in goats subjected to castration by high tension rubber band. The result of this study showed that lignocaine injection produced longer duration of antinociception with lower frequency of pain-associated behavioural changes; while treatment with epidural tramadol injection allowed the goats to continue grazing once the rubber ring had been applied. This study showed the lack of efficacy of tramadol through the epidural route to provide sufficient analgesia for castration in goats.

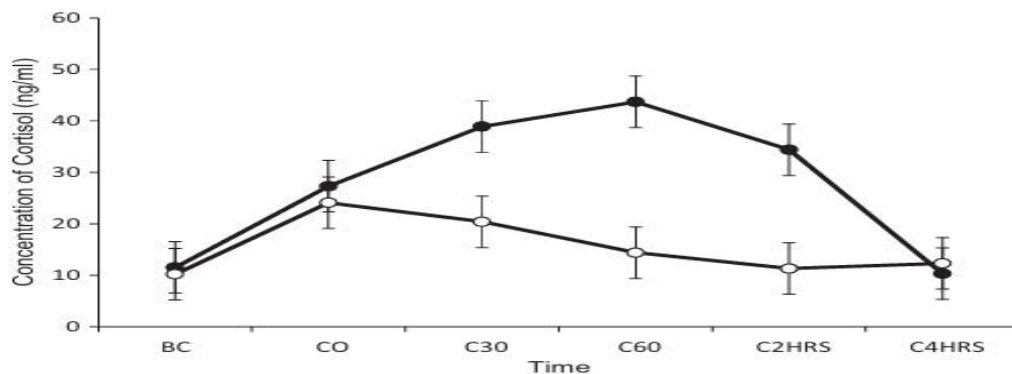


Figure 6: Changes in concentration of cortisol (mean (SD)) in plasma of 10 adult male Kano brown goats subjected to castration using high tension band following lumbosacral epidural injection of tramadol. Source: Ajadi *et al.*, 2012a

2.1.2.3 Evaluation of epidural tramadol in sheep undergoing laparotomy

Laparotomy is an invasive surgical procedure into the abdominal cavity that allows visual examination of abdominal organs and documentation and correction of pathologic abnormalities (Al- Sobayil & Ahmed, 2007; Hendrickson, 2007). Generally, it constitutes the single largest group of surgical operations carried out in ruminants (Haskell, 2004). Laparotomy is indicated for exploration of abdominal and pelvic cavities and other surgical procedures involving abdominal and pelvic organs. Other specific indications are Caesarean surgery, embryo transfer, rumenotomy, ovariectomy, abomasopexy, and ventral abdominal herniorrhaphy (Teixeira *et al.*, 2011).

Epidural injections of combinations of lignocaine and tramadol have been evaluated in goats, cattle and water buffalo (Habiban *et al.*, 2011; Dehkordi *et al.*, 2012; Ayman *et al.*, 2015) but not in sheep. The combination was found to produce a significantly longer duration of analgesia compared with epidural lignocaine injection alone. Thus, Ajadi *et al.*, (2017) evaluated the effect of tramadol-lignocaine combination on the anaesthetic indices and physiological parameters of in West African Dwarf (WAD) sheep undergoing laparo-ovariectomy. The results from this study showed that there were no significant differences in the duration of analgesia between epidural injection of lignocaine and that of lignocaine-tramadol mixture (Table 4). The rectal temperatures, respiratory rates and heart rates did not differ significantly ($p > 0.05$) between LIG-TRA and LIG, and as well as throughout the duration of study (Figure 7a – 7c). It was therefore concluded that tramadol did not improve the anaesthetic indices of epidural lignocaine injection in sheep, but increased the duration of recumbency with the tendency to cause bloat. The results of this study suggested that there are specie differences in the response to tramadol injections which is related to the pharmacokinetics of the drug.

Table 4: Anaesthetic indices of epidural lignocaine or lignocaine-tramadol mixture in West African Dwarf (WAD) sheep undergoing laparo-ovariectomy

Anaesthetic Indices	Lignocaine Group	Lignocaine – tramadol Group
	N = 5	N = 5
Onset of Action (min)	4.4 ± 2.8	1.4 ± 0.5
Duration of recumbency (min)	166.2 ± 30.6	192.6 ± 43.6
Duration of Analgesia (min)	119.4 ± 52.5	133.0 ± 19.5
Duration of Surgery (min)	42.2 ± 9.3	45.8 ± 9.4
Recovery Time (min)	34.0 ± 20.6	56.0 ± 48.0

Source: Ajadi *et al.*, 2017

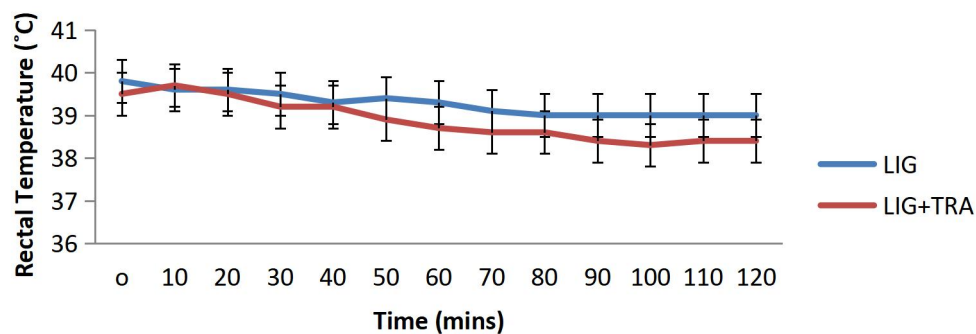


Figure 7a: Changes in Rectal temperature following epidural lignocaine or lignocaine-tramadol in WAD sheep undergoing laparo-ovariectomy. Source: Ajadi *et al.*, 2017

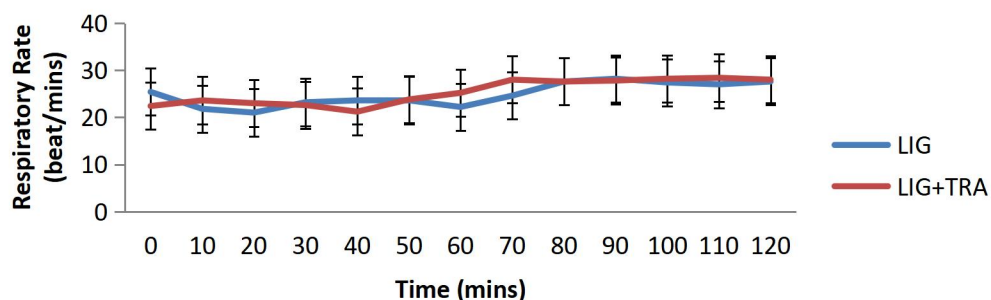


Figure 7b: Changes in Respiratory rate following epidural lignocaine or lignocaine-tramadol in WAD sheep undergoing laparo-ovariectomy. Source: Ajadi *et al.*, 2017

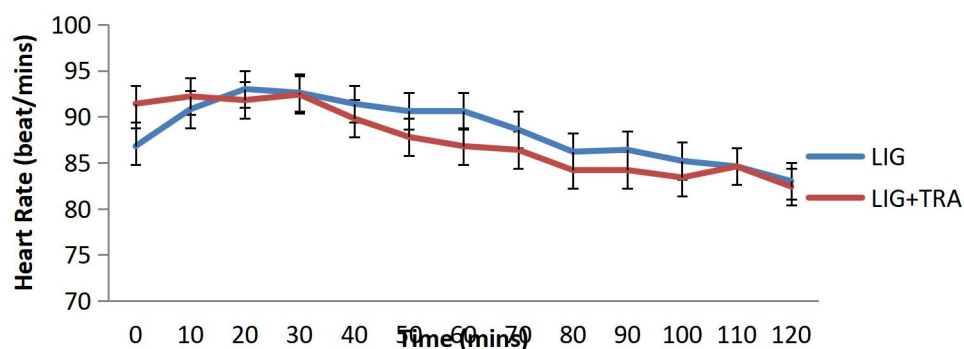


Figure 7c: Changes in Heart rate following epidural lignocaine or lignocaine-tramadol in WAD sheep undergoing laparo-ovariectomy. Source: Ajadi *et al.*, 2017

2.1.3 Evaluation of Gabapentin for pain control in dogs undergoing ovariohysterectomy.

Gabapentin is a structural analogue of gamma-aminobutyric acid, formulated for treatment of convulsion and neuropathic pain (Almeida *et al.*, 2023). Several clinical trials and meta-analyses showed that administration of gabapentin improves postoperative pain associated with abdominal hysterectomy and mastectomy in humans (Russo *et al.*, 2023). This led to the growing interest in the use of gabapentin for control of perioperative pain in veterinary medicine.

Although gabapentin has been used for pain control in dogs, there is insufficient evidence to support its analgesic efficacy. Ajadi *et al.* (2025) evaluated the efficacy and safety of oral gabapentin for perioperative pain control in dogs undergoing ovariohysterectomy (OVH). It was observed that premedication with oral gabapentin decreased postoperative pain scores in dogs undergoing elective OVH (Fig. 8). In addition, oral gabapentin did not alter the physiological parameters of the dogs undergoing elective OVH (Fig 9a – 9c). It was therefore recommended that oral gabapentin can be used as a component of multimodal analgesic agents for surgical procedure of healthy dogs in poor resource settings where access to true opioid analgesic is difficult or in cases where non-steroidal anti-inflammatory drug was contraindicated due for safety reasons.

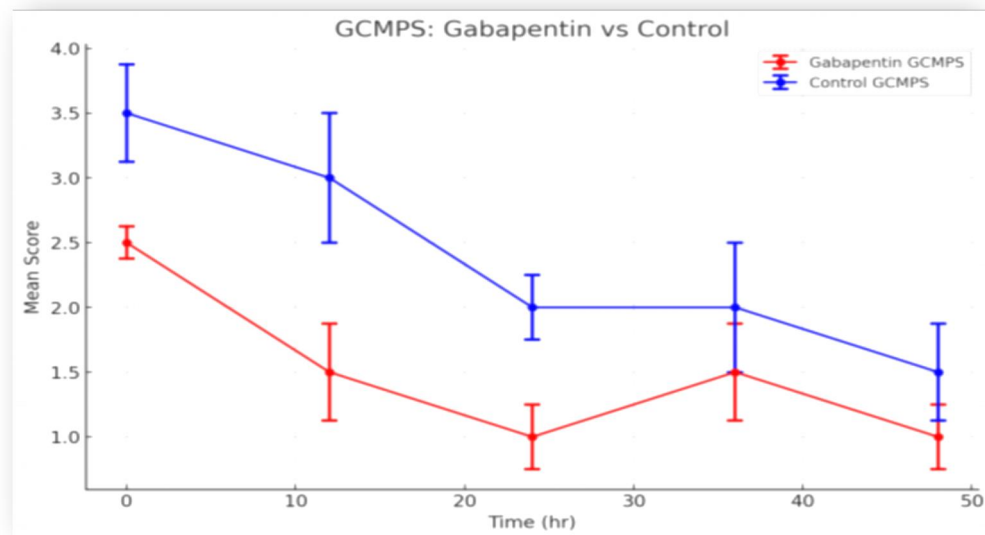


Fig. 8: Pain assessment scores of dogs subjected to elective OVH using the Glasgow Composite Pain Measure scale. Source: Ajadi *et al.*, 2025

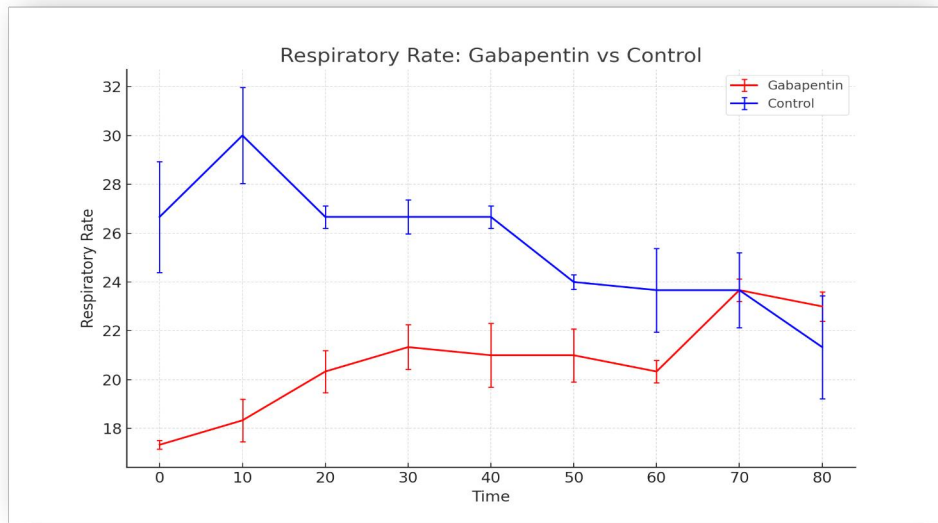


Fig. 9a: Respiratory rates of dogs undergoing elective OVH following premedication with either gabapentin or placebo (control group) and anaesthetized with propofol. Source: Ajadi *et al.*, 2025

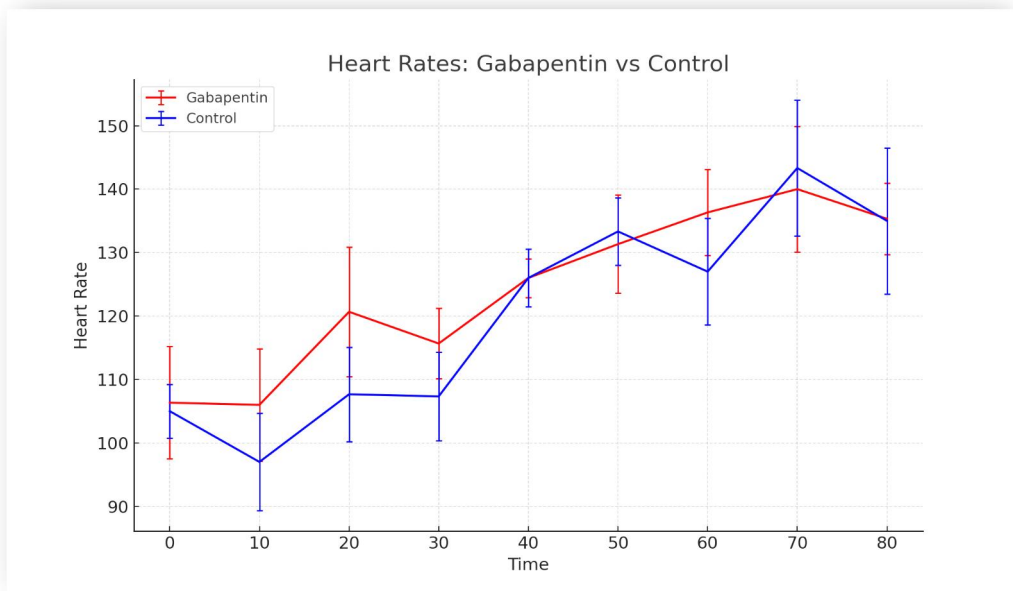


Fig. 9b: Heart rates of dogs undergoing elective OVH following premedication with either gabapentin or placebo (control group) and anaesthetized with propofol. Source: Ajadi *et al.*, 2025

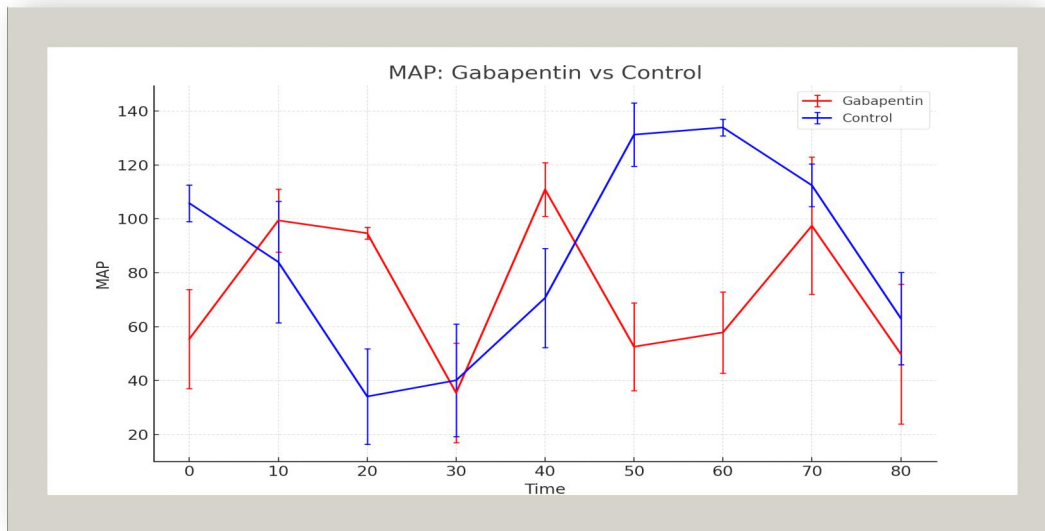


Fig. 9c: Mean arterial pressure of dogs undergoing elective OVH following premedication with either gabapentin or placebo (control group) and anaesthetized with propofol. Source: Ajadi *et al.*, 2025

2.2 Osteoarthritis: a cause of chronic musculoskeletal pain

Osteoarthritis (OA) is a degenerative joint disease characterized by damage to the articular cartilage and changes in the sub-chondral bone, and frequently accompanied by secondary synovitis (Lepine & Hayek, 2001). It is a complex disease that encompasses all the tissues within a joint and can affect multiple joints within the body. Osteoarthritis was historically regarded as a non-inflammatory arthritis, but new evidences have shown that there is an inflammatory component to OA (Scanzello *et al.*, 2008). While progressive destruction of articular cartilage with subsequent narrowing of the joint space is often considered a hallmark of OA, other intra-articular tissues are not spared.

The global prevalence of osteoarthritis (OA) has been estimated at 7.6% of the world's population in 2020, affecting approximately 595 million people (Courties *et al.*, 2024). This represents a significant increase of 132.2% since 1990. Osteoarthritis is more prevalent in

women than men and the prevalence increases dramatically with age. Forty- five percent of women over the age of 65 have symptoms of osteoarthritis, while radiological evidence is found in about 70 percent of those over 65 years (Ding *et al.*, 2024). Osteoarthritis of the knee is a major cause of mobility impairment, particularly among females. It was estimated that approximately 10 percent of the world's population who are 60 years or older have symptomatic problems that can be attributed to OA. The prevalence in developing countries is variable with some studies showing lower prevalence rates while others show similar levels to those in developed countries (Owoyemi *et al.*, 2025).

The exact prevalence of OA is difficult to determine because of the lack of use of standardized criteria. In epidemiological studies, OA is often described by radiological criteria. However, radiological disease especially when mild, has poor correlation with the presence of pain. In all populations studied so far, the prevalence of knee OA is higher than that of hip OA but this is more marked in Asian populations (Li *et al.*, 2024a).

Pain is the most important presenting sign of OA. The cause of pain is often unclear and varies in severity, location and precipitating cause between individuals. Pain in osteoarthritis has been suggested to result from erosion of joint cartilage, resulting in bone contacting bone without an intervening cushion. Pain signals are generated by sensory nerve endings intrinsic to the subchondral bone. The relevant nociceptive nerve fibers enter the bone marrow through penetrating neurovascular foramina, mostly located at the bone end, and terminate within Haversian canals in epiphyseal subchondral bone. Unlike many other pain conditions in which the underlying injury typically heals or resolves, OA is a disease that does not resolve. Thus, OA is typically accompanied by chronic pain.

2.2.1 Studies on Canine Osteoarthritis

Clinical parameters of OA such as pain, stiffness, and functional disability can be measured relatively simple. However, evaluation of structural changes demands much greater effort. Imaging technique and biomarker analyses are done to obtain information on structural changes in OA joints (Frost-Christensen *et al.*, 2008). Inflammatory markers such as erythrocytes sedimentation rates (ESR) have been evaluated in humans with osteoarthritis and have been shown to be mildly elevated in osteoarthritic patients (Dieppe and Lim 1998).

As part of our efforts towards early diagnosis of osteoarthritis, Ajadi *et al.*, (2018) evaluated the changes in erythrocyte sedimentation rates (ESR) and blood leukogram during experimental knee osteoarthritis in dogs to determine if these parameters can be used as a biomarker for monitoring the progression of osteoarthritis. Our results revealed that both ESR and neutrophil/lymphocyte (N/L) ratio increased from week 0 to week 12 of OA. However, total white bloods cell count (tWBC), neutrophil and lymphocyte counts did not differ significantly (Fig. 10). It was concluded that both ESR and N/L ratio might be useful in monitoring progression of OA in dogs.

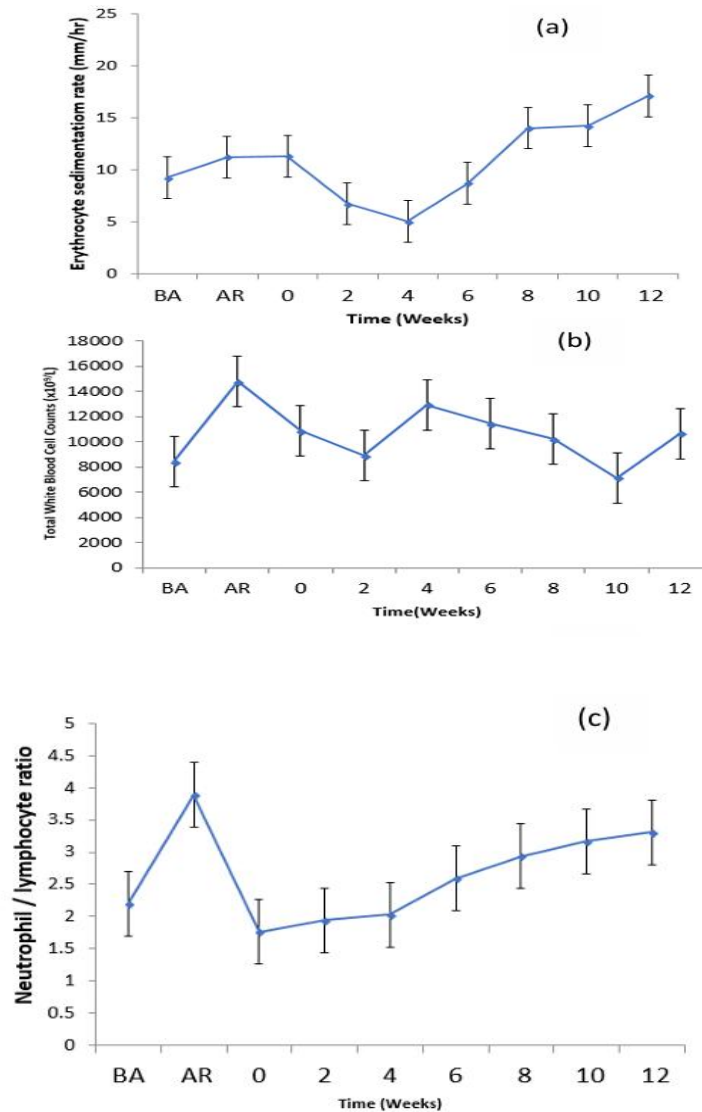


Figure 10: ESR (a), WBC (b) and N/L ratio (c) of dogs before arthrotomy (BA), immediately after arthrotomy (AR), immediately after confirmation of osteoarthritis (Week 0) and at two weeks interval up to a period of twelve weeks. Source: Ajadi *et al.*, 2018

2. 2. 2 Changes in lipid metabolism during osteoarthritis

Altered lipid metabolism has been implicated as a critical player in OA development (Mehta *et al.*, 2006). It has been shown that the lipid content of the superficial layer of normal articular cartilage increases with age (Simopoulou *et al.*, 2007). Lipid deposition, seen early in the OA process and before any histological changes, is considered to reflect lipid involvement in the

pathogenesis of OA (Simopoulou *et al.*, 2007). Furthermore, recent population studies have provided support for the hypothesis that serum cholesterol is a systemic risk factor for OA and an association has been observed between high serum cholesterol levels and radiological OA (Davies-Tuck *et al.*, 2009; Dore *et al.*, 2012). Lipid peroxidation has been linked to the structural destabilization of cartilage matrix, while lipid peroxidation inhibitors such as ascorbic acid and vitamin E have been shown to exert a protective role in extracellular matrix degradation (Henrotin *et al.*, 2003).

The effect of lipid metabolism on the development of OA may be initiated through vascular pathology on the sub-chondral bone (Dore *et al.*, 2012). These may result in subchondral bone ischemia which can contribute to decreased nutrient supply to the overlying cartilage plate. Subchondral bone ischemia can also result in osteocyte death, leading to bone resorption, reducing the viability of subchondral bone (Findlay, 2007).

In order to further elucidate the association between OA and lipid metabolism, Ajadi *et al.*, (2012b) evaluated the changes in lipid profiles of dogs following experimental OA and its relationship with the progression of the disease. Blood was obtained for determination of total plasma cholesterol (TC), triglycerides (TRIG), high density lipoproteins (HDL) and low density lipoproteins (LDL) fortnightly for twelve weeks. Radiographic scores (RAS), gait assessment score (GAS), TC, TRIG, HDL and LDL were compared by means of ANOVA. The blood TC of the dogs progressively decreased from week 4 to week 12 of OA (Table 5). Also, the LDL decreased progressively from the baseline value until the 10th week, while the HDL decreased progressively from baseline up to week 2 of experimental knee OA, and thereafter increased until the 10th week. Correlation between parameters (Table 6) showed that both TC and TRIG were negatively correlated to RAS following experimental OA in the dogs. Similarly, both TC

and TRIG were negatively correlated to the GAS in the dogs. It was therefore concluded that OA is associated with altered lipid profile in dogs.

Table 5: Short-term changes in blood lipid parameters (TC: total cholesterol; TRIG: triglycerides; LDL: low density lipoprotein; HDL: high density lipoprotein), gait assessment score (GAS) and radiographic score (RAS) following experimental knee osteoarthritis in dogs

Time intervals	TC (mmol/L)	TRIG (mmol/L)	LPL (mmol/L)	HDL (mmol/L)	GAS	RAS
Before arthrotomy	2.8 ± 0.6	1.5 ± 0.3	1.1 ± 0.3	2.1 ± 0.7	ND	0
1 day after arthrotomy	4.1 ± 0.5**	1.2 ± 0.2	0.7 ± 0.3	2.6 ± 0.3	ND	0
Week 0*	4.0 ± 0.7**	1.4 ± 0.2	0.6 ± 0.4	2.6 ± 0.5	17.0 ± 5.5	1.2 ± 0.5
Week 2	2.8 ± 0.8	1.3 ± 0.1	0.8 ± 0.4	2.3 ± 0.6	18.4 ± 6.4	1.6 ± 0.5
Week 4	4.1 ± 0.5**	1.4 ± 0.4	0.6 ± 0.2	3.1 ± 0.6	21.1 ± 2.8	2.8 ± 0.5
Week 6	3.8 ± 0.5	1.1 ± 0.2	0.7 ± 0.2	2.9 ± 0.8	17.4 ± 6.1	3.2 ± 0.8
Week 8	3.3 ± 0.9	1.0 ± 0.4	0.7 ± 0.2	2.4 ± 0.6	16.4 ± 7.2	3.0 ± 0.8
Week 10	3.0 ± 0.5	1.5 ± 0.2	0.5 ± 0.2	3.1 ± 0.7	16.4 ± 7.2	2.8 ± 0.5
Week 12	3.2 ± 1.1	1.1 ± 0.3	1.1 ± 0.2	2.4 ± 0.5	17.0 ± 6.6	2.8 ± 0.8

* After radiographic confirmation of OA; ND – not determined; ** P < 0.05

Source: Ajadi *et al.*, 2012b

Table 6: Pearson's correlation coefficients of blood lipid parameters, gait assessment score (GAS) and radiographic score (RAS) following experimental osteoarthritis in dogs. In brackets, the levels of significance are presented.

Parameters	TC	TRIG	LDL	HDL	GAS	RAS
TC		-0.185 (0.691)	0.491 (0.263)	0.601 (0.153)	0.328 (0.473)	0.458 (0.302)
TRIG	-0.185 (0.691)		-0.445 (0.317)	0.739 (0.058)	0.071 (0.850)	-0.125 (0.789)
LDL	0.491 (0.263)	-0.445 (0.317)		-0.510 (0.243)	0.027 (0.954)	0.271 (0.556)
HDL	0.601 (0.153)	0.739 (0.058)	-0.510 (0.243)		0.318 (0.487)	0.286 (0.533)
GAS	0.328 (0.473)	0.071 (0.850)	0.027 (0.954)	0.318 (0.487)		0.153 (0.496)
RAS	-0.458 (0.302)	-0.125 (0.789)	0.271 (0.556)	0.286 (0.533)	0.153 (0.496)	

Source: Ajadi *et al.*, 2012b

2.2.3 Glucosamine and snail mucin as treatment for osteoarthritis

Non-steroidal anti-inflammatory drugs are the first line of drug in the pharmacological management of osteoarthritis (Bergh and Budberg, 2005). Majority of NSAIDs act by competitive inhibition of the COX enzymes, so the effects are reversible after drug concentration decrease when drug dosing is discontinued. The exception is aspirin, which in addition to competitive inhibition, irreversibly inhibits COX through acetylation of a serine residue near the enzymes active site (Budberg, 2009).

Following the publication of *The Arthritis Cure* in 1997 (Theodosakis *et al.*, 1997), there was an explosion of interest in glucosamine as a treatment for osteoarthritis. Anecdotal reports emerged as to the benefits of glucosamine, and contentions were made that traditional medicine was

overlooking a safe and simple treatment in favour of products developed by the pharmaceutical industry (McAlindon, 2003). Since the initial publications, there have been large meta-analysis, as well as tissue culture and animal model data which support the benefit of glucosamine in osteoarthritis (Hungerford and Jones, 2003). Studies in veterinary medicine showed that the animal most commonly treated with glucosamine is the dog (Tilburt *et al.*, 2008). In addition, the clinical efficacy of glucosamine was deemed good or excellent in alleviating pain by 83 percent of Veterinarians, and for improving mobility, it was rated good or excellent by 89 percent of respondents (Anderson *et al.*, 1999). In the horse, significant recovery from lameness and overall clinical condition was reported following treatment with glucosamine (Hansen *et al.*, 2001).

The land snail has been used in medicine since antiquity. Mucus from snail has been reported to slow down the inflammation of the lungs (Bonnemain, 2005). Also the lecithin from the land snail has been used as a prognostic indicator for some cancers such as those of the breast, stomach and colon (Dwek *et al.*, 2001). Acharan sulphate, a mucin from *Achatina fulica* has been demonstrated to act as an angiogenesis inhibitor and as an antitumor agent through the inhibition of matrix metalloproteinase activity (Lee *et al.*, 2003). Mucin from jelly fish has been described to have potential disease-modifying effects on osteoarthritis in rabbit cartilage (Ohta *et al.*, 2009).

With the promise that the mucin from snail can be a potential disease modifying osteoarthritis agent (DMOA), Ajadi *et al.*, (2013) compared the potential osteoarthritic effect of snail mucin to that of glucosamine in an experimental model of knee OA in dogs. Twenty adult mongrels with mean body weight (12.4 ± 1.8 kg) were used. Experimental OA was induced surgically using the groove model. The dogs were randomly divided into three groups following radiographic evidence of OA. Efficacy of the treatment was assessed by changes in plasma IL-6 and MMP-3,

while safety was determined using the changes in packed cell volume (PCV), total white blood cell counts (WBC) and observable adverse reactions associated with treatments. In the study, plasma IL-6 and MMP-3 were significantly ($P < 0.05$) lower both in glucosamine-treated and snail mucin-treated dogs up to week 4 of treatment when compared with the control group (Fig 11 and 12). However, there were no significant ($P > 0.05$) differences in IL-6 and MMP-3 between the two treatment groups. It was concluded that both oral glucosamine and IM injection of snail mucin comparably modified the progression of OA. However, owing to the adverse reaction noted with IM injection of snail mucin, further study is required to determine the most appropriate route of its administration

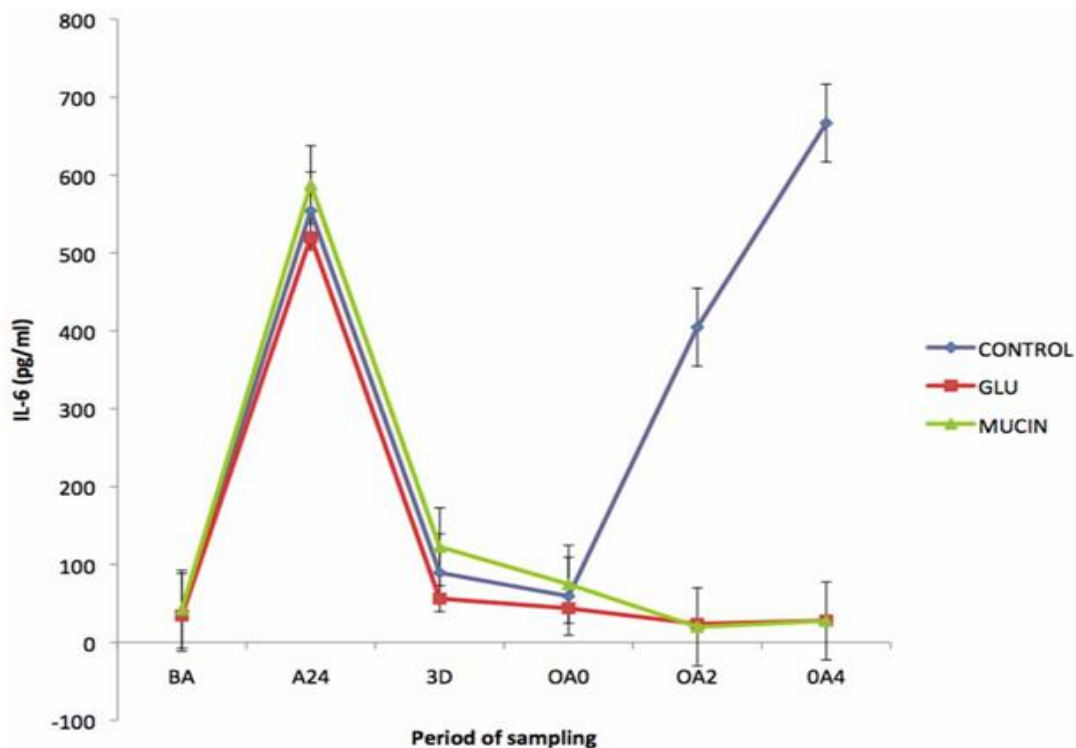


Figure 11: Changes in plasma IL-6 in dogs treated with either oral glucosamine or intramuscular injection of snail mucin following experimental osteoarthritis. Source: Ajadi *et al.*, 2013

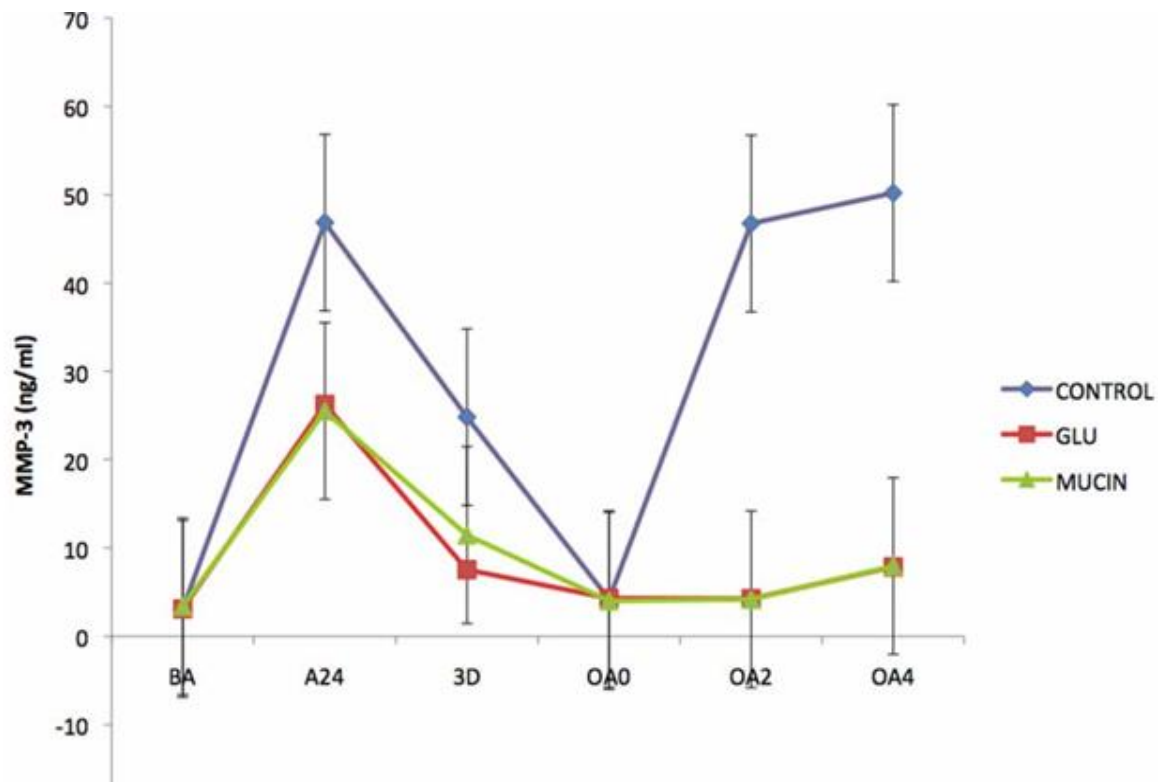


Fig. 12: Changes in plasma MMP-3 in dogs treated with either oral glucosamine or intramuscular injection of snail mucin following experimental osteoarthritis. Source: Ajadi *et al.*, 2013

2.2.4 Hip dysplasia: a major cause of osteoarthritis in dogs

Canine hip dysplasia (CHD) is a complex developmental disease of the coxo-femoral joints of rapidly growing large breeds of dogs characterized by varying degree of laxity resulting in subluxation of the femoral head, shallow acetabulum and flattening of the femoral head (Baldinger *et al.*, 2020). This leads to inflammatory response with subsequent secondary osteoarthritis. It is one of the most frequent orthopaedic illnesses in dogs, accounting for 30% of all orthopaedic cases (Ajadi *et al.*, 2018). Canine hip dysplasia is a multifactorial disease caused by genetic, environmental and epigenetic factors (Mikkola *et al.*, 2019). Excluding afflicted dogs from breeding has been found to lessen the occurrence of hip dysplasia in various nations due to its genetic potential (Baldinger *et al.*, 2020).

Radiological examination of coxo-femoral joint is done in various breeds with the purpose of assessing and determining the genetic carriers for hip dysplasia in order to remove such dogs from breeding (Ohlerth *et al.*, 2019, Baldinger *et al.*, 2020). In order to determine the prevalence of hip dysplasia in Boerboel dogs, Ajadi *et al.*, (2023) reviewed the ventrodorsal and flexed lateral hip radiographs of apparently normal Boerboel dogs presented for hip certification between 2016 and 2020 (Plate 1a & b, 2a & b). The radiographs were graded using modified Federation Cynologique International grading system. Prevalence of HD was expressed as percentages, while age and sex difference in prevalence of HD were compared using chi-square test. Relative percentages were calculated for HD grades C, D, and E. Differences were considered significant at $P \leq 0.05$. Median and modal age for the dogs was 2 years with age ranging between 1 and 6 years. Twenty seven (42.2%) were non dysplastic, while 37(57.8%) were dysplastic. Dogs with grade A accounted mostly for the non-dysplastic dogs, while dogs with grade C accounted mostly for dysplastic dogs (Table 7). Prevalence of HD was significantly ($p < 0.05$) higher in female than male (Table 8), however, there was no significant ($p > 0.05$) difference in HD prevalence between dogs 1 – 2 years of age and those that are 3 – 6 years of age (Table 9). Dogs with grade C have the highest relative percentage among the dysplastic grades (Table 9). It was concluded that HD prevalence (57.8%) in Boerboel dogs is high and dogs with grade C accounted for most of the HD cases

Table 7: Prevalence of different hip grade in Boerboel dogs

Grades	Male	Female	Total	Prevalence (%)
A	9	9	18	28.1
B	2	7	9	14.1
C	8	11	19	29.7
D	8	2	10	15.6
E	2	6	8	12.5
Total	29	35	64	100

Source Ajadi *et al.*, 2023

Table 8: Sex prevalence of hip dysplasia in Boerboel dogs

Sex	Normal	Dysplastic	Prevalence (%)
Male	11	18	28.1
Female	16	19	29.7
Total	27	37	57.8

P value $\equiv$ 0.003 Source Ajadi *et al.*, 2023

Table 9: Age prevalence of hip dysplasia in Boerboel dogs

Age (Years)	Normal	Dysplastic	Prevalence (%)
1 - 2	16	24	37.5
4 - 6	11	13	20.3
Total	27	37	57.8

P value $\equiv$ 0.18 Source: Ajadi *et al.*, 2023

Table 10: Relative percentage of different grades of hip dysplasia in Boerboel dogs

Grades	Relative Percentage (%)
C	51.4
D	27.0
E	21.6



Plate 1a: Extended ventrodorsal radiograph of a Boerboel dog with grade A (Excellent) hip.

Source: Ajadi *et al.*, 2023



Plate 1b: Flexed lateral radiograph of a Boerboel dog with grade A (Excellent) hip.

Source: Ajadi *et al.*, 2023



Plate 2a: Extended ventrodorsal hip radiograph of a Boerboel dog with grade E (severe) hip dysplasia. Note the luxation of the femoral head and severe remodelling of the femoral head and the acetabulum

Source: Ajadi *et al.*, 2023



Plate 2b: Flexed lateral hip radiograph of a Boerboel dog with grade E (severe) hip dysplasia. Note the complete luxation of the femoral head and severe remodeling of the acetabulum

Source: Ajadi *et al.*, 2023

2.2.5 Prevalence of elbow dysplasia in Boerboel dogs

Elbow dysplasia (ED) is a developmental, multifactorial, polygenic disease of rapidly growing, large breed dogs characterized by joint incongruity, primary lesions (Fragmented Medial Coronoid Process (FMCP), Un-united Anconeal Process (UAP), Osteochondritis (OCD) of humeral epicondyle), and secondary osteoarthritis (Michelsen, 2013). It is the major cause of forelimb lameness in dogs. The exact aetiology of medial coronoid disease is not fully clear, but it is thought to be due to lesions of the subchondral bone with abnormal loading leading to primary osseous fissuring, micro crack formation and elbow incongruence (Baers *et al.*, 2019). Un-united anconeal process results in medial to lateral instability of the anconeal process causing irritation, deterioration and secondary degeneration of the articular surfaces of the elbow joint (Michelsen, 2013).

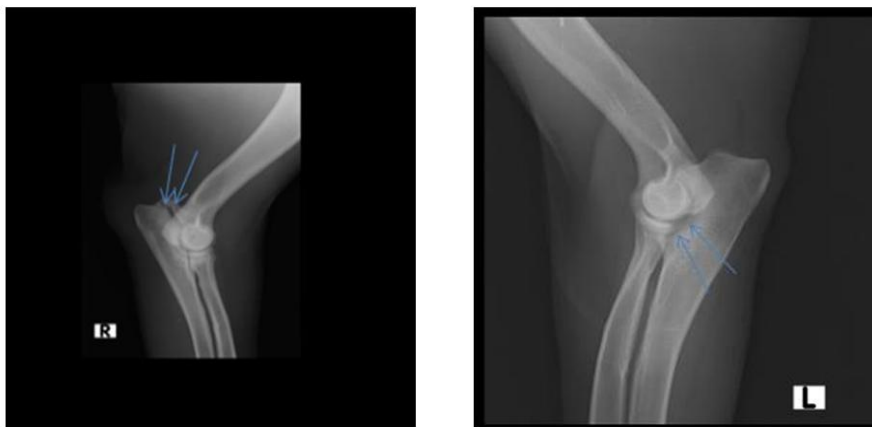
The Boerboel dog is a rapidly growing big Mollosier type of dog reported to be as a result of crossbreed between Bullmastiff and local South African dog breeds like Bullenbijter (Ajadi & Doyin-Dada, 2019). In spite of the susceptibility of Boerboels to ED, there is dearth of information on the prevalence of ED in the breed. In order to determine the prevalence of ED in Boerboel dogs, Ajadi *et al.*, (2021) reviewed the radiographs of the elbow joint of dogs presented for hip and elbow certification between 2016 and 2020 (Plate 3a & b). Radiographs were graded using international elbow working group (IEWG) criteria and grades 0-3 assigned to each joint. Elbow dysplasia prevalence expressed as percentages was obtained by dividing the number of dogs with grades 1, 2 and 3 by total number of dogs. Age and sex difference in ED prevalence were compared using chi-square test. Differences were considered significant at $P \leq 0.05$. Mean age of the dogs was 2.3 ± 0.6 years. Thirty-six (56.3%) dogs were graded as non-dysplastic, while 28(43.7%) were graded as dysplastic, with grade 3 (46.4%) accounting for majority of ED

cases (Table 11). There were no significant ($p > 0.05$) difference in sex and age prevalence of ED in the breed. In conclusion, ED prevalence (43.7) in Boerboel dog is high with majority of dogs having severe grade. Widespread phenotypic screening and strict breeding restrictions are recommended to control the disease in the breed.

Table 11: Prevalence of different elbow grade in Boerboel dogs

Elbow Grade	Male	Female	Total	Prevalence (%)
0	14	22	36	56.3
1	3	4	7	10.9
2	6	2	8	12.5
3	4	9	13	20.3
Total	27	37	64	100

Source: Ajadi *et al.*, 2021



Plates 3a & b: Extended latero-medial radiographs of Boerboel dogs showing un-united anconeal process (right radiograph) and fragmented coronoid process (Left radiograph). Source: Ajadi *et al.*, 2021

2.3 Animals' welfare

The welfare of an animal includes its physical and mental state. A good animal welfare implies both fitness and a sense of well-being. Any animal kept by man, must at least, be protected from unnecessary suffering. These include:

1. Freedom from hunger and thirst by providing ready access to fresh water and diet to maintain health and vigor.
2. Freedom from discomfort by providing an appropriate environment including shelter and a comfortable resting area.
3. Freedom to express normal behavior by providing sufficient space, proper facilities and company of the animal's own kind.
4. Freedom from fear and distress by ensuring conditions and treatments which avoid mental suffering.
5. Freedom from pain, injury or disease through prevention, rapid diagnosis, and treatment.

2.3.1 *Transportation stress: an animal welfare issue*

Road transportation stress is the acquired stress condition of animals during transportation by road in which the rules and regulations governing normal transportation welfare are not adhered to (Minka and Ayo, 2010). Most of the changes in the body parameters of transported animals are as a result of handling, loading and confinement of animals during transportation, as well as, during unloading of the animals. Other stress factors include improper restraint of the animals and non-provision of food and water during transportation (Maria *et al.*, 2007). The stress factors occurring during transportation cause physical and physiological exertion which disrupt metabolism of animals. The severity of the metabolic changes following transportation stress is

dependent on factors such as size and type of vehicle used, duration of journey, sex of the animal, age of the animal, time of transportation and the climatic condition during transportation (Ritter *et al.*, 2008).

In Ogun State, the cattle slaughtered are often transported in open, medium sized trucks over a journey of about two hours from the trans-boundary area to the central abattoir without due regard for the welfare of the animals. In order to determine the effect of transportation on the physiological status of cattle slaughtered in Abeokuta, Ajadi *et al.*, (2012c) obtained blood samples from sixty two cattle after unloading at the lirage for the determination of plasma cortisol, blood glucose and leukocyte indices, and compared the results with that of two cattle after returning from grazing (control). The result of the study revealed that plasma cortisol concentration was significantly ($P < .001$) higher in road- transported cattle (Group A) than the control (Table 12). Similarly, the blood glucose was significantly ($P < 0.05$) higher in road transported cattle than the control. However, there were no significant differences in total white blood cell counts (tWBC), absolute neutrophil counts (NEUT), absolute lymphocyte counts (LYM) and neutrophil lymphocyte ratio (N/L) between Group A and Group B cattle (Table 12). In addition, the plasma cortisol concentration and the blood glucose levels were significantly ($P = 0.05$) and positively correlated ($r = 0.230$) among the cattle (Table 13).

The results from this study showed that road transportation of cattle without adequate consideration of the cattle welfare is stressful with the attendant physiological responses such as elevated plasma concentration of cortisol and blood glucose and a tendency towards decrease in immune response of the animal if the journey is prolonged further. This effect if not prevented can lead to significant morbidity and mortality which may adversely affect the carcass quality of the animal after slaughter.

Table 12: Changes in plasma concentration of cortisol, blood glucose and leukocyte parameters of white Fulani cattle transported on road for one hour and non-transported cattle

Parameters	Cattle	
	Road Transported Cattle (Group A)	Non-Transported Cattle (Group B)
Plasma Cortisol (ng/ml)	53.7 ± 17.6	9.1 ± 3.9**
Blood Glucose (mg/dl)	112.9 ± 13	87 ± 8.3*
Total white blood cell counts (x 10 ⁶ /l)	8002 ± 3567	9280 ± 3568
Absolute neutrophil counts (x 10 ⁶ /l)	4321 ± 2318	5026 ± 2083
Absolute neutrophil counts (x 10 ⁶ /l)	3403 ± 1212	3816 ± 1757
Neutrophil/lymphocyte ratio	1.2 ± 0.28	1.5 ± 0.38

* P< 0.05,

Source: Ajadi *et al.*, 2012c

Table 13: Pearson correlation coefficient of selected blood parameters in cattle following one hour transportation

Parameters	CORT	GLU	tWBC	NEUT	LYM	N/L
Plasma cortisol (CORT)						
r	1	.230	.078	.111	.036	.135
p	1	.0508*	.500	.359	.765	.264
Blood Glucose (GLU)						
r	.230	1	-.072	-.038	-.123	.015
p	.050*	1	.556	.756	.312	.902
Total white blood cell counts (tWBC)						
r	.078	-.072	1	.958	.954	.766
p	.520	.556	1	.000*	.000*	.000*
Absolute neutrophil counts (NEUT)						
r	.111	-.038	.985	1	.892	.856
p	.359	.756	.000*	1	.000*	.000*
Absolute lymphocyte counts (LYM)						
r	.036	-.123	.954	.892	1	.553
p	.756	.312	.000*	.000*	1	.000*
Neutrophil-lymphocyte ratio (N/L)						
r	.135	.015	.766	.856	.553	1
p	.264	.264	.000*	.000*	.000*	1

Source: Ajadi *et al.*, 2012c

2.3.2 Burnout among workers: an important workplace welfare issue

Burnout is a chronic workplace stress syndrome characterized by emotional exhaustion, depersonalization and reduced personal accomplishment (Li *et al.*, 2024b). The personal cost of burnout include feelings of lonesomeness with tendency to commit suicide, anxiety, apathy, aggressive mood disorders, and frequent irritability, cardiovascular and respiratory symptoms, reduced resistance to infection, back and neck pain (Faustino *et al.*, 2009). The consequences of burnout on the employing institution include decreased productivity, increased interpersonal conflict with peers, and a tendency to abandon job. Several studies have shown that the number of workers reporting burnout is increasing in both sexes (Neil *et al.*, 2022)

Ajadi in conjunction with others carried out a study to determine the prevalence of burnout syndrome among Veterinarians in Nigeria (Adebayo *et al.*, 2009). Questionnaire comprising Copenhagen burnout inventory instrument, demographic, occupational data and health records were administered to fifty Veterinarians. The respondents were mainly men (74%), aged between 31-40 years (42%). Most of the respondents were married (90%), had higher degree in addition to their veterinary degree (54%), and had been in practice for 11-20 years (42%), been on their present job for over 10 years (42%) and work for 30-45 hours per week. Sixteen (32%) of the respondents were not satisfied with their job conditions (Table 14).

Table 14: Job satisfaction among responding veterinary surgeons

Job Satisfaction Indices	NS	%	SS	%	HS	%
Satisfaction with job	4	8	12	24	34	68
Satisfaction with salary	10	20	19	38	21	42
Satisfaction with progress at work	9	18	19	38	22	44
Satisfaction with work-place	13	26	15	30	22	44
Satisfaction with promotion criteria	13	26	10	20	27	54
Satisfaction with control at work-place	9	18	16	32	25	50

Keys: NS: Not satisfied SS: Somewhat satisfied HS: Highly satisfied Source: Adebayo *et al.*, 2009

Major areas of dissatisfaction include salary (20%), management of work place (26%) and promotion criteria (26%) (Table 15).

Table 15: Degree of burnout among responding veterinary surgeons

Burnout Indices	N	%	S	%	A	%
Work is emotionally exhausting	16	32	20	40	14	28
Work is physically exhausting	12	24	24	48	14	28
Work is often frustrating	25	50	16	32	9	18
Degree of burnout	34	68	6	12	10	20

Keys: N: Never S: Sometimes A: Always Source: Adebayo *et al.*, 2009

Only 10 (20%) of the respondents met the criteria for burnout. The major indices of burnout include emotional exhaustion (60%), physical exhaustion (72%), anxiety (52%), irritability (52%) and pain (60%) (Table 16). The study revealed that 20% of Veterinarians in Nigeria reported high levels of burnout characterized by lower job satisfaction, higher emotional and physical exhaustion, anxiety, irritability and pains.

Table 16: Health records of responding veterinary surgeons

Health Indices of Veterinary Surgeons	NS	%	SS	%	HS	%
Anxiety	24	48	20	40	6	12
Irritability	27	54	17	34	6	12
Depression	34	68	10	20	6	12
Sleeping Disorder	33	66	10	20	14	28
Experience of pain	20	40	16	32	7	14
Episode of malaria	28	56	10	20	12	24

Key: N: Never S: Sometimes A: Always Source: Adebayo *et al.*, 2009

This study was carried out in 2009 when the socioeconomic indices of Nigeria was much better compared to the current realities when the inflation rate, cost of living and available social amenities indices had worsened. The current workplace reality might also have been compounded by the increase rate of migration of skilled labour (*Japa syndrome*), embargo on employment by government and poor salary remuneration in comparison with cost of living. One can only imagine what the current prevalence of burnout syndrome will be in different work environments in Nigeria, and the university system in particular. The implication of this is a

higher prevalence of Nigerians suffering from emotional and physical exhaustion, anxiety, irritability and pains.

3.0 CONTRIBUTION TO HUMAN DEVELOPMENT

Contrary to the misconception of many that the work of an academia involves only teaching and research, I have contributed significantly to human and community development of which a few is highlighted below

3.1 Undergraduate Teaching

I have been involved in both undergraduate and postgraduate training since assumption of duty. I have also served as external examiner to the Faculty of Veterinary Medicine, University of Nigeria, Nsukka, and the Department of Veterinary Surgery and Radiology, University of Ibadan. Three of my students have recently passed the Royal College of Veterinary Surgeons (MRCVS) and are licensed to practice Veterinary Medicine in the United Kingdom, while two have recently passed the North Atlantic Veterinary Licensing Examination (NAVLE). Two of my students practicing in the UK and Sweden have also been provided with further training in surgical techniques under my supervision in order to improve their skill and confidence.

3.2 Postgraduate supervision

I have been involved in postgraduate training in the last 13 years, during which I have jointly supervised 17 post graduate students across three Departments in the University. As at today, I have supervised four PhD students, while two other doctoral candidates are at different stages of their work. I have also supervised 11 MSc and MVSc students. In addition to this, I have served as external examiner to Ahmadu Bello University, Zaria and University of Ibadan at different times to assess the theses of doctoral students and dissertations of master's student.

3.3 Curricular Development

Development of academic curriculum is the foundation upon which a sound academic program is built. In this regard, I designed a new course titled “Principles of Animal Pain Management” to the CCMAS curriculum. The curriculum for a new undergraduate program in Veterinary Radiography aimed at training required manpower had been submitted to the College of Veterinary Medicine, and is currently undergoing necessary review process. Once approved, the program will be the first in the whole of Sub-Sahara Africa and is hoped to train the necessary man-power required in this area.

3.4 Professional man-power development

Availability of affordable and high quality, locally authored text-books is one of the major challenges facing the Veterinary Profession. In 2020, I was invited by the Tertiary Education Trust Fund (TETFUND) along with other selected Veterinary Surgeons to produce a text book for the teaching of Veterinary Surgery. I contributed two chapters on wound healing and wound management towards the successful production of the book titled “Principles of Surgery: A Concise Text for Veterinary Students”.

In 2022, I was admitted as a member of the Global Pain Council (GPC) of the World Small Animal Veterinary Association (WSAVA), a body that provides advisory role on the issues of pain and pain management in dogs, cats and exotic species. In 2023, the GPC launched an online pain management certification program for Veterinarians, Veterinary Nurses and Technicians in order to provide global access to training in pain management. I contributed a section titled “Misconceptions in Pain Management” to the Module 2 of the Pain Certification program. In

addition, I have also provided lectures on Pain Management in Trauma Patient in WSAVA conferences, and contributed academic materials towards the *WSAVA Pain Awareness* month.

3.5 Development of dog breeds in Nigeria

Since 2016, I have been working with a number of dog breed clubs in Nigeria including Boerboel Alliance (BA), Boerboel Dog Breeders Association of Nigeria (BDBAN), German Shepherd Dog Breeders Association (GSDBA), and Canine Owners and Breeders Association (COBA). The focus of this collaboration is to improve the quality of dogs meant for breeding through radiographic screening. This collaboration has resulted in the official recognition of COBA as an affiliate of Federation Cynologique Internationale (FCI), a body that keeps the records of pure-bred dogs in the world. Through this effort, I have also received the World Union of German Shepherd Dog Clubs (WUSV) certification as a HD – ED radiologist and can submit radiographs of dogs for German Shepherd HD and ED screening program.

4.0 CONCLUSION

The knowledge of what animals are likely to experience and the requirements for their physical, physiological, and behavioural needs are important in addressing their welfare. Although animals might not be able to verbalize pain, changes in behavioural and physiological indicators expressed either as a development of new behaviours or a change in normal behaviours can guide veterinarians and researchers in recognizing pain in animals.

Several pharmacological options have been evaluated for their safety and efficacy in the control of perioperative pain in different species of animals such as ketamine, tramadol, midazolam and

gabapentin. Although tramadol is routinely prescribed for the control of pain, our studies showed that its efficacy differs across species and might be related to its metabolism, and the route of administration. Tramadol appeared to be less efficacious in sheep and goats when administered through the epidural route. Oral administration of gabapentin when administered preoperatively was found to provide sufficient analgesia throughout the perioperative period, and may be a viable alternative in circumstances where opioid analgesics are not available due to restrictions.

Osteoarthritis is a common cause of chronic pain in humans and animals with no known effective cure. Our studies revealed that erythrocyte sedimentation rate, and neutrophil/lymphocyte ratio can be a cheap source of monitoring the progression of osteoarthritis in dogs. In addition, our studies showed that lipid metabolism is altered during osteoarthritis, and this may be responsible for the cardiovascular effects reported in osteoarthritic patients. Also, our work on snail mucin, revealed that it can act as an osteoarthritis diseases modifying agents through its regulation of Interleukin - 6 and Matrix Metalloproteinase – 3. However, further rigorous validation to determine its safety, efficacy and route of administration is required. Our studies in Boerboel dogs reveal high prevalence of hip and elbow dysplasia. This call for urgent breeding restrictions through radiographic screening in order to control these two diseases.

Stress and pain are interconnected. Pain is a stressor that cause the activation of the autonomous nervous system. On the other hand, stress exacerbate the severity of pain. Thus, controlling stress and anxiety is an important aspect of pain control in animals. Gabapentin effect on pain control during the peri-operative period in dogs might be related to its anxiolytic effect. It is now recommended that gabapentin should be administered in cats prior to hospital visit to relieve transportation stress and provide a pain free hospital experience. Our study on transportation

stress in cattle showed that transportation is not just movement, it is a process that can affect the body metabolism due to excessive release of stress hormones such as cortisol, with its attendant immunological effect if not done with necessary welfare consideration.

Finally, our study on the prevalence of burnout among veterinarians revealed important attributes of work-place stress such as physical exhaustion, emotional exhaustion, and frustrations at work. This is associated with health indicators such as anxiety, irritability, depression, sleeping disorder, and pain. Although this study was carried out among veterinarians, findings from the study might be applicable to any settings and require that careful attention be paid to the work-place environment in order to mitigate this.

5.0 RECOMMENDATIONS

1. The slow progress recorded in the knowledge of animal sentience has been largely due to few number of researches in this area. Considering the lack of funding on research activities around animal sentience and animal welfare, it is recommended that government through the Ministry of Livestock Development should provide a dedicated fund for researches on animal sentience and animal welfare. This will provide the necessary data required for informed decisions in drafting animal welfare laws in Nigeria

2. A careful look at our curriculum will reveal large deficiency in training relating to animal sentience and animal welfare. Even though there is now an Institutional Committee saddle with research ethics, researchers, especially those employing animals in their research hardly receive appropriate training on animal welfare such as pain recognition, mitigation, and appropriate techniques for euthanasia. Introduction of topics or subjects on animal sentience or animal

welfare in the educational curriculum at every level beginning from the primary school is recommended. This will facilitate early development of the ideal culture of respect for animal welfare in the citizens. In addition to this, periodic training and certification for researchers employing animals in their studies should be incorporated into the activities of the Institutional Research and Ethics Committee. It is also the responsibility of the University and not the researcher to provide comfortable housing facilities for every animal used in research.

3, The National Assembly should promulgate the national animal welfare act to incorporate every aspect of engagement with animal use including responsible animal ownership, animal transportation, animal trade, animal slaughtering, to mention a few.

4. Owing to the inadequate data on the prevalence of musculoskeletal diseases such as osteoarthritis and other forms of arthritides in Nigeria, the establishment of a national rheumatology centre which will be saddled with the conduct and regulation of researches on musculoskeletal diseases, especially osteoarthritis and rheumatoid arthritis as it is done in many countries is recommended.

5. Access to required drugs and inputs such as anaesthetics and analgesics have been a major hindrance to appropriate care for animals. The government in conjunction with necessary regulatory agencies should remove current restrictions to essential drug access. The government should also provide subsidy for animal medicaments as it is being done for humans

6. As stated in the course of this discussion, there is increase in the number of workers reporting workplace burnout due to the worsening socioeconomic indices in the country along with the attendant health implications. Government should, as a matter of urgency, improve the

socioeconomic indices of the country and provide urgent intervention to improve the welfare of the populace. I want to plead with the Federal Government to settle all the obligations they have with the staff of universities, such as the release of all withheld salaries, payment of all outstanding allowances, and introduction of an improved welfare and salary package.

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