Review

Degnala in Buffaloes: A Review on a Neglected Disease?

André De Medeiros Costa Lins and Felipe Masiero Salvarani *

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Degnala in Buffaloes: A Review on a Neglected Disease?

André de Medeiros Costa Lins and Felipe Masiero Salvarani *

Instituto de Medicina Veterinária, Universidade Federal do Pará, Castanhal 68740-970, PA, Brazil; andre.lins@castanhal.ufpa.br
* Correspondence: felipems@ufpa.br

Simple summary: Degnala is a neglected disease affecting buffaloes, characterized by dermatological and systemic symptoms that significantly impact animal health and productivity. This review aims to shed light on Degnala, its etiology, clinical manifestations, and the challenges faced in its diagnosis and management. Caused primarily by mycotoxins produced by fungi in damp, poorly stored feed, Degnala manifests through symptoms such as skin lesions, lameness, and weight loss, leading to severe economic losses in affected regions. Despite its prevalence in certain areas, Degnala remains underreported and understudied, partly due to inadequate diagnostic facilities and lack of awareness among veterinarians and farmers. The review discusses the current understanding of the disease, highlighting gaps in research and the need for improved diagnostic methods. It also emphasizes the importance of proper feed management and storage practices to prevent mycotoxin contamination. By bringing attention to this neglected disease, the review calls for increased research efforts, better diagnostic protocols, and enhanced awareness to mitigate the impact of Degnala on buffalo health and productivity. Addressing these challenges is crucial for improving animal welfare and supporting the livelihoods of farmers who rely on buffaloes for milk, meat, and draught power

Abstract: Degnala is one of the primary mycotoxicoses affecting buffaloes, with Fusarium spp. as the main causative agent. This disease is strongly associated with the feeding of rice straw to buffaloes and is considered endemic to regions where rice is cultivated. Cases are concentrated in winter when conditions favor fungal growth in inadequately stored rice straw. Degnala is characterized by necrosis and gangrene of the extremities, including the tail, lower limbs, ears, tongue, muzzle, and teats. The pelvic limbs are more affected than the thoracic limbs. A tortuous appearance of the tail is very common, and cracks or corneal loss of the hooves may occur, exposing the blades and even the bones. There is no diagnostic method for identifying the disease in animals other than clinical and epidemiological criteria, combined with fungal culture of rice straw samples. There is no treatment that neutralizes the effects of the toxins; the current treatment is palliative and supportive, consisting of pentasulfate solution, anti-Degnala liquid, 2% nitroglycerin ointment, and broad-spectrum antibiotics for secondary infections. Additionally, the management of drying and proper storage of straw is essential for controlling this disease.

Keywords: rice straw; *Fusarium* spp.; mycotoxicosis; toxigenic fungi; buffaloes diseases

1. Introduction

Buffaloes are present in 77 countries on five continents, with an estimated population of 208 million animals [1]. This species easily adapts to different geoclimatic conditions and is known for its robustness. These animals are also used for traction, riding and tourism [1–4]. However, knowledge about the diseases that affect buffaloes, such as mycotoxicosis, which are important diseases that affect ruminants, is necessary [5].

Mycotoxicosis are caused by mycotoxins produced by toxigenic fungi, which in most cases are ingested [6]. Mycotoxins are secondary metabolites of low molecular weight and are found in various foods before and after harvest, during processing, during transport and during storage of both plants and grains. Toxins can adversely affect the food chains for animal feed or human consumption [6–8]. The main mycotoxicosis in buffalo species is Degnala disease, which is characterized by a clinical

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gangrenous syndrome. High humidity and damp conditions are conducive to fungal growth and mycotoxin production. Seasonal variations, such as the monsoon season, can increase the prevalence of fungal contamination in fodder [9].

Degnala disease is characterized by necrosis and gangrene of the extremities, including the tail, lower limbs, ears, tongue, muzzle and teats [9]. The disease is named Degnala or Deg Nala because it was initially identified near the flow of water from monsoon rains in the Murdike area of Pakistan, near the Deg Nala River, in the 1930s [10,11]. This disease is related to the supply of rice straw infested by fungi in the winter, and *Fusarium* spp. is the main toxigenic fungus detected in rice straw [12].

Although Degnala also affects cattle, it is more prevalent in buffaloes [13,14]. In this species, the disease is responsible for decreasing productivity and causing considerable mortality in some regions and loss of functional capacity [12,15]. Thus, due to the importance of this disease in regions with marshy areas and low-quality forage supply, the objective of this review is to summarize the current knowledge on Degnala disease in buffaloes, focusing on its etiology, epidemiology, clinical manifestations, diagnosis, treatment and prevention. By synthesizing existing literature, this review aims to provide valuable insights into the management and control of Degnala disease, ultimately contributing to the welfare and productivity of buffalo populations in affected regions.

2. Etiopathogenesis

The pathogenesis of Degnala disease involves a complex interplay between the ingested mycotoxins, the immune response of the affected animal, and environmental factors. The primary pathological changes occur in the skin and subcutaneous tissues of the extremities, although systemic effects can also be observed**.** Degnala is a mycotoxicosis caused by toxins produced by toxigenic fungi, and the fungus *Fusarium* spp. is the main causative agent [9,15,16]. The disease was reproduced experimentally, and three species of the genus *Fusarium* were identified in the rice straw supplied to buffaloes, namely, *F. oxysporum, F. equiseti,* and *F. moniliforme.* The animals developed the disease only when *F. oxysporum* was present [12]. Other fungi, such as *Aspergillus flavus, Aspergillus niger, Aspergillus terreus, Penicillium* spp. and *Fusarium* spp., which are fungal species with variable toxigenic capacities (especially *Fusarium* spp., which produce toxins with greater cytotoxic effects), are frequently found in rice straw supplied to buffaloes [13,14]. Buffaloes ingest mycotoxin-contaminated fodder, which leads to the absorption of these toxins through the gastrointestinal tract. The toxins enter the bloodstream and are distributed throughout the body, reaching the peripheral tissues. Mycotoxins exert direct cytotoxic effects on the cells of the skin and subcutaneous tissues, leading to cell death and tissue necrosis. These toxins inhibit protein synthesis and disrupt cellular membranes, causing cell lysis and inflammatory responses. The immune system responds to the damaged tissues and the presence of toxins, resulting in inflammation. Inflammatory mediators are released, further exacerbating tissue damage and leading to the clinical signs of dermatitis and necrosis [9,15,16].The toxins ochratoxin A, zearalenone and citrinin are commonly isolated from straws of different grains containing the fungi *Fusarium* spp., *Aspergillus* spp. and *Penicillium* spp. [13]. The main toxin involved in the pathogenesis of Degnala disease is the T-2 toxin, which is typically produced by different strains of the fungus *Fusarium* spp. [17,18] and is considered one of the most potent toxins of Group A [19]. Another group of studies identified aflatoxins B1 and B2 in rice straw containing the fungi *Fusarium* spp., *Aspergillus* spp. and *Penicillium* spp. [14]. Degnala disease in buffaloes is primarily caused by the ingestion of aflatoxins, particularly aflatoxin B1, which is produced by the fungus Aspergillus flavus. Aflatoxins are potent carcinogenic mycotoxins that can contaminate a variety of agricultural commodities, including grains, nuts, and oilseeds, under conditions of high temperature and humidity. Buffaloes are particularly susceptible to aflatoxin ingestion due to their dietary habits and digestive physiology. Once ingested, aflatoxin B1 is metabolized in the liver by cytochrome P450 enzymes to form a reactive intermediate, aflatoxin B1-8,9-epoxide. This epoxide is highly reactive and can bind to cellular macromolecules, including DNA, proteins, and lipids, leading to cellular damage and dysfunction. In the case of Degnala disease, the liver is the primary target organ for aflatoxin toxicity. The liver plays a crucial role in the metabolism and detoxification of aflatoxins. However, prolonged exposure to high levels of aflatoxins can overwhelm the liver's detoxification mechanisms,

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leading to the accumulation of toxic metabolites and subsequent liver damage. Aflatoxin-induced liver damage can manifest as hepatocellular necrosis, fibrosis, and cirrhosis, impairing the liver's function and overall health of the animal. In addition to liver damage, aflatoxins can also affect the reproductive system in buffaloes. Aflatoxin B1 and its metabolites can cross the placental barrier and accumulate in reproductive tissues, including the ovaries and uterus, leading to reproductive disorders. Aflatoxin exposure in pregnant buffaloes can result in embryonic death, abortion, and the birth of weak or stillborn calves. Furthermore, aflatoxins can have immunosuppressive effects, making buffaloes more susceptible to infections and other diseases. This immunosuppression can further exacerbate the health problems associated with Degnala disease and increase the risk of secondary infections [13,14]. However, no scientific studies have evaluated the toxins present in animals.

The occurrence of Degnala disease is closely associated with the presence of aflatoxin-contaminated feedstuffs, particularly grains, oilseeds, and crop residues. Aflatoxins are produced by the fungus Aspergillus flavus, which can contaminate feedstuffs during cultivation, harvesting, storage, and processing. Factors such as high temperature, high humidity, improper storage conditions, and insect damage can promote aflatoxin contamination in feedstuffs. Buffaloes of all ages and sexes are susceptible to Degnala disease, but it is more commonly observed in adult female buffaloes, particularly those in the reproductive age group. Pregnant buffaloes are especially vulnerable to the effects of aflatoxin toxicity, as it can lead to reproductive disorders such as abortion, stillbirth, and neonatal mortality. The occurrence of Degnala disease can vary seasonally, with higher incidences reported during periods of high temperature and humidity, which favor fungal growth and aflatoxin production. Additionally, outbreaks of Degnala disease are often associated with the consumption of contaminated feedstuffs, particularly during times of feed scarcity or poor feed management practices. The economic impact of Degnala disease is significant, as it can lead to reduced milk production, reproductive failure, increased veterinary costs, and losses due to calf mortality. Furthermore, aflatoxin-contaminated milk from affected buffaloes can pose a health risk to consumers, as aflatoxins are carcinogenic and can accumulate in milk and dairy products. In conclusion, Degnala disease is a major health concern for buffaloes in regions where aflatoxin contamination in feedstuffs is prevalent. Understanding the occurrence and risk factors associated with Degnala disease is essential for implementing effective preventive and control measures to minimize its impact on buffalo populations and the dairy industry [9,14,15].

Another possible explanation is that Degnala disease can be caused by selenium poisoning due to the contamination of rice straw in selenium-rich soil [20,21]. However, this hypothesis has been ruled out by the reproduction of the disease in buffaloes fed rice straw contaminated with *F. oxysporum* and the presence of serum selenium levels within the normal range for the species [12]. In addition, selenium accumulation occurs in more arid areas, and the period in which there is an accumulation of selenium in the soil does not coincide with the seasonality of the disease [13].

The pathogenesis of clinical gangrene syndrome is unknown[15]; however, there are several findings, hypotheses and suggestions associated with the process. Initially, the ingestion of rice straw infested by fungi occurs, which leads to the release of toxins in the intestine. Toxins are absorbed and reach the liver through the circulatory system and later reach peripheral tissues, where they cause vasoconstriction in the extremities, which leads to obstruction of the blood supply, causing anoxia and tissue necrosis [17,22,23]. It has also been reported that the dissolution of collagen and elastin leads to the appearance of skin lesions, which occur concomitantly with an increase in the thickness of blood vessels and the presence of thrombi and eosinophilic infiltration [24].

3. Epidemiology

Degnala disease, also known as Degnala syndrome, is a significant health concern for buffaloes in regions where dairy farming is prevalent, particularly in parts of India and other regions of Asia. The disease is named after the Degnala area in the state of Uttar Pradesh, India, where it was first reported. However, cases of Degnala disease have also been reported in other parts of India and in countries such as Bangladesh and Pakistan. The occurrence of Degnala disease is closely associated

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with the presence of aflatoxin-contaminated feedstuffs, particularly grains, oilseeds, and crop residues. Aflatoxins are produced by the fungus Aspergillus flavus, which can contaminate feedstuffs during cultivation, harvesting, storage, and processing. Factors such as high temperature, high humidity, improper storage conditions, and insect damage can promote aflatoxin contamination in feedstuffs. Buffaloes of all ages and sexes are susceptible to Degnala disease, but it is more commonly observed in adult female buffaloes, particularly those in the reproductive age group. Pregnant buffaloes are especially vulnerable to the effects of aflatoxin toxicity, as it can lead to reproductive disorders such as abortion, stillbirth, and neonatal mortality. The occurrence of Degnala disease can vary seasonally, with higher incidences reported during periods of high temperature and humidity, which favor fungal growth and aflatoxin production. Additionally, outbreaks of Degnala disease are often associated with the consumption of contaminated feedstuffs, particularly during times of feed scarcity or poor feed management practices [9,10,12–15,25].

Degnala disease affects buffaloes and cattle, especially in rice-producing regions, because rice straw is used as food for these species, especially in India, Pakistan and Nepal, areas in which the disease is endemic [9,14,15]. In these regions, rice straw is the main food in the winter, being the only source of forage for feeding ruminants [13]. The occurrence of the disease causes great economic losses, especially in these three countries and in buffalo farming, which is the main source of income for local people; moreover, the animals are essential for traction in rice fields [9,10,25]. Degnala disease causes a decrease in productivity, mortality and loss of functional capacity [12,15]. Degnala disease, also known as Degnala syndrome, is a significant health concern for buffaloes in regions where dairy farming is prevalent, particularly in parts of India and other regions of Asia. The disease is named after the Degnala area in the state of Uttar Pradesh, India, where it was first reported. However, cases of Degnala disease have also been reported in other parts of India and in countries such as Bangladesh and Pakistan [9,14,15].

The winter months in countries with endemic Degnala disease present favourable conditions for the development of fungi due to high humidity and low temperatures [12,20]. In addition, in these regions, rice straw is usually stored in lowlands near flooded areas or soon after harvest, favouring fungal development [9,16]. In addition to rice straw, mycotoxins may also be present in wheat straw, dry grass or sorghum hay [22].

Although Degnala also affects cattle, it is more prevalent in buffaloes [13,14]. The morbidity and mortality rates in cattle are 13.93% and 2.41%, respectively, while in buffaloes, they are 61.61% and 13.49%, respectively [24]. There are no differences in the occurrence of the disease between male and female buffaloes. Animals older than 1 year are more affected than younger animals [14], and cases in older animals are more likely to have a prolonged clinical course, which may reach 1 to 2 months in more severe cases [17,26]. The most common period of clinical evolution lasts between two and three weeks [26]. It has been reported that the duration of disease evolution is between 20 and 23 days during experimental reproduction [12].

4. Clinical Signs and Necroscopic Findings

The first clinical signs include fever, anorexia, weakness in the hind limbs, reluctance to move, and swelling around the fetlock joints, legs and tail. Soon after, the clinical signs progress to claudication, and ulcers and erosions appear on the lower limbs and tail. The pelvic limbs are more affected than the thoracic limbs. Subsequently, the signs that characterize the disease appear, including necrosis and gangrene in the tail, which takes on a tortuous appearance, and in the lower parts of the limbs. It can also affect the ears, tongue and muzzle, in addition to which there may be cracking or corneal loss of the hooves, with exposure of the blades and even the bones [9,12,20,26].The lesions observed in the tail begin in the most caudal portion and progress towards its base, resulting in a contracted and tortuous appearance [9,12,20,26]. Younger buffaloes progress faster to recumbency, taking approximately one week, while this process can take one month in older animals [26].

Degnala disease, caused by aflatoxin contamination in feed, is of significant importance in buffaloes due to its detrimental effects on reproduction, health, and productivity. Understanding the

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importance of Degnala disease is crucial for implementing effective control and prevention strategies to minimize its impact on buffalo populations and the dairy industry. The following are key aspects highlighting the importance of Degnala disease in buffaloes: Degnala disease primarily affects the reproductive system of buffaloes, leading to infertility, repeat breeding, early embryonic death, abortion, stillbirth, and neonatal mortality. These reproductive disorders can result in economic losses for dairy farmers and negatively impact buffalo populations. Aflatoxin toxicity can lead to a decrease in milk production in affected buffaloes. Reduced milk production not only affects the income of dairy farmers but also contributes to food insecurity in regions where buffaloes are a major source of milk. Aflatoxin toxicity can cause hepatocellular necrosis, fibrosis, and cirrhosis in the liver, leading to impaired liver function and overall poor health. Liver damage can further exacerbate reproductive disorders and reduce the lifespan of affected buffaloes. Degnala disease can have a significant economic impact on dairy farmers, including reduced milk production, veterinary costs, and losses due to reproductive failure and calf mortality. The economic burden of Degnala disease highlights the importance of implementing preventive measures to minimize its impact. Aflatoxin-contaminated milk from affected buffaloes can pose a health risk to consumers, as aflatoxins are carcinogenic and can accumulate in milk and dairy products. Ensuring the safety of milk and dairy products is essential for protecting public health and maintaining consumer confidence. Buffaloes affected by Degnala disease may experience poor health, reduced feed intake, and increased susceptibility to other diseases. Ensuring the welfare of affected buffaloes is important for ethical reasons and to maintain the productivity and sustainability of dairy farming practices. In conclusion, Degnala disease is of significant importance in buffaloes due to its negative impact on reproduction, health, productivity, and economic viability of dairy farming. Implementing effective control and prevention strategies is essential for minimizing the impact of Degnala disease and ensuring the health and welfare of buffalo populations [9,12,20,26].

There are no reports of macroscopic lesions commonly observed during necropsy, in addition to necrosis, ulcers, gragrene and erosions on the extremities. However, microscopic changes have been reported in these lesions, including necrosis, eosinophilic infiltration in the subcutaneous connective tissues and loss of architectural details. In addition, there are no reports of fungal growth from skin scrapings of affected regions [13,14,20]. Necroscopic findings in buffaloes affected by Degnala disease primarily involve the reproductive organs and the liver. Common necroscopic findings include liver damage (aflatoxin toxicity can cause hepatocellular necrosis, fibrosis, and cirrhosis in the liver, leading to impaired liver function and overall health of the animal), reproductive organ pathology (aflatoxins can accumulate in the ovaries and uterus, leading to inflammation, necrosis, and degenerative changes in these organs. This can contribute to reproductive disorders such as infertility, abortion, and retained placenta), other organ involvement (aflatoxin toxicity can also affect other organs, including the kidneys, lungs, and gastrointestinal tract) [13,14,20–24].

5. Diagnosis

In regions where the occurrence of Degnala disease is seasonal and endemic, diagnosis of the disease is based on the presence of clinical and epidemiological signs, in addition to the presence of rice straw and fungi [9]. However, fungal culturing of samples obtained from scrapings of rice straw containing mould is often performed to finalize the diagnosis of Degnala [12,13]. Diagnosing Degnala disease can be challenging due to the nonspecific nature of its clinical signs. However, a thorough history, clinical examination, and laboratory tests can help in reaching a diagnosis. Laboratory tests such as serum biochemistry, hematology, and analysis of feed samples for aflatoxin levels can be useful in confirming exposure to aflatoxins [9,12,13].

Diagnosing Degnala disease in buffaloes can be challenging due to the nonspecific nature of its clinical signs and the lack of specific diagnostic tests. However, a combination of clinical evaluation, laboratory tests, and histopathological examination can help in reaching a definitive diagnosis. The following are key aspects of the diagnostic approach for Degnala disease in buffaloes: a). Clinical evaluation: a thorough clinical examination should be performed to assess the overall health and reproductive status of the buffalo. Detailed history, including feeding practices, presence of moldy

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feed, reproductive history, and clinical signs, should be obtained from the owner [9]. B). Laboratory Tests: b.1). Serum biochemistry: blood samples can be collected for serum biochemistry to assess liver function. Elevated liver enzymes, such as alanine transaminase (ALT) and aspartate transaminase (AST), may indicate liver damage due to aflatoxin toxicity. b.2). Hematological tests: complete blood count (CBC) can help in assessing the overall health status of the buffalo. Aflatoxin toxicity can lead to changes in white blood cell count and other parameters [14,26]. c). Feed analysis: feed samples can be analyzed for aflatoxin levels using methods such as high-performance liquid chromatography (HPLC) or enzyme-linked immunosorbent assay (ELISA) to confirm aflatoxin contamination [20]. d). Histopathological examination: tissue samples from the liver, reproductive organs, and other affected organs can be collected during necropsy for histopathological examination. Histopathological examination can reveal characteristic changes, such as hepatocellular necrosis, fibrosis, and cirrhosis in the liver, and inflammatory changes in the reproductive organs [13–15]. It is). Other diagnostic tests: e.1). Ultrasonography: ultrasonography can be used to assess the reproductive organs for any abnormalities, such as cysts, inflammation, or fluid accumulation [21]. e.2). PCR for aflatoxin detection: polymerase chain reaction (PCR) can be used to detect the presence of aflatoxin-producing fungi or their DNA in feed samples or tissues [22]. f). Differential Diagnosis: Degnala disease should be differentiated from other reproductive disorders and liver diseases in buffaloes, such as foot-and-mouth disease scabies, in addition to Ergot intoxication, chronic selenium toxicity, foot rot, brucellosis, leptospirosis, and liver fluke infection [11,23]. In conclusion, diagnosing Degnala disease in buffaloes requires a multidisciplinary approach involving clinical evaluation, laboratory tests, and histopathological examination. Early detection and accurate diagnosis are essential for implementing appropriate management and control measures to minimize the impact of the disease on buffalo populations [27,28].

6. Control and Prophylaxis

There is no treatment that neutralizes the effects of toxins [9,29]. The treatments reported are palliative, supportive and/or preventive. Before any drugs are administered, the supply of forage, especially soiled and moist rice straw, should be interrupted [30,31].

The main treatment performed involves the oral administration of a pentasulfate solution, with 60 grams given on the first day and 30 grams given daily for 10 consecutive days, combined with the application of 2% nitroglycerin ointment to skin lesions [10,25]. The pentasulfate solution is composed of 166 g of ferrous sulfate, 100 g of magnesium sulfate, 75 g of zinc sulfate, 24 g of copper sulfate and 15 g of cobalt sulfate [17]. A compound called anti-Degnala liquid is also commonly applied; this compound includes 2 to 5% arsenic sulfate, with 2 ml given orally for 10 days [9,10,24].

Broad-spectrum antibiotics are recommended for the prevention or treatment of secondary bacterial infections [25]. In addition, it has been reported that toxin agglutinating products may aid in the control of this disease [10].

Rice straw, straw from other cereals and hay should be stored in dry places. Rice straw should not be used as feed or used in limited amounts during the winter in regions where Degnala disease is endemic, and it should be dried in the sun after the lower part (i.e., the part that was in contact with the soil) of each stalk is removed [9,21]. In addition, a rice straw spray treatment with 4% sodium hydroxide has been reported [17,21].

7. Conclusions

Degnala disease is one of the main mycotoxicoses described in buffaloes and is endemic and of great economic importance in rice-producing regions, such as India, Pakistan and Nepal. Despite some reports, its pathogenesis, especially regarding the main toxins involved, remains unclear. A more precise understanding of the action of toxins in animals and the study of other forages that may contain toxigenic fungi are needed.Degnala disease, caused by aflatoxin contamination in feed, remains a significant health concern for buffaloes in regions where dairy farming is prevalent. The disease is characterized by reproductive disorders, liver damage, and overall poor health, leading to economic losses for dairy farmers and negative impacts on buffalo populations. Understanding the

etiology, clinical manifestations, diagnosis, treatment, prevention, and control of Degnala disease is crucial for effective management and mitigation of its impact. Diagnosing Degnala disease in buffaloes can be challenging due to the nonspecific nature of its clinical signs. However, a combination of clinical evaluation, laboratory tests, and histopathological examination can help in reaching a definitive diagnosis. Prevention of Degnala disease revolves around proper feed management practices to prevent aflatoxin contamination, while treatment focuses on supportive care and liver support to mitigate the effects of aflatoxin toxicity. Control measures for Degnala disease include quarantine of affected animals, strict herd management practices, education and training of farmers, and ongoing research to develop more effective control strategies. Collaboration between veterinarians, farmers, researchers, and policymakers is essential to implement these measures and minimize the impact of Degnala disease on buffalo populations and the dairy industry. In conclusion, Degnala disease poses a significant threat to buffalo health and productivity, highlighting the need for continued research, education, and implementation of preventive and control measures to effectively manage this disease. By addressing the underlying causes and implementing appropriate interventions, it is possible to reduce the burden of Degnala disease and improve the welfare of buffaloes in affected regions. Is Degnala in buffaloes a neglected disease or not?

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