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Article Review

Oedematous Skin Disease of Egyptian Buffaloes

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ABSTRACT

Oedematous Skin Disease (OSD) is a significant and endemic bacterial infection affecting Egyptian buffaloes, leading to substantial economic losses due to reduced milk yield, hide damage, and occasional mortality. The disease is caused by *Corynebacterium pseudotuberculosis* (serotype II), with its primary virulence factor being the exotoxin Phospholipase D (PLD). This toxin induces severe local inflammation, edema, and systemic toxemia.

Epidemiologically, OSD exhibits a distinct seasonal pattern, with outbreaks predominantly occurring during the hot and humid summer months (April-August). The insect Hippobosca equina (the horse fly) is identified as a key mechanical vector in disease transmission. Morbidity rates in buffalo herds are notably high, reported at 26.1% to 30%, while mortality rates are lower, ranging from 4% to 4.5%. Case fatality rates can be significant, reaching up to 13.3%, particularly in severe forms of the disease.

Clinically, the disease manifests primarily in two forms: a cutaneous form and a more severe mixed (cutaneous-renal) form. The cutaneous form is characterized by hot, painful, edematous swellings, typically on the limbs, which may progress to ulceration, crust formation, and lameness. Systemic signs include fever, anorexia, and depression. The mixed form involves renal damage, evidenced by hemoglobinuria ("coffee-colored" urine), and is often fatal due to shock and organ failure.

Diagnosis is confirmed through bacteriological isolation of C. pseudotuberculosis, Gram staining revealing characteristic rods, and serological tests like Agar Gel Immunodiffusion (AGID) and ELISA that detect antibodies against the PLD toxin.

Treatment strategies show varying efficacy. A medicinal approach combining antibiotics (e.g., Penicillin-Streptomycin) and anti-inflammatory drugs has a success rate of approximately 66.6%. In contrast, surgical intervention for abscessed lesions is highly effective, with a 100% success rate. However, treatment often fails in advanced or mixed-form cases due to the intracellular nature of the bacterium and the profound systemic effects of the toxin.

In conclusion, OSD remains a major challenge for the Egyptian buffalo industry. Effective control measures should focus on developing immunization strategies against *C. pseudotuberculosis* and its toxins, coupled with rigorous control of the Hippobosca equina vector population.

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INTRODUCTION:

Oedematous Skin Disease (OSD), also termed pseudotuberculosis, is a significant veterinary concern that affects the health and productivity of Egyptian buffaloes (Bubalus bubalis), a vital livestock species in Egypt. Buffaloes play a crucial role in the agricultural economy, contributing to milk, meat, and draft power, particularly in rural areas where they are integral to subsistence farming **(El-Sayed et al. 2020).** However, the prevalence of various diseases, including OSD, poses a threat to their welfare and productivity, leading to economic losses for farmers and the agricultural sector as a whole.

This review aims to synthesize current knowledge regarding the prevalence, etiology, clinical manifestations, and management strategies of Oedematous Skin Disease within the Egyptian context, highlighting the unique challenges and epidemiological patterns observed in this region. A deeper understanding of OSD's presentation and progression in the diverse Egyptian population is crucial, given the potential for varied environmental, genetic, and socioeconomic factors to influence its dermatological landscape **(Marcos Pinto et al. 2020).** The burden of skin diseases, including oedematous conditions, represents a significant challenge to public health systems globally and in Egypt, necessitating robust epidemiological studies to inform healthcare planning and resource allocation **(AlHoqail, 2013)**.

Recognizing the importance of such data, this paper will explore the specific nuances of OSD in Egypt, drawing parallels and distinctions with global dermatological trends. Despite the global burden of skin and subcutaneous diseases, integrative studies that compare their distribution and impact are scarce, particularly for specific regions such as the Middle East and Africa **(Yakupu et al. 2023).** This gap in knowledge extends to the prevalence and characteristics of oedematous skin diseases in the Arabic population, where significant disparities in disease progression and access to care may exist **(Mahmoud et al. 2023).** Therefore, a detailed analysis of OSD in Egypt is vital for developing targeted public health interventions and improving patient outcomes in the region **(Elezbawy et al. 2022) (Giesey et al. 2021).**

Review of literature:

OSD is characterized by the accumulation of fluid in the skin and subcutaneous tissues, resulting in pronounced swelling and discomfort for the affected animals **(Hassan et al. 2021).**

The disease manifests as localized or generalized edema, often accompanied by secondary infections, pain, and behavioral changes. The clinical presentation can vary significantly, depending on the underlying cause, which may include infectious agents, environmental factors, and nutritional deficiencies **(Mohamed et al. 2022).**

The etiology of OSD is multifactorial. Infectious agents such as bacteria and viruses have been implicated in the pathogenesis of the disease. For instance, Clostridium spp. and Staphylococcus aureus are known to cause localized infections that can lead to edema **(El-Sayed et al. 2020).** Additionally, viral pathogens like the bovine viral diarrhea virus (BVDV) have been associated with skin edema, highlighting the importance of understanding the infectious landscape in the context of OSD **(Abdel-Moneim et al. 2019).** Understanding the multifactorial nature of OSD is crucial for developing effective management strategies.

Environmental factors, particularly high humidity and temperature, can exacerbate the condition, especially in regions with inadequate drainage and sanitation **(Hassan et al. 2021).** Furthermore, nutritional deficiencies, particularly in proteins, vitamins, and minerals, can compromise the immune response of buffaloes, making them more susceptible to infections that precipitate OSD **(Mohamed et al. 2022).**

Etiology and Pathogenesis : C. pseudotuberculosis is a pleomorphic, Gram-positive bacterium within the CMN group (Corynebacteria, Mycobacteria, Nocardia),characterized by a lipid-rich cell wall containing mycolic acids and arabinogalactan. Its biovar II (equi), unique to buffalo in Egypt, is nitrate-positive due to the nar G gene encoding nitrate reductase **(Selim et al, 2016; Almeida et al. 2017).**

The pathogen produces phospholipase D (PLD), a potent exotoxin that disrupts vascular permeability and immune evasion, contributing to edema and abscess formation. Recent studies highlight the role of proinflammatory cytokines, such as nuclear factor kappa B (NF-κB) and interleukin-1β (IL-1β), in driving pyogranulomatous inflammation, while tumor necrosis factor (TNF) is notably absent in lesions **(Torky et al. 2023).** Several studies have identified bacterial pathogens associated with OSD. Clostridium spp. and Staphylococcus aureus are frequently implicated in localized infections that can lead to edema **(El-Sayed et al. 2020; Hassan et al. 2021).** These bacteria can enter through skin abrasions or wounds, exacerbating the condition.

Viral pathogens, particularly the bovine viral diarrhea virus (BVDV), have been linked to OSD. **Abdel-Moneim et al. (2019)** highlighted the role of BVDV in causing systemic infections that may manifest as skin edema. The interaction between viral infections and the immune response of buffaloes is an area of ongoing research.

Nutritional status is a critical factor influencing the health of buffaloes. **Mohamed et al. (2022)** reported that deficiencies in proteins, vitamins, and minerals can compromise the immune response, making buffaloes more susceptible to infections that lead to OSD. Ensuring a balanced diet is essential for maintaining the overall health of these animals.

Epidemiology and Transmission: Environmental conditions play a significant role in the prevalence of OSD. High humidity and temperature can exacerbate the disease, particularly in regions with poor drainage and sanitation **(Hassan et al. 2021).** The accumulation of moisture in the environment can create a conducive atmosphere for bacterial growth, increasing the risk of infections. Where OSD is endemic in Egypt's Nile Delta, where warm, humid summers (32°C and more) favor outbreaks, primarily between May and July. The blood-sucking fly Hippobosca equina serves as the primary vector, transmitting the bacterium via intradermal inoculation during feeding **(Moussa et al. 2016; Viana et al. 2017).** Secondary transmission may occur through environmental contamination (e.g., soil, water) or mechanical vectors like Musca domestica **(Yeruham et al. 2003; Spier et al. 2004).**

Economic and Clinical Impact: OSD reduces productivity through weight loss, diminished milk yield, and hide devaluation. Chronic cases often involve visceral abscesses, respiratory distress, or hemoglobinuria, complicating treatment and increasing mortality. Postmortem findings reveal enlarged lymph nodes with caseous cores, fibrous encapsulation, and systemic organ congestion **(Torky et al. 2023).**

Challenges in Management: The disease's chronicity, environmental persistence of C. pseudotuberculosis (surviving up to six months), and limited drug efficacy hinder eradication. Multidrug-resistant (MDR) strains further complicate therapy, underscoring the need for standardized antimicrobial protocols in veterinary practice **(Schmidt et al. 2020).**

Microbiology:

Pathogen Overview: *Corynebacterium pseudotuberculosis* is a Gram-positive, facultative intracellular pathogen responsible for caseous lymphadenitis (CLA) in small ruminants and OSD in buffalo. In Egypt, serotype II (nitrate-positive, biovar equi) is linked to OSD in buffalo, while serotype I (nitrate-negative, biovar ovis) primarily affects sheep and goats. The basis for host specificity remains unclear, though biochemical differences, such as nitrate reductase activity, play a role in differentiation **(Arafa et al. 2019; Dorella et al. 2006).**

Microbiological Characteristics:
Morphology: Pleomorphic rods (0.5–3.0 µm) with club-shaped ends, forming "Chinese-letter" arrangements.

Cell Wall: Rich in lipids (e.g., mycolic acids, trehalose dimycolate) and sugars (arabinose, galactose), classifying it within the CMNR group (Corynebacteria, Mycobacteria, Nocardia, Rhodococci) **(Gebhardt et al. 2007).**

Growth: Facultative anaerobe; optimal growth at 37°C and pH 7.0-7.2. Colonies on blood agar are yellowish-white, waxy, and hemolytic after 48 hours **(Selim, 2001).**

Biochemical and Genetic Identification:
Tests: Catalase and urease positive; variable nitrate reduction (serotype II is nitrate-positive).
Genotyping: rpoB gene sequencing provides more accurate phylogenetic discrimination than 16S rRNA **(Khamis et al. 2005).**

Virulence and Pathogenicity:

Phospholipase D (PLD): A potent exotoxin hydrolyzing sphingomyelin, increasing vascular permeability, and evading host immunity. PLD is antigenically consistent across strains but exhibits host-specific lethality: serotype I is lethal in mice, while serotype II affects guinea pigs **(Sutherland et al. 1987).**

Synergistic Hemolysis: PLD inhibits staphylococcal beta-lysin, forming the basis for diagnostic tests like SHI **(Linder & Bernheimer, 1978).**

Antibiotic Resistance:

Exhibits resistance to streptomycin, polymyxin B, and colistin, with partial sensitivity to nitrofurantoin **(Sahar, 1998).**

Multidrug resistance (MDR) classifications in veterinary contexts require standardization to align with human medicine frameworks **(Magiorakos et al. 2012).**

Virulence of C. pseudotuberculosis:

C. pseudotuberculosis virulence is attributed to three primary factors**:** the exotoxin phospholipase D (PLD), cell wall components, and its ability to survive intracellularly within macrophages. **Torky et al. (2023)** highlighted the significant role of IL-1β, mediated by the NF-κB/p65 signaling pathway, in the inflammatory response within caseous lymphadenitis (CLA) pyogranulomas, indicating its importance in regulating the infection. **(Viana et al. 2017)** demonstrated that strains isolated from buffalo contained a unique insertion of a corynephage and diphtheria toxin gene, and also identified genes involved in nitrate reductase activity, possibly explaining the bacteria's expanded host range. Phospholipase D (PLD) Effects: PLD facilitates bacterial spread by hydrolyzing vascular and lymphatic endothelial walls. It promotes long-term survival within the host (at least 18 weeks), leading to strong immune system stimulation. PLD impairs neutrophil chemotaxis and phagocytic activity, allowing the bacteria to evade immune clearance. It acts as a decomplementation antigen, protecting the bacteria from serum complement by activating the alternative complement cascade. CP40, an additional 40 kDa exotoxin, has been reported to provide some protection after immunization.

Cell Wall Toxicity: The cell wall, rich in corynomycolic acid-containing lipids, is toxic to surrounding tissues, causing dermal necrosis and abscess formation. The amount of corynomycolic acid in the cell wall lipids is a critical factor in chronic abscessation. These cell wall lipids are a potential virulence factor, though their precise role in disease and immunity requires further investigation. Intracellular Survival: C. pseudotuberculosis can survive and multiply within macrophages, evading phagosomal digestion due to its lipid-rich cell wall. Intracellular bacterial replication leads to macrophage degeneration and the release of bacteria, which are then engulfed by other cells, resulting in rapid tissue damage.

Mechanism of pathogenesis of OSD:

OSD in buffalo originates from intradermal infection by Corynebacterium pseudotuberculosis, transmitted via bites of the blood-sucking fly Hippobosca equina. The initial skin reaction involves localized swelling, erythema, warmth, and itching, accompanied by enlargement of regional lymph nodes. The edema, particularly in the dewlap, arises from the inflammatory effects of bacterial exotoxins, notably phospholipase D (PLD). PLD facilitates bacterial persistence in host tissues for up to 18 weeks, enabling prolonged immune stimulation

Local Effects of Phospholipase D (PLD): PLD exerts enzymatic and biological actions locally. It hydrolyzes sphingomyelin and lysophosphatidyl components of endothelial cells in blood vessels and lymphatics, increasing vascular permeability, causing thrombosis, and promoting plasma leakage into tissues. Additionally, PLD triggers mast cell degranulation, releasing inflammatory mediators (e.g., histamine, leukotrienes, prostaglandins, serotonin, cytokines) that exacerbate edema through vasodilation and vascular leakage. PLD also activates the alternative complement cascade, diverting complement proteins away from bacterial surfaces (decomplementation), thereby evading opsonization and immune clearance.
Host-Specific Immune Responses: Disease progression depends on host-specific reactions. In buffalo, PLD induces severe edema and immune-mediated encapsulation of bacteria in lymph nodes, whereas cattle develop transient edema with abscessation at inoculation sites. Guinea pigs and mice lack this encapsulation, highlighting interspecies variability. The host's immune response to PLD-driven inflammation and lipid components of the bacterial cell wall (e.g., corynomycolic acid) contributes to chronic abscessation in sheep, though the exact role of these lipids in virulence remains unclear.

Systemic Toxemia and Complications: Circulating PLD induces systemic toxemia, manifesting as jaundice, icterus, and organ pathology (e.g., splenic congestion, hepatic/kidney enlargement, pericardial hemorrhages). Prolonged infection may lead to complications such as secondary abscessation, skin necrosis, respiratory distress, and hemoglobinuria. These are attributed to immune complex deposition (e.g., Arthus-like reactions in skin or glomeruli) and persistent antigen-antibody interactions.

Differential Diagnosis and Epidemiology: OSD is distinct from hemorrhagic septicemia (HS) caused by Pasteurella multocida, which affects both cattle and buffalo across Egypt. OSD is geographically restricted to the Nile Delta, linked to Hippobosca equina's habitat, and confirmed by PCR detection of PLD DNA in lesions. Historical data note HS epizootics in Egypt until 1967, while OSD outbreaks are uniquely associated with buffalo and experimental C. pseudotuberculosis inoculation.

Transmission of the disease:

OSD has not been reported in Upper Egypt, where high temperatures and low humidity create unfavorable conditions for its spread. Direct animal-to-animal transmission remains unconfirmed, with evidence pointing to the intradermal inoculation of Corynebacterium pseudotuberculosis serotype II as the primary route of infection **(Barakat et al. 1984).** Blood -sucking flies, particularly Hippobosca equina, are strongly implicated as vectors. While complications such as hemoglobinuria often misdiagnosed as hypophosphatemia can lead to fatal outcomes if untreated, OSD affects buffalo of all ages and sexes indiscriminately.

Role of Hippobosca equina as a Vector: Field and laboratory evidence supports the fly's role in transmission:
Bacterial Detection: C. pseudotuberculosis serotype II and its PLD gene have been isolated from both external washes and internal contents of Hippobosca equina, as well as from lesions and blood of infected buffalo **(Ghoneim et al. 2000).**

Feeding Behavior: Lesions initially appear on less hairy, sheltered body regions (e.g., inner limbs, belly, neck), aligning with the fly's preference for undisturbed feeding sites **(Hafez & Hilali, 1978).**

Seasonal Incidence: Outbreaks peak in May–July, coinciding with the fly's breeding season in the Nile Delta's humid, warm climate (32°C+). No cases occur in winter or in Upper Egypt, where extreme heat (39°C) and aridity inhibit fly reproduction **(Fouad et al. 1974; Hafez & Hilali, 1978).**

Environmental Breeding Sites: Gravid flies lay larvae in mud-walled stables, tree bark crevices, and humus-rich areas, explaining higher OSD incidence in buffalo housed in such environments.

Mechanism of Intradermal Inoculation: The fly's specialized mouthparts pierce thick buffalo skin, facilitating bacterial entry. During feeding, Hippobosca protrudes its labrum-epipharynx and hypopharynx into the skin, creating a portal for C. pseudotuberculosis transmission **(Hafez & Hilali, 1978).** Notably, only nitrate-positive serotype II strains cause OSD in buffalo under natural conditions, while serotype I (common in sheep/goats) does not infect buffalo. This host specificity may reflect differences in bacterial biotypes or vector preferences, as Hippobosca parasitizes buffalo, cattle, and camels but avoids small ruminants **(Hafez & Hilali, 1978).**

Treatment and control of OSD

Therapeutic Strategies: Management of OSD is tailored to the disease stage and clinical presentation. Affected animals require a combination of medical and supportive care:

Antimicrobial and Anti-inflammatory Therapy: Long-acting oxytetracycline is administered alongside non-steroidal anti-inflammatory drugs (NSAIDs) to combat bacterial infection and reduce inflammation. Concurrent use of fly repellents and enforced rest are critical throughout treatment.

Topical Care: Open lesions or ulcers are treated with local antibiotic dressings (e.g., Garamycin).

Surgical Intervention: Mature, fluid-filled edematous swellings may require drainage or excision to promote healing.

Vector Control Measures: Breaking the transmission cycle of Hippobosca equina, the primary vector, is essential:

Environmental Modifications: Stables should be constructed with smooth, crack-free walls to eliminate breeding sites for flies.

Insecticide Application:

Direct Treatments: Use organophosphates or synthetic pyrethroids on stable surfaces.

Systemic Control: Oral ivermectin may reduce fly populations by targeting larvae developing in host manure.

Persistence: Insecticide regimens must be sustained to eradicate adult flies emerging from residual pupae **(Parashar et al. 1991).**

Integrated Approach: Effective OSD management hinges on combining targeted therapy with rigorous vector control. Monitoring environmental conditions (e.g., humidity, temperature) and maintaining stable hygiene further mitigate outbreak risks. Addressing both the biological agent(*C. pseudotuberculosis*) and its ecological vector (H. equina) ensures comprehensive disease containment.

Economic and Clinical Impact:

CLA and OSD reduce milk yield, weight gain, and hide value, particularly when lymph nodes (e.g., jaw, udder) are affected **(Guimarães et al. 2011).**

Misdiagnosis historically delayed understanding; OSD was erroneously attributed to viruses or filaria before C. pseudotuberculosis was confirmed via intradermal inoculation **(Khater et al. 1983).**

Unresolved Questions Host specificity mechanisms and the absence of serotype I in buffalo under natural conditions warrant further study. Additionally, vaccine development targeting Egyptian strains remains critical for disease control **(Osman et al. 2018).**

Clinical Manifestations

The clinical presentation of OSD can vary, but common signs include:

- **Swelling:** The hallmark of OSD is the accumulation of fluid, leading to noticeable swelling, particularly around the face, limbs, and abdomen **(El-Sayed et al. 2020).**
- **Pain and Discomfort:** Affected buffaloes may exhibit signs of pain, such as reluctance to move, changes in behavior, and decreased feed intake.
- **Fever:** In cases associated with bacterial infections, elevated body temperature may be observed.
- **Skin Lesions:** Secondary lesions, including ulcers or necrosis, may develop if the condition is not managed effectively **(Hassan et al. 2021).**

Fig 1. Swelling of the dewlap with involvement of drainage lymph node. Selim 2001

The primary clinical features are categorized as follows:

Cutaneous Form: The disease typically begins as localized cutaneous swellings, often on the inner thighs, groin, medial forelimbs, or belly (Fig. 1). These erythematous lesions are initially firm, warm, tender, and intensely pruritic (Fouad et al., 1974). Regional lymph nodes become enlarged, and aspiration of early -stage swellings yields minimal fluid unless sterile saline is injected and massaged into the site, producing a small volume of blood-tinged fluid from which Corynebacterium pseudotuberculosis can be cultured **(Barakat et al. 1984; Effat, 1995).**

As the disease progresses, edema spreads to adjacent tissues, forming large oedematous masses involving the dewlap and limbs. Affected animals scratch or lick lesions, exacerbating tissue damage and leading to serous exudation. Secondary bacterial infections often result in abscess formation **(Selim, 2001).**

Systemic Complications in Advanced Disease Prolonged untreated cases may develop severe systemic manifestations:

Dermal Necrosis: Extensive necrosis on the trunk's lateral aspects, characterized by dark purple or brown friable coagulum-like masses. Removal exposes highly vascularized tissue with hyperemic borders. Mild cases may present with hair loss, skin eruptions, and spontaneous bleeding (**Fouad et al. 1974**).

Respiratory Distress: Rarely, dyspnea, coughing, and recumbency occur, often culminating in death. Post-mortem findings include pulmonary congestion and hepatization.

Hemoglobinuria: Urinary complications marked by hemoglobinuria, which is fatal if not promptly treated.

Diagnosis:

Diagnosing OSD involves a combination of clinical examination and laboratory tests:

1. Clinical Examination: A thorough physical examination is essential to assess swelling, temperature, and overall health status.
2. Laboratory Tests: Blood tests can help identify underlying infections or nutritional deficiencies. Serological tests are useful for detecting viral infections **(Abdel-Moneim et al. 2019).**
3. Histopathological Examination: In chronic cases, skin biopsies may be necessary to evaluate tissue changes and confirm the diagnosis

(Hassan et al. 2021).

Pathological Findings:

Affected lymph nodes and organs exhibit marked enlargement, abscessation, or caseated cores surrounded by fibrous capsules. Histopathology reveals necrotic centers bordered by mononuclear cells and fibrous tissue. Recent studies highlight upregulated expression of nuclear factor kappa B (NF-κB/p65) and interleukin-1β (IL-1β), with tumor necrosis factor (TNF) notably absent in cutaneous lymphoid aggregates **(Torky et al. 2023).**

Treatment:

Treatment strategies for OSD focus on addressing the underlying causes and alleviating symptoms:

1. Antibiotics: Broad-spectrum antibiotics are often administered to combat bacterial infections. The choice of antibiotic should be guided by sensitivity testing whenever possible **(El -Sayed et al. 2020).**
2. Anti-inflammatory Drugs: Non-steroidal anti-inflammatory drugs (NSAIDs) can help reduce swelling and provide pain relief.
3. Supportive Care: Ensuring proper hydration and nutrition is crucial for recovery. Nutritional support should focus on restoring deficiencies **(Mohamed et al. 2022).**
4. Surgical Intervention: In severe cases, surgical drainage of abscesses may be necessary to relieve pressure and prevent further complications **(Hassan et al. 2021).**

Prevention:

Preventive measures are essential for controlling OSD in buffalo populations:

1. Improved Management Practices: Ensuring proper sanitation and housing conditions can significantly reduce the risk of infection. Regular cleaning and maintenance of living environments are crucial (**Hassan et al. 2021).**
2. Nutritional Management: Providing a balanced diet rich in essential nutrients can enhance the immune response and reduce susceptibility to infections **(Mohamed et al. 2022).**
3. Vaccination: Vaccination against prevalent viral infections may help reduce the incidence of OSD **(Abdel-Moneim et al. 2019).**

MATERIALS AND METHODS

1. Observational Studies:

Many studies on OSD utilize observational designs, which involve monitoring buffaloes in natural settings to assess the prevalence and clinical manifestations of the disease. For example, **El-Sayed et al. (2020)** conducted a cross-sectional study to evaluate the incidence of OSD in various herds across different geographic regions in Egypt. This approach allowed researchers to gather data on the clinical signs, environmental conditions, and management practices associated with OSD.

2. Experimental Studies:

Experimental studies are also employed to investigate the pathogenesis of OSD. For instance, researchers may induce OSD in controlled settings to study the effects of specific pathogens or environmental factors on the disease's development. Abdel-Moneim et al. (2019) utilized an experimental model to assess the role of viral infections, such as bovine viral diarrhea virus (BVDV), in the etiology of OSD, allowing for a controlled examination of the disease mechanisms.

Sample Selection:

1. Population Sampling:

Selecting an appropriate sample population is critical for the validity of research findings. Studies often involve random sampling of buffaloes from various farms to ensure representativeness. For example, **Hassan et al. (2021)** selected buffaloes from different regions with varying environmental conditions to assess the impact of these factors on OSD prevalence. This method enhances the generalizability of the results.

2. Inclusion and Exclusion Criteria

Researchers typically establish clear inclusion and exclusion criteria to define the study population. For instance, only buffaloes exhibiting specific clinical signs of OSD may be included in a study, while those with other concurrent diseases may be excluded to minimize confounding variables **(Mohamed et al. 2022).**

Data Collection:

1. Clinical Examination:

Clinical examinations are a fundamental

component of OSD research. Veterinarians or trained personnel conduct thorough physical assessments to document clinical signs, such as swelling, pain, and skin lesions. **El-Sayed et al. (2020)** emphasized the importance of standardized examination protocols to ensure consistency in data collection.

2. Laboratory Testing:

Laboratory tests play a crucial role in diagnosing OSD and understanding its etiology. Blood samples may be collected for serological testing to identify viral infections, while skin biopsies can be performed for histopathological examination. **Abdel-Moneim et al. (2019)** utilized serological assays to detect BVDV antibodies in buffaloes with OSD, providing insight into the viral contribution to the disease.

3. Environmental Assessments:

Environmental factors are assessed through observational studies and data collection on temperature, humidity, and sanitation practices in buffalo housing. **Hassan et al. (2021)** conducted environmental assessments to correlate these factors with the prevalence of OSD, highlighting the significance of environmental conditions in disease manifestation.

Data Analysis:

1. Statistical Methods:

Statistical analysis is essential for interpreting data and drawing conclusions. Researchers often employ descriptive statistics to summarize clinical findings and prevalence rates. Inferential statistics, such as chi-square tests or logistic regression, may be used to assess associations between risk factors and OSD incidence **(Mohamed et al. 2022).** For example, **El-Sayed et al. (2020)** used logistic regression to analyze the relationship between nutritional deficiencies and the occurrence of OSD.

2. Qualitative Analysis:

In addition to quantitative methods, qualitative analysis may be employed to gain insights into management practices and farmer perceptions of OSD. Interviews and surveys can be conducted to gather information on farmers' experiences with the disease, which can inform prevention strategies and educational initiatives.

Bacteriological Examination:

Samples should be collected aseptically from clinical cases by aspiration of pus from closed lesions or through aseptic swabbing from opened lesions and sent on ice to the laboratory at which microbiological investigations are performed. All samples from lymph nodes and edematous skin lesions are inoculated on trypticase soy broth (TSB) and incubated for 37°C for 24 h. All samples are cultured on duplicated blood agar (incubation at 37°C for 24 h to 48h in complete aerobic conditions supported with 10% CO2), MacConkey agar, Pseudomonas agar, mannitol salt agar (incubation for 24h at 37°C) **(Quinn et al. 2002).** All suspected colonies were put forward for Gram staining and different biochemical identification tests **(Quinn et al. 2002).**

Hemolytic colonies and non-hemolytic creamy in color on blood agar and in trypticase soy broth, it forms a surface film, though the culture remains clear; this film is broken by agitation, forming flakes were submitted for catalase, oxidase and confirmed for Corynebacterium species by S.R.O GP24.

RESULTS

Prevalence and Clinical Findings:

Recent studies have reported varying prevalence rates of Oedematous Skin Disease (OSD) in Egyptian buffalo populations. **El-Sayed et al. (2020)** conducted a cross-sectional study across several regions in Egypt and found that the prevalence of OSD ranged from 10% to 25%, with higher rates observed in areas with poor sanitation and high humidity. Clinical examinations revealed that the most common signs included swelling of the face, limbs, and abdomen, along with associated pain and behavioral changes. In severe cases, secondary skin lesions such as ulcers and necrosis were noted **(Hassan et al. 2021).**

Etiological Factors:

The etiology of OSD has been linked to various infectious agents and environmental factors. **Abdel-Moneim et al. (2019)** identified Bovine Viral Diarrhea Virus (BVDV) as a significant viral contributor to OSD, with serological tests revealing a high prevalence of BVDV antibodies in affected buffaloes. Bacterial pathogens, particularly Clostridium spp. and Staphylococcus aureus, were also frequently isolated from skin lesions, indicating a polymicrobial infection pattern **(El-Sayed et al. 2020).**

Environmental assessments conducted by **Hassan et al. (2021)** indicated that high humidity levels and inadequate drainage systems significantly correlated with increased OSD incidence. Nutritional deficiencies, particularly in protein and vitamins, were reported to compromise the immune response of buffaloes, making them more susceptible to infections leading to OSD (**Mohamed et al. 2022**).

Treatment Outcomes:

Treatment strategies varied across studies, with most veterinarians employing a combination of antibiotics, anti-inflammatory drugs, and supportive care. **Mohamed et al. (2022)** reported that the use of broad-spectrum antibiotics significantly reduced the severity of clinical signs in affected buffaloes. In cases where abscesses developed, surgical drainage was necessary, leading to improved outcomes and recovery rates.

DISCUSSION

Oedematous Skin Disease represents a multifactorial challenge in the management of buffalo health in Egypt. The findings from various studies underscore the importance of understanding the interplay between infectious agents, environmental conditions, and nutritional status in the pathogenesis of OSD.

Infectious Agents:

The identification of both viral and bacterial pathogens as contributors to OSD highlights the need for comprehensive diagnostic approaches. The presence of BVDV in affected buffaloes suggests that vaccination programs targeting this virus could be beneficial in reducing the incidence of OSD **(Abdel-Moneim et al. 2019).** Furthermore, the isolation of bacterial pathogens emphasizes the necessity for improved biosecurity measures and management practices to prevent infections.

Environmental and Nutritional Factors

The correlation between environmental conditions and OSD prevalence is particularly concerning. High humidity and poor sanitation create an environment conducive to the proliferation of infectious agents **(Hassan et al. 2021).** Implementing better drainage systems and sanitation protocols in buffalo housing could significantly mitigate the risk of OSD. Additionally, addressing nutritional deficiencies through balanced diets rich in proteins, vitamins, and minerals is crucial for enhancing the immune response of buffaloes **(Mohamed et al. 2022).**

Treatment and Management Strategies

The treatment outcomes observed in various studies indicate that a multifaceted approach is necessary for managing OSD effectively. The combination of antibiotics and anti-inflammatory medications has shown promise in alleviating clinical signs **(Mohamed et al. 2022).** However, reliance solely on pharmacological interventions may not be sufficient. A holistic approach that includes preventive measures, such as vaccination, improved management practices, and nutritional support, is essential for long-term control of OSD.

CONCLUSION

Oedematous Skin Disease poses a significant threat to the health and productivity of Egyptian buffaloes. The disease's multifactorial nature necessitates a comprehensive understanding of its etiology, clinical manifestations, and management strategies. The findings from recent studies emphasize the importance of addressing infectious agents, environmental conditions, and nutritional deficiencies to reduce the incidence of OSD effectively.

Future research should focus on developing targeted vaccination programs, improving management practices, and enhancing nutritional strategies to combat OSD. By implementing these measures, veterinarians and livestock producers can work towards improving the welfare and productivity of buffalo populations in Egypt.

OSD remains a persistent challenge in Egyptian livestock due to its complex interplay of environmental, microbiological, and immunological factors. Advances in understanding its pathogenesis, particularly cytokine dynamics and biovar-specific virulence, offer pathways for targeted vaccine development and improved diagnostic strategies. Addressing antibiotic resistance and enhancing vector control are critical for mitigating this economically devastating disease.

Oedematous Skin Disease represents a significant challenge to the health and productivity of Egyptian buffaloes. Understanding its etiology, clinical manifestations, and management strategies is essential for veterinarians and livestock producers. Continued research and education are necessary to develop effective prevention and treatment protocols, ultimately improving animal welfare and productivity in the buffalo farming sector.

The methodologies employed in researching Oedematous Skin Disease in Egyptian buffaloes encompass a range of observational and experimental approaches, sample selection techniques, data collection methods, and analytical strategies. Understanding these methodologies is essential for evaluating the validity and reliability of research findings. Continued research utilizing robust methodologies will enhance our understanding of OSD, ultimately contributing to improved management practices and animal welfare in buffalo farming.

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