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Article Review

A Review on Hemorrhagic Septicemia

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ABSTRACT

Hemorrhagic septicemia (HS) is an acute, fatal septicaemic bacterial disease, affecting mainly cattle and buffalo, but it is widely considered that buffaloes are the most susceptible. The disease is an important cause of high morbidity and mortality in tropical regions of Asia, Africa and the Middle East. It is caused by *Pasteurella multocida* serotype B: 2 (Asian countries) and serotype E:2 (African countries). Respiratory system plays the main role in the route of transmission of the HS disease where the *Pasteurella multocida* enters the respiratory tract of infected animals through inhalation and passes into the bloodstream thus producing clinical signs which usually progress rapidly from fever and depression to death within hours to a few days. Because the disease course is so short, few animals can be treated in time, and recovery is rare. Outbreaks mostly occur during the changed climatic conditions (high humidity and high temperatures). This review aims to summarize the latest developments of the disease with the focus on its spread, etiology, transmission, clinical presentations, diagnostics and control measures.

INTRODUCTION

Hemorrhagic septicemia is a serious acute, highly fatal, and highly prevalent disease in livestock. It considered the most economically important bacterial disease of water buffalo and cattle in tropical areas of Asia, particularly in India and other parts of Southeast Asia where water buffalo populations are high. The disease is most devastating to smallholder farmers where husbandry and preventive practices are poor and free-range management is common. Hemorrhagic septicemia may be

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asymptomatic or unnoticed until onset of the acute stage, which is characterized by rapid onset (within a few hours) and progression. Hemorrhagic septicemia is also an important disease in Africa and the Middle East, with sporadic outbreaks occurring in southern Europe **(Spickler 2019).**

Etiology

Hemorrhagic septicemia is caused by certain members of *Pasteurella multocida* subsp. multocida, a Gram-negative coccobacillus in the family Pasteurellaceae. *Pasteurella multocida* can be found in the upper respiratory tract as normal flora or can act as a primary or secondary pathogen depending on the species of animal. *Pasteurella multocida* isolates are traditionally identified by a letter designating the organism's serogroup (A, B, D, E, F), based on the capsular antigen, and a number for the somatic antigen accordingly HS is caused by *Pasteurella multocida* serotypes B:2 and E:2 (Carter and Heddleston classification system). The B:2 serotype has been seen in Southern Europe, the Middle East, Southeast Asia, Egypt, and the Sudan. The E:2 serotype has been reported in Egypt, the Sudan, the Republic of South Africa, and several other African countries **(De Alwis 1999 and Boulianne et al. 2019)**

Stability and sensitivity

Pasteurella multocida is susceptible to mild heat (55°C) and most disinfectants. *Pasteurella multocida* does not remain viable for long periods in the environment, but it can survive for hours and possibly days in damp soil or water. Rainy conditions and high humidity facilitate transmission **(Cuevas et al. 2020).**

Transmission

It has been estimated that up to 5% of healthy water buffalo and cattle are colonized by small numbers of *P multocida* serotype B:2 or E:2, which can be shed during periods of stress. Common stressors associated with outbreaks of hemorrhagic septicemia include high temperature and humidity, concurrent infection, poor nutrition, or work stress. Although outbreaks can occur at any time, disease is most prevalent during the rainy season. Increased outbreaks associated with high rainfall are most likely due to the multiple stressors present during this time and the moist conditions, which prolong the survival time of the organism in the environment. Infection occurs by contact with infected oral or nasal secretions from either healthy carrier animals or animals with clinical disease, or by ingestion of contaminated feed or water. Infection begins in the tonsil and adjacent nasopharyngeal tissues. Subsequently, bacteremia leads to dissemination and rapid growth of bacteria in various locations, tissue injury, a host cytokine response, and release of lipopolysaccharides, that results in a rapidly progressing endotoxemia. Clinical signs can appear 1–3 days after infection, and death can occur within 8–24 hours after the first clinical signs develop. Biting arthropods do not seem to be significant vectors **(Benkirane and De Alwis, 2002; Brown C. and Torres, 2008)**

Host range

Hemorrhagic septicemia affects mainly cattle and buffalo, in tropical regions of the world. Hemorrhagic septicemia is caused primarily by *P. multocida* serotypes B:2 and E:2 and is thought to occur at the later stages of pasteurellosis disease. Hemorrhagic septicemia is observed less commonly in swine, sheep, goats, deer, and elk and then is mostly associated with serotype B:2 strains. The only confirmed outbreaks of HS in the Americas occurred in bison in Yellowstone National Park, most recently from 1965–1967. Hemorrhagic septicemia is observed less commonly in swine, sheep, goats, deer, and elk and has been reported in camels, elephants, rhinoceros, horses, donkeys, yaks, and various species of deer and other wild ruminants. In areas where animals have no immunity, severe disease is expected to occur in all ages **(De- Alwis 1992; Ahmed 1996).**

Transboundary spread

The estimated global population of buffalo is 204.3 million, with 97.09% found in Asia, followed by Africa (1.7%), America (0.97%), and Europe (0.22%), whereas the estimated global population of cattle is 1.5 billion, with 34.9%

distributed in America, followed by 31.1% in Asia, 23.8% in Africa, and 7.8% in Europe **(Almoheer et al. 2022)**.

Several outbreaks have been reported since 2010 in Central Europe (e.g., Germany, Hungary, Serbia), suggesting that the causative organisms may have been introduced to this region after apparently being absent for decades. Hemorrhagic septicemia-causing strains of *P. multocida* are not thought to circulate in North America, Australia or New Zealand. They were also thought to be absent from South and Central America; however, this disease was reported to the World Organization for Animal Health (OIE) from Colombia in 2007, Venezuela in 2015 and Ecuador in 2018. There seems to be little or no published information about these outbreaks. Serotype B:2 is the major cause of hemorrhagic septicemia in Asia, although a few clinical cases are apparently caused by other serotypes, including members of serogroup E. B:2 is also prominent in Europe and the Middle East. At one time, most cases of hemorrhagic septicemia in Africa were thought to be caused by serotype E:2. However, B:2 organisms have increased in frequency there, and the relative contributions of these two serotypes are currently unclear.

The importance of Hemorrhagic septicemia (HS) to buffaloes rearing in Iraq is highlighted by a survey, which indicated its prevalence up to 38.74 % (National survey, 2008). The disease causes many outbreaks and infections in cattle, buffaloes and sheep in Basra **(Al-Hamed, 2010),** Al-Qadisyia **(Salah, 2012)** and Baghdad **(Al-Shemmari, 2013)**. **Khan et al. (2012)** reported an outbreak of hemorrhagic septicemia in buffalo calves in Pakistan, 31.48% mortality was recorded. Mortality significantly peaked on 8th day (37%). **Fraz (2011)** stated that an extensive outbreak of an HS occurred in the dromedary population of Greater Cholistan from mid of November 2010 to the mid of December 2010

Moreover, in a study on HS done by **Farooq et al .(2011)** whose reported that the overall morbidity, mortality and case fatality rates were 17.39, 14.66 and 84.30%, respectively, from 10 infected/outbreak villages in Pakistan with the total population of 4248 animals. **Khan et al. (2013)** stated that HS is a widespread disease in India, occurs more frequently in poor farming conditions. In the present instance, the animals were brought up under an extensive, free-range system. Such conditions are ideal surroundings for the spread of HS. **McFadden et al. (2011)** stated that an acute outbreak of septicemia in cattle in New Zealand resulting in high mortality and added that all ages of cattle was affected. **Waffa et al. (2014)** recorded an outbreak of hemorrhagic septicemia (HS) with 100% morbidity and 27.5% mortality was reported in a herd of domestic water buffalo at Thi Qar / the south west of Iraq. Haemorrhagic Septicaemia was reported during July, 2016 in buffaloes of village Ranipur, district Patna, Bihar, India by **Sinha et al. (2018). Brown et al. (2021)** reported an outbreak in 2019 in New Zealand, where ≤48-hour-old calves became acutely ill. The hygiene, biosecurity and ventilation in the pens were poor. Of the 15 calves, 11 died while four calves became acutely ill later in the outbreak were treated with cefquinome and recovered. Around 40 buffaloes have died within four days due to suspected Sahana disease (hemorrhagic septicemia) in a number of villages located in the Garadapur block of Odisha's Kendrapara stated by **Ashis (2020).**

The data used in the current systematic analysis were extracted from the World Organization for Animal Health (OIE-WAHIS) for the prevalence of HS among buffaloes, cattle, sheep, and goats in 41 countries in 2005–2019.The infection rate among cattle worldwide dropped from 77.4% in 2005 to 72.4% in 2019, while the infection rate among buffaloes declined from 15.6% in 2005 to 2.8% in 2019. In Africa, the infection rate among cattle decreased from 100% in 2005 to 63.8% in 2019, whereas the infection rate among sheep and goats increased to 20.7% and 15.5%, respectively, in 2019. In Asia, the infection rate among cattle, sheep, and goats increased from 64.7%, 4.2%, and 6.7% in 2005 to 77.6%, 9.4% and 8.2% in 2019, respectively, while the infection rate among buffaloes decreased from 24.4% in 2005 to 4.7% in 2019 **(Almoheer et al. 2022).**

Clinical signs

Most cases in buffaloes are acute or peracute. In peracute cases of hemorrhagic septicemia that result in death within 8–24 hours, animals often have fever, hypersalivation, nasal discharge, and rapidly followed by respiratory distress, septic shock with widespread hemorrhaging, and death within 1 to 3 days **(Shivachandra et al. 2011).** However, because of the short duration of the disease, these clinical signs may easily be overlooked. Acute disease can persist for up to 3 days, and less often up to 5 days, and is characterized by fever (40°–41.1°C), restlessness and reluctance to move, hypersalivation, lacrimation, nasal discharge that begins as serous and progresses to mucopurulent, oedematous swellings become apparent in the pharyngeal region; these swellings spread to the ventral cervical region and brisket, Respiratory distress occurs, progressive respiratory distress, cyanosis, terminal recumbency, and sometimes abdominal pain with diarrhea, and the animal usually collapses and dies 6–24 hours after the first signs are seen. Animals with clinical signs, particularly buffalo, rarely recover. Chronic cases do not seem to occur in buffalo. In endemic areas most deaths are confined to older calves and adults **(Wilkie et al. 2012)**

Lesions

Widespread haemorrhages, oedema, and hyperaemia, consistent with severe sepsis. Oedema consists of a coagulated serofibrinous mass with straw-coloured or blood stained fluid. Swelling of the head, neck, and brisket occurs in nearly all cases. Similar swellings can also be found in the musculature. Subserosal petechial haemorrhages may occur throughout the body, and the thoracic and abdominal cavities often contain blood-tinged fluid. Scattered petechiae may be visible in the tissues and lymph nodes, particularly the pharyngeal and cervical nodes; these nodes are often swollen and haemorrhagic. Pneumonia or gastroenteritis occasionally occurs, but usually is not extensive. Atypical cases, with no throat swelling and extensive pneumonia, are sometimes seen. There are no microscopic features that are specific for hemorrhagic septicaemia – all lesions are consistent with severe endotoxic shock and massive capillary damage **(Radostits et al. 2007; Naz et al. 2012)**

Economic importance

Buffaloes show a shorter course of the disease and are more susceptible to HS than cattle with a mortality rate reaching 100% in untreated cases at an early stage **(Rafidah et al. 2012)** and because the disease course is so short, few animals can be treated in time, and recovery is rare, so due to severe economic losses and is ranked as the most important contagious disease of cattle and buffaloes **(Benkirane and De ALwis 2002).**

Diagnosis and differential diagnosis

Clinical diagnosis based on history, lapses in vaccination, environmental conditions, and clinical signs and characteristic lesions. Laboratory diagnosis based on culture and biochemical tests **(Quinn et al. 2006).** More recently, molecular techniques, including agar gel electrophoresis **(Ranjan et al. 2011).**

Shipping fever is often mistakenly confused for HS, but has a multifactorial aetiology (often Mannheimia haemolytica), is not septicaemic, and does not cause multisystemic petechial haemorrhages. The peracute nature of the disease and the extensive oedema and haemorrhage make it difficult to differentiate from blackleg and anthrax. Acute salmonellosis and mycoplasmosis should also be considered.

Treatment

Antibiotic treatment can be effective against hemorrhagic septicemia if administered very early in the disease. However, because HS progresses rapidly, treatment is often unsuccessful. During outbreaks, any diseased animal with a fever should be treated with intravenous Antibiotic as soon as possible to quickly obtain systemic bactericidal antimicrobial concentrations. Antimicrobial susceptibility testing (AST) is particularly necessary for *P.* multocida for which resistance to commonly used antimicrobial agents has occurred Antibiotics like Penicillin, Amoxicillin, Cephalothin, Ceftiofur, Cefquinome, Streptomycin, Gentamicin, Spectinomycin, Florfenicol, Tetracycline, Sulfonamides, Tri-

methoprim/Sulfamethoxazole, Erythromycin, Tilmicosin, Enrofoxacin and Norfoxacin can be effectively used have been used effectively to treat HS **(OIE, 2008).**

Prevention and control

Avoiding crowding, especially during wet conditions, will also reduce the incidence of the disease, medical prophylaxis and sanitary prophylaxis Vaccination is routinely practiced in endemic areas **(Verma and Jaiswal, 1998).**

Killed vaccines are most commonly used for prevention and include bacterins, alum-precipitated and aluminum hydroxide gel vaccines, and oil-adjuvant vaccines. In animals >3 years old, an initial two doses, 1–3 months apart, are recommended, followed by booster vaccinations once or twice yearly. The oil-adjuvant vaccine provides protection for 9–12 months and is administered annually. It is most effective when administered 1 month before the monsoon or rainy season. Although it provides the strongest immunity, it is unpopular in the field because of its viscosity and difficulty of administration **(OIE, 2019).**

The commonly used alum-precipitated and aluminum hydroxide gel vaccines have shorter durations of immunity (approximately 4–5 months with variable protective efficacy), and twice yearly booster vaccinations are recommended. It is important that the vaccines are made from the strains of *P multocida* circulating in the regions of intended use to obtain maximal effectiveness. Maternal immunity can interfere with vaccine efficacy in calves.

Attenuated or modified-live vaccines have been used with some success. A live, avirulent, intranasal vaccine prepared from a *P multocida* serotype B:3 of fallow deer origin seems generally effective; however, this vaccine has been associated with sporadic outbreaks and virulence in young animals. Various modified-live and subunit vaccines made from either purified or recombinant bacterial components have also been investigated experimentally but are not widely available **(Rafidah et al. 2012).**

Failure of vaccination to control HS is common due to inadequate vaccine coverage (< 70%), mostly due to variable management systems that make annual vaccination difficult.

CONCLUSION

It can be concluded that HS is highly fatal disease. Because the disease course is so short, few animals can be treated in time, and recovery is rare. Young animals are mainly affected in endemic regions, and outbreaks are particularly common during rainy weather, when the organism can spread readily. In areas where animals have no immunity, severe disease is expected to occur in all ages. In addition, vaccination against HS before transportation consider as important factors in the initiation of the disease also. *Pasteurella multocida* B: 2 and E: 2 are the causative agent of HS that occurs mainly in water buffaloes and cattle. It has been found in almost all parts of the world as a costly animal disease that causes billions of dollars in losses annually. Vaccination against HS remains the most effective way to prevent the disease, and the antibiotics are inefficient.

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