



## Heat Intolerance Associated with Foot and Mouth Disease in Cattle: A Neglected Syndrome

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### ABSTRACT

Heat intolerance (HI) syndrome is a chronic condition sequel to Foot and Mouth Disease (FMD) in cattle. FMD is a highly contagious viral disease affecting cloven-hoofed animals and is endemic in many regions of Africa, Asia, and the Middle East. FMD is typically characterized by fever, anorexia, excessive salivation, and vesicular lesions on the mouth, teats, and feet, often resulting in mastitis, lameness, and some cases, complications such as heat intolerance. HI syndrome has been reported in some cattle following FMD outbreaks in Egypt, Ethiopia, Iraq, and Tanzania. The syndrome is characterized by shade-seeking behaviour, panting, hair overgrowth, hyperthermia, weight loss, and reduced milk production. Despite extensive research on the pathogenesis and economic burden of FMD, HI syndrome remains poorly understood. This review synthesizes the existing knowledge on HI syndrome, highlights key knowledge gaps, and recommends future research directions for this neglected syndrome associated with FMD in cattle.

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### INTRODUCTION

Foot and Mouth Disease (FMD) is a highly contagious viral disease that affects cloven-hoofed animals, including cattle, goats, sheep, pigs and various wildlife species. The disease is caused by the FMD virus (FMDV), which is a member of the genus Aphthovirus in the family Picornaviridae (Zell et al. 2017; Azeem et al. 2020). The virus is primarily transmitted through direct contact with infected animals or contaminated materials. The disease is endemic in many countries in Africa, Asia and the Middle East (Byomi and Zidan 2023; Aslam and Alkheragia 2023). However, FMD outbreaks can also occur in countries considered free of the disease, impacting animal health and resulting in severe economic losses (Knight-Jones and Rushton 2013).

The clinical signs of FMD in cattle, especially young calves and highly productive breeds are normally severe. In young calves, heart failure is the most common outcome without developing lesions like vesicles in adults (Salim et al. 2019; Alagmy et al. 2022). In adults, the most common characteristic signs and lesions are fever and vesicles that appear in the mouth on the dental pad, gums, tongue, soft palate, nostrils, and muzzle (Azeem et al. 2020). As a result of the vesicles in the mouth, the animal becomes reluctant to eat, hence anorexia. Furthermore, the lesions may ulcerate, causing affected animals to produce copious

amounts of saliva and nasal discharge, which starts as mucoid and eventually turns mucopurulent (Islam et al. 2017; Azeem et al. 2020). Animals that are affected become lethargic, may quickly experience weight loss and progressive or abrupt, significant declines in milk output. In certain circumstances, milk production may stop until the following lactation or may permanently decrease. In addition to other manifestations like mastitis or foot deformities, it has been observed that some cattle that recover from clinical FMD also acquire heat-intolerance (HI) syndrome (Radostitis et al. 1994; Pereka et al. 2000; Chibunda et al. 2006; Ghanem and Abdel-Hamid 2010). Heat intolerance is normally a failure of the heat-regulating mechanisms of the body, resulting in an inability to cope with high environmental temperatures. Failure of the heat-regulating mechanisms has been exhibited in cattle, especially as a sequel to foot-and-mouth disease. This syndrome has been observed and reported to be associated with previous outbreaks of FMD in various countries, including Egypt (Ghanem and Abdel-Hamid 2010), Ethiopia (Jibat et al. 2013), Iraq (Abbas et al. 2012) and Tanzania (Pereka et al. 2000; Catley et al. 2004; Chibunda et al. 2006). The syndrome is referred to as 'luzwiga' by the Sukuma people in Tanzania (Chibunda et al. 2006), as Mahrorah in Iraq (Abbas et al. 2012) and as hairy panting syndrome in Egypt (Ghanem and Abdel-Hamid 2010). In Cambodia, farmers referred to HI animals as cattle that

'like to swim a lot' and their 'coats changed colour' (Young et al. 2016). The syndrome is characterized by hair overgrowth, shade-seeking behaviour, panting, loss of body weight, increased body temperature, high respiration rate and reduced milk production (Pereka et al. 2000; Chibunda et al. 2006). Furthermore, affected animals reduce grazing and rumination time, especially on sunny days. These clinical presentations can affect the general well-being of animals, resulting in poor health and productivity. For instance, shade-seeking behaviour may cause reduced grazing time, which may also affect fertility and productivity. Similarly, HI syndrome associated with FMD may lead to substantial economic losses resulting from reduced milk production and fertility rate. As a result, the syndrome can impact the livelihoods of livestock keepers, who depend on cattle production as a source of income.

Although FMD in cattle has been extensively studied, with good documentation on its epidemiology, pathogenesis and economic impacts, its potential association with HI syndrome remains relatively underexplored. However, HI syndrome may significantly affect productivity loss in affected animals, especially in the tropics. This scoping review explores the knowledge gaps related to HI syndrome associated with FMD, highlighting the importance of understanding the pathophysiology of the syndrome and its possible economic impacts on cattle productivity.

#### **Pathogenesis of Foot and Mouth Disease in Cattle**

Foot and Mouth Disease (FMD) is caused by the FMD virus (FMDV), a member of the Aphthovirus genus which belongs to the family Picornaviridae (Zell et al. 2017). The virus has seven serotypes namely, O, A, C, SAT1, SAT2, SAT3 and Asia1 (Byomi and Zidan 2023). The virus is transmitted through direct contact with infected animals or contaminated materials. The virus enters the animal body through the epithelium or mucosa of the nose and mouth. After entry, the virus multiplies in the epithelial cells of the oropharynx leading to a primary viremia. Following the primary replication site, the viruses are spread to regional lymph nodes, lungs and then disseminates to the rest of the body via the bloodstream resulting in systemic infection (Arzt et al. 2017). The systemic disease is characterized by fever, vesicular lesions on the tongue, gums and between the hooves. These lesions are caused by the necrotic change in epithelium and inflammation related to the viral attack of the skin (Kumar et al. 2017). These lesions may impair animal's feeding and movement ability leading to a lot of economic loss in the affected herds (Knight-Jones and Rushton 2013; Ali et al. 2024).

Although FMD in cattle is normally characterized by severe fever, vesicles and lameness, most cattle recover within 2-3 weeks depending on nutrition, environment and absence of secondary infections (Kumar et al. 2017; Ghonaim et al. 2025). However, some recovered cattle can remain viral carriers, particularly in lymphoid tissues (Stenfeldt et al. 2016). Furthermore, some cattle recovered from FMD develop heat intolerance (HI) syndrome (Radostitis 1994; Catley et al. 2004; Chibunda et al. 2006; Ghanem and Abdel-Hamid 2010; Young et al. 2016). Unfortunately, the main cause of the syndrome and its pathogenesis in cattle recovered from clinical FMD are not

clear. Therefore, there is a need for a comprehensive study to examine the way FMD virus affects host cells and tissues in a way that alters thermoregulation in cattle. Similarly, there is a need for efforts to determine if some specific FMDV types or serotypes are associated with long-term sequelae including heat intolerance syndrome in cattle.

#### **Association of Heat Intolerance Syndrome with Foot and Mouth Disease in Cattle**

Heat intolerance (HI) syndrome which is a chronic condition, develops in some cattle following an outbreak of clinical FMD (Radostitis 1994; Chibunda et al. 2006; Ghanem and Abdel-Hamid 2010). The occurrence of the syndrome and its association with FMD appear to be very well-known among livestock keepers in Africa (Catley et al. 2004; Chibunda et al. 2006; Jibat et al., 2013) and in the middle East (Abbas et al. 2012). In Tanzania, Catley et al. 2004, using the matrix scoring and proportion piling of participatory appraisal methods revealed that heat intolerance syndrome is common in some FMD recovered cases. The study revealed further that whereas Sukuma livestock keepers in Mwanza region did not associate the HI syndrome with previous FMD outbreak, higher agreement that HI syndrome is associated with previous FMD outbreak was evident among Maasai pastoralists in Morogoro region (Catley et al. 2004). In Ethiopia, Jibat et al. (2013) used also the participatory appraisal methods to estimate the impacts of FMD on the livelihood of livestock keepers. The study revealed that all informant groups recognized HI syndrome as a sequela of FMD in cattle. The informants in Ethiopia were also conversant with clinical manifestations of the syndrome.

The syndrome is characterized by hair overgrowth, shade-seeking behaviour, panting, salivation, loss of body weight, increased body temperature and respiration rate and reduced milk production (Ghanem and Abdul-Hamid 2010; Chibunda et al. 2006; Abbas et al. 2012; Jibat et al. 2013). The affected animals also tend to reduce grazing and rumination time in the evening and during sunny days, and animals tended to wallow in water bodies at animal drinking points (Chibunda et al. 2006). The pathogenesis of HI syndrome associated with FMD is not fully understood, but hormonal disruption has been proposed (Radostitis 1994). However, association of HI syndrome with disruption of thyroid hormone has been disproved (Maddur et al. 2011). Unfortunately, to date there is no further study that has established pathogenesis of heat intolerance syndrome associated with FMD outbreaks in cattle. Unfortunately, to date there is no extensive epidemiological investigation that has been carryout to determine prevalence of HI syndrome associated with FMD in cattle.

#### **Possible Impacts of Heat Intolerance Syndrome on Cattle productivity and welfare**

Heat intolerance syndrome associated with FMD in cattle is characterized by increased body temperature, hair overgrowth, weight loss, panting, decreased grazing and rumination activity, and shade-seeking behaviour (Ghanem and Abdul-Hamid 2010; Chibunda et al. 2006; Abbas et al. 2012; Jibat et al. 2013). These symptoms can reduce cattle productivity in numerous ways. Cattle affected by HI syndrome exhibit persistently increased body temperature,

even under moderate environmental conditions. The inability to dissipate heat efficiently leads to excessive metabolic heat accumulation, exacerbating oxidative stress and increasing cellular damage. Persistent hyperthermia impairs enzymatic activity and metabolic pathways, leading to oxidative stress and reduced productivity (Collier et al. 2018).

The mechanisms underlying impaired thermoregulation in HI-affected cattle remain poorly understood. However, impaired thermoregulation may result in inadequate heat dissipation responses such as sweating and vasodilation (Sejian et al. 2019). Neurological dysfunction may also contribute to an impaired ability to activate thermoregulatory responses, further compounding heat stress. Neuromuscular damage further exacerbates the condition by weakening coordination and reducing the ability to seek cooler environments (Cheshire 2016). Excessive heat exposure leads to increased sweating and respiratory evaporation, resulting in the loss of essential electrolytes such as sodium, potassium, and chloride. Loss of electrolytes leads to electrolyte imbalances and dehydration, compromising circulatory and neuromuscular functions (Baumgard and Rhoads 2013). Electrolyte depletion may disrupt neuromuscular function, exacerbating symptoms such as weakness, and fatigue. The increase in the body temperature and panting in heat intolerance syndrome may result in additional energy costs to animal health and welfare (Das et al. 2016). As a result, cattle use much more energy to cool their bodies, which is likely to lead to negative energy balance and deteriorated body condition. The weight loss may lead to more adverse effects on dairy cows leading to decreased milk yield.

The reduction of grazing and rumination time in heat intolerant animals can also negatively affect cattle productivity due to reduced digestive efficiency. Grazing and rumination are crucial for appropriate digestion and nutrient absorption. This would impede cattle's natural grazing and ruminating behavior and, over time, they risk being underfed on the important nutrients which is detrimental to their overall health and productivity (Iqbal et al. 2023). This, in turn, can magnify weight loss and impair the efficiency of converting feed into body weight or milk. In addition, heat intolerance induced stress can have a long time effects on animal health and productivity.

#### **Knowledge gaps and future research direction**

Despite some reports on the occurrence of HI syndrome following FMD outbreaks in Africa, Asia and the Middle East, its association with FMD in cattle remains limited. The precise mechanisms through which FMD virus (FMDV) may disrupt thermoregulation are not yet well understood. It also remains unclear whether specific FMDV serotypes have a greater propensity to induce HI syndrome. Furthermore, evidence regarding breed-specific susceptibility is limited, particularly whether indigenous cattle breeds exhibit greater resilience compared to high-yielding exotic breeds. Identifying genetic or physiological markers of heat tolerance among different cattle breeds is therefore of significant importance.

Given these knowledge gaps, urgent research is needed to elucidate how FMDV infection affects thermoregulatory pathways at the cellular and tissue levels. This includes understanding the roles of stress hormones, inflammatory

mediators, and other biochemical processes that may link viral infection to impaired thermoregulation. Investigating these pathways could shed light on how post-FMD complications contribute to chronic heat intolerance. Moreover, large-scale epidemiological studies are required to determine the prevalence of HI syndrome among cattle that have recovered from FMD, as well as to assess whether particular FMDV serotypes are more frequently associated with long-term sequelae such as HI. In parallel, there is a critical need to evaluate the economic impact of HI syndrome, especially the losses related to reduced milk yield, impaired recovery of muscle mass, and diminished meat productivity due to prolonged thermal stress. Addressing these research priorities will require a multidisciplinary approach integrating virology, immunology, animal physiology, and agricultural economics. Ultimately, a better understanding of HI syndrome will support the development of targeted interventions and improved management practices to enhance thermal resilience and productivity in cattle populations affected by FMD.

#### **Conclusions**

In conclusion, this paper documents a neglected heat intolerance syndrome in cattle recovered from FMD. Despite the increasing incidences of FMD, its association with HI syndrome remains insufficiently studied. The association of heat intolerance syndrome and FMD in cattle underscores a critical yet often overlooked area of research that may have significant implications for animal health, cattle productivity and welfare. This neglect not only limits our understanding of the disease pathogenesis but also underrates the economic losses associated with the syndrome. Despite its massive possible consequences, this syndrome has not been a focus for researchers, and its pathogenesis remains largely unexplored. Since climate change increases the intensity of heat stress it makes research of this 'silent' disorder crucial for a sustainable and healthy future of cattle production in areas where FMD is endemic.

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