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***RESEARCH ARTICLE***

# RABIES EPIDEMIOLOGY AND HEALTH AUTHORITIES' EFFORTS IN CONTROL AND PREVENTION OF THE DISEASE IN THE KINGDOM OF SAUDI ARABIA: A NARRATIVE REVIEW

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***Abstract***

Rabies, a fatal zoonotic disease, has significant public health and economic impacts globally. In the Kingdom of Saudi Arabia, rabies presents a significant challenge due to its prevalence among both domestic and wild animals. This review provides a comprehensive overview of rabies epidemiology in Saudi Arabia, detailing the clinical forms, pathogenesis, transmission modes, and clinical manifestations in humans and animals. The control and prevention strategies employed by Saudi health authorities, including public health policies and vaccination campaigns, are critically analyzed. Despite the implementation of advanced healthcare and preventive measures, rabies persists as a significant threat, particularly in regions with a high incidence of animal bites. This review emphasizes the necessity for continuous monitoring, enhanced public awareness, and improved diagnostic capabilities to mitigate rabies transmission and ensure public health safety in Saudi Arabia and the broader Gulf region.



## Introduction:-

Since 1980, there has been a remarkable increase in the incidence of infectious disease outbreaks globally. In fact, new viruses are being identified at a rate of approximately three to four per year(Otte and Pica-Ciamarra, 2021). A significant proportion of emerging human pathogens, exceeding 60%, exhibit zoonotic characteristics, indicating the potential for animal-to-human transmission. These conditions result in 2.5 billion infections and 2.7 million deaths annually, with the most recent emergence being the coronavirus disease 2019 (COVID-19)(Otte and Pica-Ciamarra, 2021; Rahman et al., 2020; Sharan et al., 2023)**.**The economic impact of these diseases is considerable, resulting in significant costs for medical interventions, lost productivity, and disease control efforts (Elsohaby and Villa, 2023). As explained by Rahman et al. (Rahman et al., 2020), rabies, a fatal zoonotic condition, causes 30,000 to 70,000 yearly human casualties. While dogs are the primary reservoir, wild animals such as cats and jackals can also act as vectors for the transmission of the disease.The first documented case of rabies was in Babylon in 2300 B.C.(Gholami et al., 2014). In developing countries, the majority of cases are attributed to stray dog bites, while in developed nations, bat, fox, and other wild animal transmissions are the primary sources of infection(Rahman et al., 2020).

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**Types of rabies**

According to Fooks et al. (Fooks et al., 2017), rabies can be classified into two traditional forms: furious (encephalitic) and paralytic. Encephalitic cases usually occur unexpectedly, while paralytic cases occur in about 20% of cases. The condition is fatal once noticed and affects only a small percentage of those bitten(Dutta, 2014).

The prodromal symptoms of furious rabies include parasthesia, itching, fever, headache, tachycardia, anxiety, insomnia, restlessness, and myalgias. After two to three days, excitement develops, causing mental excitement, restlessness, hyperesthesia, and hydrophobia. Hydrophobia is expressed by an abrupt spasm of the mouth, pharynx, larynx, and respiratory muscles. It can be induced by offering water(Fooks et al., 2014; Jackson, 2011; Warrell and Warrell, 2015; Plotkin, 2000; Setiawan et al., 2018).

Rabies can be characterized by flaccid paralysis, fever, and profuse sweating(Ghosh et al., 2009; Dutta, 2014). This type of rabies is correlated with rare distal paraesthesiaand percussion myoedema and has a longer survival period (Hemachudha et al., 2005). The disorder has been identified in various species, including dogs, cats, foxes, sheep, goats, dromedaries, and horses. The initial outbreak was first reported in 1992/1993, affecting 44 animals and four species. The first documented case of human infection with this strain of rabies was declared in 1990, affecting a young schoolboy who had been bitten by a fox(Wernery, 2014). Cases of rabies have been recorded in different countries within the wider Gulf region over the years(Wernery, 2014; Bannazadeh Baghi et al., 2018). As reported by Wernery(Wernery, 2014), the disorder spread across Oman, where foxes serve as the primary reservoir for rabies, yet they are behind in terms of animal bites to humans.

In 2013, a recurrence of rabies was observed in the Arabian Peninsula, with infected animals including six feral cats, two red foxes, and one horse(Wernery, 2014). Epidemiological data from Kuwait indicates that dogs, bats, and other mammals may be the hosts of the disorder. It is uncertain whether Bahrain, Qatar, and the UAE are truly free of dog-mediated rabies, given that the classification is based on incomplete data and the lack of designated reference laboratories (Bannazadeh Baghi et al., 2018). In Saudi Arabia, rabies is a well-documented disease, with the majority of human bites occurring from canines, felines, rodents, and foxes(Memish et al., 2015). Despite advancements in healthcare, there has been a dearth of inquiries into rabies, with only one confirmed case reported. It is of interest to public health to continue to investigate animal-associated injuries. It is also noteworthy that Dhayhi et al. (Dhayhi et al., 2019) and Alknawy et al. (Alknawy et al., 2018) have provided evidence of the first verified cases of local human rabies in the country.

The clinical incidence of rabies in Saudi Arabia is attributed to a number of different animal species, including dogs, cats, rodents, camels, foxes, monkeys, and wolves (Algahtani et al., 2020; Kasem et al., 2019; Al-Tayib, 2019; Memish et al., 2015). In 2007, a study conducted in Al-Qassim examined 4,124 camels and found that the incidence of clinical rabies was 0.2 percent among camels that were most likely infected by bites from wild dogs (70%) or foxes (17%) (Kasem et al., 2019). From 1997 to 2006, a total of 26 dogs, 10 foxes, 8 camels, and 7 cats were reported to have rabies in Al-Qassim region(Memish et al., 2015; Kasem et al., 2019).

A revised report from 2007 to 2009 revealed that 11,069 animal bites had occurred in the country, with dogs (49.5%) and cats (26.6%) being the most prevalent(Memish et al., 2015; Kasem et al., 2019). The most common wild animals infected with the virus in the country are foxes and wolves, with the illness also being diagnosed in monkeys at a prevalence rate of 1.3%(Kasem et al., 2019).

The greatest burden of rabies-positive animals is observed in Al-Qassim, Eastern province, Riyadh, and Al-Madina territories. There is a prominent seasonal variation in the monthly incidence of bite injuries, with dog and cat bites demonstrating a year-long pattern of occurrence, while fox bites tend to increase in August and September (Memish et al., 2015; Al-Tayib, 2019). Despite the advances in healthcare in Saudi Arabia, there has been a paucity of inquiries into rabies in society, with only one confirmed case report in the previous decade. Animal-associated injuries remain a significant public health concern, and Dhayhi et al. (Dhayhi et al., 2019) and Alknawy et al. (Alknawy et al., 2018) provide compelling evidence of the first verified cases of local human rabies in the country.

**Pathogenesis**

The most significant risk factor pertains to bites on the hands, neck, face, and head, predominantly involving puncture(Singh et al., 2017; Chhabra et al., 2015; Consales and Bolzan, 2007). Such cases are correlated with shorter incubation periods due to the reduced length and greater number of neurons(Singh et al., 2017).

In most cases, the virus can persist in the muscle for an extended duration, which may provide an opportunity for post-exposure intervention and clearance by the host's immune system (Singh et al., 2017; Consales and Bolzan, 2007). The virus attaches to G-protein receptors on target cells (myocytes, local sensory, and motor neurons) and amplifies in muscle cells and macrophages(Singh et al., 2017).

The virus has been observed to persist for up to 18 days before migrating upwards and reaching the CNS, where it infects nerve cells(Singh et al., 2017). The virus travels retrogradely along peripheral nerves, affecting both motor and sensory nerves (Singh et al., 2017; Warrell and Warrell, 2004; Mazarakis et al., 2001). Additionally, RABV may enter the bloodstream due to a large inoculum at the bite site or in cases with short incubation periods(Singh et al., 2017; Burrell et al., 2017).

In accordance with the findings of Hemachudha et al. (Hemachudha et al., 2013), the dissemination of RABV infection is contingent upon the quantity of virus inoculum and the tissue tropism of the virus. It is most probable that dog-specific variants will infect deep bites that penetrate muscle tissue. Furthermore, Hemachudha et al. (Hemachudha et al., 2013) indicated that the virus's entry via the motor route is based upon the presence of the nicotinic acetylcholine receptor at the neuromuscular junction.

**Mode of transmission from animals to humans**

In their respective studies, Singh et al. (Singh et al., 2017),Noman et al.(Noman et al., 2021), Li et al.(Li et al., 2021), and Ngugi et al. (Ngugi et al., 2018) have identified the most common mode of transmission of the disorder as bites from animals, such as dogs and cats, which carry the infection due to their close association with humans. In Asia and Africa, canid bites account for 85-95% of cases, often resulting in physical and emotional trauma(Singh et al., 2017).

The risk of infection by bite is 5-80% higher than the chance of tissue invasion from licks or scratches, with a 0.1-1% chance(Singh et al., 2017). The mortality rate is dependent on the severity of the infection, the location of the wound, and the potency of the virus in the saliva. Bat-specific RABV isolates exhibit greater virulence in superficial epidermal injections and at lower temperatures, as evidenced by studies by Singh et al. (Singh et al., 2017)andConsales and Bolzan(Consales and Bolzan, 2007). In accordance with the findings of Consales and Bolzan (Consales and Bolzan, 2007), Singh et al. (Singh et al., 2017) propose that percutaneous infection may occur as a result of undetected skin contact and bites.

Over the past 50 years, a few non-bite rabies cases have been reported, but the incidence is lower than previously thought (Singh et al., 2017; Samad et al., 2024). The most efficient transmission route is saliva from bites, but other routes include inhalation of aerosolized RABV, tissue and organ transplants, handling of carcasses, and contamination of wounds. Inhalation exposure represents a potential transmission route(Singh et al., 2017; Hemachudha et al., 2013).

In 2005, corneal transplantation resulted in the acquisition of the infection in patients in the United States and in Germany, all of whom ultimately died. This incident highlighted the necessity for diagnostic testing, particularly in individuals presenting with nervous symptoms (Singh et al., 2017; Lu et al., 2018).

Rabies-infected individuals may transmit the disease through bites, although this is less well-documented(Singh et al., 2017; Feder et al., 2012). Unprotected contact with affected individuals and secretions with high virions can pose risks to relatives and healthcare professionals. Standard barrier precautions are crucial for minimizing transmission risk. Airborne exposure during vaccine production and animal vaccinations also pose risks. It is imperative to implement pre- and post-exposure prophylaxis to effectively manage these conditions(Singh et al., 2017; Weese, 2004; Bertozzi et al., 2016; Lodha et al., 2023; Costescu Strachinaru et al., 2024).

The skinning and handling of carcasses infected with rabies represent a significant transmission pathway, with dog slaughtering being a major pathogenic avenue(Nguyen et al., 2021; Tasiame et al., 2022; Ekanem et al., 2013). The consumption of dog meat is a delicacy in some societies. The presence of rabies virus in healthy dogs used for slaughtering predisposes butchers to rabies. The dog trade, slaughter processes, and consumption of dog meat represent fundamental elements of the rabies-specific epidemiological triangle. Congested trucks have been identified as a significant risk factor for the propagation of disorder among canines(Singh et al., 2017; Tasiame et al., 2022; Ekanem et al., 2013; Mshelbwala et al., 2013).

Singh et al. (Singh et al., 2017) and Mshelbwala et al.(Mshelbwala et al., 2013) emphasize the potential risk of rabies in the dog trade, where butchers handle animals without the necessary precautions and are not subject to government regulation. Furthermore, the unhygienic conditions prevalent in slaughterhouses and the dissemination organs of slaughtered animals serve to exacerbate the risk (Singh et al., 2017). The consumption of dog meat does not directly cause rabies transmission; however, the risk of transmission arises during the catching, handling, transporting, and slaughtering of the animals. The majority of butchers lack an understanding of the zoonotic significance of rabies, thereby exacerbating the risk element inherent to their trade(Singh et al., 2017; Mshelbwala et al., 2013; Garba et al., 2013).

**Clinical signs and symptoms in humans**

The disorder manifests in various ways, as evidenced by the findings of Plotkin (Plotkin, 2000), Warrell and Warrell (Warrell and Warrell, 2015), Consales and Bolzan (Consales and Bolzan, 2007), and Fooks et al. (Fooks et al., 2017), with an average incubation period of 20-60 days. The symptoms may manifest within five to six days, or in some cases, over a period of six months(Plotkin, 2000). However, the average phase lasts one to three months in approximately 60% of cases(Takayama, 2008).

Salomão et al. (Salomão et al., 2017) emphasize the considerable variability in the incubation periods for pathogens, which can range from two to three months. The time required for the pathogen to manifest in a host is influenced by various factors, including location, wound depth, and virus strain. The duration of infection can extend up to seven years following exposure. The initial symptoms of the disease include fever, anxiety, malaise, paraesthesia, and pruritus(Fooks et al., 2017; Warrell and Warrell, 2015; Plotkin, 2000).

A neuropsychiatric disorder of a particularly intense and distressing nature is typified by a constellation of symptoms including agitation, confusion, hydrophobia, hyperventilation, hypersalivation, priapism, and convulsions (Jackson, 2011; Plotkin, 2000). Hydrophobia, or fear of water, is a common symptom indicative of cerebral and autonomic dysfunction (Jackson, 2011). The disorder is episodic, with patients exhibiting cooperative and oriented behavior. In some cases, peripheral nerve paralysis is present, often accompanied by fever. Eventually, individuals exhibit symptoms and become paralyzed(Jackson, 2011; Plotkin, 2000; Hemachudha et al., 2005).

While paralytic rabies and Guillain-Barré Syndrome (GBS) share clinical points of similarity, GBS is distinguished by its sensory involvement and the absence of fever and encephalitic signs in oxygenated patients(Jackson, 2011; Plotkin, 2000; Hemachudha et al., 2005). It is of the utmost importance to conduct diagnostic investigations to distinguish between the two conditions. Recovery from rabies is limited, and patients who have received only partial vaccinations may experience severe neurological complications. No known treatment is currently available(Plotkin, 2000; Hemachudha et al., 2005; Manoj et al., 2016).

**Manifestations in animals**

Rabies in animals presents with a range of symptoms, including hyperexcitability, autonomic dysfunction, and aerophobia a(Burgos-Cáceres, 2011; Rohde, 2016; Lackay et al., 2008). However, the most common presentation is that of unexplained paralysis and behavioral changes, including loss of appetite, interest in unusual objects, pawing, breathing difficulties, swallowing difficulties, seizures, and hypersensitivities to touch or sound (Abdulkhazhieva and Abdulkhazhieva, 2023; Rohde, 2016).

Dogs, cats, and domestic ferrets are subjects of intense study in the rabies ecosystem due to their close contact with humans (Lackay et al., 2008). The incubation period for rabies virus in canines can range from seven days to several months, during which time the animal may exhibit symptoms including drooling, aggression, anxiety, and whining. The initial signs of rabies infection in canines include fever, nervousness, irritability, atypical behavior, and itching at the bite site (Burgos-Cáceres, 2011; Abdulkhazhieva and Abdulkhazhieva, 2023).

Dogs exhibit excitement for up to a week, followed by an encephalic and paralytic stage (Lackay et al., 2008). The excitement phase is characterised by aggressiveness, attacks, wandering movements, voicechanges, and seizures. The paralytic phase is characterised by the loss of voice, depression, and paralysis, which may ultimately result in a coma(Abdulkhazhieva and Abdulkhazhieva, 2023). The disease typically results in respiratory failure and death, with an average duration of three to eight days. Cats exhibit similar symptoms, yet they tend to conceal themselves and display greater viciousness(Lackay et al., 2008). Behavior that is inexplicable or that exhibits an abrupt adjustment should be regarded as suspicious (Frymus et al., 2009). Cats may present with nonspecific symptoms, such as fever, anorexia, vomiting, and diarrhea, and later, uncharacteristic behaviors. The typical interval between the onset of symptoms and death is 1-10 days(Frymus et al., 2009).

Small domestic animals like ferrets and rabbits are becoming popular companions, with an elevated risk of infection(Quesenberry and de Matos, 2020; Sujatha et al., 2023). The symptoms of this condition include lethargy, ataxia, paresis, paraparesis, paralysis, constipation, hypothermia, inappetence, anorexia, abnormal vocalization, sneezing, paraesthesia, and ptyalism. These symptoms are described in detail by Lackay et al. (Lackay et al., 2008). In rabbits, the symptoms include weakness in the forelimbs, palpable crepitus, head tremors, ear infection, nasal discharge, and anorexia(Lackay et al., 2008). In the case of foxes, increased aggressiveness may be observed (Rohde, 2016). It is of paramount importance to observe and understand the diversity of presentations exhibited by species in order to develop effective responses.

**Laboratory investigations**

Laboratory investigations for rabies can take various forms, including direct microscopy for interpreting histological sections and the World Health Organization-recommended direct fluorescent antibody test (DFAT) (Singh et al., 2017; Hemachudha et al., 2013; Mani and Madhusudana, 2013; Duong et al., 2016). Histopathological image analysis can reveal the Negri body, but these techniques have poor sensitivity and are not recommended for primary diagnosis (Singh et al., 2017; Mani and Madhusudana, 2013). Fluorescent testing has been demonstrated to have nearly 99% specificity and sensitivity(Mani and Madhusudana, 2013).

Another viral antigen investigative tool is rapid rabies enzyme immunodiagnosis (RREID), which identifies the presence of RABV antigens in specimens using monoclonal or polyclonal antibodies(Mani and Madhusudana, 2013; Duong et al., 2016).The utilization of rabies virus antigen in animal diagnostics has been investigated, with the rapid immunodiagnostic test (RIDT) being a cost-effective and efficacious method for animal rabies diagnosis. Nevertheless, the findings indicate that the low specificity of RIDT for human brain specimens renders it unsuitable for the diagnosis of zoonotic diseases in humans(Mani and Madhusudana, 2013).

Reverse-transcriptase PCR (RT-PCR) is a crucial diagnostic tool for rabies due to its high sensitivity and specificity(Duong et al., 2016). Nevertheless, Duong et al. (Duong et al., 2016) advised that it is a time- and resource-intensive process, while Mani and Madhusudana(Mani and Madhusudana, 2013) acknowledge that the risk of cross-contamination represents a significant flaw in its application. Additionally, practitioners may employ real-time reverse transcriptase PCR (RT-qPCR) in diagnostic procedures. Duong et al. (Duong et al., 2016) have expressed confidence in the potential of this approach, particularly with regard to the lower cross-contamination risk associated with the assays.

The direct rapid immunohistochemical test (dRIT), developed by the US Centers for Disease Control and Prevention (CDC), is a rapid, sensitive, and specific method for detecting rabies virus antigen in suspected brain smears, as compared to the fluorescent antibody technique(Mani and Madhusudana, 2013; Duong et al., 2016; Lembo et al., 2006).

**Control and prevention of rabies in Saudi Arabia and Gulf Area**

In Saudi Arabia, rabies is a reportable disease, and the Ministry of Health requires that all healthcare facilities in the country report suspected or confirmed cases to the Public Health Directorate(Memish et al., 2015; Algahtani et al., 2020).

Nevertheless, underreporting persists as a significant challenge across the Middle East, even in countries where the issue is perceived as endemic(Bannazadeh Baghi et al., 2018). Three National Reference Laboratories have been designated for testing the disease in animals in Saudi Arabia: one in Qassim, one in Al-Ahsa, and one in Jeddah (Memish et al., 2015; Algahtani et al., 2020). Additionally, the government provides healthcare facilities with a policy delineating the practices for handling rabid animal brain specimens and the protocols for submission(Memish et al., 2015; Kasem et al., 2019).

Furthermore, the Ministry of Health has disseminated a synopsis of pre- and post-exposure prophylaxis and treatment for rabid animal human bite victims to all healthcare professionals in the country(Memish et al., 2015). Additionally, the Ministry of Environment, Water, and Agriculture program is focused on the eradication of canine-transmitted human rabies by 2030(Kasem et al., 2019) and is worthy of note in the context of rabies control in Saudi

Arabia. The program's core strategies include "advocacy by the authorities for the prevention and control of rabies, community mobilization, dog immunization, resource allocation, public awareness, provision of post-exposure prevention, and facilitation of coordination between human and animal health sectors(Kasem et al., 2019).

The measures currently in place in Saudi Arabia are consistent with the findings of scholarly research indicating that the most effective approach to preventing and controlling the zoonosis is through the management of animals. As Singh et al. (Singh et al., 2017) posit, canine and feline vaccination, in conjunction with the management of stray animal populations and public health education, represent fundamental elements of animal rabies control.

While Saudi Arabia's actions in the prevention, treatment, management, and control of rabies are praiseworthy, there are shortcomings in its response, paralleling those observed in other countries within the broader Gulf region. Memish et al. (Memish et al., 2015) argued that a more comprehensive understanding of the epidemiology of animal bites and animal rabies in the largest country in the Peninsula would be of significant value. Indeed, reflecting the overall paucity of statistical information in the larger Gulf area, Baghi et al. (Bannazadeh Baghi et al., 2018) found that very little data on the problem are available in Oman, while several other countries, including Kuwait, Bahrain, and Qatar, are also hampered by reporting inadequacies, with some localities having no data at all. The accessible information is frequently out of date, as it does not account for changes over time and therefore may not be accurate (Bannazadeh Baghi et al., 2018).

The implementation of robust surveillance, data reporting/sharing, and monitoring mechanisms could facilitate the elimination of rabies in Saudi Arabia and the wider Gulf region, as proposed by Baghi et al. (Bannazadeh Baghi et al., 2018). The availability of rigorous empirical epidemiological data on the problem could enhance the efficacy of interventions. For Saudi Arabia, enhanced rabies control strategies are of particular significance, given the country's cultural and religious importance. Al-Tayib(Al-Tayib, 2019) reports that Saudi Arabia annually hosts the largest assembly of Hajj, where millions of pilgrims congregate in a small geographical area. In light of the nature of this gathering, Al-Tayib(Al-Tayib, 2019) acknowledges that the event places the country at the forefront of pandemic threats. Consequently, it is of the utmost importance to maintain a high level of vigilance in monitoring the pathogen in order to prevent the further spread of the virus locally, regionally, and internationally. Additionally, there is a significant economic aspect to the necessity of a more robust response to rabies in Saudi Arabia and other Gulf countries. This is particularly evident in the context of the livestock trade. Baghi et al. (Bannazadeh Baghi et al., 2018) posit that rural areas in the Middle East often exhibit a higher incidence of human rabies, as residents are more engaged in livestock farming and utilize canines for protection. Moreover, these populations have limited awareness of the risks of the zoonosis, are misinformed about it, or fail to fully adhere to post-exposure prophylaxis recommendations compared with their urban counterparts (Bannazadeh Baghi et al., 2018). Accordingly, Baghi et al. (Bannazadeh Baghi et al., 2018) posit that it is imperative to reinforce biosecurity and management protocols for farm animals to diminish the probability of pathogen emergence and mitigate the potential for economic losses.

## Conclusions:-

Rabies remains a significant public health problem in the Kingdom of Saudi Arabia, exacerbated by the prevalence of animal bites from both domestic and wild animals. Epidemiological data indicate the need for sustained and coordinated efforts to control and prevent rabies. Despite the existence of vaccination programs and reporting mechanisms, challenges remain due to incomplete data and the presence of stray animals. Enhanced public health strategies, including comprehensive human and animal vaccination campaigns, improved diagnostic facilities, and robust public awareness initiatives, are essential to reduce the spread of rabies. In addition, regional cooperation among Gulf countries could strengthen rabies control efforts and ensure a unified approach to this zoonotic threat. Continued research and surveillance are essential to adapt to the evolving epidemiological landscape and implement effective measures to protect public health and reduce the incidence of rabies in the region.

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