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Review Article

Bovine Rabies - A Neglected Livestock Disease: A Looming Concern in the Indian Subcontinent

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A B S T R A C T

Bovine rabies is a global animal and public health concern. There remains a poor understanding of the true disease burden and economic impact. In low-income developing countries that rely primarily on livestock, the losses are substantial. Because of the total dependence on cattle rearing for the rural economy in the Indian subcontinent countries, it is becoming a matter of concern. Considering the overwhelming effects of livestock rabies, especially bovine rabies in the Indian subcontinent region, this article collates information regarding various aspects of the issue and highlights the importance of developing targeted bespoke intervention strategies.

Cattle are always at higher risk of exposure facilitated by traditional rearing and farming practices. Economic impact includes trade restrictions on livestock products, losses in the livestock industry, and financial burdens on the government and farmers due to control measures. Epidemiology of rabies in cattle is multifactorial, but more or less similar in the Indian subcontinent. Under-reporting, poor surveillance, lack of facilities to diagnose animal rabies, lack of internationally approved protocols for vaccination, knowledge gap on the management of exposed and diseased animals, neglect in the government livestock disease control programs, and the utopian task of canine rabies control are the major challenges. Successful bovine rabies control would need targeted measures at the species level such as investing in vaccination and control measures, strengthening surveillance, and improving farmer awareness. Simultaneous efforts in controlling rabies in livestock along with canine rabies control can contribute to achieving the global goal of 'zero rabies by 30'. With little emphatic support from the global community to address bovine rabies, countries of the Indian subcontinent may have to develop indigenous capacity, as the depth of the issue is regional rather than global.

Keywords: Rabies, Livestock, Bovine, Indian Subcontinent, Spillover, Veterinary PEP

Introduction

Rabies, a neglected tropical disease, has significant public and animal health implications globally.[1] The disease has recently received much global attention with the launch of a global strategic plan to eliminate dog-mediated rabies by 2030 by a quadripartite body consisting ofWorld Health Organization(WHO), Food and Agriculture Organization (FAO), World Organization for Animal Health (WOAH) and Global Alliance for Rabies Control (GARC). However, the focus is mainly on human rabies death elimination through canine rabies control. Canine rabies is endemic in the Indian subcontinent region and its control is facing many challenges such as a huge free-roaming dog population, poor accessibility to quality vaccines, lack of political will, and the perceived high cost of vaccination.[2,3]

The livestock industry stands as a pillar of the agricultural sector in the Indian subcontinent. Livestock, especially cattle, play a significant role in the rural economy as 70% of the population depends on agriculture. Rabies in livestock is becoming an emerging problem as its incidence has been increasing in the last decade.[2] Rabies is commonly reported in livestock across various regions globally, with cattle being the most significantly impacted species among all livestock.[2–6]

All warm-blooded animals are susceptible to rabies; however, carnivores are the primary vector species in the majority of the tropical areas of the world. Apart from dog-mediated rabies, intermittent involvement of wildlife does occur. Bovine and other livestock infections are spillover from vector species. It is a cause of regional concern where cattle are reared for livelihood and play a major role in the rural economy, and canine rabies control is still a distant dream. Analysis of livestock rabies remains limited worldwide. This review paper aims to provide insights into this neglected livestock disease and to highlight the importance of initiating a targeted approach to bovine rabies control.

Bovine Rabies Burden

The Indian subcontinent comprises India, Bangladesh, Afghanistan, Bhutan, Nepal, Myanmar, Maldives, Sri Lanka and Pakistan. Rabies is considered enzootic in these countries with the exception of Maldives.[7] Due to the lack of structured surveillance programs in these countries, there is a considerable knowledge gap on the livestock rabies burden.[2,7] Rabies outbreaks in cattle and other livestock species are reported frequently in India,[8–12] Bangladesh,[13] Bhutan,[14,15] Nepal,[16,17] Pakistan,[18] and Sri Lanka[19,20]. Cattle constitutes the second most common species affected by rabies after dogs in many of these countries.[13,15,16] In rural areas, the most affected animals are bovines.[21] The true burden of bovine rabies in India, the largest milk producer in the world, is not fully known. It is of great socio-economic concern in rural India.[10] A study conducted in India revealed that the incidence of rabies in stray cattle is four times higher than that in stray dogs.[8]

Opportunities for Exposure

Cattle are more prone to attack from rabid animals than any other animal species because of their open or semi-open housing, and while grazing on pasture.[22,23] Cattle are naturally curious and will approach a dog that is behaving strangely and will usually be attacked.[24] Additionally, the degree of injury is usually severe, with multiple injuries to the face, neck and muzzle, possibly due to their natural way of defending with their head.[24] Most dog bites in livestock occur in the muzzle area, which is highly innervated, and bites in other areas may go unnoticed due to the hairy skin. Dog bites while on grazing pasture may go unnoticed by the owner leading to more chance of developing clinical rabies in unvaccinated cattle.[2,8] The tethering system commonly used in cattle ranching may increase the risk of a dog attack as it limits their chance of escape by running.[13]

Feeding domestic ruminants by tethering them in public fields, roadsides or rice fields after harvest is a common practice in the Indian subcontinent region, providing more opportunities for dog attacks.[8,25] In contrast, they are kept housed in urban areas, which may be the reason for the lower incidence of bovine rabies in urban areas.[25,26] Contrary to the situation in developed countries, where livestock are typically stall-fed, cattle in developing countries are free-ranging on available pasture.

In the forest fringes , there are more opportunities for exposure. Cattle are usually granted unattended free-range grazing access, encompassing forested areas, exposing them to wild animals such as jackals, foxes, wolves and dogs, the common wildlife reservoirs.[25] Cases in cattle have recently been on the rise, even in countries where dog rabies has been eliminated and the majority of these cases are attributed to bat variant rabies.[4,5,27] Cattle on farms represent the primary food source for bats.[28] There is evidence that deforestation and agricultural expansion have enhanced rabies virus persistence in the bat-cattle cycle.[5,6]

Female, aged and cross-bred cattle are reported as being at higher risk.[25,26] Poor bodily thrift, the manner in which they are managed, lack of horns for protection and body color attractive to dogs are presumed as probable reasons for the increased level of risk.[13] Seasonality is another factor in bovine rabies. Monsoon precipitation is found positively associated with rabies cases in livestock.[13] The breeding season of dogs plays a key role in the bovine rabies outbreaks. The observed increase in cases in the December–January months can be correlated with the dog breeding season in the Indian subcontinent.[13,16,29] The

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impact of anthropogenic environmental changes, primarily for cattle pasture expansion, on bovine rabies outbreaks has been demonstrated.[28] Social characteristics such as economic status, literacy, awareness, and exposure to feral dogs can influence the epidemiology of rabies in cattle.[16,30]

Animal Health and Economic Implications

Rabies is one of the most prevalent neurological diseases of ruminants in endemic countries. As in the case of humans, the lethality of rabies in animals is invariably 100%. Rabid cattle may potentially infect other animals as they shed virus in saliva and other secretions. A calf nursing a rabid cow or vice versa is considered exposed to rabies.[31] Livestock rabies causes significant economic losses in the livestock sector besides its public health significance, in developing countries. Due to their total reliance on the livestock sector for their livelihoods, losses are relatively higher on account of direct and indirect damages. The economic impact may be significant at both the household and national levels, alongside its effects on human health.[32] Losses and economic impact of rabies in livestock are often overlooked and include expenses for treatment and handling, loss from rejection of milk, and death. The livelihoods of individuals are impacted by diminished food security, a reduction in protein resources, and a decrease in draught power. Additionally, trade restrictions on livestock products, as well as the financial burden on the government and farmers due to control measures adversely affect the economy.[4,8]

Rabies has encroached on livestock yield, with an approximate loss of USD 12.3 billion in Asia and Africa.[8] Livestock death of USD 512 million is estimated in rabies-endemic countries.[33] The financial burden of animal rabies in India is estimated to be approximately INR 100 crore.[34] Studies based on surveys indicate significant regional variation according to the region where it was conducted. There is a considerable shortage of data on the economy of bovine rabies worldwide.

Public Health Implications

Rabies in cattle represents a public health threat in endemic areas as these animals are in regular contact with humans. Though they are considered dead-end hosts, cattle shed virus in saliva and the virus is found in neural tissue. The possibility of getting infected on exposure to these tissues cannot be excluded. Handling and consumption of tissues from rabid or exposed animals may carry a risk of rabies transmission.[31,35] Additionally, they pose a potential occupational risk to veterinarians and farmers who are in regular contact with these animals. Rabies occurrence in cattle often leads to mass rabies post-exposure prophylaxis (PEP) in humans at risk. There are no evidence-based reports of human rabies from consumption of milk. However, there are reports of mass PEP in humans who drank unpasteurized milk from rabid cows.[36,37] Because of the 100% fatality of the disease and effectiveness of PEP, mass exposure incidents prompt clinicians to administer PEP, to pacify and alleviate public panic, even though circumstances do not meet the criteria for exposure.[37–39] There are anecdotal accounts of rabies being spread to animals through the consumption of infected animal milk.[3] The theoretical risk of rabies transmission through ingestion of unpasteurized milk may warrant PEP in rural areas of India, given the continued use of unpasteurized milk and milk products in rural households. Religious and traditional beliefs about the benefits of raw milk do not deter most people from consuming it, despite the zoonoses scare.[40]

Challenges and Barriers

To a certain extent, major barriers to controlling livestock rabies are similar in the Indian subcontinent region.[18] Insight on the economic impact of bovine rabies remains limited globally.[30] Numerous nations have undertaken research on the economic effects of bovine rabies; however, these studies mostly focused on public health rather than the cattle industry.[41] Nevertheless, rabies in livestock remains under-reported in developing countries because they lack adequate and efficient surveillance systems.[2,8,10] Moreover, public awareness of the risk of contracting zoonotic pathogens is generally poor in rural areas.[40]

Although vaccination is the key pillar of rabies control in animals, there are no internationally approved or established protocols for rabies vaccination in cattle and veterinary PEP. International guidelines recommend that exposed naive cattle may be euthanized or quarantined for six months which is not practical in developing countries due to religious, cultural and economic reasons.[23,42] Religious and cultural attitudes make implementation difficult in countries like India.[43] Veterinary PEP has been restricted to treating valuable, owned pet animals.[3]

International guidelines recommend an antigenicity of a minimum of 1 IU/mL (in contrast to 2.5 IU/mL for human vaccines) for animal vaccines, which is in fact intended for preventive vaccination.[44] Hence, good quality, high potency vaccines may not be readily available everywhere for PEP. However, most of the animal vaccines used in India have a potency of 2.5 IU/mL. The unavailability of vaccines that are licensed for all livestock species is another barrier. Vaccinating animals for which there are no approved products can create a false sense of security. Furthermore, most inactivated animal rabies vaccines are in liquid form, in contrast to freeze-dried human vaccines. Dry vaccine formulations are generally thought to be less susceptible to temperature-induced deterioration.[45] Hence, the thermal stability and shelf life of animal vaccines may be compromised in tropical countries.

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Pre-exposure vaccination has been found to be effective in reducing rabies occurrence in cattle in many countries,[2,23,41,46] but its economic aspects have not been well assessed in resource-poor countries. Rabies vaccination is not included in the mandatory vaccination list for cattle in low-income countries.[8,15,46] Hence, preventive vaccination in livestock is often based on perception of risk and hence, the coverage is poor. Moreover, bovine rabies does not impose the kind of livestock disease burden in resource-poor countries that contagious diseases such as foot and mouth disease, hemorrhagic septicemia, brucellosis, or lumpy skin disease do. Consequently, rabies control in livestock is not often considered a cost-effective investment in animal health in government programs.[47] Rabies is generally considered a companion animal disease in the animal health sector. Animal insurance, a common tool in use to address the financial burden of farmers in unforeseen events, is of little help in rabies deaths as rabies is listed as a vaccine-preventable disease.

Control Measures

The epidemiology of rabies in cattle is multifactorial, but more or less similar across the Indian subcontinent.[16] Success of rabies control in cattle would need effective control at the source and a combination of measures applied at the species level such as vaccination at least in high-risk areas, adopting veterinary PEP, good farm practices, surveillance and improving awareness among farmers.[2,5,15,45] Management strategies should include addressing environmental factors and habitat management that facilitate virus transmission.[4,6] Appropriate measures can better safeguard our priceless animals.

Preventive Vaccination in Cattle

In endemic locations, prophylactic rabies immunization is advised for cattle.[48] Effectiveness of pre-exposure rabies vaccination of cattle with inactivated vaccines is well documented.[5,23,46] However, there is a lack of consensus regarding the minimum age for vaccination and the number of doses required, with manufacturers and country-specific guidelines offering differing recommendations.[49,50] In many countries, vaccination is voluntary and based on the perception of risk.[22,47] Research showed that calves older than four months react favorably to vaccination, and two doses produce protective antibody levels.[23] In an economic analysis comparing vaccination cost to rabies fatality, regardless of herd size, the average cost of vaccination was found to constitute only 10% of the estimated economic loss demonstrating the economic viability of pre-exposure vaccination.[5] However, potential economic benefits in resource-poor countries with huge cattle populations need further validation and convincing. Despite all economic limitations, vaccination represents a significant measure to control bovine rabies by protecting them from unnoticed exposure in pastures, improving the efficacy of PEP by inducing an anamnestic immune response, reducing the cost of treatment and minimizing economic hardship of farmers. An Indian study reported that a single intradermal pre-exposure vaccination is effective and can be a cost-effective option in rabies-endemic countries[2] and is worth considering.

Veterinary PEP in Cattle

Currently, there are no internationally licensed products or established regimens for rabies PEP in naïve exposed animals, let alone cattle.[42] PEP is not recommended by WHO in animals but is practiced in countries like India due to socio-economic reasons.[3,51] The general practice of using a protocol similar to PEP in humans is limited to valuable owned dogs. There are reports of PEP failures when applied to exposed naive cattle.[8,52] It is proven that vaccines alone cannot always prevent rabies. Availability, affordability and ethical considerations prohibit the use of immunoglobulin in veterinary PEP in developing countries that face critical shortages for human use.[43]

There is a paucity of information on the efficacy and feasibility of rabies PEP in cattle. The available documentation is mostly from India. Recent studies on cattle PEP from India report promising results.[43,53,] It is demonstrated that tissue culture rabies vaccine could elicit a satisfactory immune response in cattle sufficient to protect them when exposed to virulent rabies virus.[53] PEP has been proposed as an alternative to euthanasia or six-month quarantine for animals.[42,54,55,56,57] Abraham et al. proposed a new schedule, the "Modified Essen Regimen" for PEP in cattle, which could achieve sufficient immunity as early as day 3 in a significant number of animals and showed better immunogenicity in comparison to the standard Essen regimen.[43] The study claimed that it can save more exposed cattle from clinical rabies. The clinical effectiveness of a novel low-cost protocol, the 'Madhusudana-Bharti-Uppinder protocol", for pre- and post-exposure in cattle has been reported from Himachal Pradesh, India.[56] Studies suggested that the total cost of PEP using intradermal rabies vaccination (IDRV) was 13.6% less than that of intramuscular rabies vaccination (IMRV).[56,58] The recent interest shown by researchers from India is hopeful and indicates the impact of the issue in the livestock sector.

Conclusion

Bovine rabies in the Indian subcontinent is clearly a "neglected" livestock disease. Existing control activities are inadequate. From a broader perspective, "control at the source" looks more attractive as the benefits would be shared by the public health sector as well. However, given the impact of economic loss on the farming community, the impact on public health, and the unpredictability of

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the time required to achieve the utopian task of canine rabies control in endemic areas, simultaneous species-level intervention is the need of the hour. Vaccines and regimens should be robust enough to provide protection under all conditions. Vaccinating cattle should also be an essential part of the strategy to control rabies. There is an urgent need to develop pre- and post-exposure vaccination protocols along with increased surveillance and farmer awareness. Simultaneous efforts to eliminate rabies in cattle and other livestock can significantly contribute to the global goal of eliminating dog-mediated human rabies by 2030. With minimal interest from the global community to address bovine rabies, countries in the Indian subcontinent may need to develop indigenous capacity, as the depth of the problem is more regional than global.

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