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Review

Epidemiology and Diagnosis of Rinderpest: Pakistan and Global Eradication Programme

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ABSTRACT

The genus Morbillivirus, within the family Paramyxoviriidae has three important animal disease viruses i.e., Rinderpest virus (RPV), Peste des petits ruminants virus (PPRV) and the Canine distemper virus (CDV). The RPV nucleic acid (RNA) is surrounded and protected in the cytoplasm by the nucleocapsid protein. Rinderpest can affect all the species of the order Artiodactyla – cloven footed animals/ even footed ungulates. The disease is characterized by the "the 3 D's: discharge, diarrhea and death. The spread of the disease is caused by the introduction of live infected animals into rinderpest free areas. Geographical distribution of rinderpest has been confined to only three "defined foci". There are several serological and molecular methods for the detection of the Rinderpest virus, but the PCR (Polymerase Chain Reaction) is the most sensitive method for the detection of minute quantities of nucleic acid material, so RT – PCR (Reverse Transcription-PCR) is used to diagnose the RPV. Infection can easily be controlled by proper quarantine and hygienic measures, owing to virus, need of close contact in order to be transmitted. The Global Rinderpest Eradication Programme (GREP) is a time bound activity aiming at the total elimination of rinderpest from the world by the year 2010. There had been two epidemics of rinderpest in Pakistan. Thereafter the disease occurred sporadically. The present study is carried out to assess the status of the disease in Asia and particularly in Pakistan, thus providing help in part to eliminate this disease.

Key Words: Rinderpest; Epidemiology; Diagnosis: Pakistan

INTRODUCTION

Rinderpest is one of the oldest known diseases of cattle and has recognized as distinct clinical entity since 376 A.D (Barrett, 1999). Owing to its highly contagious nature and consequent capacity of rapid spread , it is regarded as List A disease by the Office International des Epizooties and is subjected to total elimination from the world by the year 2010.

History. The German "Rinderpest" is the English euphemism for the murrain known as "Cattle Plague" . The name hides the desolation wrought by a disease that ravaged cattle herds domesticated in Asia 9000 years ago. The English name "steppe murrain" reflects the belief in Europe that its homeland was the steppes between Europe and Asia from where the waves of rinderpest swept west to Atlantic and east to Pacific in the retinues of marauding Asia armies (Scott, 1999).

In the eighteenth century, rinderpest entered Europe through Venice and had spread as far as Great Britain by 1714. This epidemic resulted in the establishment of first veterinary school at Lyon, France in 1762 (Barrett & Rossiter, 1999). Similarly, rinderpest was introduced in Africa , by cattle brought from Asia ,during the latter part of the nineteenth century. This was the first epizootic of rinderpest in Africa and a total of 2.5 million cattle died in South Africa (Mack, 1970).

In twentieth century, rinderpest reappeared in Europe through the transportation of live, infected animals from India to Brazil (Pastoret *et al.,* 1991). This was the last serious outbreak in domestic cattle of Europe that took place in Belgium in 1920. The same shipload of Indian cattle caused the only outbreak of rinderpest in Brazil (Roberts, 1921). Following the 1920 outbreak in Europe, the Office International des Epizooties (OIE) was established in Paris to deal with matters concerning animal health in relation to international trade (Barrett, 1999).The last rinderpest outbreak in Europe occurred in 1948 in Rome zoo and was caused by importation of an infected Antelope (Tassi, 1949).

In 2002, there was growing confidence , based on sound scientific evidences, that the geographical distribution of rinderpest has been confined to only three "defined foci", and these were located in the Somali pastoral ecosystem of Somalia and Kenya, the pastoral systems east of the Nile in southern Sudan and the Indus River buffalo tract of Pakistan (Roeder, 2002).

Geographic distribution. According to Roeder (2002a), recent national eradication campaigns have freed three of the last remaining, reservoirs of the virus in Sudan, Pakistan

and Yemen of the disease. But the virus persists in the southern part of the so called Somali pastoral ecosystem.

Phylogenetic studies carried out on the different strains of rinderpest virus, isolated from Africa and Asia over the past ten years, showed three distinct lineages – one lineage is confined in Asia while the other two circulate in Africa (Chamberlain *et al.,* 1993; Wamwayi *et al.,* 1995; Barrett *et al.,* 1998).

Host range. Rinderpest can affect all the species of the order Artiodactyla – cloven footed animals/ even footed ungulates (Scott, 1964), which includes both domestic and wild animals. Some species are most susceptible than others, and the manifestations of the infection can range from acute and lethal in species such as Buffalo and Warthog to very mild or undetectable in Thomson's gazelle and Hippopotamus (Plowright, 1984). In domestic buffaloes, the mortality rate may be as high as 80% while yalks almost invariably die (Roeder & Xie, 1997; Rossiter *et al.,* 1998). Laboratory animals like mice, guinea pigs and rabbits can also contract the disease (Kahrs, 2001).

Transmission. Rinderpest is transmitted by contact with infected animals, or with infected feed and water sources; aerosol transmission is not a significant means of transmission (it occurs only in a confined area over a short distance).There is no vertical transmission, arthropod vector, or carrier state. The spread of the disease is caused by the introduction of live infected animals into rinderpest free areas. It is transmitted as a consequence of military campaigns, the trade in livestock and the movement of wild game (Mebus, 1998).

Epizootology. Traditionally, rinderpest outbreaks follow wars and civil disturbances i.e. when there is unrestricted movement of people with animals, which can carry the virus. The outbreak in Lebanon, Middle East and Sri Lanka followed this pattern. The likely source of the outbreak in Sri Lanka in 1987 was live goats brought from India with the troops and traded locally (Anderson *et al.,* 1990). Similarly rinderpest reappeared in Turkey as a consequence of the Gulf War (Barrett, 1999). Transmission by the infected meat is very rare and considered to be a low risk. The most dangerous source of virus is sub clinically infected animals. In such cases the incubation period for these viruses can be up to 15 days and this, along with low transmission rates, means that they can persist unnoticed for many years in cattle populations. It is possible that disease may flare up clinically when animals are put under stress, such as when they are moved to markets (Barrett, 1999).

Pathogenicity. The incubation period varies with the strain of virus, dosage, and route of exposure. Following natural exposure, the incubation period ranges from 3 to 15 days but it is usually 4 to 5 days. The virus penetrates through the epithelium of the upper respiratory tract and multiplies in the tonsils and the regional lymph nodes from where it enters the blood in mononuclear cells, which disseminate the virus to other lymphoid organs, epithelial cells of the gut and mucous membranes. The lymphoid tissue and alimentary mucosa are preferred sites for virus growth (Radostits *et al*., 1994).

Clinical signs. Rinderpest is manifested by a short period of fever, lymphocytolysis, erosive stomatitis, and gastroenteritis. Infected animals salivate profusely, show severe mucopurulent ocular and nasal discharges and suffer from severe diarrhea. The disease is characterized by the "the 3 D's: discharge, diarrhea and death. Infected animals usually die as a result of the dehydrating effects of diarrhea. However they can also die from a latent parasitic or bacterial infection, which can be exacerbated because of the immunosuppression of the animal, caused by the destruction of the lymphoid organs by the virus (Taylor, 1986; Radostits *et al.,* 1994; Wamwayi *et al.,* 1995). Genus Morbillivirus, in addition to rinderpest virus, also include measles virus (MV), Peste des petits ruminants (PPR), Canine distemper virus (CDV), Phocid distemper viruses (PDV), and Cetacean morbilliviruses, which include Dolphin Morbillivirus (DMV) and Porpoise Morbillivirus (PMV) (Barrett *et al.,* 1995).

Classic rinderpest can be diagnosed clinically on the basis of outbreaks, clinical findings, gross lesions, post mortem lesions, morbidity and mortality rates (Anderson *et al.,* 1996).

Diagnosis. Laboratory diagnosis requires either identification of specific antigen or virus specific nucleic acid in the field samples to confirm the presence of this disease (Anderson *et al*., 1996).The methods available to identify the causative agent are Agar gel immunodiffusion (AGID) test (White, 1958) which is a general Morbillivirus specific antigen detection test, but can not distinguish between viruses of RP and PPR. Agar-gel precipitation test (AGPT) and Counter Immunoelectrophoresis (CIEP), (Asif & Akhtar, 1997). Bruning *et al.* (1999) reported the development of a simple, rapid and accurate pen side test for the detection of antigen in lachrymal fluid of experimentally and naturally infected cattle using the Clearview chromatographic strip test technology. Immunocapture (ic) ELISA, used for differential diagnosis, is based on antigen detection in morbid samples (Libeau *et al.,* 1994). This test is more sensitive than other antigen detection systems. Ismail *et al*. (1994) developed a recombinant baculovirus that express the N protein of RPV-K in insect cells and larvae (*Spodoptera frugiperda*). This recombinant protein was used as a coating antigen in an ELISA to distinguish vaccinated animals from those infected with RPV and was also used successfully in the diagnosis of two other morbilliviruses, measles virus and PPR virus. Immunohistochemistry, using virus monoclonal antibodies, can be used to detect virus antigens in fixed tissue specimens.

Molecular techniques i.e. nucleic acid hybridization, performed on either extracted nucleic acid material or in situ on histological sections, has greatly speeded up the differential diagnosis (Diallo *et al., 1989*). Pandey *et al.* (1992) described the detection of RPV and PPRV using

biotinylated cDNA probes based on N gene of RPV and PPRV respectively. Polymerase chain reaction (PCR) is the most sensitive method for the detection of minute quantities of nucleic acid material. RT–PCR is used to diagnose RNA viruses like morbilliviruses (Forsyth & Barrett, 1995).

Disease control. Morbilliviruses are extremely fragile; they are sensitive to high temperature, sunlight, low and high pH, and those chemicals which can destroy their outer lipid containing envelope. The virus is inactivated in dead animals within 24 h, as a result of pH variations and putrefaction. Moreover, outside the host, the virus can not survive for longer time (Bellini *et al.*, 1997).

As all the Morbilliviruses require close contact between infected and susceptible populations for transmission plus there is no arthropod vector involved in transmission, therefore Morbillivirus, infection can easily be controlled by proper quarantine and hygienic measures, owing to virus, need of close contact in order to be transmitted. Rinderpest was successfully controlled and eliminated from Europe by these means without the use of vaccination (Barrett & Rossiter, 1999).

Although there are several different strains of rinderpest virus, there is only one serotype therefore a vaccine, which protects against one strain, will also, protects against all the others. Moreover, there is no evidence of persistent or carrier state in recovered animals. Furthermore, after recovery of infection, an animal is immune for life; consequently, vaccination is a very effective mean of controlling this disease (Barrett, 1999).

The most effective and now widely used vaccine was developed by Plowright and Ferris in 1959 by passaging the the virulent Kabete 'O' strain of rinderpest in primary bovine kidney cells (Plowright & Ferris, 1962). This attenuated virus, known as the RBOK (Rinderpest of Bovine Origion Kabete), now used as a vaccine to protect susceptible population from virulent virus. Immunity following vaccination is complete and lifelong in cattle (Plowright & Taylor, 1967), and the vaccine virus does not replicate at the epithelial surfaces and so can not be transmitted by contact (Plowright & Ferris, 1962). The improvement in the freezdrying techniques has greatly increased the stability (shelf life) of the vaccine dried form (Mariner *et al*., 1990). This freeze-dried virus is to be kept cold until used. The combination of maintenance of the cold chain and remoteness of vaccination sites made RP vaccination very expensive (Mebus, 1998). Keeping in view the problems of Plowright tissue culture vaccine, the greater heat stability of poxvirus has been exploited to produce recombinant vaccine (Yamanouchi *et al*., 1993; Ohishi *et al*., 2000).

In the final stages of eradication campaign it is required to distinguish serologically between animals recovered from a natural infection and the vaccinated ones. Therefore, a genetically marked rinderpest vaccine, containing a marker protein to which animals were not normally being exposed in the environment, desired. For this purpose, a marker vaccine expressing green fluorescent protein (GFP) gene has been produced (Walsh *et al.*, 2000).

Economic importance. Rinderpest has had more influence on world's food supply than any other animal disease and has tremendous destructive potential in Africa. Rinderpest has caused both direct and indirect losses in domestic livestock enterprises. Losses in Asia and African countries were economically disastrous on account of deaths, loss of productivity, expert restrictions and the cost of effective prevention and control. A rinderpest outbreak that raged across much of Africa in 1982-84 was estimated to have cost at least US$2 billion (Roeder, 2002a).

Eradication programme. The Global Rinderpest Eradication Programme (GREP), established in 1987, is a time bound activity aiming at the total elimination of rinderpest from the world by the year 2010 (FAO, 2003). The ability to eradicate rinderpest and prevent its reintroduction is considered to be a measure of the effectiveness of a country's veterinary service. For countries that wish to eradicate rinderpest, an international agreed on protocol known as the "OIE Pathway" has been established. Before a country can declare itself free of rinderpest, there must be a period of freedom from disease, after which vaccination is stopped to allow the development of a susceptible population of cattle. Virus eradication is then confirmed by thorough random sampling for disease and antibodies (FAO, 2003a). Roeder (2002) reported that only Syria and Iran maintain routine mass vaccination programmes, the latter because of the perceived risk of invasion from neighboring countries (Pakistan and Afghanistan).

In Nov 2002, experts were increasingly confident that the rinderpest virus responsible for the devastating livestock disease rinderpest is no longer present in three of its last reserves, in Pakistan, Sudan and Yemen. Efforts are underway to eradicate the last traces of the disease in the northeast Kenya and southern Somalia in order to meet a global deadline of 2010 for declaring the world completely free from the disease (Roeder, 2002a).

Pakistan and rinderpest. Ghulam *et al.* (2000) reported that there had been two epidemics of rinderpest in Pakistan since 1947 i.e. 1947 to 1951 and 1959 to 1962. Thereafter the disease occurred sporadically. The disease was reported from Punjab in 1988, 1994, 1995 and 1997, and from Balochistan in 1986, 1987, 1991 and 1995 (Hussain, 1997; Hussain *et al.*, 2001). In last decad, between April and August 1994, a major epidemic had has been reported from Gilgit and Hunza (Rossiter *et al*., 1998). Rinderpest has remained endemic in dairy colonies of Karachi especially Landhi Cattle Colony (Raja, 1995; 1996). These colonies once appeared to be a major reservoir of rinderpest not only for spreading the disease within Pakistan but also throughout the region particularly South East Asia and the Middle East (Asif & Akhter, 1997; Durrani *et al.*, 1998; Hussain *et al.*, 1998).

Rinderpest in neighboring Afghanistan in mid 1995 also appeared to have been introduced by the transportation of the animal from Pakistan (Hussain *et al.*, 1998). Similarly, it is also conceivable that the outbreak, which occurred in Turkey in 1995-96, was also a related event through the trade in livestock from Balochistan (Pakistan) to Turkey via Iran (Roeder, 2000).

Rinderpest was last reported and confirmed by laboratory tests in buffalo herds close to Karachi in September 2000. Its eradication is being actively pursued by the Government of Pakistan with assistance from the European Union and FAO (European Union funded project GCP/ PAK/088/EC; FAO funded project TCP/PAK/GREP had been coordinating a random serological survey in Afghanistan during 2000-2001 and detected 0.2% seropositive animals among 20,000 cattle (Majok *et al.*, 2000; FAO, 2001). Similarly a survey conducted in Balochistan, NWFP, Northern Areas and Jammu and Kashmir in 2001 found 0.3% positive reactions among 2,697 sera (FAO-funded project TCP/PAK/8923). These serological studies in the region over the last two years provide a degree of confidence that rinderpest has not been circulating in the border regions of Afghanistan and in the contagious, ecologically related, areas of Pakistan in recent years. This confirms the understanding gained from clinical surveillance.

Roeder (2002) reported in March 2002 that Indus River buffalo tract of Sindh Province (Pakistan) was the last reservoir in Asia. Roeder (2002) further high lightened the urgent need to focus on eliminating rapidly this last Asian reservoir of rinderpest i.e. only when the last reservoir has been consigned to history will the risk of rinderpest resurgence disappear. Later same year i.e. in November 2002, Roeder (2002) confirmed that no case of rinderpest was reported from this area since September 2000, so it is conceivable that Asia is now free from rinderpest for the first time in millennia, although of course it will take some time before freedom can be proved in accordance with internationally accepted guidelines.

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