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Peste des petits ruminants Indian Perspective



**ICAR–National Institute of Veterinary
Epidemiology and Disease Informatics (NIVEDI)
Bengaluru**

February 2023

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Institute Ref. No.: F.No. 13/NIVEDI/PMEC/EM&TB/2021-2022/19(2)

Citation: V. Balamurugan, K. Vinod Kumar, G. Govindaraj, K.P. Suresh, B.R. Shome, B. R. Gulati (2023), Status Paper on Peste des petits ruminants Indian Perspective, ICAR-National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), pp: 1-47

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Published by: The Director: ICAR-National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), Indian Council of Agricultural Research (ICAR), Post Box No. 6450, Yelahanka, Bengaluru -560 064, Karnataka, India.

Printer: Cnu Graphic printers, Maleshwaram, Bengaluru, India

Peste des petits ruminants Indian Perspective

Summary

Peste des petits ruminants (PPR) otherwise known as “small ruminant plague”, is considered as a major constraint in augmenting the productivity of small ruminants in developing countries like India. PPR is one of the priority animal diseases that affects sheep and goats. The disease is an acute, highly contagious, World Organization for Animal Health notifiable, and economically important transboundary viral disease of domestic and wild small ruminants. The disease is associated with high morbidity and mortality in sheep and goats and is caused by the PPR virus, which belongs to the genus *Morbillivirus* of the family *Paramyxoviridae*. The disease is clinically manifested by pyrexia, oculo-nasal discharges, necrotizing and erosive stomatitis, gastroenteritis, diarrhoea, and bronchopneumonia. PPRV needs close contact between infected and susceptible animals to spread because of the lability of the virus outside the environment. The most important epidemiological risk parameters of PPR in sheep and goats are the introduction of animals in the flocks from an unknown source, along with other management factors and rearing patterns. Though the natural transmission of the virus occurs in other species *viz.*, cattle, buffaloes, etc., the clinical form of the disease is generally not observed. The temporal and spatial epidemiological analysis of PPR using national surveillance outbreaks/cases reports data from 1995 to 2019 available in the National Animal Diseases Referral Expert System revealed that PPR features among the top ten diseases in sheep and goats and stands first among viral diseases, and accounts for 36% mortality in sheep and goats. PPR outbreaks occur around the year in all seasons but are encountered most frequently during the lean period, especially, in the winter (January to February) in different regions/zones. The disease can be diagnosed based on clinical signs, pathological lesions, and specific detection of virus antigen/antibodies/genome in the clinical samples by various serological tests and molecular assays. Considering the importance of sheep and goats in food security and socio-economic growth, and the availability of effective and safe live attenuated cell culture PPR vaccines and diagnostics, the Government of India launched a centrally sponsored PPR control program in India in line with PPR Global Control and Eradication Strategy to control and eradication of PPR by 2030. The reported outbreaks in India over the years have progressively declined in most of the states, especially Andhra Pradesh, Telangana, Karnataka, and Chhattisgarh due to the implementation of a strategic mass vaccination programme since 2011. Andhra Pradesh, West Bengal, and Karnataka states were the top three states on the reported outbreaks during 1995-2010, whereas, during 2011-15 and 2015-2019, Jharkhand and West Bengal states reported more PPR outbreaks. Decreased numbers of outbreaks in recent years, as well as changes in the disease patterns, severity, and distribution, might be due to the effectiveness of vaccines, timely vaccination, circulation of a single lineage virus, and most importantly, effective planning and implementation of the vaccination programme in sheep and goats. Sharing the experiences on the PPR control strategies adopted by some of the states in India may motivate other Indian states of similar socio-economic and small ruminant rearing patterns to vaccinate and control PPR. This status paper provides current comprehensive aspects of the PPR epidemiology with special reference to disease distribution, prevalence, transmission, risk factors of the disease, host susceptibility to PPRV infection, diagnosis and management, socio-economic and policy implication, and control measures with perspectives on its control and eradication.

Peste des petits ruminants in Indian Perspective

1. Introduction

In India, the livestock sector contributes 25.6% of total Agriculture Gross Domestic Product (GDP) and 4.11% to national GDP and 16% to the income of small farm households as against an average of 14% for all rural households and employs about 8.8 % of the population in India (Dash, 2017). The small ruminant sector is a significant contributor to the income and livelihoods of the poorest segments of society, and provides sustenance to the rural population, and contributes significantly to poverty alleviation (Chakraborty and Gupta, 2017). The husbandry of small ruminants plays an important role in maintaining the sustainable agriculture and livelihood of the small, marginal, and landless rural farmers by providing meat, fiber, milk, skin, and manure in underdeveloped and developing countries in the world. The small ruminants are “Any Time Money-ATM” of the poor landless farmers and also provide employment, raise income, improves household nutrition, hence, it is called as “poor man cow”.

PPR stands for “*Peste des Petits Ruminants*”, otherwise known as “*Plague of small ruminants*” and is one of the priority animal diseases whose control is considered important for poverty alleviation in underdeveloped and developing countries. PPR is one of the highly contagious, World Organisation for Animal Health (WOAH) notifiable, economically important devastating viral diseases of sheep and goats. The PPR, being the plague of goats and sheep associated with high morbidity and mortality, poses a heavy threat to the national economy of the countries, where the disease is endemic. As a transboundary animal disease (TAD), the presence of PPR can limit export and import, which in turn diminish the consumption of animal protein in humans. The disease is caused by the PPR virus-PPRV. Clinically, the disease is characterized by pyrexia, necrotizing and erosive stomatitis, catarrhal inflammation of the ocular and nasal mucosa (oculo-nasal discharges), enteritis, diarrhea with respiratory distress followed by bronchopneumonia, which leads to either recovery or death of the affected animal. The causative agent is an enveloped RNA virus that belongs to the genus *Morbillivirus* of the family *Paramyxoviridae* (subfamily *Paramyxovirinae*) under the order *Mononegavirales* (https://talk.ictvonline.org/ictv-reports/ictv_online_report/negative-sense-rna-viruses/w/paramyxoviridae/1183/genus-morbillivirus) with other members of the genus, which include rinderpest virus (RPV), measles virus, canine distemper virus, phocine distemper virus, and dolphin and porpoise morbillivirus. The genome is a negative sense single-stranded-RNA, approximately 16 kb long and the PPRV is a single genotype and genetically grouped into four lineages (I, II, III, and IV) based on the fusion (F) and nucleocapsid (N) gene sequences analyses (Shaila et al., 1996; Dhar et al., 2002; Balamurugan et al., 2010b).

Many outbreaks of PPR are being reported from several countries in Africa and Asia and at present more than 70 countries have confirmed PPR affecting ~1.7 billion of the global sheep and goats population (<http://www.fao.org/ppr/en/>) in Africa, the Middle East, and Asia including the Indian subcontinent. The disease was first described in 1942 in Côte d'Ivoire (Ivory Coast), West Africa, then the disease has spread to different regions in sub-Saharan Africa, the Arabian Peninsula, the Middle East, and Asia. The spread of disease to several new countries in Africa, Asia, and Europe with the involvement of various lineage of PPRV is a cause of global animal

health concern especially with the recent introduction of Asian lineage in some African countries and African lineage into Asian countries and the entry of PPR in Southern Europe through Turkey (Baron et al., 2016; Kamel and El-Sayed, 2019). Because of the huge impact on production and socio-economics of the livestock farmers, and the transboundary nature of the disease, it is considered as one of the main constraints in augmenting the productivity of small ruminants in enzootic countries. For effective control and eradication of PPR, the strong support of accurate diagnostics for mass screening and timely availability of vaccines and vaccination of the susceptible population are imperative. PPR recently become a major international target for improved control, marked by the adoption of a resolution in 2014 by the WOAHP to establish a control program to eventually eradicate the disease (OIE, 2019). Considering the importance of small ruminants in ensuring food security and socio-economic growth in many parts of the world, mainly in Africa and Asia, following the eradication of rinderpest, a global consensus was agreed on the need to eradicate PPR with the adoption of the PPR Global Control and Eradication Strategy (GCES) with a vision to make the world free from PPR by 2030 (OIE and FAO, 2015). European Commission for International Cooperation and Development, Food and Agriculture Organization (FAO), and WOAHP jointly launched an international strategic plan for control and eradication intending to gather all stakeholders behind the PPR-Global Eradication Programme (PPR-GEP) and mobilize the additional support required for the eradication (OIE and FAO, 2015). The campaign will make PPR only the second animal disease ever to be eradicated, after rinderpest. In this direction, FAO and WOAHP, launched the PPR global eradication program (PPR-GEP) for the period 2017-2021 with the adoption of GCES for the global elimination of PPRV by 2030 (OIE and FAO, 2015; Parida et al., 2015).

India is a vast country with a population of ~148.88 million goats and 74.26 million sheep (as per the 20th Livestock census-2019)(DAHD, 2020a), as against approximately 2.1 billion world population of sheep and goats. In India, PPR was first reported in Arasur village, Villupuram district in Tamil Nadu state in 1987 (Shaila et al., 1989). The disease was believed to be restricted to Southern parts of India until severe epidemics swept through the rest of India in 1994 and onwards (Kulkarni et al., 1996). Since then, the disease became enzootic in many states of India (Balamurugan et al., 2014b, 2021a). Despite strict control measures including statutory regulations along with the availability of vaccines and diagnostics, PPR remains a constant threat (Singh et al., 2009). To control PPR, the Department of Animal Husbandry and Dairying (DAHD), Government of India (GoI) during 2010-2011 implemented a national PPR control programme PPR-CP) even before GCES (DAHD, 2020b), to control and eradicate PPR from India in a time-bound manner on the line of RP eradication. In the first phase of PPR-CP, the states and Union Territories (UTs) in Southern India were included in the vaccination, and the remaining states and UTs of India were included in the second phase during 2014-2015 (Balamurugan et al., 2016). The activities aimed under PPR-CP include vaccination, pre-and post-vaccination monitoring, acquiring PPR free zone with vaccination, syndromic surveillance, outbreaks investigation, response, and communication, and implementation of focused ring vaccination in place with biosecurity precautionary measures for prevention and spread of PPR outbreaks

or to minimize the risk of spread including containments of the infectivity, severity, and transmissibility into an animal population.

In India, many outbreaks of PPR in sheep and goats remain un-reported and underreported owing to inadequate animal disease surveillance and reporting systems (Balamurugan et al., 2011, 2012b). As of now, the disease has been brought under control in India although the occurrence and severity of the disease have progressively and substantially declined in areas under progressive vaccination (Balamurugan et al., 2016). The epidemiological analysis of outbreaks/cases data from different geographical areas with varying agro-climatic conditions may help in devising effective vaccination and control strategies, to prevent disease incursion, and to acquire disease-free status by implementing the effective comprehensive active surveillance and intensive monitoring programme. This would help in sustainable small ruminant production and pave a way for increasing small ruminant export after attaining disease-free status (Balamurugan et al., 2019, 2020g, 2021a). This status paper comprehends valuable information on PPR epidemiology, with special reference to disease prevalence, transmission, host susceptibility, epidemiological risk factors, diagnosis and management, socio-economic and policy implication, and control measures, with perspectives on its control and eradication. This paper also provides information on hotspot areas and identifies when and where intensive surveillance and vaccination along with biosecurity measures could be implemented for the control and eradication of the disease from India in consonance with the global strategic plan.

2. Regional Distribution

The first confirmed outbreak of PPR in sheep with 25 % mortality was reported in Arasur village, Villupuram district of Tamil Nadu in 1987, where characteristic clinical signs of PPR were noticed (Shaila et al., 1989). The PPR was believed to be restricted in Southern India until severe epidemics swept in the rest of India from 1994 onwards. The disease was reported first time in Karnataka in 1992 (Srinivas and Gopal, 1996) and Maharashtra in 1994 (Kulkarni et al., 1996) and started spreading across varied agro-climatic conditions with varying intensities. Since then, the disease has become enzootic in many northern states of India (Mondal et al., 1995; Nanda et al., 1996). Outbreaks in other species like buffaloes have also been reported (Govindarajan et al., 1997). The PPR extended its geographic distribution to North-Eastern (NE) states, as PPR outbreaks were reported regularly in Assam and Tripura states (De et al., 2016; Devi et al., 2016). PPRV isolated from an outbreak in Tripura during 2012, revealed a high degree of identity with Bangladesh isolates, which indicates the cross-border movement of animals between the international borders of both countries (Chaudhary et al., 2013). Several PPR outbreaks have occurred in the past and now occurring regularly, in almost all seasons round the year and throughout India, as the disease is enzootic (Balamurugan et al., 2021a). Further, details of breed, sex, age of the animals involved in outbreaks were also not available. However, It is still not clear whether the apparent geographical spread of the disease in the last two decades is real or reflects increased awareness, wider availability of diagnostic tools, or even a change in the virulence of the virus and public and regulatory concerns (Singh et al., 2009; Balamurugan et al., 2014b). It seems most likely that combinations of these factors are responsible for the present knowledge of the disease distribution/dynamics.

3. Epidemiology

3.1. PPR Virus

Molecular evolution, emergence and re-emergence, and characterization of different PPRV isolates/ strains across Africa, the Middle East, Asia, and Southern Europe regions and from different countries have been reported. However, Sequences and phylogenetic analyses based on the F and N gene of the different PPRV isolates/strains from different parts of the world has defined the presence of four different lineages (I, II, III & IV) of the virus (Shaila et al., 1996; Dhar et al., 2002; Kerur et al., 2008; Balamurugan et al., 2010b). The lineage IV (Asian lineage) is represented by isolates from the Arabian Peninsula, the Middle East, Asia, including India. Till now, there was no report of circulation of other lineages of PPRV except Asian lineage IV in India. Further, molecular characterization of PPRV isolated from an outbreak in the Indo-Bangladesh border of Tripura state of North-East India, also suggests the transboundary circulation of virus between India and Bangladesh border (Muthuchelvan et al., 2014). Similarly, the spread of the disease to many new countries in Africa and Asia with the involvement of different lineages of PPRV has been reported as recently (Balamurugan et al., 2020a).

3.2. Environment

PPR virus is fragile and cannot survive for a long time outside the host but survives for long periods in chilled and frozen tissues. The virus is inactivated at 50°C for 60 min. and its half-life has been estimated to be 2.2 min at 56°C and 3.3 h at 37°C. PPRV is sensitive to ether or similar lipid solvent agents but is relatively stable between pH 5.8 to 10.0 (OIE, 2019). The presence of PPRV antibodies in camels, cattle, and wild ruminants besides sheep and goats suggests the natural transmission of PPRV infection among these animals under field conditions (Balamurugan et al., 2012a, 2014c). Transmission of PPRV either directly or indirectly from sheep or goats to cattle/buffaloes or camels or other hosts provides a mechanism for the virus to survive outside of the environment in the unnatural hosts. The virus excreted in the secretions or the discharges from eyes, nose, and mouth, as well as the excretion through faeces of affected animals during infection before and after the onset of the clinical signs, are the important source of virus (Balamurugan et al., 2006; Balamurugan, 2017; Tripath et al., 2018). These discharges form fine infectious droplets in the air particularly when the affected animals cough and sneeze and animals in close contact inhale the infectious droplets and are likely to become infected. The infectious aerosols can also contaminate water, feed troughs, and bedding, turning them into additional sources of infection, but this indirect mode seems to be less important since the PPRV is not expected to survive for a long time outside the host and is also sensitive to lipid solvent. Trade of small ruminants at markets where animals from different sources are brought into close contact with one another provides increased opportunities for PPRV transmission. Nomadic/migratory animals will often come into contact with local sheep and goat populations from whom they may contact the virus (Singh et al., 2004a) subsequently, infected migratory animals may transmit the virus to other susceptible local sheep and goats. Therefore, the movement of animals plays an important role in the transmission and maintenance of the PPR virus in nature.

3.3. Host

Interaction of the host and virus is initiated by specific receptor binding, which is mediated by the hemagglutination (H) protein of PPRV and sialic acid on the host cell membrane. Cellular receptors are the major determinants of the host range and tissue tropism of a virus (Balamurugan et al., 2015). The multiplication and pathogenicity of the virus are proportional to that of the innate resistance of the host, the host's immune response, parasitic infection in the host, the nutritional level of the host, the breed, sex and age of the animal, etc. (Balamurugan et al., 2020a). Evidence from the experimental studies on PPRV infection and results based on accurate field observations in sheep, goats, and cattle have suggested that natural infection occurs through the entry of the virus through the upper respiratory tract epithelium. However, the initial site for virus replication is not within the epithelial cells of the respiratory mucosa, as has been previously reported, but is within the tonsillar tissue and lymph nodes draining the site of inoculation. The virus is taken up by immune cells within the respiratory mucosa which then transports the virus to lymphoid tissues where primary virus replication occurs, and from where the virus enters circulation.

3.4. Epidemiological risk factors

The PPRV primarily affects sheep and goats and occasionally some other artiodactyls including camels and wildlife small ruminants. Many authors believe that although PPRV infects sheep and goats, the severity of the clinical symptoms is more predominant in goats than sheep (Tripathi et al., 1996a; b; 2018; Singh et al., 2004a). PPRV shedding plays a possible role as the source of silent infection especially when there is no history of an outbreak in a nearby flock or area. The breed of the animal may also affect the infection due to their differential susceptibility to PPR. Some breeds are more susceptible to disease than others, however, many studies on breeds have not been carried out except one or a few *in vitro* studies (Balamurugan et al., 2015). Association between age and severity of the PPR has also been reported with young animals aged from 6 months to 1 year old being more susceptible than adult animals. Most authors have linked the outbreak of PPR with the introduction of new animals to the flocks from unknown sources as a major risk factor. The disease occurs throughout the year in the endemic country of India but was encountered most frequently during the lean period or during the cold dry season (January to February) (Singh et al., 2004a; Balamurugan et al., 2011, 2012a, 2016, 2021a). Further, abortion and various associated risk factors in small ruminants is a challenge to farmers, and PPR was chiefly linked to it. Feeding patterns including stall feeding and grazing were not found to be a significant risk factor as reported, although this has been considered as a risk factor for acquiring infectious diseases. Stallfeeding might have other management practices like the purchase of animals that increasing the risk for PPR transmission. Even though grazing was not a significant risk factor, there is still a possibility of domestic livestock interactions, pastures, and water sources for feed and water reservoirs for spillover of PPR. Seropositivity results revealed higher proportions of seropositive female sheep and goats were observed compared to male animals, which may be related to the physiological differences between females and males, where females reveal some degree of infection resulting from stress due to milk production and pregnancies. Further, females maintained for a longer period as compared to

males, thus increasing the likelihood of female animals being exposed to PPRV over time. PPRV actively circulating in the endemic regions and the migration of animals was considered to be the main source of spreading PPR in these regions (Singh et al., 2004a; Balamurugan et al., 2021a).

4. Epidemiological analysis

The national surveillance epidemiological data on PPR in India from 1995-2019 were obtained from the National Animal Diseases Referral Expert System (NADRES) database of the Indian Council of Agricultural Research-National Institute of Veterinary Epidemiology and Disease Informatics (ICAR-NIVEDI). The passive disease surveillance data available at the NADRES database was analyzed and were grouped into three periods as, before the implementation of the national PPR-CP (1995-2010), after the implementation of the first phase (2011-2015), and after the second phase of PPR-CP (2016-2019) (Balamurugan et al., 2021a).

The results of outbreaks and cases in proportion to the population for different periods are presented in Figure 4. Himachal Pradesh (HP), undivided Andhra Pradesh (AP), and West Bengal (WB) states were the top three states reporting the highest number of outbreaks per 100 thousand population during 1995–2010, whereas Jharkhand and Haryana states were highest during 2011–15 and 2016–2019 periods, respectively. The proportion of reported cases to the population was highest in HP, WB, Odisha states in 1995–2010, Tripura & Kerala states in 2011–2015, and Jharkhand and Haryana in 2016–2019.

Further, passive surveillance data were collated at the regional level, and cumulative monthly outbreaks/cases of PPR were calculated for identifying the seasonal occurrence of the disease in different zones (Balamurugan et al., 2021a). Based on the cumulative outbreaks/cases reports, the status of the disease in sheep and goats, disease burden, regional distribution, host susceptibility, the decadal, quinquennial, and yearly and seasonal patterns, spatial distribution, risk zones/areas, endemicity, etc. in the different zones and states of India was analyzed and discussed (Balamurugan et al., 2021a).

4.1. Disease Burden

In India, based on the NADRES data from the ICAR-NIVEDI, a total of 8168 outbreaks of PPR were reported from 1995 to 2019 with the highest 3844 outbreaks in goats followed by 3473 outbreaks in sheep and 851 outbreaks in the flocks where sheep and goats are reared together. Among different geographical regions, the South zone reported the highest proportion (4029 outbreaks; 49.33 %) of reported outbreaks followed by the East (2896 outbreaks; 35.46 %), North (600 outbreaks; 7.35 %), and West (449 outbreaks; 5.50 %) zones, whereas the Central (140 outbreaks; 1.71 %) and North-East (54 outbreaks; 0.67 %) zones reported fewer outbreaks. Further, it has been observed that PPR features among the top ten sheep and goats diseases (PPR, sheep & goat pox, Rabies, Enterotoxaemia, Bluetongue, Coccidiosis, Babesiosis, Theileriosis, Footrot, and Fascioliasis) in sheep and goats and stands first among viral diseases, and accounts for 36 % of the mortalities among reported deaths based on the analysis of the outbreaks/case reports in NADRES database from 1995 to 2019. On analysis of 25 years data, it was observed that 95,492 deaths were reported, of which 59.76 % in

goats (n=57,066), 23.98 % in sheep (n=22,901) and 16.26 % in sheep and goats together (n=15,525). Further, on comparison, the East zone (45.69 %) showed the highest proportion of reported deaths followed by the South (26.29 %), West (12.23 %), North (12.12 %), Central (2.84 %), and North-East (0.83 %) zones. The cumulative deaths reported during 1995-2010 was highest (76.89 %; n=73,428) followed by 11.82 % (n=11,286) during 2011-2015 and 11.29 % (n=10,778), during 2016-2019 and 2.86 % (n=2729) deaths only in 2019 were reported.

The details of the PPR outbreaks and cases in sheep and goats in different zones in different periods of analysis are presented in **Fig. 1**. Further, the mean cases per outbreak with the measure of dispersion like range and standard deviation were summarized in **Fig. 2**. Furthermore, the results of outbreaks and cases in proportion to the population for different periods are presented in **Fig.3**. Himachal Pradesh (HP), undivided Andhra Pradesh (AP), and West Bengal (WB) states were the top three states reporting the highest number of outbreaks per 100 thousand population during 1995-2010, whereas Jharkhand and Harayana states were highest during 2011-15 and 2016-2019 periods, respectively. The proportion of reported cases to the population was highest in HP, WB, Odisha states in 1995-2010, Tripura & Kerala states in 2011-2015, and Jharkhand and Haryana in 2016-2019.

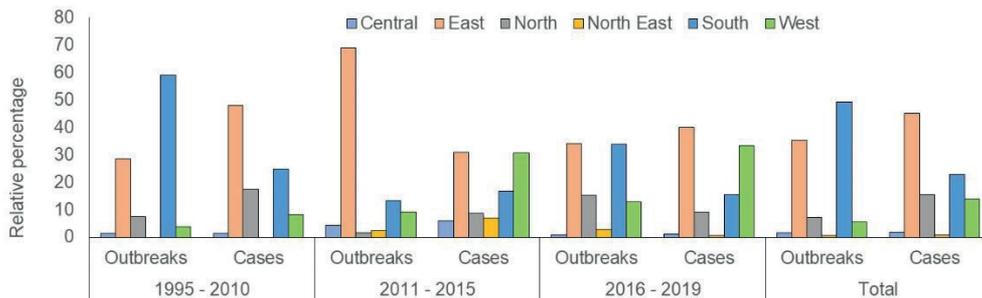


Figure 1. Analysis of cumulative PPR reports (Zone-wise) in different periods (1995-2019). Relative percentages of the cumulative outbreaks, cases, and deaths in sheep and goats in different zones of the country during the different analyzed periods. C-Central zone; E-East zone; N- North Zone; NE-North-East Zone; S-South Zone; W-West zone.

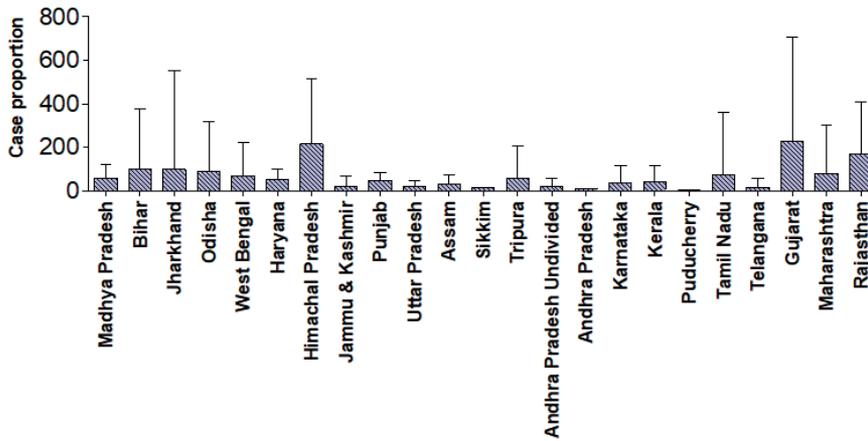


Figure 2. Dispersion analysis (Statewise) of the cumulative PPR reports in India (1995-2019). The mean cases per outbreak with the measure of the variation was calculated.

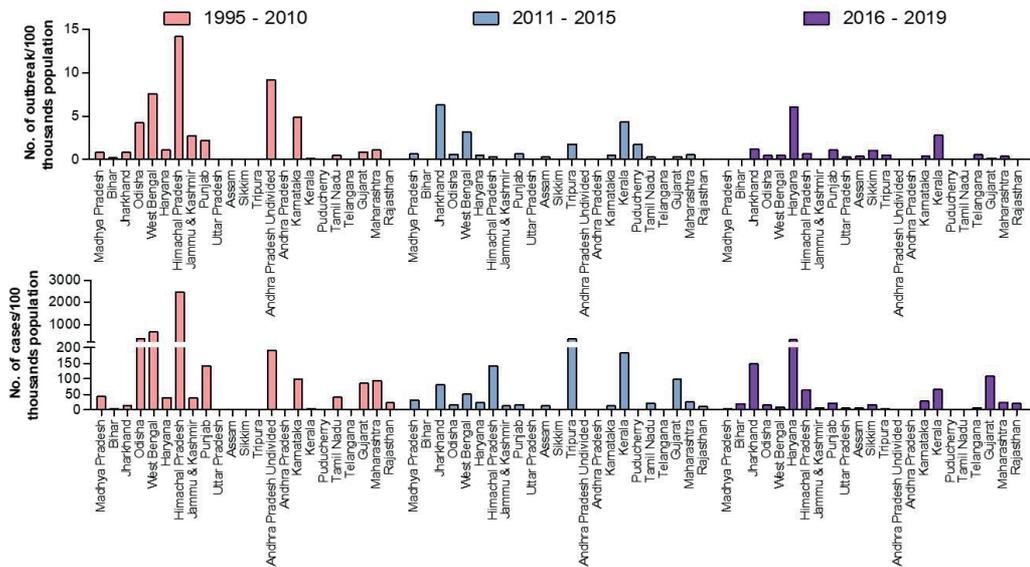


Figure 3. The state-wise proportion of the cumulative PPR reports in India (1995-2019) with the population. [A]. Outbreaks [B]. Cases. Himachal Pradesh, West Bengal, and Odisha were the top three states reporting the highest number of cases per 100 thousand population during 1995-2010, whereas Tripura & Kerala and Jharkhand & Haryana states were highest during 2011-15 and 2016-2019 periods, respectively.

4.2. Temporal patterns

The year-wise trend analysis of cumulative PPR reports in India (1995-2019) from NADRES database showed a gradual increase in outbreaks and cases since 1995 and the highest numbers were reported between 2000 and 2007, which probably due to the availability of diagnostic assays since 2002 (Singh et al., 2004a; a; b, 2009). Further, the number of reported outbreaks and cases showed a declining trend from 2005, which might be due to the implementation of focussed vaccination in some states since 2002 (Singh et al., 2009), and the strategic vaccination under PPR-CP in a few states from 2011, besides implementation of the biosecurity measures to prevent the spread and control of PPR outbreaks. However, during 2018-2019, the marginal increase in the number of outbreaks only in some defined geographical areas in Maharashtra, Haryana, Jharkhand, and West Bengal when compared to 2017 (**Fig. 4**), might be due to the migration of the non-vaccinated animals for grazing/ trade as well as non-implementation of the vaccination as per the direction of the strategic vaccination in a year under PPR-CP (Balamurugan et al., 2019, 2020f, b; c, g; e, 2021a). Further, the multivariable regression analysis of outbreaks revealed disease occurrence in the East zone was positively associated and significant, as in this zone more outbreaks were being reported than other zones, and extensive vaccination is not being practiced. The decline in outbreaks in India, in general, might be due to the extensive adoption of strategic vaccination in the sheep and goats under the national PPR-CP since 2011 by the major states. In recent years, especially from 2018 onwards the occurrence of PPR in Jharkhand, Maharashtra, West Bengal, Haryana states, had increased, which might be due to the non-implementation of the vaccination or movement of non-vaccinated animals through migrants shepherd in these states (Balamurugan et al., 2021a). Karnataka and AP have shown a decline in the number of outbreaks during 2011-15 and 2016-19 with sporadic outbreaks in 2018 and 2019; whereas Chhattisgarh state reported no outbreaks since 2013-2014, even though PPR is still reported in some areas of the country (Balamurugan et al., 2016). However, West Bengal and Jharkhand states have reported the highest outbreaks during the 2011-2015 and 2016-2019 periods, respectively (Balamurugan et al., 2021a).

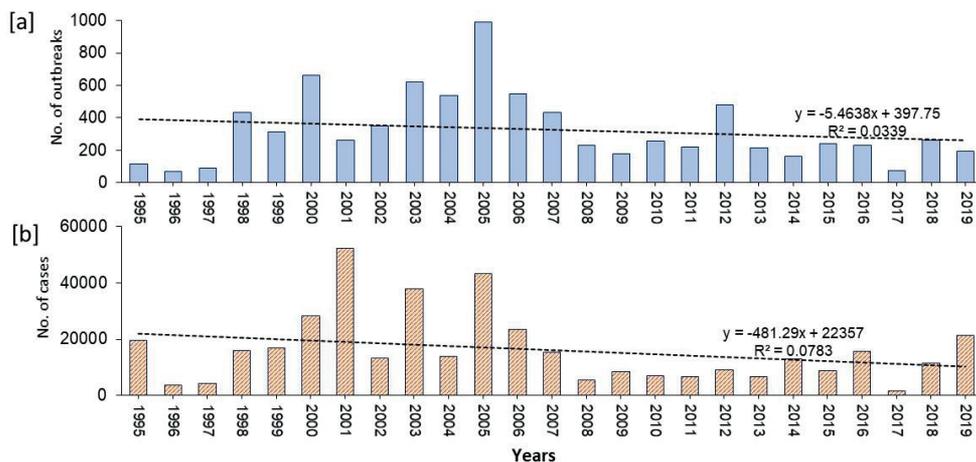


Figure 4. Year-wise trend analysis of cumulative PPR reports in India (1995-2019). [A]. Outbreaks [B]. Cases. A gradual increase in outbreaks and cases since 1995 and the highest numbers between 2000 and 2007, with a declining trend from 2005 was observed.

Further, the zone-wise analysis revealed that East zone reported highest cases (181,824 cases; 45.17 %) followed by the South (92,018 cases; 22.86 %); North (62,288 cases; 15.48 %); West (55,701 cases; 13.85%) zones, whereas the Central (7,252 cases; 1.80 %) and North-East (3,412 cases; 0.85 %) zones reported the lowest number of cases (**Fig. 5**). Furthermore, the highest (74.62 %) proportion of reported outbreaks (n=6095) were during 1995-2010 followed by 16.12 % (n=1317) during 2011-2015 and 9.26 % (n=756) during 2016-2019. Nevertheless, the reported outbreaks during 1995-2010, ranged from 2 to 2,807 with least in Kerala and highest in Andhra Pradesh with an average of ~380 outbreaks, whereas 1 to 451 outbreaks were reported during 2011-2015, with least in Puducherry and highest in Jharkhand, and 1 to 136 outbreaks with least in Sikkim and highest in Telangana (n=136) followed by 121 outbreaks in Jharkhand during 2016-2019 (Balamurugan et al., 2021a).

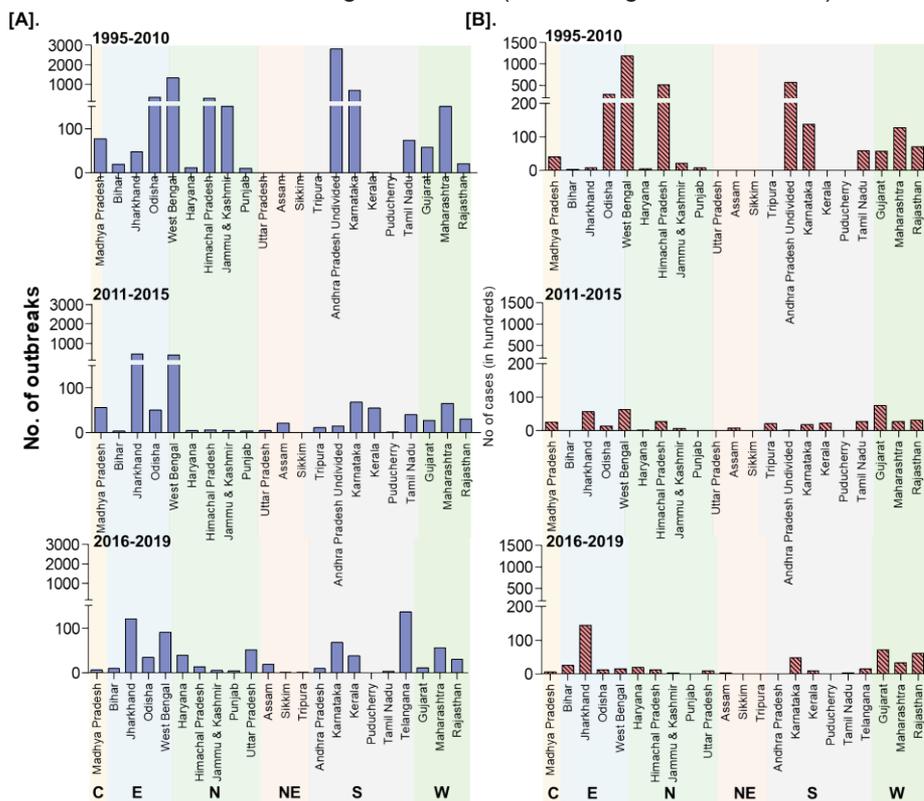


Figure 5. The state-wise occurrence of cumulative PPR reports in India (1995-2019). [A]. Outbreaks [B]. Cases. C-Central zone; E-East zone; N- North Zone; NE-North-East Zone; S-South Zone; W-West zone. Karnataka and Andhra Pradesh have shown a decline in the number of outbreaks during 2011-15 and 2016-

19 with sporadic outbreaks in 2018 and 2019; West Bengal and Jharkhand states have reported the highest outbreaks during 2011-2015 and 2015-2019 periods, respectively.

4.3. Seasonal variations

The month-wise reports indicated that PPR has been found to occur throughout the year and more outbreaks occurred from January to March (**Fig. 6**). However, the outbreaks were predominantly observed between January to March in the South zone, whereas October & November in the East zone and April & May months in the Central zone. In the North-East zone, the highest outbreaks were observed in June months only (Balamurugan et al., 2021a). In the Western zone, most of the outbreaks were reported from January to March followed by November month, whereas in the North Zone, the highest outbreaks were reported between November and January followed by June and July. Further, on comparison, more cases were recorded during June and July months in the East and North zone, respectively, whereas in the West, Central and North-East zones, during November, May, and June months and in the south zone more cases were recorded during December to April months (Balamurugan et al., 2021a).

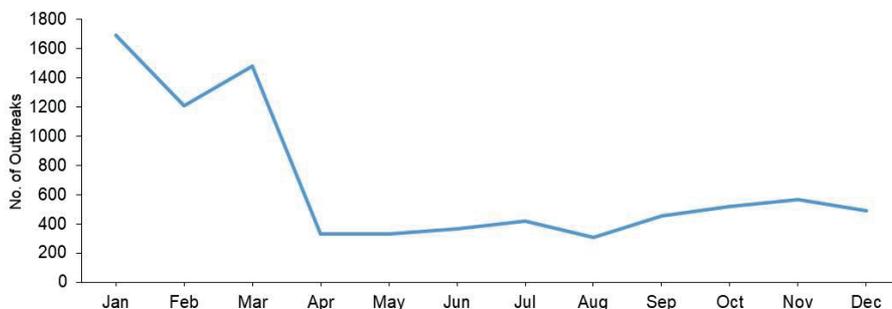


Figure 6. Month-wise analysis of cumulative PPR outbreaks in different zones in India (1995–2019).

Seasonal variations (**Fig. 7**) in PPR outbreaks have been recorded in different states in different zones of India. Generally, animal husbandry practices, agro-climatic conditions, and geographical locations affect the seasonal distribution of the disease (Singh et al., 2004a; Balamurugan et al., 2012b, 2016). The disease occurs in all seasons but is encountered most frequently during the lean period either in the wet season/ rainy season/ summer or during the cold dry season (December to February) (Singh et al., 2004a) as small ruminants in India are reared on free-range pastureland, shrubs, and forest. The observed significance with the Winter season in sheep and goats and Spring and Winter season in sheep was positively associated with the outbreaks, which is probably due to the various causal factors associated with the occurrence of the disease during January to March. In recent years, with the decline in available pastureland and forest area, these animals will often travel long distances during the dry season in search of fodder and water. Temporally, most outbreaks were observed during the Winter and early fall (November to March) than other seasons. On

the commencement of monsoon, an increase in the availability of local fodder restricts migration of animals which results in a substantial decrease in the frequency of outbreaks in the sub-Himalayan region as well as in dryland areas (Rajasthan and Gujarat states) as reported earlier (Singh et al., 2004a). The increased animal trade / the movement of animals during December, lambing seasons, seasonal environmental conditions /summer or wet season or lean period (animals are usually under stress due to long-distance traveling and nutritional deficiency) might be the epidemiological or risk factors associated with the occurrence of the disease (Singh et al., 2004a; Soundararajan et al., 2006; Balamurugan et al., 2012a). During their migration, infected animals may transmit the virus to susceptible local sheep and goats (Singh et al., 2004a; Balamurugan et al., 2012b). Furthermore, climatic factors favorable for the survival and spread of the virus may also contribute to the seasonal distribution of PPR outbreaks in different geographical regions. With the start of the rainy season (between June/July and August/September), the migratory activity of animals is reduced due to the increased availability of local fodder. In conclusion, the most appropriate time to vaccinate against PPR is August / September and March /April in a year and well before the migration of the animals.

4.4. Species susceptibility

On analysis of the reported outbreaks and cases (outbreaks n=8168, cases n=402495) from 25 years (1995-2019), the highest outbreaks in goats (47.06 %) followed by 42.52 % in sheep and 10.42 % in sheep and goats together with 53.52 % (n=215425), 22.91 % (n=92202), and 23.57 % (n=94868) cases in goats, sheep, and sheep and goats together, respectively. The detailed species-wise reported PPR cases/outbreaks are presented in **Fig. 7**. An increased number of outbreaks have been reported in goats than in sheep in the different zones of the country, except in the south zone where the number of outbreaks was higher in sheep (**Fig. 7**).

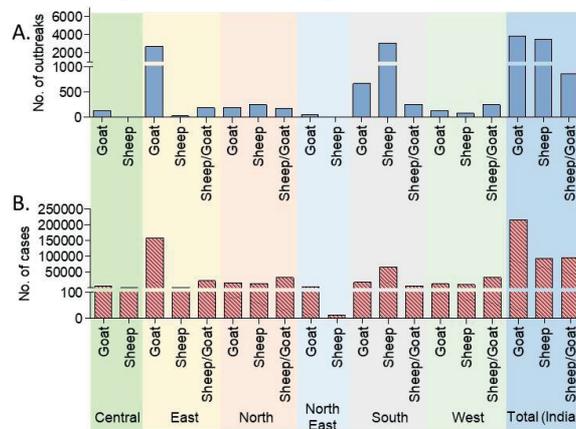


Figure 7. Species-wise occurrence of cumulative PPR reports in different zones/regions of India (1995-2019).[A]. Outbreaks [B]. Cases. An increased number of outbreaks have been reported in goats than in sheep in the different zones of the country, except in the south zone where the number of outbreaks was greater in sheep.

Eventhough susceptibility of sheep and goats are equal chance, PPR affects goats more than sheep and the population of goats to sheep is almost 2:1 in India as per the 20th livestock census 2019 (DAHD, 2020a) and in South-zone, the population of sheep is higher than goats in Andhra Pradesh, Telangana, and Karnataka states. Many authors believe that although PPRV infects both sheep and goats, the severity of the clinical symptoms is more predominant in goats than sheep (Tripathi et al., 1996a; b; 2018; Singh et al., 2004a). Outbreaks are relatively more common in goats than sheep in northern (Singh et al., 2004a; b; c), as the goat population is more in northern India (Singh et al., 2004a). Severe outbreaks of PPR have been noticed in regions having large sheep populations, indicating PPRV causes serious clinical disease in sheep as well (Singh et al., 2004a). Curiously, in some studies, PPRVs isolated from goats from north India have been shown to cause severe infection in goats as compared to sheep (Nanda et al., 1996; Singh et al., 2004a). However, a PPRV isolated from goats did not induce apparent clinical signs in sheep in the few initial passages. This isolate induced clinical signs in sheep after few passages of adaptation in sheep (Balamurugan, 2017). Nevertheless, it cannot be undermined that, the recovery rate in goats is comparatively less than that in sheep after infection. Generally, small ruminants have a high reproductive rate (fecundity), under normal circumstances (no drought), tropical sheep/goats should be lambing/kidding at least three times in two years. This combined with the higher rate of slaughtering of male goats at an early market age and fecundity of female goats (Balamurugan et al., 2011, 2016), results in appears of approximately 30-40% naïve population every year (Singh, 2011). These newly born animals become susceptible to the infection; presumably, another reason for greater susceptibility of the goat population as reported earlier (Singh et al., 2004a). Further, it was observed that deaths were reported more in goats (60 %) than in sheep (23.98 %), which is corroborated with most of the earlier reports stating that though the PPRV infects both sheep and goats, the severity of the clinical symptoms was more predominant in goats than sheep (Singh et al., 2004a) and goats were severely infected than sheep (Singh et al., 2004a; Balamurugan et al., 2012a, 2016). The studies at the molecular aspects of virus affinity and species susceptibility would unravel the greater susceptibility of a goat than sheep. The research work need to be undertaken to find out the hypotheis. In tropical areas, the fertility rate is higher in goats than sheep, which accounts for larger flock replacement by goat offspring. Balamurugan et al., (2012b) attributed greater PPR positivity in clinical samples from goats to the fact most of the suspected samples were from regions, which had a larger goat population.

4.4.1. Unnatural Host

The occurrence of PPR in un-natural /atypical hosts is still a matter of dispute. There have been several reports of subclinical PPRV infection occurring in ruminant species of animals. Although cattle are susceptible to PPRV infection following contact with the sick sheep and goats, they do not exhibit clinical signs and do not transmit the disease to other animals but seroconvert (Sen et al., 2014). There is no evidence of carrier state, however, they may play a role in the epizootiology of PPR because they are apparently unable to transmit the disease to other animals. The PPRV may be

adapted in bovine, which is subclinically infected without showing any symptoms of illness under natural conditions. Cattle and Pigs were considered dead-end hosts for PPRV. However, the virus was also isolated from a natural outbreak in buffaloes caused by fatal syndrome (Govindarajan et al., 1997). The circulation of PPRV in the unnatural host(s) may have a significant role or may help in the control or restrict the spread of PPR in small ruminants in a particular geographical area (Balamurugan et al., 2012a). This assumption may be due to the possibility of adaptation and change in virulence of the virus where natural and unnatural hosts are reared together in integrated farming systems. It is believed that, in the situation, where large and small ruminants co-exist, seroconversion in cattle of cross-reacting PPRV antibodies might have also helped to eradicate RP. Subsequent to the development of specific diagnostics, the presence of PPRV antibodies has also been reported in cattle, buffaloes (Balamurugan et al., 2012a), and PPRV antibodies and antigens detected in experimental cattle over one year (Sen et al., 2014). All these reports showed that PPR could also be transmitted directly or indirectly from sheep or goats to cattle, providing a mechanism for the virus to survive outside of the environment in the unnatural host.

PPR in wild small ruminant species has been reported and the role of wild animals in the epizootiology of PPR has been realized and could be of considerable significance for virus perpetuation. Antelope and other small wild ruminant species have been reported to be severely affected. However, In India, the presence of the infectious virus in seropositive wild ruminant has not yet been reported except in a Chowsingha (*Tetracerus quadricornis*), a member of the subfamily Bovinae (Jaisree et al., 2018). Further, PPRV in the nasal swabs of dogs by microarray screening (Ratta et al., 2016) and detection of PPRV nucleic acid in the tissue samples of Lion died of Trypanosomiasis (Balamurugan et al., 2012c), provided new insight or suggest possible crossing of species barrier in the PPR epidemiology. However, a detailed study is needed to conclude. Wild ruminants have been suspected to play a role in spreading the disease, sharing the same grazing field or areas and water bodies with domestic animals may potentially result in the spillover of PPRV from domestic to wild ruminants in the ecosystem. However, the actual role of the wildlife on the epizootiology of the disease remains unclear for the moment and is to be investigated (Balamurugan et al., 2015). Moreover, the presence of PPR virus-specific antibodies in cattle/buffaloes and wild ruminants suggests the natural transmission of infection among these animals. Hence, there is a possibility of wildlife-livestock interactions resulting in the spillover of PPR to wildlife.

4.5. Spatial distribution

The spatial maps were generated using the open-source GIS software QGIS (Quantum GIS Development Team 2018, QGIS version number 2.18.0) to visualize risk zones/ areas and outbreak locations of the districts in the different states of India. The categorization of endemicity was based on the scale of the cumulative outbreaks that occurred in the area (district) per year in the given period of analysis and classified into different categories of risk (if the outbreaks numbers as 0 –no risk, 1- very low, 2- low, 3- medium, 4- high and >4 very high-risk districts). Further, this categorization is also classified as sporadic (very low=1 outbreak), low endemic [mild=2 outbreaks and moderate=3 outbreaks]), highly endemic (high=4 outbreaks), and hyperendemic (very

high = >4 outbreaks] districts, respectively to present the different endemicity levels in the Indian states. Based on the occurrence of the cumulative outbreaks in the endemic districts per year in the given period of analysis, the districts in four different categories in different states of India were obtained as sporadic (1 outbreak), low endemic (2-3 outbreaks), highly endemic (4 outbreaks), and hyperendemic (>4 outbreaks) districts, respectively. Furthermore, the different categories of endemic districts are depicted in six-scale classification at different periods of analysis and are depicted in the map (**Fig. 8**) to visualize risk zones/areas and the number of outbreaks that occurred in district locations in different states of India. Many districts of Andhra Pradesh, Karnataka, West Bengal, Jharkhand, Tamil Nadu, Maharashtra, Gujarat, Himachal Pradesh, Jammu and Kashmir, and Odisha fall under the highly endemic and hyperendemic risk areas categories, whereas many districts in the states of Central and North-East zones belongs to sporadic and low endemic risk areas. An increasing number of districts were affected with PPRV infection during 1995-2010 compared to the 2011-2015 and 2016-2019 periods and further, a few sporadic outbreaks occurred in only a few of the districts in different states of the country in 2019 and 2020 (**Fig. 8**). Further, on analysis of cumulative data, Andhra Pradesh, West Bengal, and Karnataka states were the top three states during 1995-2010, whereas, during 2011-15 Jharkhand, West Bengal and Karnataka, and during 2016-2019, Jharkhand, West Bengal, and Maharashtra & Karnataka had reported the highest number of outbreaks (**Fig. 8**). Furthermore, East and South zones had reported more outbreaks than other zones during 1995-2010, whereas during 2011-15 and 2016-19 more outbreaks were observed only in the East zone. States like Jharkhand, West Bengal, Kerala, and Rajasthan have reported an increasing trend of PPR outbreaks during 2011-2015. Although South zone states like Karnataka, Andhra Pradesh have shown a decline in the number of outbreaks, the disease is still reported sporadically. PPR endemic risk areas showed a wide variation in the different states/zones of India at different periods. The variation in disease endemicity might be due to differences in animal husbandry practices and the agro-climatic conditions affecting the pattern of the natural vegetation which indirectly influences the socio-economic factors, the migration patterns of small ruminants, flock size, and the population density of the animals in the different states (Balamurugan et al., 2021a). Although India is endemic to PPR, north-eastern states are either free from disease or have very few reports (Singh et al., 2004a; Balamurugan et al., 2014a, 2020f). North-East states have a relatively small sheep and goats population and intermixing of these animals with the small ruminants population from the rest of the country is usually limited. Further, the hilly terrain characterizing this region may restrict the movement of animals and disease transmission (Balamurugan et al., 2020c).

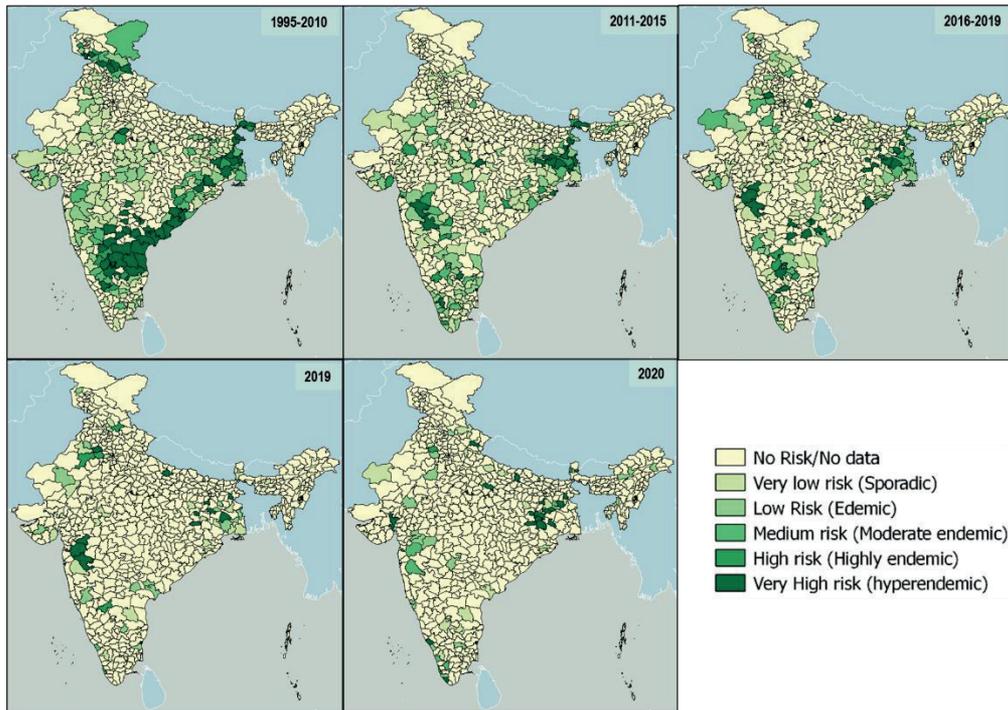


Figure 8. Endemic districts of PPR in different states of India (1995-2019). The endemicity categorization is based on the scale of the cumulative outbreaks, that occurred in the districts per year in the given period of analysis and classified as in the categories of risk.

5. Seroprevalence

The prevalence of PPRV antibodies in sheep and goats indicates subclinical or inapparent or non-lethal infections, as vaccinations against the disease are generally limited and irregular in the endemic countries, which could be of epidemiological significance. However, the prevalence of antibodies in adult sheep or goats is not always indicative of infection, as there is always a high probability of these animals receiving vaccination once during a lifetime. The data on the seroprevalence of antibodies to PPRV in small ruminants (sheep and goats) and large ruminants (Cattle, Buffaloes, Camels) are available from many countries including India from low to high based on the endemicity of the disease (Singh et al., 2004a; Balamurugan et al., 2011, 2012c, 2015). A systematic or organized serological survey for PPR prevalence has not been conducted in India and the majority of the reports indicate only regional data, barring a small number. A nation-wide systematic serosurvey conducted by employing the PPR competitive ELISA (Singh et al., 2004c) in sheep and goats during 2017-2018 showed a wide variation in the prevalence status of PPRV antibodies (seroprevalence/immune population) in the different states of India as vaccination strategies employed and coverage by the states varied significantly, even though it is not possible to distinguish the vaccinated and infected animals, as the DIVA vaccine was not being used in the PPR-CP (Balamurugan et al., 2021a). The prevalence of

PPRV antibodies in southern peninsular India (TN, Karnataka, AP, Kerala, and Telangana) varied significantly due to variation in risk population, disease incidence, and extent of vaccination coverage in the PPR-CP. Further, the observed prevalence of antibodies level in the states in the Southern Peninsular covering two zones (Southern plateau and hills, and West coastal plateau and hills zones) was high (population immunity) due to continuous vaccination coverage in the states due to PPR-CP implementation since 2010–2011 (www.daahd.nic.in) when compared to non-vaccination implemented states of India, where baseline 30 % prevalence was observed (Balamurugan et al., 2020f). Similarly, the earlier reported seroprevalence in other agroclimatic zones/states was also varied. The reported seroprevalence from the Eastern Himalayan zone (covering north-eastern states of India) showed 34.3%, 10.3%, 4.7%, 15.7%, 14.7%, and 5.5%, in small ruminants in Assam, Manipur, Meghalaya, Mizoram, Nagaland, and Tripura, respectively (Balamurugan et al., 2020f), whereas the Central and Western plateau and hills and Western Dry as well as Gujarat plains and hills zones covering the central and western India, showed seroprevalence of 34.4%, 20.8%, 51.6%, 74.1%, 68.3%, and 64.8% in Madhya Pradesh, Goa, Chhattisgarh, Maharashtra, Gujarat, and Rajasthan states respectively (Balamurugan et al., 2018, 2020, 2021a). Similarly, the Western Himalayan zone and Upper and Trans Gangetic Plains zones covering North Indian states showed that seroprevalence of 57.32%, 55.22%, 65.69%, 37.09%, 32.73%, and 29.35% in small ruminants in Haryana, Punjab, Uttar Pradesh, Himachal Pradesh, Jammu and Kashmir, and Uttarakhand states, respectively (Balamurugan et al., 2020b). The East coast plains and hills and Middle Gangetic Plains and Western plateau and hills zones covering Eastern India, and island zone of Andaman and Nicobar, showed the seroprevalence of 30.91% and 54.20% in Bihar and Odisha states, respectively (Balamurugan et al., 2020d) with only 1.16% in the Sikkim, 1.28% in the Andaman Islands (Balamurugan et al., 2019, 2020c). Overall, the reported prevalence of PPRV antibodies in small ruminants in India as a whole in a large scale study varied between 33.0 to 43.7% (Singh et al., 2004a; Raghavendra et al., 2008; Balamurugan et al., 2011), which indicated the need for vigorous vaccination among small ruminants in the country to be continued to achieve desired population immunity status for the eradication of PPR from India.

6. Transmission

PPRV needs close contact between infected and susceptible animals to spread because of the lability of the virus outside. PPRV is transmitted mainly by inhalation of infectious aerosol materials between animals living in close contact. Quantities of the virus are excreted in the secretions or the discharges from eyes, nose, and mouth, as well as the excretion through faeces of affected animals during infection especially at least 7 days after onset of the disease and, are the important source of virus infection (Singh et al., 2004b; Balamurugan et al., 2006). These discharges form fine infectious droplets in the air particularly when the affected animals cough and sneeze. Animals in close contact inhale the infectious droplets and are likely to become infected. The infectious aerosols can also contaminate water, feed troughs, and bedding, turning them into additional sources of infection, but this indirect mode seems to be less important since the PPRV is not expected to survive for a long time outside the host and is also sensitive to lipid solvent. Trade of small ruminants at markets where animals from different sources are brought into close contact with one another provides increased opportunities for PPRV transmission. Although cattle and pigs have been shown to seroconvert the following contact with the sick sheep and goats, the development of clinical disease in these animals has not been reported. Transmission of PPRV either directly or indirectly from sheep or goats to cattle provides a mechanism for the virus to survive outside of the environment in the unnatural host. The presence of PPRV antibodies in unnatural hosts besides sheep and goats suggests the natural transmission of PPRV infection among these animals under field conditions (Balamurugan et al., 2012a, 2014c). Nomadic animals will often come into contact with local sheep and goat populations from whom they may contact the virus (Singh et al., 2004a); subsequently, infected migratory animals may transmit the virus to other susceptible local sheep and goats. Therefore, the movement of animals plays an important role in the transmission and maintenance of the PPR virus in nature.

7. Clinical Manifestations

PPR can be diagnosed tentatively based on clinical and pathological lesions. The clinical manifestation of PPR is more or less similar to RP except for the remarkable affinity of the PPRV to the lung tissues. Clinically, the disease is characterized by high fever (pyrexia), oculo-nasal discharges, necrotizing and erosive stomatitis, gastroenteritis, diarrhea, and bronchopneumonia, followed by either death of the animal or recovery of the animal from the disease (Balamurugan et al., 2014c). The clinical picture of PPR could be characterized by “3Ds”, i.e. discharge, diarrhea, and death, with an additional fourth component, bronchopneumonia. The case definition of PPR include five specific cardinal clinical signs viz., pyrexia, oculo-nasal discharge, oral lesions, respiratory signs, and diarrhoea (Fig. 9) (Balamurugan et al., 2019). Generally, the incubation period is 4–6 days but may range from 3 to 10 days. The disease exhibits different stages, viz. (i) incubation period (short) 5–7 days, (ii) prodromal phase (febrile reaction), (iii) mucosal phase (pyrexia, ocular and nasal discharges, hyperemia of the conjunctiva, and mucosa of anterior nares and erosions on the tongue, palate, lips and other parts of the oral mucosa), (iv) diarrhoeal stage (diarrhea, pneumonia, dehydration, death) and, (v) in nonfatal cases, “recovery stage” in which sheep and goats that recover from PPR develop active lifelong immunity. PPR

may manifest in different forms like peracute, acute, and mild depending on the severity of the disease (OIE, 2019). The peracute form is seen in young goats with an incubation period of 2 days followed by hyperthermia (41–42 °C), prostration, piloerection, anorexia, oral and ocular discharges, and constipation, and later leads to profuse diarrhea. Death occurs within 5–6 days of infection. The acute form is characterized by a fever followed by oculonasal discharges (watery to mucopurulent with eyelids sticking together) and partial blockage of the nose due to nasal discharges. Later, diarrhea followed by necrotic lesions appears in the oral cavity. The mortality rate is 70–80 % and death occurs within 7-10 days after the onset of disease. The severity of the disease depends on various factors, namely, the PPRV virulence/lineage, species, breed, immune status, and age of the animals. PPR is frequently confused with other diseases that present fever and grossly similar clinical signs, especially when it is newly introduced. The other diseases with similar signs for differential diagnosis are bluetongue (BT), contagious ecthyma (Orf), foot and mouth disease (FMD), contagious caprine pleuropneumonia (CCPP), pasteurellosis, etc., Sometimes, mixed infection of PPR either with goat pox, sheep pox, Orf, BT, etc., have also been reported (Saravanan et al., 2007; Mondal et al., 2009; Malik et al., 2011).



Figure 9: The case definition of PPR include five specific cardinal clinical signs viz., A) pyrexia, B) oculo-nasal discharge, C) oral lesions, D) respiratory signs, and E) diarrhoea

7.1. Pathological Lesions

The pathology of PPR is characterized and dominated by retrogressive and necrotic changes in lymphoid tissues and epithelial cells of the gastrointestinal and respiratory systems. The prominent lesions in PPR infected animals include consolidation, changes in the color of lungs, and sometimes, frothy mucus is observed in cut pieces of the lung on squeezing, anteroventral areas of right lung are frequently involved; areas of lungs become dark red or purple, firm to touch mainly in the anterior and cardiac lobes (Kumar et al., 2002). Consolidation of lobes of lungs and occlusion of the airway caused by secondary bacterial pneumonia are common. The congested alveolar border was found to be one of the most characteristic clinical and pathological

changes of PPR in goats (Tripathi et al., 1996a; b; 2018; Kumar et al., 2002). The involvement of the respiratory system in PPR is remarkable and pneumonia is a predominant sign in PPR. Most reports found lung involvement in almost more than 90 % of cases dying during the outbreak of PPR (Tripathi et al., 1996a; b; 2018; Aruni et al., 1998). Bronchopneumonia is a constant lesion, with the possibility of pleuritis and hydrothorax. Lymph nodes associated with the lung (mediastinal) and intestine (mesenteric) are most commonly affected which are generally enlarged, oedematous, and congested. Spleen become congested and engorged, and at times showed petechiae on the capsular surface. Severe congestion and necrotic lesions in the gastrointestinal tract are normal features. Necrotic or hemorrhagic enteritis or congestion around the ileocecal valve, at the caeco-colic junction, and in the rectum are seen usually. In the posterior part of the colon and rectum, discontinuous streaks of congestion (“Zebra” stripes or “Zebra markings”) on the mucosal folds are observed, which are typical of PPR (Balamurugan et al., 2014b).

8. Socio-economic impact

As a TAD, the presence of disease can limit trade and export, import of new breeds, and development of intensive livestock production, which in turn diminish the consumption of animal protein in humans. Due to the occurrence of other diseases, the economic impacts of PPR are probably underestimated, but it is believed that PPR is one of the major constraints for augmenting small ruminant production. Epidemics affect not only individual farmers but also the agricultural industry and as a consequence, the national economy. Further, the control costs burden the exchequer and crowd-out investment growth of the sector. PPR is present in countries, which are either developing or under-developed thereby adding to the economic woes. Sheep and goats are numerically and economically important livestock species in developing countries like India with a population of ~148.88 million goats and 74.26 million sheep (as per the 20th Livestock census-2019, DADF, Gol, www.dahd.nic.in) as against approximately 2.1 billions world population of sheep and goats, are contributing much too small, marginal and landless rural farmers to sustain their livelihood. Economic loss due to PPR is not quantified comprehensively so far either at the national or regional/state levels. Due to the occurrence of other diseases, the economic impacts of PPR are probably underestimated, but it is believed that PPR is one of the major constraints of small ruminant productivity. The quantification of economic loss due to any disease in animals is very important since it helps in prioritizing the research on animal health issues, and designing an appropriate control program. Some economic loss reports in India are based on reported cases and deaths and some are based on primary surveys from few geographical locations. In India, the economic loss due to PPR was reported during different periods of study. As per a rough estimate, the disease causes an annual loss of 1, 800 million INR (Venkataramanan et al., 2005) or 4,000 million INR (DAHD, Gol, www.dahd.nic.in), or a value of 4610.3 million (3,323.2 million USD for goats and sheep 1,287.1 million USD) USD with 28.39 % loss due to PPR in small ruminants (Singh et al., 2009), or an annual estimated financial loss of INR 16,110 million at 10% incidence rate (Govindaraj et al., 2016) in sheep and goats.

In developing countries, sheep and goats are generally reared by landless and marginal farmers and the majority of their income source depends on the production

potential and health status of the animals. The health of the animals is directly correlated with the income security of these farmers. Any animal disease event in the farms devastates the major income source and affects the socio-cultural fabric of the farm families significantly. In the normal course, the sheep and goats act as an asset and cushions the farm families against the vagaries of monsoon and unemployment. But the disease like PPR affects the regular family income source their by affecting the family consumption, saving and investment pattern, and affects the overall growth and development of farm families in all spheres of life. The downward spiral of income due to PPR makes them remain in the lower socio-economic base for a very long period. To leapfrog from this level, urgent attention is needed on the adoption of PPR preventive methods like vaccination and biosecurity by the farmers.

9. Diagnosis

PPR is tentatively diagnosed by clinical observations with characteristic symptoms and post-mortem lesions. The laboratory confirmation is by various serological and molecular techniques. Serological tests such as agar gel immunodiffusion test (AGID)/AGPT, counter immuno-electrophoresis (CIE) and indirect ELISA, although popular in earlier days for tentative diagnosis, do not differentiate PPR and RP infections. The advent of cell culture and molecular biological techniques has allowed the development of specific, rapid, and sensitive diagnostics. In general, virus isolation, AGID/AGPT, CIE, nucleic acid hybridization, hemagglutination using piglet or chicken red blood cells, immune-histochemical detection, serum or virus neutralization test (VNT), and ELISA using PPRV-specific monoclonal antibodies (MAbs) are used for diagnosis of PPR. The specific diagnosis of PPRV infection can be achieved by cDNA hybridization, mobility of N protein, neutralization test and MAb-based ELISA, RT-PCR, and real-time RT-PCR. A battery of serological tests and molecular assays are available to detect and identify PPRV antigen/nucleic acid and antibodies. Balamurugan (2014b), comprehensively reviewed the diagnosis of PPR in India. Most of the conventional tests are time-consuming, labor-intensive, less sensitive, and not rapid and therefore, not suitable for primary diagnosis but useful in secondary confirmatory testing and retrospective epidemiological studies. To overcome the drawbacks associated with these tests, molecular biology tools and techniques like real-time RT-PCR and loop-mediated isothermal amplification (LAMP) assays have been used for the rapid and sensitive detection of PPRV RNA from clinical samples.

9.1. Conventional diagnostic techniques

PPRV-specific antibodies have been used for the detection of virus antigen in tissue, swabs, conjunctival smears, and formalin-fixed tissues by various researchers in different assays/tests. Earlier, AGID/AGPT was a frequently used method for the detection of PPRV antigens in clinical and post-mortem samples. CIE was a comparatively more sensitive and rapid method than that of AGPT but failed to differentiate between PPRV and RPV infection. Indirect immunofluorescence test (IFAT) and Immunoperoxidase test (IPT) utilizing polyclonal and MAb provide rapid detection of virus antigen *in situ* in the infected cells or tissue samples. IPT could be a test of choice for localization of PPRV antigen in samples where antigen has not been reported previously. Among all the methods, isolation of the virus remains the “gold

standard” for the diagnosis of PPR. Virus isolation cannot always be done as routine diagnostic assays because they are time-consuming and cumbersome and require cell culture facilities, and they are not as sensitive as RT-PCR. VNT was performed for confirmation and differentiation of viruses, for the detection of PPRV antibodies in serum samples. Differential neutralization test is one of the important means to distinguish RP and PPR viruses.

9.2. Enzyme-linked immunosorbent assay (ELISA)

As a rapid, simple, and sensitive assay, ELISA has been widely used in the serological profiling of PPRV in the mass screening of samples for seromonitoring/serosurveillance or syndromic surveillance. Various researchers have used MAb produced against PPRV for the detection of antibodies and antigens in ELISA. Singh (2004c) developed a MAb-based c-ELISA for the detection of PPRV antibodies using a virus-neutralizing MAb directed against an epitope in ‘H’ protein specific MAb (4B11) to PPRV and cell culture propagated vaccine virus antigen. This c-ELISA had high diagnostic specificity-DSp (99.8 %) and diagnostic sensitivity- DSn (90.5 %) for detection of PPRV antibody in convalescent sera, when compared with VNT and also the commercially available kit, where, it had high DSn (92.2 %) and DSp (98.4 %) (Singh et al., 2004c, 2006). This assay is currently being employed extensively throughout India for monitoring/serosurveillance of PPR. Further, a polyclonal antibody-based indirect ELISA was also developed for the detection of antibodies to PPRV in the serum samples of goats and sheep using Vero cell culture propagated purified PPRV antigen. This assay had a high degree of specificity and sensitivity (DSp 95.09, DSn 90.81 %) and (DSp 100, DSn 80 %), when compared with c-ELISA (Balamurugan et al., 2007) and VNT, respectively. This may be a good alternative tool to c-ELISA for seroepidemiological surveys. Further, MAb-based immunocapture ELISA and sandwich ELISA (s-ELISA) have been used extensively for the detection of PPRV antigen in clinical specimens. The s-ELISA kit developed at IVRI, Mukteswar, uses a MAb (4G6) directed against an epitope of N protein of PPRV (Singh et al., 2004b), which is routinely being used for the prevalence or detection of PPRV antigens in syndromic surveillance in India (Singh et al., 2004b). This assay was efficacious, with diagnostic sensitivities (89 %) and specificities (93 %), comparable to the commercial immunocapture-ELISA. Further, an assay using synthetic peptide antigen or multiple antigenic peptides (MAPs), specific to PPRV polypeptides as isotope, for the detection of PPRV antibodies in serum samples has also been developed by IVRI for diagnosis or serosurveillance and seromonitoring.

Due to the advancement in rDNA technology, gene expression technology, the production of recombinant viral proteins has become easier and more efficient. The ease of genetic modification, the yield of recombinant proteins, and the maintenance of post-translational modifications often determine the choice of the host systems. Recombinant complete PPRV N protein-based antigen capture ELISA was developed as an improved version of the s-ELISA kit using N protein-specific Mab for the detection of PPRV antigens in the clinical samples (Yadav et al., 2009; Basagoudanavar et al., 2018). Further, indirect ELISA was developed using the recombinant non-structural V protein and it has only a relative sensitivity and relative specificity of 77.73% and 73.775%, respectively as compared to c-ELISA (Yadav et al., 2019). Recently,

Balamurugan et al. (2021c) produced polyclonal antibodies against the recombinant truncated PPRV N protein expressed in *E. coli* and developed Avidin-Biotin recombinant ELISA for PPRV antigens detection in clinical specimens and Avidin-Biotin recombinant Competitive ELISA for PPRV antibodies detection in the serum samples (Balamurugan et al., 2021b). After extensive field evaluation of the ABrAC ELISA (Balamurugan et al., 2022a), it can be used as a mass screening assay as well as for routine diagnosis along with the existing improved version of the PPR s-ELISA kit (Singh et al., 2004b; Basagoudanavar et al., 2018) for surveillance of PPR in India. These assays are safe and better alternatives to live PPRV antigen in ELISA for clinical or sero-surveillance of PPR in enzootic India during the eradication and post-eradication phase. As of now, the MAb-based PPR-s-ELISA kit and PPR c-ELISA kit have been recommended for the detection of PPRV antigen in the clinical specimens and the detection of PPRV antibodies in the sera of animals, respectively in the national strategic plan for PPR eradication 2030, by DAHD, Gol.

9.3. Molecular diagnostic techniques

Due to an improved understanding of the viral genome and molecular biological techniques, nucleic acid-based specific and sensitive assays were also developed. Nucleic acid hybridization, RT-PCR, simple, and aqueous phase ELISA, PCR-ELISA, and nucleic acid hybridization have also been used for the detection and differentiation of PPRV (Shaila et al., 1989; Forsyth and Barrett, 1995; Saravanan et al., 2004; Balamurugan et al., 2006; George et al., 2006). RT-PCR and cDNA hybridization techniques are the two sensitive means to diagnose PPRV infection but are time-consuming and cumbersome for routine diagnosis with a large sample size. Nucleic acid hybridization is also suitable for providing diagnosis utilizing field materials, which are either collected from the putrefied or semi-putrefied carcasses or get putrefied during the transit period (Pandey et al., 1992). Despite the high sensitivity, radiolabelled probes were not widely used because of the short half-life of ^{32}P and the requirements of fresh specimens and isotopes handling facility. This led to the development of non-radioactive probes using biotinylated DNA or digoxigenin (DIG) labeled oligonucleotides. This assay was very specific and rapid but its sensitivity was not less than radioactively labeled probes. Of late, RT-PCRs and real-time qRT-PCR with different chemistry either single or duplex format have been reported for detection and differential diagnosis of PPR in clinical specimens (Balamurugan et al., 2010b; a). Further, a rapid and sensitive diagnostic tool, the LAMP technique (Dadas et al., 2012) has also been developed for the detection of PPRV using field clinical samples in less equipped rural diagnostics laboratory settings.

9.4. Pen-side tests

A simple dot-ELISA has also been developed using anti-N protein MAb (Saravanan et al., 2006) for the detection of PPRV antigen in tissue homogenate/swab materials of sheep and goats origin. This test is useful for screening a large number of clinical samples and suitable for animal disease investigation laboratories in the field and could be used as a penside test for diagnosis of PPR. This assay had relative DS_n (82.5 %) and DS_p (91 %) compared to s-ELISA for PPR diagnosis. Lateral flow test for detection of PPRV antigen and antibody was also developed, but not up to the mark in

regular usage. However, this test has the advantages of being quick, easy to perform, and does not involve technical skill or expertise, and hence user-friendly and useful as a pen-side diagnostic test. Raj et al., (2008) developed immunofiltration and antigen-competition ELISA methods for the detection of PPRV antigen, which showed a sensitivity of 80 % and specificity of 100 %. These two tests can serve as a screening (immunofiltration) and confirmatory (antigen-competition ELISA) test, respectively, in the diagnosis of PPR in sheep or goats. Moreover, this test has the advantages of being quick, easy to perform, and does not require technical skill or expertise, and hence user friendly.

10. Prevention and Control measures

PPR has a massive impact on sheep and goat production and productivity in endemic settings and therefore, its control and eradication are of high priority. The strong support of accurate diagnostics for mass screening and timely availability of vaccines and vaccinating all susceptible populations is highly imperative for the effective control of PPR (Balamurugan et al., 2021a). Other methods like isolation and movement control to reduce the disease spread is difficult to implement in the field due to various problems in developing countries. All the animals in the affected flock should be under quarantine for at least one month after the last clinical case. Animal movements need to be strictly controlled in the area of the infection. Unfortunately, such sanitary and phytosanitary, and control measures are difficult to maintain in the majority of the PPR endemic countries including India. Hence, the control of PPR can be ensured only through the implementation of effective prophylactic measures like mass vaccination, and the adoption of quarantine/biosecurity measures. Some of the sanitary prophylaxis measures that can prevent the occurrence of PPR infection are strict quarantine and control of animal movements; quarantine of newly purchased or newly arriving goats/sheep for at least two to three weeks before allowing them to mix with the regular flock and know the health status and the source of new animal(s) brought into the flock; reducing migratory flocks mixing with the local sheep and goats; effective cleaning and disinfection of contaminated areas, equipment and clothing with lipid solvent solutions of high or low pH and disinfectants; dead animal/carcasses should be burnt/ buried deeply; monitor animals closely and frequently for any illness or signs of disease; isolate any sick animals from the flock and contact the veterinarian immediately to examine sick animals in the herd /flock; use separate facilities and staff to handle the isolated animals; educate and train the employees about PPR and the signs of illness and monitoring of wild and captive animals, especially that are in contact with sheep and goats.

Since PPR is a viral disease, there is no specific treatment for this disease. Post-exposure therapeutic approaches for PPR infections are not mentioned much in the literature. The treatment regime of affected animals includes the use of broad-spectrum antibiotics plus fluid therapy along with vaccinating the flock against PPR during the first week of the outbreak in endemic disease conditions (Balamurugan, 2017; Tripath et al., 2018). Treatment of affected animals is by administration of antibiotics (long-acting oxytetracycline, chlortetracycline) to prevent secondary bacterial infections and anti-diarrhoeal medicines have been practiced with supportive therapy (B-complex and

Dextrose saline) for 5 to 7 days, which may be useful to reduce the severity of the disease (Balamurugan, 2017).

10.1. Prophylaxis measures

The control of PPR can be ensured only through the implementation of effective prophylactic measures. Vaccination is a recommended tool to support control and eradication efforts and thus to limit the economic loss due to PPR (Balamurugan et al., 2016). Three homologous PPR vaccines using Indian isolates of PPRV (goat origin-Sungri 1996 and Coimbatore-1997; sheep origin-Arasur-1987) have been developed and evaluated (Saravanan et al., 2010). These vaccines also provide satisfactory protection against the challenge and are equally safe and protective as Sungri-96 in sheep and goats and suited for commercial vaccine production (Saravanan et al., 2010). A minimum WOAHA recommended dose i.e., 10^3 TCID₅₀, of vaccine each animal should receive for the protective response. Live attenuated PPR vaccine (Sungri 1996 strain) has been tested extensively in in-house as well as by field trials and is safe and potent in small ruminants (Sreenivasa et al., 2000; Singh et al., 2009, 2010) and about 90% of the animals have been found to have protective levels of antibodies under field conditions (Sreenivasa et al., 2000). Using this vaccine, studies have been undertaken for thermostability, pathogenicity, and immunogenicity at various *in vitro* passages (Sreenivasa et al., 2000; Sarkar et al., 2003; Rajak et al., 2005; Saravanan et al., 2010). Thus, Sungri 96 PPR vaccine is safe for mass vaccination campaigns under field conditions and is presently used throughout India to vaccinate sheep and goats with great efficacy.

10.2. Planning of Control Programme

The PPR control depends mainly on rapid and effective diagnosis, surveillance, monitoring, and implementation of the vaccination programme. Control strategies may vary in different countries based on the prevalence of the disease, however, in developing or underdeveloped countries the choices of control strategies are limited, as the stamping out policy is not feasible for socio-economic reasons. Rigorous stamping out policy involving quarantine and slaughter can control the spread of the disease and aid in eradication, but difficult to follow in developing countries like India due to various socio-economic and sentimental reasons. However, in the final stage of eradication, elimination of the virus is possible through slaughter or restriction in the movement of animals. Generally, social acceptance, public and regulatory support are essential for the success of any disease control and eradication programme. Hence, vaccination is a recommended tool to support control and eradication efforts (Singh et al., 2009; Singh, 2011). In many countries including India, vaccination is an important strategy to control the disease (Singh et al., 2009; Singh, 2011) and to minimize the immediate loss to the farmers. In India, the success of the national rinderpest eradication programme (NPRE) has provided the confidence that it is required to launch a similar programme with PPR. There is a need for a disease registry, both at the state and national level, to ensure effective reporting and coordination of outbreak occurrence and monitoring (Balamurugan et al., 2014b). This would help to provide a rapid appraisal of the vaccination status, serological and epidemiological status, target population identification, movement of animals, and tracking and locating prospective

animal target foci (Singh et al., 2009; Balamurugan et al., 2016; 2021a). A better knowledge of sheep and goat population dynamics, herd management practices, and animal movement patterns will be a critical condition for the success of any control programme (Singh et al. 2009; Balamurugan et. al., 2016; 2021a) besides, the local management of the PPR by farmers, animal health workers, veterinary professionals, and services. Further, improvements in the governance of the surveillance systems and veterinary services for better coordination with the private and public sectors of animal health management are highly imperative. Though a good PPR vaccine is available, the implementation of a relevant vaccination and monitoring strategy will have to find its way, though more lessons learned from RP eradication (Singh et al., 2009; Balamurugan et al., 2016).

In India, currently, the PPR vaccine (Sungri 96 strain), developed by Indian Veterinary Research Institute (IVRI), Mukteswar has undergone extensive field trials (Singh et al., 2009; Singh, 2011) and is being used in the PPR-CP of GoI. All Indian PPR vaccine virus strains belong to Asian lineage IV and the use of any PPR vaccine may be sufficient to protect against the circulating field isolates/strains of PPRV in India. These vaccines can be used for the control and eradication of the disease not only from India but also from other countries following the example of the global RP eradication programme (GREP), as one single vaccine of any lineage may provide a protective immune response against any four lineage viruses so far identified in various geographical areas in the world. Experimental vaccination against PPR after field testing has been practiced in 15 states of India since 2002 to combat the disease as “focus vaccination” targeting the area of the outbreak (Singh et al., 2009). Further, the vaccine production and quality control technology has been transferred to different national and multinational companies in India {three multinational companies (MNCs) viz. M/s Intervet India Pvt Ltd. (MSD Animal Health), Pune India, M/s Indian Immunologicals Limited (IIL), Hyderabad, India, and M/s Hester Bioscience, Ahmadabad, India}, apart from a few Veterinary Biological Production Units (VBPUs) and Institute of Animal Health and Veterinary Biologicals of different states of India (Balamurugan et al., 2021a). The availability of an effective vaccine, accurate mass screening diagnostic assays, an experienced or improved infrastructure, expertise, success with the eradication of RP under the NPPE programme, have provided confidence and prompted India to propose a national level PPR control programme initially on the line of NPPE. Besides the availability of aforesaid elements (Singh et al., 2009; Singh, 2011) in India, the Department of Animal Husbandry, Dairying, and Fisheries (DADF) the Central Government of India, has better coordination and cooperation with the state animal husbandry departments in the federal setup. Therefore, the launching of a control and eradication programme appears technically feasible, economically viable, and a practically attainable proposition. It was decided by DAHD, Government of India to undertake a PPR control programme (PPR_CP) in the 11th five-year plan (2007-2012) similar to FMD Control Programme (FMD-CP) (DAHD, 2020b), to control and eradicate this disease from India in a time-bound manner on the lines of RP eradication (<http://dahd.nic.in/>). Accordingly, this proposed programme has been initiated by following the eradication pathway of WOAHP during the year 2010-2011 with a sum of INR 432.5 million in the first phase for undertaking various activities of the programme (<http://dahd.nic.in/>). During the first phase,

vaccination was planned in Southern peninsular India and the remaining states and UTs were included in the second phase of PPR-CP from 2014 to 2015 (Balamurugan et al., 2016).

The expertise in the country, especially, scientific and technical manpower, trained veterinarians, technical and para-veterinary staff for handling vaccines at various stages from production to delivery in the field are available. These prophylactic services are being gradually expanded by involving public-private partnerships (PPP) especially, the participation of non-governmental organisations (NGOs), cooperatives, and private veterinary practitioners in implementing and executing disease control programs as stated by Singh et al., (2009). Further, setting up a network cum database would be of help in developing a coordinated approach towards the effective implementation of the control programme. At present, the disease occurrence, severity of the clinical disease, and the number of outbreaks in India have progressively and substantially declined in areas under regular mass vaccination mostly under national PPR-CP and partly under Assistance to States for Control of Animal Diseases (ASCAD) of the Government of India. The disease incidence has been in decline over the past five years as per outbreak data analysis (Balamurugan et al., 2021a). In India, the decreased numbers of outbreaks, as well as changes in the severity of disease patterns recently observed, might be due to the effectiveness of live attenuated vaccines, timely vaccination of sheep and goats, and circulation of a single serotype Asian lineage virus, since the disease was first reported in India (Balamurugan et al., 2021a) as any vaccine lineage virus can protect against all other field viruses/ field isolates/strains of PPRV lineages and provide complete clinical protection against challenges with all four lineages of PPRV (Mahapatra et al., 2020).

10.3. Vaccination strategies

Vaccination strategies for the control of PPR would be slightly different from vaccination programmes implemented for rinderpest. A mass vaccination to cover 80% of the population to achieve herd or flock immunity would be needed to account for the population dynamics of sheep and goats, differences in sheep and goats husbandry practices, and the agro-climatic conditions affecting the pattern of disease (Singh, 2011). The slaughtering of male goats at an early age combined with the high fecundity of the caprine species results in the replacement of population (~30-40% naïve population appears) every year and thus a different approach is needed to control the PPR. In the strategic vaccination of the control programme, mass vaccination of the entire population within a specified area, subsequently 'vaccinations on younger animals' at approximately >6 months of age need to be undertaken (Singh, 2011) to avoid window of susceptibility in kids to PPRV infection and to eliminate PPR infection from susceptible populations (Balamurugan et al., 2012d). In a given time, 4 to 6 months old young ones in and around the vaccinated flocks will be 20 to 30% of the population then but the vaccinated flocks will be 70 to 80% thus provides the flock immunity. Vaccinated animals, infected and recovered animals are protected from re-infection for the remainder of their lives. Hence, in this direction, the strategies were proposed in the PPR_CP involving mass vaccination of all susceptible sheep and goats and their three subsequent generations (approx. 30%) with 100% fund from central assistance. In other way, vaccinations should be focused initially on high-risk group

animals, for example, young animals (6 months to 1 year), migratory flocks (Singh 2011) in suitable periods preferably in lean period. Alternatively, mass vaccination can be carried out based on populations to make disease-free areas (zone) by identifying the areas of infection and implementing vaccinations followed by screening, testing, and overall revaccination, if required, in those areas. The time of vaccination of young animals is an important issue in PPR control. There are few reports on the duration of persistence of maternal antibodies in lambs/kids born to vaccinated dams. Maternal antibodies in young animals were detectable up to 6 months of age but fell below the protection threshold level at 3 or 4 months in lambs and kids, respectively (Balamurugan et al., 2012d). Similarly, the neutralizing maternal antibodies were detectable up to 4 months compared to 3 months with competitive ELISA. These findings lead to the suggestion that lambs and kids from immunized or exposed dams should be vaccinated at 4 and 5 months of age, respectively. In case of outbreaks situation, in general, the age of vaccination which was recommended as 3 to 4 months in non-endemic areas (or regularly vaccinating areas), while in endemic areas (or non-vaccinated areas) vaccination may be practiced after 3 months.

In India, PPR-CP involves intensive mass vaccination of all susceptible sheep and goats above 4-6 months age group of animals in pulse vaccination mode, and two successive annual vaccination of their subsequent generations (30-40 % naïve young population every year) (Govindaraj et al., 2019) to reach 70-80 % immunity level and again mass vaccination of the entire sheep and goats population in each of the states. This strategy is to cover the naïve population appearing in the flock continuously due to high reproductive rates, fecundity, and slaughtering of male goats at an early age (Singh, 2011; Balamurugan et al., 2016). As of now, in some Indian states viz. Karnataka, Andhra Pradesh, Telangana, and Chhattisgarh the PPR outbreaks in sheep and goats have declined after implementing the strategic vaccination under control programme. The decreased number of outbreaks in the recent past, as well as changes in the disease severity patterns and distribution, might be due to the existence of institutional infrastructure, the effectiveness of the vaccine, timely vaccination, and most importantly effective planning and implementation of the vaccination programme (Balamurugan et al., 2018). Overall, fixed strategies may not work for all the states or regions, or countries. However, the mass vaccination in pulse polio model with two to three cycles of vaccination, with each cycle of covering the entire population of sheep and goats initially, subsequently bi-annual vaccination covering the naïve young population in a pre-designated stipulated period for two years, followed by the entire population, will have a tremendous impact on the control of PPR outbreaks in sheep and goats and subsequent eradication. Thus, after three to four rounds of vaccination, the population in the state may be immune to the disease, but the threat persists from ingress of disease from other bordering states, hence vaccinating the migratory population at the check post or border regions of the states or inter-state border or in the place of entry or place of trade market of the animal through transport from other states are to be targeted for mass vaccination as and when required. Sharing the experiences on the PPR vaccination strategies adopted by some of the successful states in India may provide directions for other Indian states of similar socio-economic and small ruminant rearing patterns to vaccinate and control PPR. Further, the geographic distribution of both PPRV and goatpox or sheepox virus infection and the

occurrence of mixed infections due to these viruses, necessitate the use of a combined vaccine {available as PPR and goat pox; and sheep pox and PPR (Hosamani et al., 2006; Chaudhary et al., 2009)} for control of these infections in the endemic areas, in lines with the mass immunization programs.

10.4. Effect of vaccination

India previously practiced focused vaccination (vaccination limited to the place of the outbreak within a radius of 3–10 km to contain the disease spread) during outbreaks to control and prevent the disease spread in 15 states (AP, Karnataka, Himachal Pradesh, Uttar Pradesh, Madhya Pradesh, Uttarakhand, Chhattisgarh, Haryana, Jammu and Kashmir, Jharkhand, Maharashtra, Odisha, Punjab, Rajasthan, and West Bengal) of India since 2002 under the respective state's sponsored or Assistance to States for Control of Animal Diseases (ASCAD) program of the Gol. Further, besides immunization of susceptible animals, implementation of biosecurity measures during outbreaks has been carried out by the State Government to prevent the spread and control of outbreaks. The biosecurity measures advised to different stakeholders are strict quarantine of sick and exposed animals in cases; restriction of animal movements; quarantine of newly purchased animals for at least two to three weeks; decontamination of the premises with common disinfectants; proper disposal of carcasses and contact fomites on-site, restriction on the importation of sheep and goats from affected areas; infected and suspected flocks must be placed under quarantine; personnel should ensure that shoes, clothes, vehicles, and equipment are disinfected. Further, the Gol-sponsored PPR-CP has been implemented during FY 2010-2011 to control and eradicate PPR in Southern peninsular India. During 2011 in the first phase of PPR-CP, Karnataka, Andhra Pradesh, Telangana, Tamil Nadu, Kerala, Maharashtra, Goa and Lakshadweep, Daman and Diu, Dadra and Nagar Haveli, Puducherry, and Andaman and Nicobar Island state and UTs in Southern peninsular India were planned and the remaining states and UTs were included in the second phase of PPR-CP from 2014 to 2015 (Balamurugan et al., 2016). However, this strategic vaccination in the PPR-CP was carried out only in some states of India since 2011. In 2019, the PPR outbreaks were reported in 16 states and confined to a few districts in the mass vaccination program implemented states and more districts in the vaccination program not implemented or focused vaccination practiced states (Balamurugan et al., 2021a). The highest PPR outbreaks were reported from Jharkhand, followed by Maharashtra, Uttar Pradesh, West Bengal, Haryana, Rajasthan, Karnataka, Kerala states, etc. with more outbreaks from November to March with a peak during January (Winter season) (Balamurugan et al., 2021a).

10.4.1. Case studies of the states

In the South Zone, in Karnataka state, after adopting vaccination since 2004, the number of outbreaks declined and reached as low as four outbreaks during the financial year (FY) 2011-2012 & 2012-2013 from 156-206 outbreaks during FY 2004-2006. Since 2011, under PPR-CP, the state continued vaccination in the program mode and covered the entire population (80-90 %) within 24 days in pulse vaccination mode. Subsequently, one-third of the naïve population was taken as the target for subsequent vaccination after 6 months, and thereafter every vaccination six-month interval along with leftover animals in previous vaccination. Due to the strategic vaccination, the

diagnosed PPR cases and deaths reduced, with only four outbreaks during FY 2011-2012 from the reported 206 outbreaks during FY 2005-2006. As per recent reports from 2017-2020, in Karnataka 4-7 outbreaks were reported in the FY and confined to the three (Belagavi, Bellary, and Kolar) districts (**Fig. 9**). Similarly, in the undivided Andhra Pradesh (Telangana carved from AP during 2014) state during the year 1999, approximately 552 outbreaks were reported and become persistent with continuously reported outbreaks of ~ 157 to 420 from 2002-2006 every year with a peak of 418 during FY 2005-2006. The undivided AP adopted focused vaccination since 2002, and a strategic annual vaccination program during FY 2007-2008, with two cycles of intermittent mass vaccination and selective vaccination to cover the new-born young stock above five months of age and unvaccinated animals to contain the outbreaks and reduced the epidemic level to 95 % until 2010 (Balamurugan et al., 2021a). After adopting the PPR-CP since 2010-2011, mass vaccination of small ruminants was carried out in pulse vaccination mode followed by bi-annual vaccination (based on the lambing/kidding pattern) to cover naïve young population from 2012 to 2014, which resulted in three outbreaks during FY 2012-2013 & 2013-2014 and reduced the burden by about 99 % (one reported outbreak in the FY 2011-2012) against about 377- 418 outbreaks in the FY 2004-2005 & 2005-2006. In FY 2019-2020, nine outbreaks in three districts (Khammam, Nalgonda, and Warangal-urban) in Telangana state and three outbreaks in Krishna and YSR (Kadapa) districts in Andhra Pradesh were reported. Further, the different categories of endemic districts in Karnataka and undivided AP are depicted in a six-scale classification (**Fig. 9**) at different periods of analysis (Balamurugan et al., 2021a).

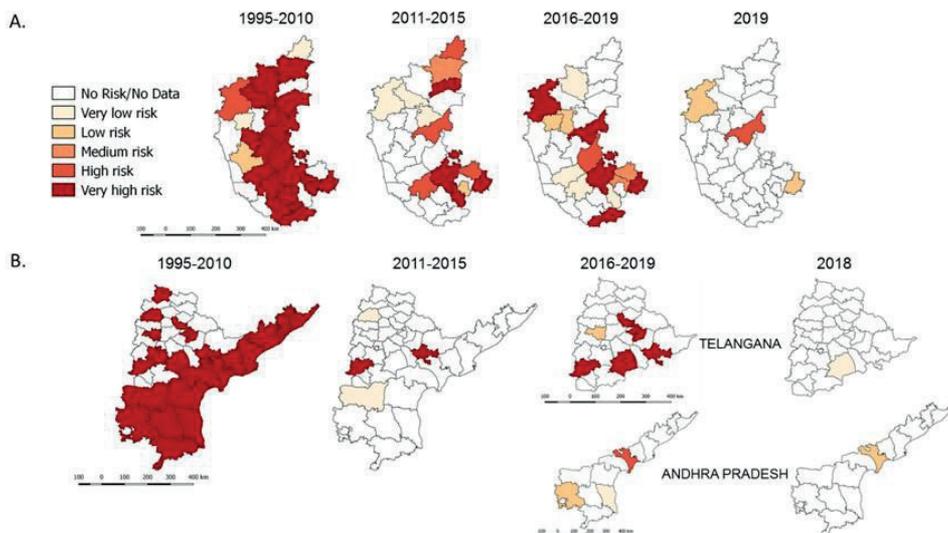


Figure 9. The reported outbreaks in different categories of endemic districts of Karnataka (A) Andhra Pradesh (B) with risk areas are depicted in six scales at different periods of analysis using QGIS-2.18 in the maps of the respective states.

The vaccination coverage percentage was 44, 37, and 4.0% in MP; 80, 71, and 80%, in Chhattisgarh; 61, 29, and 79% in Gujarat and 15, 51, and 74% in Maharashtra during FY 2016–2017, 2017–2018 and 2018–2019, respectively, with the required vaccination coverage in Rajasthan and no vaccination in Goa state during these periods. Further, based on the passive surveillance official data, the total number of reported PPR outbreaks for the last five FY from 2015 to 2016 to 2020–2021 was 12, 119, 20, 44, and four (4) for MP, Maharashtra, Gujarat, Rajasthan, and Goa states, respectively. In 2020, 39 outbreaks were reported from 15 districts in the studied regions, of which Maharashtra had the highest (33 outbreaks from nine districts) and the lowest two outbreaks from either one or two districts of other states. The state-wise details of the number of vaccinations carried out in small ruminants' populations were depicted in Fig. 10, along with the FY reported outbreaks in each of the studied states. In the states where continuous vaccination is being adopted, disease outbreaks are being reported sporadically. Further, a decline in the number of reported year-wise outbreaks was depicted in these states since disease reports and PPR were restricted to only a few districts in 2020 (Fig. 11)(Balamurugan et al 2022b).

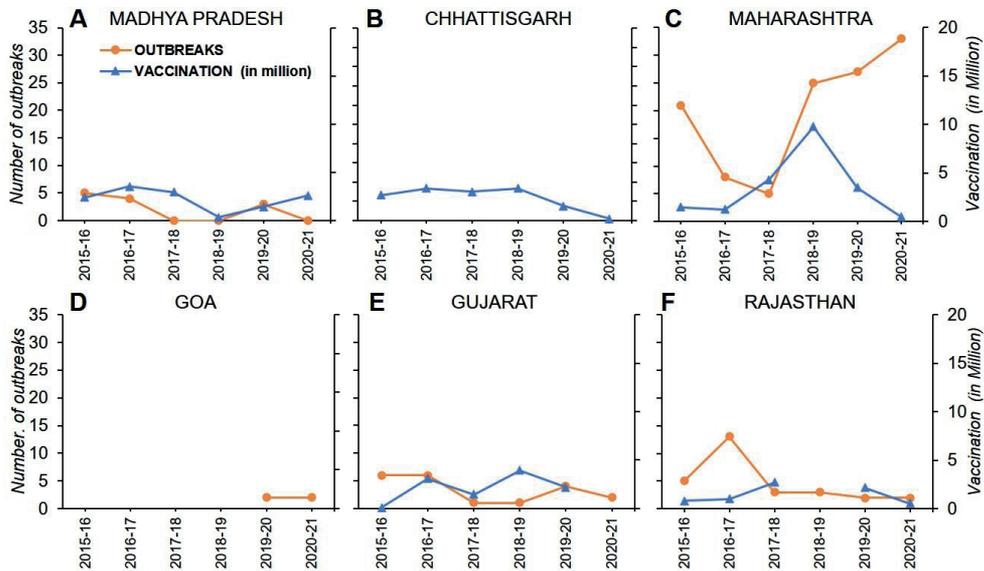


Fig. 10 Trend of reported outbreaks in the states of Madhya Pradesh (A), Chhattisgarh (B), Maharashtra (C), Goa (D), Gujarat (E), and Rajasthan (F) from the financial year 2015–2016 to 2020–2021 versus the doses of vaccine used (in million) in the vaccination program during the preceding years against the small ruminant population (outbreaks in number, vaccination in million)

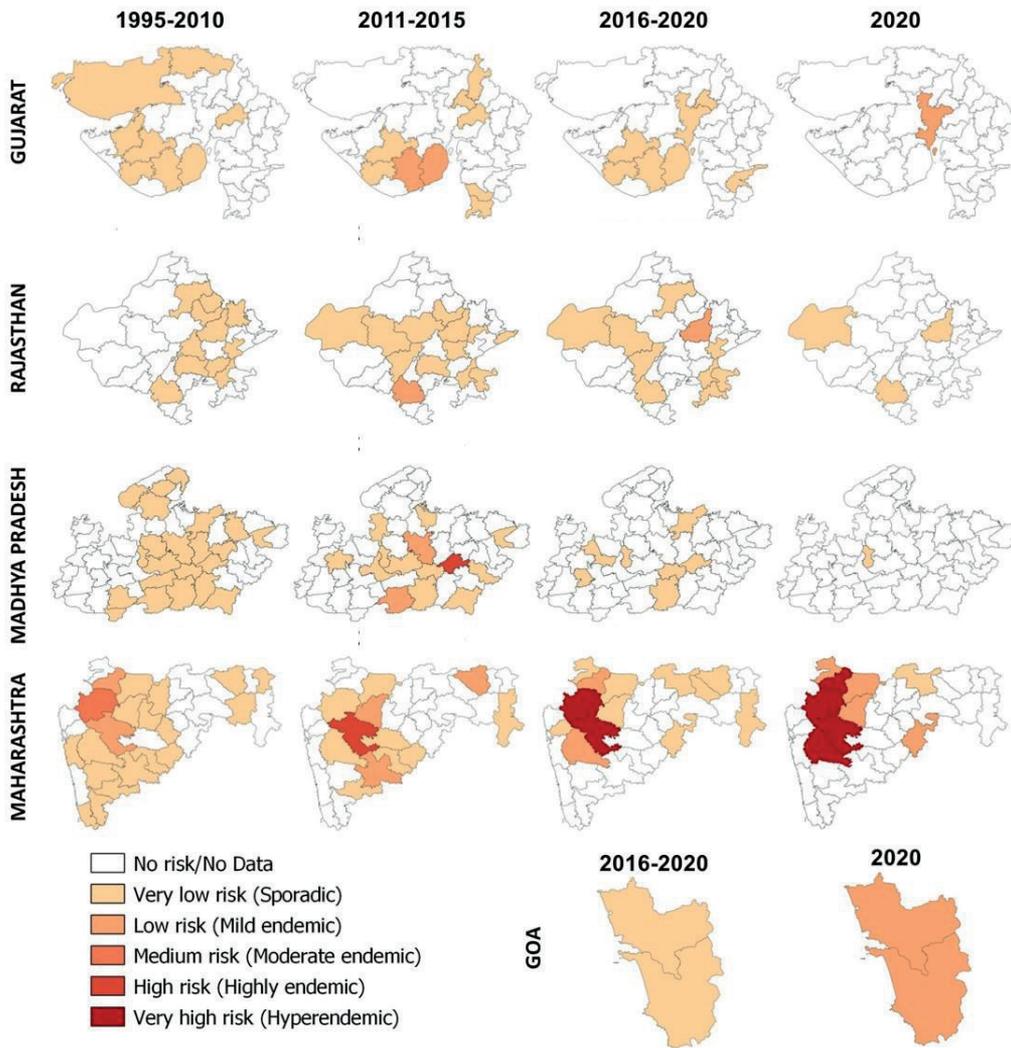


Figure 11 : The reported outbreaks in different categories of endemic districts of the studied states with risk areas are depicted in six scales at different periods of analysis using QGIS-2.18 in the maps of the respective states. The endemicity of PPR outbreak categorization is based on the scale of the cumulative outbreaks that occurred in the districts per year in the given period of analysis and classified into different risk levels (if the outbreaks numbers in the district as 0—no risk, 1—very low, 2—low, 3—medium, 4—high and > 4 very high- risk districts). No official outbreaks have been reported in Chhattisgarh state since 2014; however, two outbreaks were observed, with 647 diagnosed and 272 death cases during 2010–2012 as per a published report (Govindaraj et al. 2019)

Among the zones, the effect of vaccination was more effective and pronounced in the South zone result in a drastic reduction in the reported outbreaks and cases. Karnataka state reported the disease for the first time in 1992 (Srinivas and Gopal, 1996) it progressed later across varied agro-climatic conditions with varying intensities and reached a peak during 2004-2006 (Hegde et al., 2009). Since 2004, the state has followed mass vaccination, and in consonance with PPR-CP during 2011, which resulted in a decline in the number of outbreaks. Further, the undivided AP followed focused vaccination since 2002 to contain the outbreaks and reduced the epidemic level by 95 % (Singh and Bandyopadhyay, 2015), and the state implemented a mass vaccination during 2007-2008 and followed annual programs until 2010 (Sireesha et al., 2014) and in consonance with PPR-CP from 2012 to 2014, which reduced the burden by about 99 % with the flock immunity of 81 to 95.6 % (Singh and Bandyopadhyay, 2015; Balamurugan et al., 2016). This is due to systemic vaccination programs followed in these states during the first phase of PPR-CP (Balamurugan et al., 2020e). In the Central zone, Chhattisgarh state-initiated the PPR annual vaccination program (as mass vaccination campaign) since 2010 on the lines of 'pulse polio program' in the designated period (11-12 days) with a mass media campaign to reach out to livestock farmers (Balamurugan et al., 2016) resulting in no report of PPR since 2013-2014 (Roy et al., 2014). Besides farm-reared animals, goat markets, nomadic and selling units, check posts, etc., were also vaccinated to maximize the vaccination coverage. Further, emergency vaccination in the face of disease incidence, outbreaks, and/or epizootics (if any) and vaccination in villages that missed out during the campaign were also carried out subsequently as follow-up vaccination to cover unvaccinated animals in the regular program. Through a strategic annual vaccination program in pulse vaccination mode, PPR has been kept under control in the state (Govindaraj et al., 2019) and it may eventually assist in its eradication.

Strategic vaccination has been systematically followed in the states like Karnataka, Andhra Pradesh/Telangana, and Chhattisgarh since the beginning of PPR-CP, and these states controlled the PPR outbreaks successfully (Balamurugan et al., 2016). Further, the other states have implemented focused ring vaccination in the outbreak areas along with the biosecurity measures to contain the outbreaks. In the recent past, since 2015 in the second phase of PPR-CP, most of the states and UTs in India followed strategic vaccination, thereby the reported overall outbreaks and disease threat have been reduced significantly in India. Due to PPR-CP, the disease has been brought under control in Indian states and the disease threat declined progressively and substantially in areas under continuous vaccination (Balamurugan et al., 2016) and benefits outweigh the cost of a vaccination program (Govindaraj et al., 2019). The PPR outbreaks trend at the national level showed about 75-80 % decline (Singh and Bandyopadhyay, 2015), however, there was no further definite declining trend during the years (2009-2013) (Balamurugan et al., 2016). However, in some states, where focused/targeted vaccination is adopted, disease outbreaks are being reported sporadically. Generally, the success of the vaccination and control of disease depends on various factors, like animal husbandry practices, population density, lambing and kidding seasons, movement / migratory population of animals, etc., including the observed vaccination-related field problems, like vaccine-chain mechanism, identification of unvaccinated animals, farmers insistence on repeat vaccination and

cold chain maintenance for storage of vaccines, timely supply of the vaccine, and wastage of vaccines in the field due to high package vaccine doses supplied, etc., (Sireesha et al., 2014; Balamurugan et al., 2016). All these factors and constraints need to be addressed for the success of the program, along with the adoption of biosecurity measures.

11. National strategic plan for PPR eradication (NPPE)

India has a cost-effective potent vaccine (which provides immunity for more than 3 to 6 years -lifetime immunity in small ruminants), diagnostic kits, and identification mechanism, sero-surveillance and monitoring infrastructure, and competent human resources to run a successful PPR eradication program. Further strengthening of existing disease diagnostics laboratories, surveillance infrastructure, and continuous availability of vaccines with diagnostic kits will support the PPR eradication plan for 2030. Still, India, being a large country with a huge sheep and goat population spread all over the country, needs regional coordination and harmonization of national strategies for achieving this eradication goal.

The salient features of this plan include strategic vaccination with complete blanket coverage of sheep and goats' populations till 2025/26, attaining targeted herd immunity and stoppage of virus circulation through clinical surveillance by 2026/27, and freedom from PPRV infection by 2030. The strategic vaccination, include mass vaccination targeting the defined populations (above 4 months of age of sheep and goats) in "pulse vaccination mode" in the designated period through annual mass vaccination covering the entire population for 3 to 4 years in each of the states and union territories till to reach 70-80 % immunity level for eradication. Further, Sero-monitoring, sero-surveillance and population immunity assessments including outbreaks investigations, syndromic surveillance and surveillance in un-natural hosts and livestock -wildlife interface of buffer zones are the national action plan for surveillance and monitoring of PPR including the further strengthened of surveillance mechanism by State/UTs animal husbandry and veterinary departments.

As of now DAHD, Gol-approved ICAR-IVRI developed PPR competitive ELISA and PPR sandwich or antigen capture ELISA kits/assays for sero-monitoring/surveillance of PPR in sheep and goats and are currently being employed extensively throughout India. The ICAR-NIVEDI (WOAH Reference Laboratory Network for PPR- South India) shall be the apex body for the serosurveillance / sero-monitoring of PPR in the country to provide the national database on the surveillance and to develop strategies and take adequate measures to prevent and control PPR and shall be responsible for the epidemiology of PPR including surveillance in other hosts, syndromic surveillance, capacity building training, etc., ICAR-NIVEDI plays a significant role under PPR-EP in India in Sero-monitoring and surveillance of PPR through strategic systematic sampling plan and testing of samples.; Sero-monitoring and surveillance data management and analysis taking village as epi-unit as per WOA format including syndromic surveillance and need-based capacity building training to the different stakeholder, etc., besides, the participating laboratories network/animal husbandry department from each state/ UT to be involved in the collection of primary and secondary data for the impact assessment of the PPR control and eradication program. Besides, supporting the state animal diseases diagnostic

laboratory in harmonization and quality assurance of the participating laboratories and impact assessment of PPR control and eradication programme in the country, associating with different stakeholders and other organizations (ICAR-IVRI, RDDDL of DAHD, Gol, State AHD -Disease Diagnostics laboratories, etc.) is needed for the success of the programme.

The ICAR-IVRI, Morbillivirus Laboratory, Division of Virology (WOAH Reference Laboratory Network for PPR- North India) Mukteswar, is the National apex laboratory for confirming the PPR diagnosis and molecular characterization of the virus and supplying of diagnostic kits. Proficiency testing of the PPR vaccine as per IP Vet including challenge testing shall be carried out at the Division of Standardisation, ICAR-IVRI, Izatnagar/ Bengaluru and CCSNIAH, Baghpat, or at any other Institute approved by DAHD, Gol. Similarly, the Central Disease Diagnostics Laboratory (CDDL)/Centre for Animal Disease Research and Diagnosis (CADRAD) of ICAR-IVRI/NPRE -IVRI will play the role of official Proficiency Testing provider for PPR diagnosis. The other activities of NPPE include training of field veterinarians, vaccinators, and supporting staff which will increase the program efficiency as well as state-level pre-and post-vaccination sero-monitoring during the program period. Further, overall monitoring of the programme includes the real-time vaccination data flow from the field level, procurement of vaccine, storage, shipments, cold chain maintenance, and other vaccine-chain mechanism and logistics till the delivery of the vaccine to the animals through different departmental units of the state/UT for effective implementation (Balamurugan et al., 2021a).

12. Conclusions and perspective

This status paper provides insight into the temporal patterns and spatial distribution of PPR in India as well as disease burden, host specificity, diagnosis, prevention and control measures, the control programme, and time of outbreaks/cases to support policymakers to take appropriate decisions towards PPR control and eradication. PPR is one of the priorities of transboundary animal viral disease of sheep and goats, whose control is considered important for poverty alleviation in endemic India. At present, the disease has been brought under control by effective and safe live attenuated PPR vaccine, but only with effective implementation of a strategic vaccination, complete control and eradication of the disease from India is possible. Vaccination needs to be carried out more intensively and more frequently as per the strategic plan to control and eradicate PPR in India. vaccination to be carried out to reach 70–80% level immunity status in the state/region. Further, vaccination may be restricted to bordering districts, animal markets, and check posts only, after the state/UT reached the desired 70% cluster level PPRV antibodies prevalence (immunity levels) without the occurrence of PPR outbreaks (known from syndromic surveillance). In the continued vaccinated regions, the incidence of the disease will reduce significantly. However, some sporadic outbreaks we may experience in some pockets, where mixing of the infected /vaccinated and non-vaccinated animals gathering especially in the local market, transportation for trade, nomad/ migratory of animals (known from surveillance). Once vaccination continues in all the parts of India simultaneously, we can expect only a few sporadic outbreaks restricted to trade and marketing places in a few districts. During these sporadic outbreaks, focused

vaccination (vaccination limited to the place of the outbreak with a radius of 3-10 km to contain the disease spread) should be implemented additionally for the control of the PPR. Later post eradication stage, if outbreaks happened due to ingress of animals, we may think of a stamping-out policy with adequate compensation especially in the international border areas and interface areas.

If needed, Epi-zone or risk zone /area may be identified in the state and vaccination to be initiated first in the high-risk area followed by the low risk area in the various districts of the state/UT concerning the risk/target population. Thus, after a few rounds of vaccination, the population in the state may be immune to the disease, but the threat persists from ingress of disease from other bordering states, hence vaccinating the migratory population at the check post or border regions of the states or inter-state border or in the place of entry or place of trade market of the animal through transport from other states are to be targeted as and when required. The vaccination strategies adopted in India will alter PPR epidemiology in general and disease severity pattern in particular, as changing patterns in terms of the severity of gross lesions and clinical signs observed in the region, where regular vaccination is carried out. Therefore, the disease conditions may not always produce all the clinical signs of PPR but may produce one or more of the classical clinical signs. Notably, the observed mild form of rinderpest (RP) in the last phase of eradication caused the delay to declare the eradication of RP. In this situation, syndromic surveillance with a survey instrument tool will help to identify the single case in the flock or the case reported to the veterinary dispensary. The spillover effect of the virus in the sporadic outbreaks in the sheep and goats to wild small ruminants and vice versa at the domestic-and wildlife interface will happen, so thorough monitoring of the interface will be needed through clinical/syndromic /serosurveillance. Further, the other unnatural/atypical hosts namely, wild ruminants, captive ruminants, and camel, or cattle/buffaloes need to be monitored for the clinical signs of PPR, as PPR has been reported from these species from different parts of the world. The unusual-host cattle and buffaloes, will not exhibit the clinical signs, however, seroconversion will take place in these hosts, should be monitored for the clinical signs of PPR during surveillance.

Most of the associating laboratories including the RDDDL of DAHD, GoI, already regularly carrying out disease diagnostic activities and they were trained in the NPPE program earlier. Through the necessary capacity-building training under this programme, their competence will improve. Besides, training the laboratory personal on ELISA, as well as data management, will be done as a part of the synchronization of laboratories and laboratory capacity. Mass awareness is very important for the success of the PPR virus elimination and therefore action programs for mass awareness had already been drawn by the respective states/UT's. Farmers are already aware of PPR and are willing to vaccinate their animals to prevent PPR. However, awareness to be created every year before the vaccination drive through mass media, local panchayat, TV, Radio, newspaper, etc. Further, Veterinarian may be emphasized about the importance of the PPR eradication program and their role in the program and their efforts in vaccinating all the eligible target animals, without leaving single animal under their jurisdiction within the stipulated schedule and time frame. The stakeholders' networks are very much vital for the success of the program (Laboratory network to be established for surveillance and monitoring; Veterinarian network for vaccination

coverage and collection of appropriate samples including survey data of the PPR program; Expert core teams networks from ICAR, DAHD, GoI, State AH Department, for coordination of all the activities related to the PPR-EP, planning, rollout, monitoring of the implemented program; Network for vaccine supplier and DAHD, and State AH Department, to ensure regular supply of the Quality Vaccine for field use, including production and supply and QC; Each state AH department should have an ad-hoc institutional mechanism to plan, implement and monitor the program in a regular basis and interact with DAHD, GoI, as per the national strategic plan). To assess the impact of the PPR control and eradication programme including cost-benefit of PPR, chronological activities initiated in each of the states need to be collected /documented and collated to understand the status of the disease in sheep and goats during various periods, regional distribution, disease burden, temporal and seasonal patterns, spatial distribution, risk zones/areas, endemicity, etc. The historical data, baseline, concurrent assessment, and ex-post implementation data need to be collected from primary and secondary sources using appropriate and validated survey instruments developed for the purpose.

Since the present PPR vaccine is not the DIVA vaccine, it is difficult to differentiate both the infected and vaccinated animals using this PPR vaccine and ELISA kit, however, Rinderpest was successfully eradicated without using the DIVA vaccine. Therefore, the following strategies surveys need to be initially used for serosurveillance and seromonitoring of PPR to know the status of PPRV antibodies in sheep and goat populations using the present PPR-c-ELISA kit, as per WOAHA global control and eradication strategies (GCES). Baseline pre-vaccination serosurvey need to be carried out in different age groups (i) 6-12 months; ii) 1 year to 2 years iii) > 2 years to know the status of the PPRV antibodies in sheep and goat population (baseline seroprevalence of PPR), as different states are at a different level of implementation of the PPR-CP. The post-vaccination seromonitoring serosurvey needs to be done targeting only the animals of the 6–12-month age group within 90 days after two months of vaccination drive (between 60- 90 days after vaccination) to know the efficacy of the vaccination at field scenario. Further, population immunity serosurvey needs to be taken in sheep & goats after 8 months of vaccination to assess the status of PPRV antibodies in the age group of 1 year and above (part (i) 1 year to 2 years part ii) > 2 years age group). Finally, syndromic surveillance using schedule /questionnaire survey tool during the years needs to be undertaken to know the status of clinical diseases, if any. Continued surveillance in Captive and wild small ruminants including camel during the course of the PPR eradication programme needs to be strictly monitored to understand the extent and change in dynamics of PPRV in wild small ruminants due to the pressure exerted by the progressive vaccination drive in sheep and goats under the eradication program.

Further, a review of population immunity/herd immunity at the end of 5 years needs to be assessed and analyzed with progressing OB and syndromic surveillance information to decide the further course of action required for a successful PPR eradication program. In case of the evidence-based decision of continuance of the eradication effort, actions as necessary would be taken to continue the vaccination drive for the period to be decided with continued surveillance, or else if the satisfactory results are obtained after 5 years, the vaccination drive would be discontinued and the

process of syndromic surveillance would be continued for three more years. This would be followed by freedom serosurvey in the 8th year, three years after cessation of complete vaccination using an appropriate sampling plan for the declaration of India provisionally free from PPRV. Finally, the central, state and district-level technical working group on various elements of PPR control and eradication viz., diagnostics, surveillance, disease prevention, and control, legal framework, and involvement of different stakeholders need to be established in the national strategic plan for PPR eradication in the direction of PPR-GEP for overall monitoring and effective implementation of the programme and successful eradication of PPR from India.

Acknowledgments

The authors wish to thank the Indian Council of Agricultural Research (ICAR), New Delhi, India, for providing the facilities, and the ICAR–National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI) staff for their constant support and encouragement. The authors also thank the Directors of the state Animal Husbandry Departments for sending the monthly outbreaks information to the ICAR-NIVEDI, for the generation of national animal disease surveillance database (NADRES), at ICAR-NIVEDI. The authors also thank DAHD, Gol, New Delhi for their support and encouragement of involving ICAR-NIVEDI in the national PPR-CP and EP. All the authors who contributed to the understanding of the PPR virus pathobiology including in diagnosis and prophylaxis of PPR irrespective of their citation being figured or not in this paper are acknowledged. Further, the authors apologize for the non-inclusion of some of the references, if any, which is unintentional.

Authors Contribution:

VB-Conceptualization, investigation, visualization, supervision, review, analyses and wrote & edited the draft of the manuscript. KVK-designed and ran the statistical analyses and prepared all the figures. GG- statistical analyses and copy-editing. KPS-datasheets and outbreak details. BRS- key inputs, guidance and support. BRG-editing, guidance and support.

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