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Foot and mouth disease prevalence in cattle and buffaloes from India determined by systematic review and meta-analysis

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ABSTRACT

In the present study, Foot and Mouth Disease (FMD) prevalence in cattle and buffaloes from India was determined by employing systematic review and meta-analysis. The FMD prevalence studies (73) reported during 1986-2021 were obtained from online databases, offline literatures and meta-analysis by using meta package in R-Software was done. The pooled FMD prevalence in India was 43% (95% level CI 35-52%, PI 3-94%) obtained by using 5,00,267 samples. Period-wise analysis revealed a higher prevalence of 68% during 1986-2000 than recent years. A higher FMD prevalence in east zone (59%), and lower in central zone (24%) was observed. Among 19 states, a higher prevalence of FMD was detected in Rajasthan (81%) and lower in Andaman and Nicobar (3%). Species-wise analysis indicated a higher prevalence in cattle (45%) than buffaloes (30%). The method-wise analysis revealed a higher prevalence in antigen detection (49%) than the antibody detection (42%) methods. The FMD seroprevalence was 59% against the FMD vaccination obtained by liquid phase blocking ELISA. In India, a higher FMD prevalence by serotype O (64%) than other serotypes was observed. Thus, the higher FMD prevalence zone, states, species, methods and serotypes identified may be employed by policy makers for making informed decisions to maximise the use of scarce resources available. There was a decreasing trend in FMD prevalence in the recent years, however, need is there to prevent FMD by vaccination to move in the progressive control pathway stages. This will help in increasing export trade and eventually result in economic benefits to dairy farmers.

Keywords: Foot and Mouth disease, India, Meta-analysis, Prevalence, Systematic review

Livestock is a major sector of agricultural production system in India and it plays a significant part in the farming community's socio-economic growth. India has a total of 536 million livestock population as per 20th Livestock census (BAHS 2019) and ranks first in milk production in the World. However, the diseases like Foot and Mouth Disease (FMD) causes tremendous burden and higher production losses to farmers. FMD is a contagious illness that affects cloven-footed animals and poses a severe threat to the livestock industry. It is characterised by fever, followed by vesicles and erosions on the tongue, gums, lips, interdigital space and in mammary glands (Meyer and Knudsen 2001). These vesicles often join to form enormous, inflated blisters that burst, leaving raw, painful ulcers behind. Although FMD has a low mortality rate in adult animals, it has debilitating symptoms such as weight loss, decreased milk production, reproductive failures, and loss of draught power, all of which result in lower productivity and economic losses. FMD virus (FMDV), the causative agent, is a member of the aphthovirus genus of family Picornaviridae. The virus occurs as seven major serotypes, viz. O, A, C, Asia-1, SAT-1, SAT-2, and SAT-3 (Domingo *et al.* 2003). Within each of these serotypes, however, there are a number of immunologically and serologically distinct sub types with varying degrees of virulence, and the virus appears to be capable of infinite mutations, resulting in the appearance of new, antigenically different sub types (Akhoon *et al.* 2015).

FMD is endemic in India and has been reported throughout the year in almost all parts of the country. Disease occurrence, severity of clinical disease, and number of outbreaks have decreased significantly in areas where regular vaccination is carried out, mainly under the FMD control programme and partially under the *Rashtriya Krishi Vikas Yojona* (RKVY) and Assistance to States for Control of Animal Diseases (ASCAD) of the Government of India (Pattnaik *et al.* 2012). In recent times, the National FMD Control Programme (FMDCP) in India is mostly carried out by mandating domestic large ruminant vaccination twice a year. The first case of FMD in India was recorded in 1864, afterwards it was reported in many parts of the country (Pattnaik *et al.* 2012).The direct loss due to FMD amounting to USD 2684 (₹ 20,000 crores) per annum have been reported (Venkataramanan *et al.* 2006). Further, 80% of the total direct loss caused by FMD was due to drop in milk production (Mathew and Menon 2008). The total

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estimated loss due to FMD in cattle and buffalo in India was USD 2804 million (₹ 20,897 crores) during 2013–14 with wide variation in magnitude of economic losses across the states studied in India (Govindaraj *et al.* 2020). As a result, it is critical to focus on FMD prevalence in cattle and buffaloes, and to understand the disease current status or burden in India. Several researchers have reported the prevalence estimates obtained by using meta-analysis for various livestock diseases (Krishnamoorthy *et al.* 2019a, 2021a, b,c) except FMD. A recent study from Bangladesh reported the prevalence estimates for FMD by using meta-analysis and no studies from India was available. Further, it was considered as an innovative technique to determine the livestock diseases prevalence estimates and not widely used in the field of Veterinary Sciences (Krishnamoorthy *et al.* 2020). Hence, the present study was conducted to determine the prevalence estimates for FMD along with various subgroup analyses based on year-wise, zone-wise, state-wise, host species-wise, antigen or antibody detection methods, method-wise, and FMDV serotype-wise in India.

MATERIALS AND METHODS

Search strategy for studies: Using appropriate keyword searches, a systematic literature search was conducted on the FMD prevalence in cattle and buffaloes in India. The PubMed, Science Direct, Springer's Scopus, Google Scholar, Indianjournals.com, J-Gate @ Consortium of e-Resources in Agriculture (CeRA) under Indian Council of Agricultural Research (ICAR), research abstracts in proceedings/compendiums of conferences, seminars, symposia, and other published works of literature were among the databases used in the search. To determine the prevalence estimates, more than 500 publications were searched, evaluated, and selected, and the data obtained was subjected to meta-analysis. Based on the Indian states, the prevalence studies were categorized into five zones, viz. north, east, west, south, and central. The author's name, year, state, diagnostic techniques used, FMDV serotype, number of samples tested, and number of positive samples in cattle and buffaloes are among the information collected. The retrieval period for the studies was between 1986 and 2021, based on availability, and the language was confined to English only. Additionally, the peer-reviewed articles, original research articles, and references cited from the retrieved studies were re-searched to track down published articles on FMD prevalence from previous years.

Selection criteria of studies: The cross-sectional and longitudinal studies on FMD prevalence conducted on cattle and buffaloes in India was chosen for this study. The studies selected met the following criteria: (1) FMD prevalence frequency or antigen/antibody detected, (2) FMDV serotype detected, (3) total number of animals tested or screened, (4) year of the study conducted, (5) studies with prevalence values reported, (6) geographical location of the study, (7) study type and (8) studies which have used the standard methodology of confirmatory tests including, molecular methods by different PCRs and serological diagnosis by different ELISA's. Exclusion criteria for the studies were: (1) FMD positive frequencies were not reported, (2) studies such as case reports, review articles and outbreaks investigations were not included for analysis purpose. Furthermore, the quality of the study was assessed using a specified rating system as reported earlier (Krishnamoorthy *et al.* 2021a, b, c). It includes sample representativeness, sample size, methodology employed, prevalence values, and outcome assessment, with maximum scores of 2, 1, 3, 2, and 2, respectively. The maximum score for study quality assessment was ten, and the lowest score was determined by the study requirements.

Data curation: Before beginning the data entry process onto predesigned Microsoft Excel sheets, the FMD seroprevalence studies were properly examined and analysed. These included the authors names, the year of publication, study period, numbers of animals positive for FMD, total number of cattle and buffaloes tested, and FMD diagnosis confirmation methods. The confirmation methods used for the diagnosis of FMD prevalence were clinical examination, molecular methods using different PCRs, serological diagnosis by using different types of ELISA's, compliment fixation test, etc.The FMD prevalence used to calculate overall prevalence estimate was the value of the highest prevalence obtained in a study by using various diagnostic methods.

Meta-analysis methodology: The meta-analysis on FMD prevalence in cattle and buffaloes in India was conducted by using the R Open source scripting software (Comprehensive R Archive Network) version 3.2.5 and the R package used was "meta" as reported earlier (Schwarzer 2007). A forest plot or a confidence interval plot were used to show meta-analysis graphically. The proportion was transformed using the generalised linear mixed model and the Logit transformation, i.e.'sm=PLOGIT'. A square representing a point estimate of prevalence and a horizontal line extending either side of the square block depicting a 95% confidence interval (CI) were used to illustrate the studies. The prediction interval (PI) at the 95% level is represented by the shaded dark line beneath the forest plot. The I-square, Tau square, H value, and P values calculated and given in the last line of the forest plot were used to determine the heterogeneity between studies. Subgroup analysis was performed based on the various characteristics indicated earlier to reduce heterogeneity between studies on FMD prevalence (Krishnamoorthy *et al.* 2019a, b, Krishnamoorthy *et al.* 2021a, b, c). The Cochran Q statistic was derived as previously published in the studies (Krishnamoorthy *et al.* 2017, Krishnamoorthy *et al.* 2019a, b, Krishnamoorthy *et al.* 2021a, b, c). For the FMD seroprevalence estimation, forest plots were prepared for overall prevalence estimate, year-wise, zone-wise, state-wise, host species-wise, method-wise, and FMD serotype-wise. The prevalence of FMD in cattle and buffaloes in India was calculated as a percentage, with CI and PI calculated at the 95% level.

RESULTS AND DISCUSSION

FMD prevalence studies: Apart from wild life, India has a large livestock population with a susceptible population of 535 million and monitoring livestock diseases status in the population relies on accurate diagnostic and rapid disease reporting systems (Singh *et al.* 2019). The details of FMD prevalence studies from India included in the meta-analysis are shown in Fig. 1. The number of prevalence studies included for meta-analysis was 73 from India after the systematic review. The year-wise and state-wise number of studies from India included for meta-analysis are given in Fig. 2. More studies (12) were reported during the year 2014 (12). The prevalence studies included were 4, 19, and 54 during the period 1986–2000, 2001–10, and 2011–21, respectively and with 5,00,267 samples obtained from cattle and buffaloes in India. The prevalence studies from India covered 17 states and two union territories, with more number of studies from Uttarakhand (20), followed by Haryana (14), Uttar Pradesh (10), Karnataka (7), Andhra Pradesh (4), Andaman and Nicobar Islands (4), Jammu and Kashmir (2), Kerala (2), Assam (2), Gujarat (2), Odisha (2), and one study each from Chhattisgarh, Madhya Pradesh, Maharashtra, Mizoram, Punjab, Rajasthan, Tamil Nadu, and West Bengal. The details of the studies on FMD prevalence with author name, year, states, zones, along with their quality assessment scores are presented in Table 1. The studies with a quality assessment score of 5 and above were included for the meta-analysis. It was observed that more number of studies reported on the prevalence was for FMDV Serotype O (29) followed by A (25), Asia 1 (21) and one study for serotype C. In India, serotypes O, A, and Asia 1 are the most common serotypes reported (Singh *et al.* 2019). SAT serotypes have never been found in India, whereas serotype C has not been found since 1995 as described (Pattnaik *et al.* 2012). Serotype O has historically dominated field outbreaks, followed by serotypes Asia 1 and A (Pattnaik *et al.* 2012) and concurred with the present study.

FMD prevalence in India: The particulars of meta-analysis results on FMD prevalence in India are presented in Table 2. The pooled estimates for FMD prevalence was 43% (95% level, CI 35–52%, PI 3–94%). However, a lesser prevalence was reported from Bangladesh (25%) by using meta-analysis of 30 studies (Hasan and Mia 2021). The forest plot for FMD prevalence studies from different states in India during the period 2011 to 2021 is depicted in Fig. 3. The FMD prevalence was high during 1986– 2000 (68%) than the recent period i.e., 2011-2021 (43%). Over a ten-year period in India, the temporal distribution of FMD cases with different serotypes showed a significant decline in the number of FMD outbreaks, which is linked to the incremental improvement in herd immunity due to regular immunization under the FMDCP since 2007. From 2006 to 2017, the total incidence of FMD and individual serotype specific incidences showed a downward trend, with rare surges in the number of outbreaks at different times (Singh *et al.* 2019) and corroborated with the present study. The zone-wise and state-wise FMD prevalence in India are presented in Table 2 and Fig. 4. The zone-wise analysis revealed a higher FMD prevalence in the East zone (59%) and lower in the Central zone (24%). This may be due to the differences in agro-climatic factors, dairy animal rearing systems, management practices, cattle, and buffalo breeds in that particular geographical area. The highest prevalence of FMD was observed in Rajasthan (81%), followed by Assam (74%), Andhra Pradesh (52%), Kerala (44%), and lowest in Andaman and Nicobar Islands (3%), and Chhattisgarh (12%). The host species-wise analysis indicated a higher FMD prevalence of 45% in cattle when compared to buffaloes (30%). This might be due to the fact that buffaloes are resistant to various diseases and they belong to indigenous breeds of a geographical area rather than more of crossbreeds in cattle, which are less resistant to diseases. The FMD prevalence was higher in antigen detection methods (49%) when compared to antibody detection methods (42%). Hence, the antigen detection methods may be used for the diagnosis of FMD in cattle and buffaloes in future. Based on the method of detection of FMD, it was observed that the prevalence was higher by molecular methods (64%) followed by Differentiating Infected from Vaccinated Animals (DIVA) ELISA and Compliment Fixation Test (63%), Sandwich ELISA (60%), Non Structural Proteins (NSP) ELISA (59%) and Indirect ELISA (42%). The DIVA and NSP ELISA's are used to detect the prevalence of FMD infection in endemic regions and the sero-surveillance to detect the prevalence of FMD in livestock can be accomplished by using NSP based tests as reported (King *et al.* 2015). The FMD antibody ELISA methods showed a slightly higher prevalence of 49%

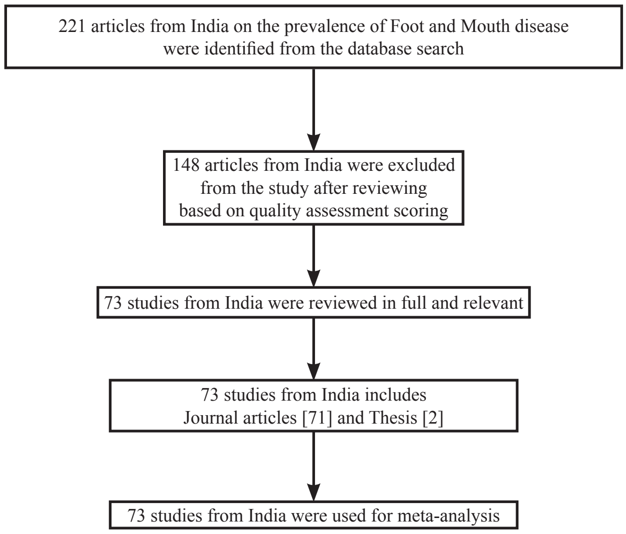

Fig. 1. Number of FMD prevalence studies obtained for meta-analysis.

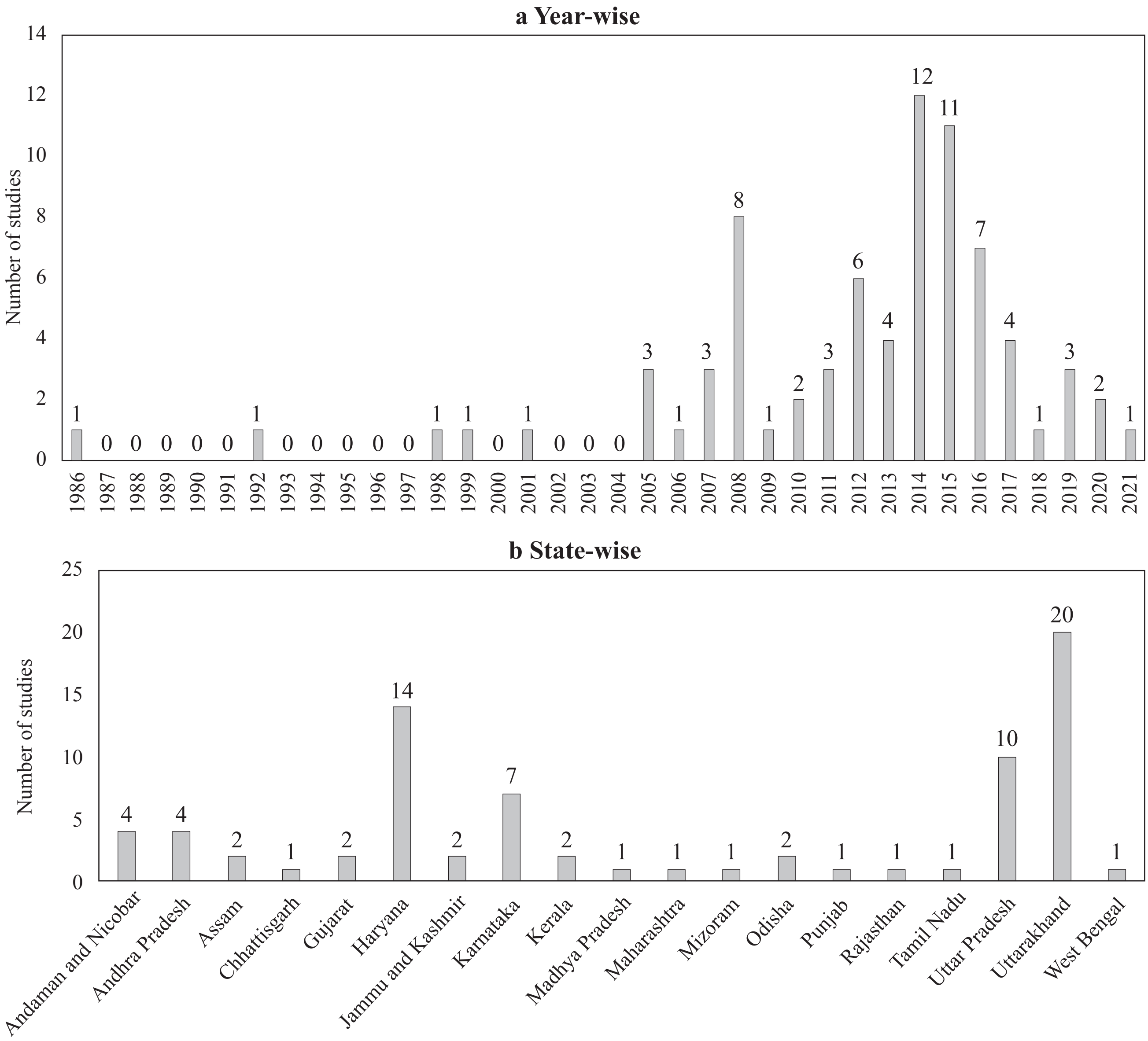

Fig. 2. Number of FMD prevalence studies included for meta-analysis based on Year-wise (a) and State-wise (b).

when compared to antigen detecting ELISA (48%). The serological tests were used in monitoring the immune status of animals exposed to FMDV or FMD vaccines (King *et al.* 2015) and concurred with present study. FMD virus serotype-wise analysis indicated a higher prevalence of serotype O (64%) followed by serotype A (29%), serotype Asia 1 (24%) and less prevalence in serotype C (3%). As previously reported, 80% of confirmed outbreaks or cases in India are due to serotype O and it concurred with the present study. Further, the FMD was mainly caused by serotype O, which caused the maximum number of outbreaks and cases during 2006-11 (Subramaniam *et al.* 2013). The Cochran Q statistic showed a highly significant ($P<0.01$) difference between the studies based on year-wise, zone-wise, state-wise, host-wise, method-wise, and FMDV serotype-wise except for Odisha which showed no significant difference. Since the introduction of mass vaccination programmes in India, there has been a significant reduction in FMD outbreaks in terms of the number of cases and the duration of the epidemics (Singh *et al.* 2019). Further, there was high heterogeneity between these studies that was observed for FMD prevalence estimates which could be due to innumerable factors comprising age, breed, sex, parity of cattle, genetic characteristics, weather conditions, and management practices in that particular geographical area. There was no FMD genotypes or lineages particular to geographical area occur in the India was observed (Subramaniam *et al*. 2013).

FMD control and prevention is mainly by targeting effective livestock management practices and reducing the associated risk factors (Hasan and Mia 2021). In several South American countries, preventive vaccination has

Study	Events	Total	Proportion	95%-CI
Akhoon et al.. 2015 Jammu and Kashmir	412	10870	0.04	[0.03: 0.04]
Anil et al.. 2021 Andhra Pradesh	8	200	0.04	[0.02: 0.08]
Arun 2012 Kerala	6	30	0.20	[0.08: 0.39]
Baro et at.. 2019 Assam	72	88	0.82	[0.72: 0.89]
Bhanot et al.. 2013 Haryana	5	15	0.33	[0.12: 0.62]
Bhanot et al.. 2015 Haryana	10	15	0.67	[0.38: 0.88]
Biswal et al.. 2014 Uttarakhand	730	2500	0.29	[0.27: 0.31]
Biswal et al.. 2015 Uttarakhand	1859	2628	0.71	[0.69: 0.72]
Biswal et al.. 2016 Uttarakhand	734	1800	0.41	[0.38: 0.43]
Biswal et al.. 2017 Uttarakhand	188	210	0.90	[0.85: 0.93]
Biswal et al.. 2019 Uttarakhand	33	54	0.61	[0.47: 0.74]
Bora et at.. 2014 Haryana	1596	4200	0.38	[0.37: 0.39]
Bulbul et al.. 2015 Jammu and Kashmir	168	200	0.84	[0.78: 0.89]
Das et al.. 2016 Uttarakhand	241	3903	0.06	[0.05: 0.07]
Gowane et at.. 2013 Rajasthan	321	395	0.81	[0.77: 0.85]
Hayer et al.. 2017a Chhattisgarh	222	1836	0.12	[0.11: 0.14]
Hayer et al.. 2017b Uttarakhand	64	78	0.82	[0.72: 0.90]
Hegde et al.. 2016a Karnataka	3041	8877	0.34	[0.33: 0.35]
Hegde et al.. 2016b Karnataka	1992	6002	0.33	[0.32: 0.34]
Hegde et al.. 2016c Karnataka	3067	5399	0.52	[0.51: 0.53]
Hemalatha et at.. 2020 Tamilnadu	45	83	0.54	[0.43: 0.65]
Hosamani et al.. 2015 Karnataka	826	3454	0.24	[0.22: 0.25]
Kakker and Sharma. 2012 Haryana	34	56	0.61	[0.47: 0.74]
Lather et al.. 2014 Haryana	174	800	0.22	[0.19: 0.25]
Lather et al.. 2015 Haryana	1017	1600	0.64	[0.61: 0.66]
Longjam et al.. 2011 Assam	65	100	0.65	[0.55: 0.74]
Longjam et al.. 2012 Mizoram	55	84	0.65	[0.54: 0.76]
Madhanmohan et al.. 2012 Andhra Pradesh	76	84	0.90	[0.82: 0.96]
Mahajan et al.. 2013 Uttarakhand	2383	7947	0.30	[0.29: 0.31]
Mahajan et al.. 2014 Uttarakhand	2280	6750	0.34	[0.33: 0.35]
Mohan et al.. 2013 Uttarakhand	641	900	0.71	[0.68: 0.74]
Mohan et al.. 2014 Uttarakhand	188	300	0.63	[0.57: 0.68]
Mohan et al.. 2015 Uttarakhand	68	269	0.25	[0.20: 0.31]
Mohanty et al.. 2015 Odisha	17	51	0.33	[0.21: 0.48]
Mohapatra et al.. 2011 Uttarakhand	200	585	0.34	[0.30: 0.38]
Mohapatra et al.. 2014 Uttarakhand	1721	6618	0.26	[0.25: 0.27]
Ranabijuli. 2011 Odisha	595	1400	0.42	[0.40: 0.45]
Rout et al.. 2014a Karnataka	3	7	0.43	[0.10: 0.82]
Rout et al.. 2014b Gujarat	191	317	0.60	[0.55: 0.66]
Rout et al.. 2016a Uttarakhand	67	140	0.48	[0.39: 0.56]
Rout et al.. 2016b Uttarakhand	687	1320	0.52	[0.49: 0.55]
Sharma et at.. 2012 Uttarakhand	587	2175	0.27	[0.25: 0.29]
Sharma et at.. 2014 Andaman and Nicobar	7	203	0.03	[0.01: 0.07]
Sharma et al.. 2014 Gujarat	67	203	0.33	[0.27: 0.40]
Sharma et at.. 2014 Kerala	140	203	0.69	[0.62: 0.75]
Sharma et al.. 2014 Maharashtra	67	203	0.33	[0.27: 0.40]
Singh et al.. 2015a Uttar Pradesh	90	119	0.76	[0.67: 0.83]
Singh et at.. 2015b Uttar Pradesh	1941	10422	0.19	[0.18: 0.19]
Singh et al.. 2017 Uttar Pradesh	79	120	0.66	[0.57: 0.74]
Singh et al.. 2020 Uttar Pradesh	111	400	0.28	[0.23: 0.32]
Soni et al.. 2012 Madhya Pradesh	210	500	0.42	[0.38: 0.46]
Subramaniam et al.. 2018 Uttarakhand	38	40	0.95	[0.83: 0.99]
Sunder et al.. 2015 Andaman and Nicobar	210	2632	0.08	[0.07: 0.09]
Sunder et at.. 2019 Andaman and Nicobar	4	12	0.33	[0.10: 0.65]
Common effect model		**99897**	**0.30**	**[0.29: 0.30]**
Random effects model			**0.43**	**[0.35: 0.52]**
Prediction Interval				**[0.05: 0.92]**

Heterogeneity = I^2=100%, τ^2=1.7317, p = 0

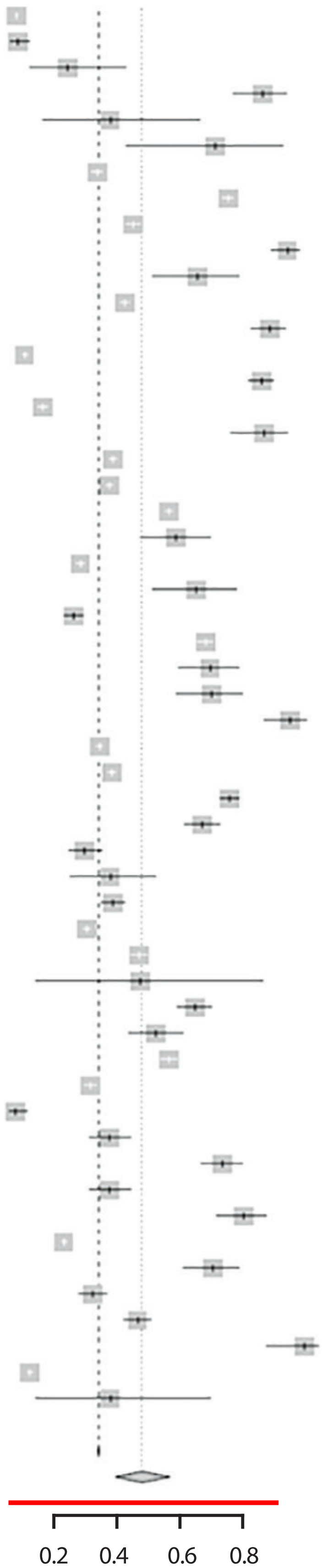

Fig. 3. Forest plot showing FMD prevalence in India during 2011-2021.

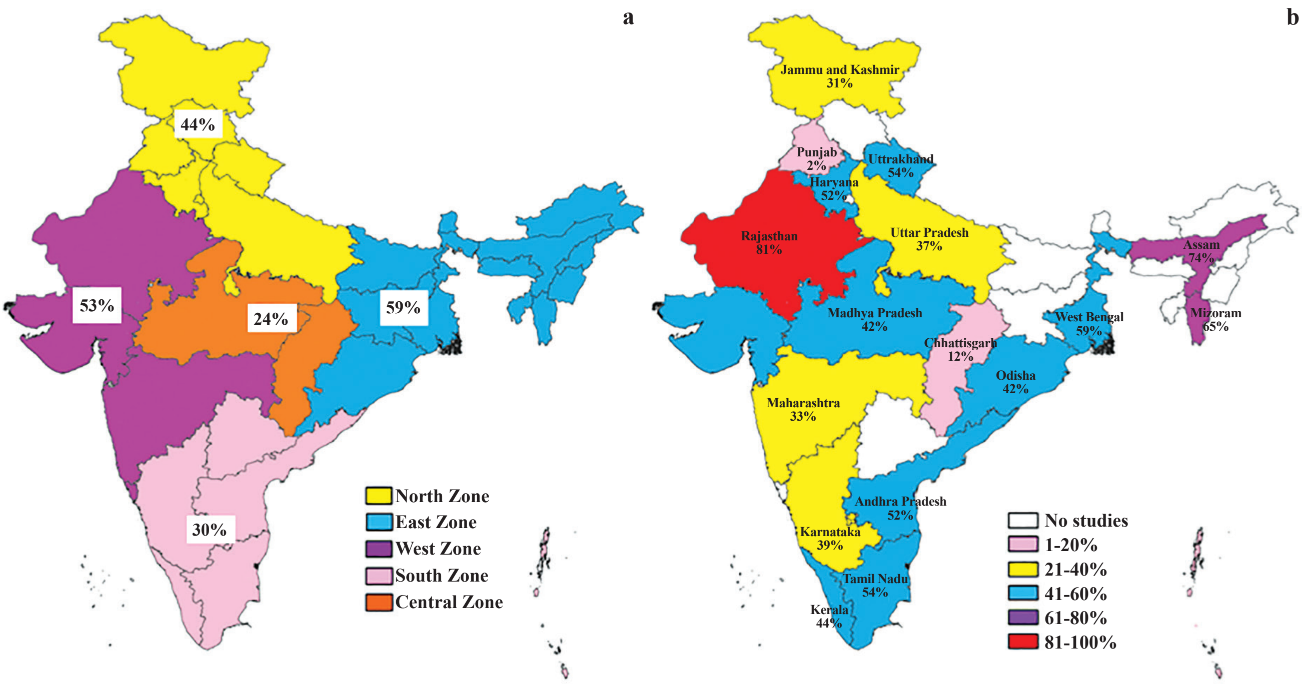

Fig. 4. India map showing zone wise (a) and state-wise (b) FMD prevalence estimates.

been successful in not just controlling but also eradicating this disease (Singh *et al.* 2019). The unrestricted animal movement in the country plays an important role in the FMD spread across the geographical locations (Subramaniam *et al*. 2013). Further, the uncontrolled movement of animals, the infection immunity effect and the presence of carrier animals for FMD may be the main reasons for the occurrence of FMD outbreaks at particular intervals as reported (Subramaniam *et al.* 2013). As a result, enhancing the effectiveness of FMD vaccines and the epidemiology of FMD virus serotypes causing the FMD outbreaks, should be the top priorities in FMD research. Field diagnostics must be utilised in combination with the vaccination programmes to effectively manage FMD in the field conditions. Disease containment will be more effective if early diagnosis and disease transmission are prevented by following biosecurity measures in the farms or villages with FMD cases. In India, where culling of infected animals cannot be practiced, it is preferable to detect and confine clinically diseased and suspected animals to prevent virus transmission and allow animals to recover on their own with effective therapeutic measures. India was placed in the category 5 (High incidence with outbreaks throughout the year) country based on the under reporting are most expected, no incentives for reporting the outbreaks or cases to authorities were limited, as reported (Sumption *et al.* 2008). However, the situation is changing with continuous vaccination of the cattle and buffalo population in India under the FMD control programmes regularly. There is zoning of the areas which are free of FMD cases or outbreaks for long period such as in Andhra Pradesh, Punjab and Telangana states. Further, there is requirement of the State Animal Husbandry Departments to encourage the field veterinarians to report the livestock disease outbreaks, by providing incentives to them for reporting the disease outbreaks.

In the present study, the high risk zones, states, methods, serotypes identified will help the various stakeholders and policy makers to utilize the available scarce resources effectively and also to make informed decisions. However, there is decreasing trend in the FMD prevalence in the recent years as observed from the present study. The associated risk factors for the occurrence of FMD should be taken in to account before planning and implementation of control programmes to yield the desired effects. There is a need for the continuous FMD vaccination in cattle, buffaloes, sheep, goat and pig population in India and it was planned to achieve under National Animal Diseases Control Programme launched by Government of India by the year 2024. This programme would result in reducing the FMD occurrences and for moving up in the stages of the progressive control pathway. This will help in improving the export trade of buffalo meat and also increasing the milk production in cattle and buffaloes, eventually result in the economic benefits to the dairy farmers.

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Table 1. Quality assessment scores for Foot and Mouth disease prevalence studies from India included in the meta-analysis

Studies (Author and year)	Study state	Zone	Quality assessment of prevalence studies[#]					
			Sample representativeness (Maximum score=2)	Sample size (Maximum score=1)	Methodology employed (Maximum score=3)	Prevalence value (Maximum score=2)	Assessment of outcome (Maximum score=2)	Total score (Maximum score=10)
Ahuja *et al.* 1986	Haryana	North	1	1	2	2	1	7
Akhoon *et al.* 2015	Jammu and Kashmir	North	1	1	1	2	1	6
Anil *et al.* 2021	Andhra Pradesh	South	1	1	2	1	1	6
Arun 2012	Kerala	South	1	1	2	2	1	7
Baro *et al.* 2019	Assam	East	1	1	3	1	1	7
Bhanot *et al.* 2013	Haryana	North	2	1	2	1	1	7
Bhanot *et al.* 2015	Haryana	North	2	1	2	1	1	7
Biswal *et al.* 2014	Uttarakhand	North	2	1	2	2	1	8
Biswal *et al.* 2015	Uttarakhand	North	2	1	2	1	1	7
Biswal *et al.* 2016	Uttarakhand	North	1	1	2	1	1	6
Biswal *et al.* 2017	Uttarakhand	North	1	1	3	1	1	7
Biswal *et al.* 2019	Uttarakhand	North	1	1	3	1	1	7
Bora *et al.* 2014	Haryana	North	2	1	2	2	1	8
Bulbul *et al.* 2015	Jammu and Kashmir	North	2	1	1	2	1	7
Dana *et al.* 2001	West Bengal	East	2	1	1	2	1	7
Das *et al.* 2016	Uttarakhand	North	2	1	2	2	1	8
Giridharan *et al.* 2005	Uttarakhand	North	1	1	3	1	1	7
Gowane *et al.* 2013	Rajasthan	West	1	1	2	2	1	7
Hayer *et al.* 2017a	Chhattisgarh	Central	1	1	2	2	1	7
Hayer *et al.* 2017b	Uttarakhand	North	1	1	2	2	1	7
Hegde *et al.* 2016a	Karnataka	South	2	1	2	2	1	8
Hegde *et al.* 2016b	Karnataka	South	2	1	2	2	1	8
Hegde *et al.* 2016c	Karnataka	South	2	1	2	2	1	8
Hemalatha *et al.* 2020	Tamil Nadu	South	2	1	2	2	1	8
Hosamani *et al.* 2015	Karnataka	South	2	1	2	2	1	8
Kakker and Sharma 2008	Haryana	North	2	1	2	1	1	7
Kakker and Sharma 2012	Haryana	North	2	1	2	2	1	8
Kumar *et al.* 2007	Haryana	North	2	1	2	2	1	8
Lather *et al.* 2014	Haryana	North	2	1	2	2	1	8
Lather *et al.* 2015	Haryana	North	2	1	2	2	1	8
Longjam *et al.* 2011	Assam	East	1	1	3	2	1	8
Longjam *et al.* 2012	Mizoram	East	2	1	3	2	1	9
Maan *et al.* 1998	Haryana	North	2	1	2	2	1	8
Madhanmohan *et al.* 2012	Andhra Pradesh	South	1	1	3	1	1	7
Mahajan *et al.* 2013	Uttarakhand	North	2	1	2	2	1	8
Mahajan *et al.* 2014	Uttarakhand	North	2	1	2	1	1	7
Maroudam *et al.* 2008	Andhra Pradesh	South	1	1	2	2	1	7

Studies (Author and year)	Study state	Zone	Quality assessment of prevalence studies[#]					
			Sample representativeness (Maximum score=2)	Sample size (Maximum score=1)	Methodology employed (Maximum score=3)	Prevalence value (Maximum score=2)	Assessment of outcome (Maximum score=2)	Total score (Maximum score=10)
Mohan *et al.* 2008	Karnataka	South	1	1	3	1	1	7
Mohan *et al.* 2013	Uttarakhand	North	2	1	2	2	1	8
Mohan *et al.* 2014	Uttarakhand	North	2	1	2	2	1	8
Mohan *et al.* 2015	Uttarakhand	North	2	1	2	2	1	8
Mohanty *et al.* 2015	Odisha	East	2	1	2	2	1	8
Mohapatra *et al.* 2011	Uttarakhand	North	2	1	2	2	1	8
Mohapatra *et al.* 2014	Uttarakhand	North	2	1	2	2	1	8
Mohapatra *et al.* 2007	Uttarakhand	North	1	1	3	1	1	7
Muthukrishnan *et al.* 2008	Andhra Pradesh	South	1	1	3	1	1	7
Prasad *et al.* 1992	Haryana	North	2	1	2	2	1	8
Ranabijuli 2011	Odisha	East	2	1	2	2	1	8
Rout *et al.* 2014a	Karnataka	South	2	1	2	2	1	8
Rout *et al.* 2014b	Gujarat	West	2	1	2	2	1	8
Rout *et al.* 2016a	Uttarakhand	North	2	1	2	2	1	8
Rout *et al.* 2016b	Uttarakhand	North	1	1	2	2	1	7
Sharma and Kakker 2005	Haryana	North	2	1	2	2	1	8
Sharma *et al.* 2006	Haryana	North	2	1	2	2	1	8
Sharma *et al.* 2012	Uttarakhand	North	1	1	2	1	1	6
Sharma *et al.* 2014	Andaman and Nicobar, Gujarat, Kerala, Maharashtra	South, West	2	1	2	2	1	8
Singh *et al.* 2008a	Uttar Pradesh	North	2	1	2	2	1	8
Singh *et al.* 2008b	Punjab and Uttar Pradesh	North	2	1	1	2	1	7
Singh *et al.* 2010	Uttar Pradesh	North	2	1	2	2	1	8
Singh *et al.* 2015a	Uttar Pradesh	North	2	1	2	2	1	8
Singh *et al.* 2015b	Uttar Pradesh	North	2	1	2	2	1	8
Singh *et al.* 2017	Uttar Pradesh	North	2	1	2	2	1	8
Singh *et al.* 2020	Uttar Pradesh	North	2	1	2	2	1	8
Soni *et al.* 2012	Madhya Pradesh	Central	2	1	1	2	1	7
Subramaniam *et al.* 2018	Uttarakhand	North	1	1	3	1	1	7
Sunder *et al.* 2005	Andaman and Nicobar	South	2	1	2	2	1	8
Sunder *et al.* 2015	Andaman and Nicobar	South	2	1	2	2	1	8
Sunder *et al.* 2019	Andaman and Nicobar	South	1	1	3	1	1	7
Suryanarayana *et al.* 1999	Karnataka	South	1	1	2	1		5
Verma *et al.* 2007	Haryana	North	2	1	2	2	1	8
Verma *et al.* 2008	Uttar Pradesh	North	2	1	2	1	1	7
Verma *et al.* 2009	Uttar Pradesh	North	2	1	2	2	1	8
Verma *et al.* 2010	Uttar Pradesh	North	2	1	2	2	1	8

[#]Representativeness of samples: 1 Representative 2 Truly representative; Sample size: 1-Given; Methodology used: 1-Clinical examination 2 Serology, 3-Molecular methods; Prevalence values: 1-Calculated, 2-Mentioned; Outcome assessment: 1-Individual assessment, 2-Double assessment. Details of the references are provided in Supplementary File 1.

Table 2. Foot and Mouth disease prevalence estimates in India for various parameters based on meta-analysis

Parameter	Period	Number of studies	Total	Prevalence (%) [CI at 95% level]	PI (%) at 95% level	Tests for Heterogeneity				
						I^2 Value (%)	Tau square value	H value	Degrees of Freedom	Cochran Q statistics
India	1986-2021	77	500267	43 [35-52]	3-94	99.9	2.387	30.36	76	94057.1**
India period-I	1986-2000	4	1210	68 [56-77]	22-94	86.1	0.162	2.68	3	23.0**
India period-II	2000-2010	19	399160	38 [18-62]	1-99	99.9	4.873	30.66	18	14843.0**
India period-III	2011-2021	54	99897	43 [35-52]	5-92	99.5	1.732	14.35	53	15933.2**
North Zone	2005-2020	47	478636	44 [33-55]	3-95	99.9	2.335	35.57	46	70837.5**
Haryana	1986-2015	14	10241	52 [37-67]	8-94	98.7	1.324	8.84	13	1272.5**
Jammu and Kashmir	2015	2	11070	31 [1-93]	-	99.8	5.997	24.55	1	869.1**
Punjab	2008	1	300000	2	-	-	-	-	-	-
Uttarakhand	2005-2019	20	38388	54 [39-68]	6-95	99.5	1.746	14.02	19	5089.6**
Uttar Pradesh	2008-2020	10	107227	37 [18-60]	1-96	99.9	2.354	34.66	9	12396.1**
East Zone	2001-2019	6	1823	59 [45-71]	16-91	93.6	0.431	3.97	5	91.4**
Assam	2011 and 2019	2	188	74 [60-84]	-	84.6	0.1391	2.55	1	6.84**
Mizoram	2012	1	84	65	-	-	-	-	-	-
Odisha	2011 and 2015	2	1451	42 [40-45]	-	40.3	0.0	1.29	1	1.74^{NS}
West Bengal	2001	1	100	59	-	-	-	-	-	-
West Zone	2013 and 2014	4	1118	53 [32-73]	1-99	98.3	0.806	7.61	3	200.6**
Gujarat	2014	2	520	47 [28-66]	-	97.2	0.301	5.97	1	37.3**
Maharashtra	2014	1	203	33	-	-	-	-	-	-
Rajasthan	2013	1	395	81	-	-	-	-	-	-
South Zone	1999-2021	18	28064	30 [15-51]	1-96	99.1	3.440	10.36	17	2714.0**
Andaman & Nicobar	2014-2019	4	3158	3 [0-27]	0-100	77.8	4.973	2.12	3	60.8**
Andhra Pradesh	2008-2021	4	315	52 [12-90]	0-100	97.4	4.429	6.20	3	237.6**
Karnataka	1999-2016	7	24275	39 [30-49]	14-72	99.3	0.240	12.04	6	892.6**
Kerala	2012 and 2014	2	233	44 [14-79]	-	95.2	1.130	4.54	1	26.4**
Tamil Nadu	2020	1	83	54	-	-	-	-	-	-
Central Zone	2012 and 2017	2	2336	24 [9-50]	-	99.5	0.984	14.37	1	202.6**
Chhattisgarh	2017	1	1836	12	-	-	-	-	-	-
Madhya Pradesh	2012	1	500	42	-	-	-	-	-	-
Cattle	1986-2020	54	64673	45 [36-54]	4-94	99.3	2.018	12.18	53	12186.7**

Parameter	Period	Number of studies	Total	Prevalence (%) [CI at 95% level]	PI (%) at 95% level	Tests for Heterogeneity				
						I^2 Value (%)	Tau square value	H value	Degrees of Freedom	Cochran Q statistics
Buffaloes	2006-2020	18	14887	30 [21-42]	4-82	99.1	1.187	10.63	17	2136.2**
Cattle and Buffaloes	1992-2021	34	458040	40 [28-53]	2-95	99.9	2.535	42.75	33	72870.3**
Antigen detection	1986-2021	33	419786	49 [33-65]	2-98	99.9	3.669	31.54	32	30256.8**
Antibody detection	1992-2020	50	81180	42 [34-50]	6-88	99.3	1.327	11.66	49	8079.6**
CFT	1992	1	423	63	-	-	-	-	-	-
Clinical examination	1998-2016	10	409632	30 [9-64]	0-99	99.9	5.191	50.13	9	18794.3**
C-ELISA	2014	4	812	27 [8-62]	0-100	97.7	2.142	6.55	3	220.1**
DIVA ELISA	2019 and 2020	2	171	63 [30-87]	-	96.7	0.933	5.52	1	34.9**
I-ELISA	1999 and 2011	2	1413	42 [40-45]	-	0.0	0.0	1.00	1	0.09^{NS}
LPB ELISA	2008-2017	16	10374	59 [49-68]	20-89	98.9	0.614	9.41	15	1690.1**
NSP ELISA	2007-2020	26	69200	36 [30-43]	10-74	98.9	0.587	9.48	25	2628.5**
S-ELISA	2005-2019	8	1177	60 [44-74]	13-94	93.7	0.774	3.99	7	170.0**
Molecular methods	1999-2019	17	6913	64 [45-79]	6-98	99.0	2.298	10.06	16	2474.6**
ELISA	1986-2021	56	65798	47 [38-55]	6-93	99.1	1.758	10.31	55	7288.0**
Antigen ELISA	1986-2021	12	3641	48 [31-66]	5-95	96.9	1.614	5.72	11	587.3**
Antibody ELISA	1999-2020	45	64278	49 [41-57]	9-90	99.2	1.163	10.92	44	6123.8**
Serotype A	1998-2017	25	26360	29 [20-39]	3-84	99.1	1.439	10.79	24	3526.2**
Serotype Asia 1	1992-2017	24	14917	24 [15-36]	2-86	98.9	2.007	9.67	23	2533.2**
Serotype C	2005	1	151	3	-	-	-	-	-	-
Serotype O	1992-2019	29	17714	64 [52-73]	12-96	98.8	1.481	9.13	29	4099.9**

CI, Confidence interval; PI, Prediction interval; H, Heterogeneity; CFT, Complement Ffixation test; C, Competitive; ELISA, Enzyme linked immuno-sorbent assay; DIVA, Differentiation from infected and vaccinated animals; i, Indirect; LPB, Liquid phase blocking; NSP, Non structural proteins; s, Sandwich. Significance levels = ^{NS}Not significant, *Significant ($P<0.05$), **Highly significant ($P<0.01$).

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