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REVIEW

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Foot and mouth disease in Ethiopia: a systematic review and meta-analysis in the last fifteen years (2007–2021)

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Abstract

Background Foot and Mouth disease (FMD) is an acute contagious and highly infectious disease of domesticated and wild cloven-hoofed animals characterized by the appearance of vesicular lesions at the epithelium of the mouth, nares, muzzle, feet and udder, causing repeated outbreaks every year in Ethiopia, thereby causing production loss and the banning of exportation of livestock, products and their by-products. The prevalence of foot and mouth disease in Ethiopia has been reported from different parts of the country, but a pooled quantitative estimate of foot and mouth disease has not been done so far; therefore this meta-analysis sought to determine FMD status in Ethiopia.

Main body Literature search was conducted by the main search engines and indexing services: Google, Google Scholar, PubMed, and Science Direct. Additionally, university repositories were discovered to retrieve unpublished MSc theses. All studies dealt with the prevalence of FMD. Raw data were extracted in Microsoft Excel and then imported into R Studio. Random effects model was used to pool estimates of outcomes at 95% confidence interval. Heterogeneity level was computed by Higgins's I^2 statistics. Publication bias was checked using funnel plots for standard error augmented by Begg's and Egger's tests. In total, 27 reports with 13,510 cattle were included in this study. An estimate of prevalence across reviews for the entire literature collected from the period 2007 to 2021 was 21.39% (16.53–26.56). Sub-analysis for herd size, animal composition, age group and sex of cattle identified as potential significant factors for FMD. FMD prevalence in cattle at early age and adult age was 19.5% and 14.6%, respectively ($P < 0.01$). Compared to intensive production, FMD occurrence was 4.3 times higher in extensive production (P value = 0.003).

Conclusions FMD is prevalent in Ethiopian cattle, and the disease is a list A disease which could affect the export of live animals and their products since FMD is a trans-boundary disease. Therefore, it is imperative to have strategic implementation of effective prevention, control, and robust eradication policies.

Keywords Cattle, FMD, Ethiopia, Systematic review, Meta-analysis

Background

In Ethiopia, agriculture contributes roughly 45–48% of gross domestic production (GDP). Livestock contributes about 20% of the country's agriculture GDP, excluding other roles, such as traction power, fertilizer, and transportation (Dubie and Negash 2021). The livestock sector is the largest in Africa with an estimated number of cattle, 65.35 million; sheep, 39.89 million and goats, 50.50 million (CSA 2020). However, the country has not been benefiting from the sector due to various constraints. Constraints include wide spread potential endemic disease, insufficient veterinary services, and a lack of a responsive system (Abdela 2017; Metages 2018). In Ethiopia, livestock diseases contribute to substantial economic losses for producers, who are responsible for hundreds

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of millions of birr every year (Jibat et al. 2013; Jemberu et al. 2014). Accordingly, diseases hinder the production and productivity of the sector by roughly 50–60% every year (Wagari 2016). Of the known livestock diseases that reduce productivity, foot and mouth disease is predominantly endemic, highly spread and has major socio-economic significance in the country (Bayissa et al. 2011; Jemberu et al. 2016; Molla et al. 2017).

Foot and mouth disease (FMD) is the most economically significant trans-boundary viral disease of ruminants affecting cattle, particularly at national, regional, and individual producer levels, preventing the country from generating revenue from livestock and limiting its ability to engage in international trade (Jibat et al. 2013; Knight-Jones and Rushton 2013; Jemberu et al. 2014; Abdela 2017). This is due to the extremely contagious and acute nature of the FMD virus, which affects all cloven-hoofed animals. Thus, it poses trade embargoes on live animals and on their products, being a bottleneck for production and productivity (Abdela 2017). As per the World Organization for Animal Health, FMD is list A disease and ranks first among animal infectious diseases (OIE 2021). The virus causing FMD is categorized under the genus *Aphthovirus*, which belongs to the family Picornaviridae. Infection with FMD virus is characterized by febrile illness, appetite loss, vesicular eruptions in the mucosa of the mouth, salivation, and vesiculitis in inter-digital spaces and coronary bands of feet and teats, as well as sudden demise of calves (Alexandersen and Mowat 2005).

The FMD virus has immunologically proven seven serotypes, namely O, A, C, Asia 1, Southern African Territories (SAT)-1, SAT-2 and SAT-3 (OIE 2021). Immunologically, multiple subtypes are segregated with distinct antigenic and genetic properties due to the high mutation rate of the virus (Brito et al. 2018). There is a difference between the seven serotypes of the virus and their distribution around the world (Ayelet et al. 2012; Brito et al. 2018). Out of these serotypes, five serotypes (O, A, C, SAT-1 and SAT-2) have been documented in Ethiopia (Ayelet et al. 2009; Negusssie et al. 2010). Moreover, within each serotype, there are numerous bio-typical strains and topotypes which could be typified by genetic and serological tests, where infection with one serotype may not give immunity against other strains (Singh et al. 2019; Wubshet et al. 2019). Serotypes O and A are responsible for considerable economic losses in the livestock sector in Ethiopia (Negusssie et al. 2010; Kassaw et al. 2013; Legesse et al. 2013).

Foot and mouse disease occurrence at the national level decelerates income generation by severely limiting trade opportunities (Bayissa et al. 2011; Jibat et al. 2013). In the case of small-scale mixed farming systems heavy losses occur when outbreaks affect draught oxen during the cropping season; FMD also causes considerable losses in milk yield and weight among dairy and fattening stock, respectively. For rural children especially, milk is a central food at the household level (Jibat et al. 2013). The significant death and suffering of cattle due to FMD is particularly observed during periods of drought or at an early age which limit access to feed and water. Moreover, the FMD status of a nation is a key contributor to international trade in livestock products, which means the presence of FMD is an operational blockade. Furthermore, it can lead to substantial destruction in tourism due to the limitation of human movement (Wubshet et al. 2019).

The contributing factors to the spread of FMD are livestock movement and trade. Hence, despite significant economic losses, movement and trade restrictions at domestic and international levels are crucial to controlling the disease (Knight-Jones and Rushton 2013). Although it is a disease of low mortality, the infection caused by FMD is colossal and impacts huge numbers of animals posing a global impact. This impact could be described in two modules: (1) through direct loss as a result of reduced production and changes in herd compositions; and (2) indirect losses effected by costs of control, access to markets and inadequate use of capable production technologies. The annual economic discrepancy due to FMD in terms of observable production losses and vaccination in endemic regions alone is estimated to be between US$6.5 and 21 billion (Knight-Jones and Rushton 2013).

Sero-prevalence studies conducted in Ethiopia so far have estimated FMD prevalence ranges from 4.8% to 72.1% in cattle (Sahle et al. 2004; Rufael et al. 2008; Megersa et al. 2009; Molla et al. 2010; Bayissa et al. 2011; Abunna et al. 2013; Yahya et al. 2013; Alemayehu et al. 2013; Zerabruk et al. 2014; Beyene et al. 2015; Belina 2016; Tesfaye et al. 2016; Wagari 2016; Jemberu et al. 2016; Sulayeman et al. 2018; Tadesse et al. 2019; Tesfaye et al. 2020; Dubie and Negash 2021). In addition, studies have shown that prevalence ranges from 4 to 11% among small ruminants (Sahle et al. 2004; Beyene et al. 2015). A report indicated that it is the leading and most substantial cause of direct production loss and blockage of exports of live animals, products, and their derivatives (Aman et al. 2020). FMD has been documented in different parts of Ethiopia, but until now, there has not been a careful systematic review and pooled quantitative documentation of the status of FMD in Ethiopia, which are crucial in developing strategies for preventing and controlling the disease so as to reduce its prevalence.

Main text

This systematic review and meta-analysis study are carried out according to PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Moher et al. 2009). The PRISMA checklist is used to ensure that eligible studies are included in the analysis. This study examines the prevalence of foot and mouth disease in cattle across Ethiopia, which is the outcome of interest.

Study area description

This meta-analytic study was carried out in Ethiopia, a country found in the horn of Africa, positioned between 3°00′–15°00′ N latitude and 32°30′–48°00′ E longitude. Ethiopia possesses a 1.04 million km^2 land area (Etana et al. 2020) and a human population of 115 million, which is most populous and the second country in Africa next to Nigeria (Varrella 2021). The country's climate is ideal for agricultural activity and is also home to an estimated 65.35 million cattle population (Central Statistical Agency 2020). Due to its diverse topography, Ethiopia's climate provides the basis for diverse agro-climatic zones. The agro-climatic zone heighted above 2300 m above sea level (m.a.s.l.) is taken as highland, which is surrounded by a temperate changeover zone between 1500 and 2300 m.a.s.l termed as midland, whereas zone having an altitude beneath 1500 m.a.s.l is categorized as lowland (Etana et al. 2020; Hassen et al. 2021).

Literature search strategy

Comprehensive search of literature was performed to extract articles on the sero-prevalence of FMD in Ethiopia that effected from February, 2021 to August, 2021. Among the search engines used were Google, Google Scholar, PubMed, and Science Direct. Bulletin of Animal Health and Production in Africa and the Ethiopian Veterinary Journal were also searched for directly unavailable online databases. Moreover, university repositories were discovered to retrieve unpublished MSc and PhD theses. The following Medical Subjects Headings (MeSH) terms were used for searching relevant literature in the search engine: "FMD", "Sero-prevalence" and "Ethiopia". In addition, search terms used included "Prevalence", "Cattle", and "Foot and Mouth Disease". By cross-referencing the collected studies, the selection of the studies was checked.

Selection of studies and data extraction

Up to now, reports that document the sero-prevalence of foot and mouth disease in Ethiopia have been downloaded and fed to the Mendeley reference manager. Both inclusion and exclusion criteria were developed for eminence prior to the commencement of the review process. Then, all articles selected through the searching strategy were individually extracted by the two authors. The objectives of the study were used as criteria for the selection of articles to be included. Accordingly, a study to be part of the meta-analysis has to fulfill the following eligibility criteria: (1) be published in English, (2) be cross-sectional, (3) 3ABC ELISA and/or clinical examination (in case of an outbreak), and PCR, molecular characterization (4) use of a sample size above 65. In extraction studies, both title and abstract were considered for relevance to the outcome and eligibility criteria, otherwise excluded.

Authors (ET and WS) collected applicable data related to study characteristics. The primary data extracted from eligible studies were the year of study, method of diagnosis, total number of observations, and cases. For samples that underwent molecular characterization, the major serotype isolates were identified and extracted based on the number of cases. Furthermore, the first author's name, publication year, study year, study site, production system, breeds, commingling of animals, agro-ecological zone, and diagnosis methods were key attributes of the extract. All the extracts found eligible were imported into a Microsoft Excel (2010) spreadsheet. The screening strategy of studies and exclusion reasons are presented (Fig. 1).

Critical appraisal of studies

The Joanna Briggs Institute's critical appraisal tool developed for the assessment of generalizability of articles in order to minimize publication biases was assessed for prevalence studies (Munn et al. 2015) and was rated for 9 points. The two authors were averaged out of 9 points and a final decision was made on studies with a score above or equal to five to be included.

Data synthesis and analysis

All analyses were conducted using RStudio (version 4.0.4) ("R core team, R: A language and environment for statistical computing" R core team 2021) where the "metafor" package was employed to estimate models (Viechtbauer 2010). Different steps are followed to analyze the data. First, apparent prevalence was calculated, using the summation of the frequency of cases in all reports included, divided by the summation of the frequency of cattle sampled. The 95% level of confidence interval (95% CI) was calculated by the binomial method. Then, prevalence estimates for every study were logit-transformed, and the pooled prevalence was computed based on meta-analytic models. The random effects model meta-analysis was used to estimate the pooled prevalence and 95% CI level of FMD in the overall population in Ethiopia (Hedges and

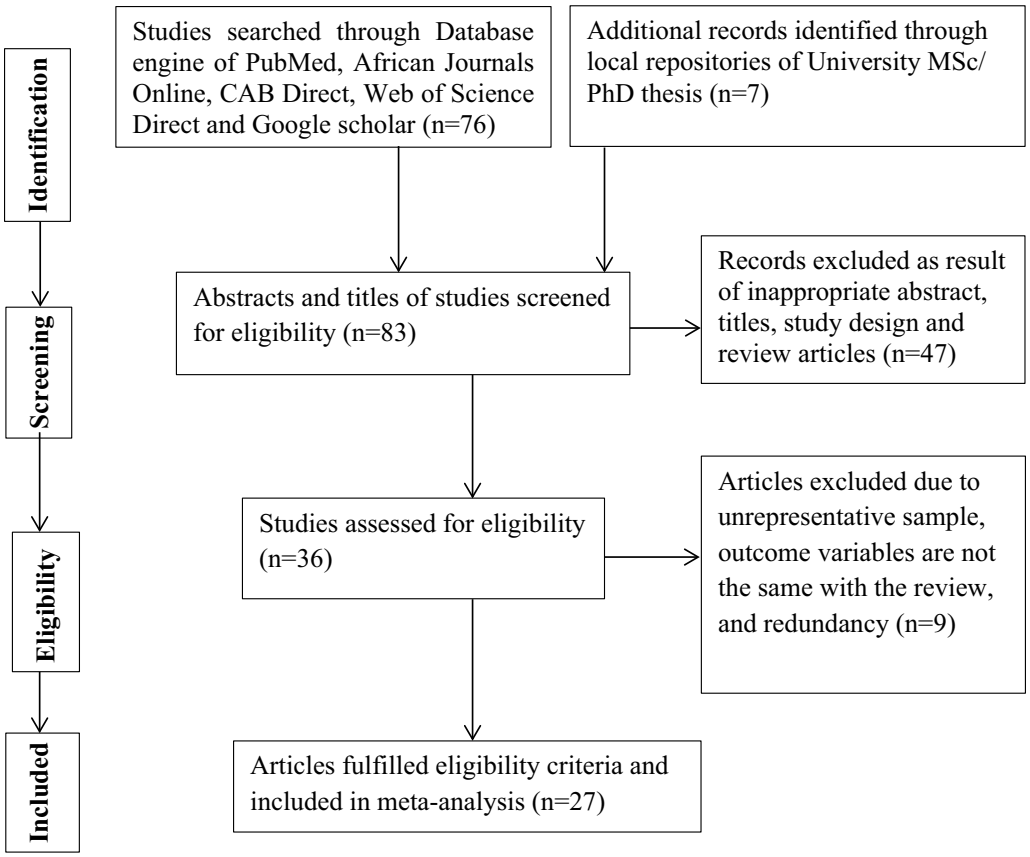

Fig. 1 Schematic representation of literature selection procedure adopted for the systematic review of Foot and Mouth Disease prevalence in Ethiopia. This Flowchart shows the literature search and inclusion/exclusion process

Vevea 1998). The spatial distribution of FMD prevalence per study was dotted proportionally on a map showing distribution, which was generated using ArcGIS version 10.3.1 software (ESRI, Redlands, California, USA).

Heterogeneity analysis

Cochran's Q statistic (Cochran 1954) and Higgin's statistic (I^2) were used to test heterogeneity and quantify the proportion of the true variation due to heterogeneity among studies, respectively (Higgins et al. 2003). Higgin's statistic (I^2) is computed to describe the variation among studies in the pooled prevalence due to heterogeneity. The I^2 scores of 25, 50, and 75% show low, moderate, and high degrees of heterogeneity, respectively. The I^2 value of 0% indicates no heterogeneity was detected. Cochran's Q is the number of squares measured on a standardized scale. Accordingly, the P value indicates the presence of heterogeneity with a lower cut point value (Higgins and Thompson 2002). Pooled prevalence for the category of the moderator was calculated by subgroup analysis. Moderators' category results with $P \leq 0.05$ were statistically significant. Sub-group analyses were undertaken to assess potential sources of heterogeneity between studies. The moderators included in the sub-group analysis were: study area (region), size of sample and year of the study.

Meta-regression

Univariable meta-regression was conducted to identify the parsimonious moderators; following it multivariable analysis was conducted to identify significant predictors. Initially, both random effects and fixed effects models were considered for each potential moderator. Later, random effect model was used only due to observed heterogeneity. Moreover, moderators were checked for collinearity using Goodman's and Kruskal gamma statistics, where moderators with gamma values between -0.6 and $+0.6$, were added to the multivariable meta-regression model. Finally, the multivariable meta-regression model was fitted using the moderators with P values < 0.25 in the univariable analysis. Moderator testing for collinearity and P value revealed the relevant moderators that had statistically significant relations with computed effect sizes and explained the explainable

proportion of heterogeneity within the model attributed to recognized moderators (R^2).

Assessment of bias

The study design and sample size of reported studies were used to exclude small study bias when assessing literature quality. The fitness of multivariable meta-regression models and the likelihood of publication bias were assessed through funnel plots, Egger's asymmetry test (Egger et al. 1997) and Begg's rank correlation test (Begg and Mazumdar 1994). A statistical test of Begg's and Egger's significance was also used in order to determine whether there is a bias. The logarithm function of the effect size and standard error for the effect size was shown by a funnel plot. This is used to indicate the visual appearance of cross-study bias. An influence plot analysis was conducted to determine whether any of the study reports had a significant effect on the estimated effect size (Borenstein et al. 2009). Initially, across study bias was examined visually by a funnel plot, then Egger's regression analysis was used to test asymmetry existence of studies by testing the statistical significance of the across study bias (Egger et al. 1997). The Duval and Tweedie nonparametric 'fill and trim' linear random method was used to check unbiased estimates existence (Duval and Tweedie 2000).

Results

Literature search

About 83 reported articles were retrieved and sorted from various database sources. Twenty of the articles were excluded during the initial screening due to inappropriateness of abstract and title by manual tracing. Further, 63 articles were subjected to inclusion criteria. Among these, 27 articles were removed due to the presence of an unrepresentative sample, redundancy of reports and inadequate methodology. Inadequate methodology includes poor sampling strategy, data management and presentation of results. The remaining 36 articles were again tested for sample size and 9 articles were dropped due to small sample size where the studies were only based on molecular characterization. Thus, only 27 full-length studies which met the eligibility criteria for the systematic review and meta-analysis (Fig. 1) were incorporated into the analysis of the pooled prevalence of foot and mouth disease.

Study Characteristics

The details of the selected studies for the meta-analysis are described (Table 1). All of the retrieved studies were written in English. The 83 obtained research articles and MSc theses were examined to estimate FMD prevalence during the literature search period. However, about 56 reports were excluded due to unfitting abstract, title, study design and insufficient sample size, and were review articles. Likewise, reports were excluded for the absence of information on the required moderators. As a result, fewer studies have been included in meta-analysis in our datasets. Accordingly, only 27 full-length reports qualified the inclusion criteria. This systemic review and meta-analysis include articles that were studied between a period from 2007 and 2021. A total number of cattle involved in the studies and found diseases were 13,510 and 2,705, respectively. The sample size stretched from 126 to 1020 cattle (mean: 501; standard error [SE]: ± 62). The prevalence range of FMD occurrence reported in the literatures varied from 4.7 to 80% (mean: 24.8%; standard error [SE]: ± 18.2%) (Abunna et al. 2013; Gelana et al. 2016; Ahmed et al. 2020; Awel et al. 2021).

Geographical distribution of study locations

A total of 27 study locations were recognized to map the spatial distribution of the studies. A graphic depicting the distribution of studies in the country and their observed prevalence, which is based on a point size proportional to the prevalence, is found in Fig. 2. Of the studies conducted, most were spatially located in the western and southwestern parts of Ethiopia. Some states, namely Tigray, Oromia and SNNPR contain a high number of survey locations. However, other states, namely Afar, Benshangul and Somali regions had only a few disease surveys published. The average apparent prevalence of FMD ranged between regional states: Amhara 7.4%, Benishangul Gumuz 19.8%, Oromia 51.8%, Tigray 11.1% and SNNPR 11.1%. An overview of the identified survey districts with disease prevalence data is provided (Table 1).

The distribution of studies from 2007 to 2021 provides an indication of the temporal pattern of studies. It was found that there was a fairly uniform distribution of studies but substantial variation in prevalence (Fig. 2B).

Meta-analysis

A forest plot presenting the results from each study along with the pooled estimate is shown in Fig. 3. A random effects meta-analysis was computed using the reports of logit-transformed data. The random effects meta-analysis was chosen due to the expected variation among studies. Thus, the pooled prevalence of FMD in cattle was 21.39% (95% CI 16.53–26.56), with a separate study prevalence estimate ranging from 4.8 to 72.1%. The meta-analysis revealed between-study variation as moderate ($\tau^2 = 0.001$; heterogeneity $I^2 = 98\%$ with Heterogeneity chi-square = 1377.39, degree of freedom = 26 and a $P < 0.01$). The random effects of studies were weighted roughly the same as the fixed effects of studies, ranging between 0.9 and 7.3%.

Table 1 Study articles comprised in a meta-analysis of foot and mouth disease in cattle in Ethiopia

Author publication year	Year of study	Cases	Sample size	App	Study location	Part of country	Region
Abbuna et al. 2013	2011	79	986	0.801	Eastern Zone	Eastern Ethiopia	Dire Dawa
Ahmed et al. 2020	2019	155	384	0.404	West Shewa Zone	Central Ethiopia	Oromia
Awel et al. 2021	2020	276	383	0.72	Ada Berga	Central Ethiopia	Oromia
Bayissa et al. 2011	2011	177	768	0.23	Borena zone	Southern Ethiopia	Oromia
Belina et al. 2016	2015	69	634	0.108	Eastern Shewa	Central Ethiopia	Oromia
Beyene et al. 2015	2012	69	181	0.381	Asosa	Western Ethiopia	Beneshangul
Desissa et al. 2014	2012	82	384	0.214	Kellem Wollega Zone	Western Ethiopia	Oromia
Dubie and Negash 2021	2019	76	384	0.198	Zone one, Afar	Northern Ethiopia	Afar
Azeb, G/tensay 2015	2015	39	400	0.098	North and Eastern zone	Northern Ethiopia	Tigray
Gelana et al. 2016	2016	13	271	0.047	Wollega Zones	Central Ethiopia	Oromia
Gelaye et al. 2009	2008	33	273	0.121	Benchi Maji	Southern Ethiopia	South
Hordofa et al. 2018	2009	63	421	0.151	West Shewa	Central Ethiopia	Oromia
Jibril et al. 2013	2013	65	301	0.216	Bale Zone	Southern Ethiopia	Oromia
Megersa et al. 2009	2008	97	1020	0.095	Gamo Gofa	Southern Ethiopia	Southern
Mekonen et al. 2011	2008	113	460	0.246	Guji Zone	Southern Ethiopia	Oromia
Mesfine et al. 2019	2018	145	1009	0.144	Northern	Northern Ethiopia	Amhara
Mohamoud et al. 2011	2010	56	384	0.146	Jijiga zone	Eastern Ethiopia	Somalia
Molla et al. 2010	2009	63	770	0.081	South Omo	Southern Ethiopia	Southern
Rufael et al. 2008	2007	194	920	0.211	Borena zone	Southern Ethiopia	Oromia
Negusssie et al. 2010	2009	219	496	0.441	Addis Ababa, Oromia	Central Ethiopia	Oromia
Sulayeman et al. 2018	2016	139	574	0.242	East shewa	Central Ethiopia	Oromia
Taye et al. 2020	2016	71	340	0.209	Southern Tigray	Northern Ethiopia	Tigray
Tegegne et al. 2020	2019	76	384	0.198	Chifra	Eastern Ethiopia	Afar
Tesfaye et al. 2016	2015	155	363	0.427	Borena zone	Southern Ethiopia	Oromia
Urge et al. 2020	2019	62	126	0.292	Welmera district	Central Ethiopia	Oromia
Yahya et al. 2013	2009	59	504	0.117	Hararghe Zones	Eastern Ethiopia	Oromia
Zerabruk et al. 2014	2009	60	390	0.154	Central Tigray	Northern Ethiopia	Tigray

Subgroup meta-analysis

Subgroup analysis of covariates was run to obtain predictor level estimates, which were computed for valid predictors. Totally, nine covariates were considered in the analysis. Accordingly, the breed level pooled estimate of foot and mouth disease was 7.5% (95% CI 3.87–16.82) in local breed, while that of cross breed was 15.1% (95% CI 10.21–22.62). Likewise, the estimate for the young age group was 14.64% (95% CI 11.93–18.86) and that of adults was 19.52% (95% CI 14.46–25.81). For female animals, the estimate was 13.28% (95% CI 10.77–16.19), while for male animals, the estimate was 7.31% (95% CI 5.21–9.89). When the overall status of FMD is considered from a herd size perspective, there were 10.82%, 8.18% and 5.86% in large, medium and small herd sizes, respectively. Furthermore, the pooled estimates for cattle composition with other animals on the farm, not mixed, and mixed were 3.58% and 17.62%, respectively. Agro-ecology, movement history, grazing system, and production system were included in the analysis, and additional details on the estimates and related statistical significance are provided in Table 2.

Meta-regression models

Univariable meta-regression

Univariable meta-regression was employed for every moderator variable included separately in the analysis. Among the moderators considered in this analysis, system of production, sex of animal, age group, wildlife contact history and animal composition had statistically significant effects on the observed variability between the reports (Table 3). These moderators accounted for 31.06%, 14.59%, 28.74%, 18.64% and 12.1% of the heterogeneity, respectively.

Multivariable meta-regression

All the moderators with p-values less than 0.25 in the univariable analysis were analyzed in the subsequent multivariable meta-regression. In this case, the predictors considered were system of production, sex of animal,

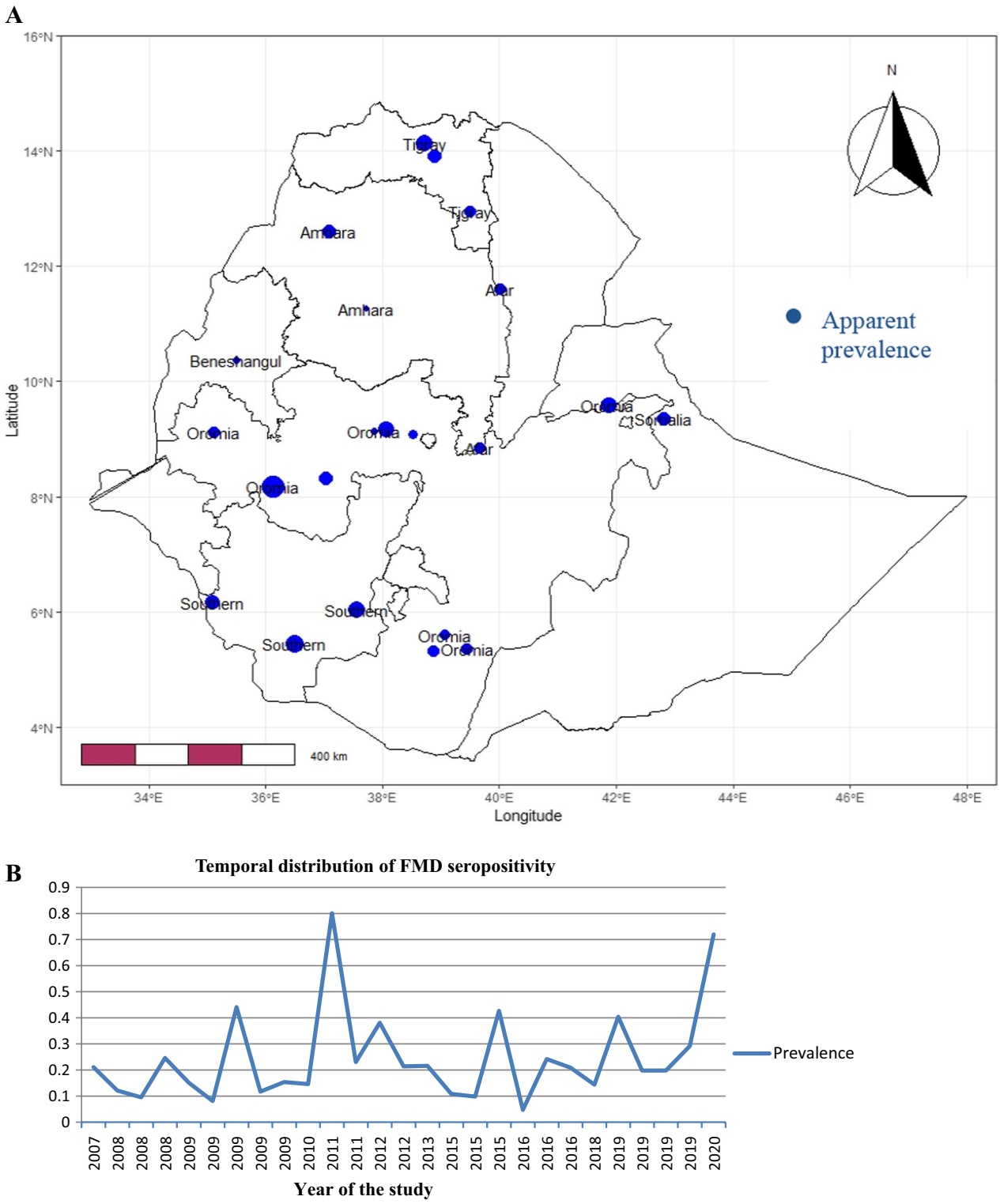

Fig. 2 **A** Shows the spatial distribution of studies from 2007 to 2021 across the country, Ethiopia. The prevalence was mapped using a point size proportional to the pooled prevalence, with data presented proportionally to allow for visual analysis. **B**: Shows the temporal distribution of studies from 2007 to 2021 across the country, Ethiopia

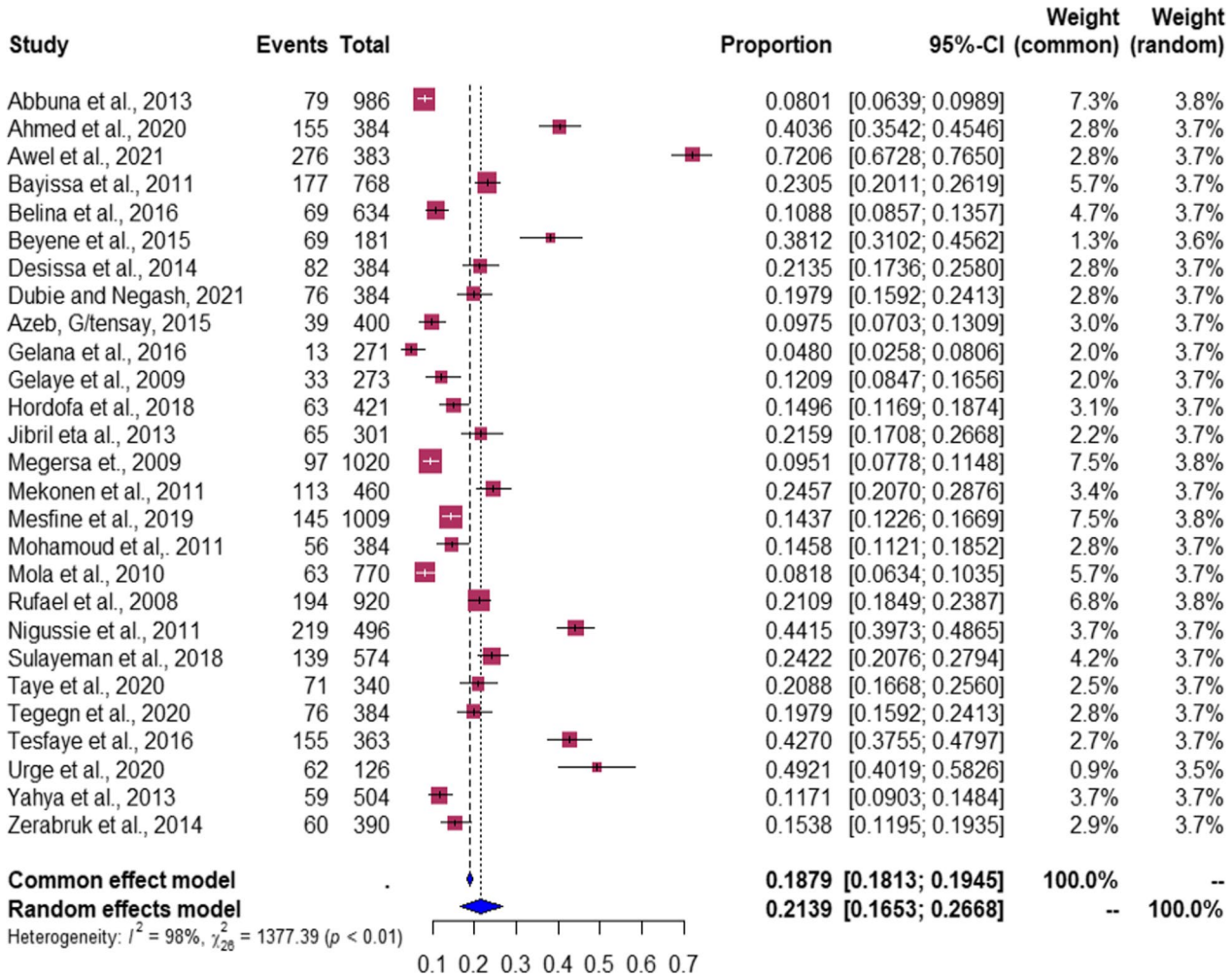

Fig. 3 Forest plot visualizing the varying FMD sero-prevalence reported for each included publication in the meta-analysis. Weightage given to each included publication by both Random Effects and Fixed Effect models have been shown for rigorous comparison. "Total" refers to the number of cattle in each publication, while "Events" refers to the number of FMD-seropositive cattle. "Proportion" reports the FMD prevalence for each publication

cattle breed, age group, wildlife contact history and animal composition (Table 4). Finally, system of production, sex of animal, age group, wildlife contact history and animal composition fitted to the final multivariable meta-regression model are statistically significant at ($P \leq 0.05$). Moreover, findings from the multivariable meta-regression are presented in Table 4.

The model explained 58.2% of the observed variability among the studied articles ($R^2 = 0.582$, τ^2unexplained = 1.032). The prevalence of foot and mouth disease was noted to be higher by 74% in the presence of wildlife contact as compared to no contact history with wildlife (Table 4). In the case of cattle mixed with other animals of the same age group, the prevalence can rise to 94% from the baseline of not mixed. Likewise, the odds of foot and mouth disease occurrence may increase 4.3 times in intensive compared to extensive production system, and it can increase 2.07 times in semi-intensive system as compared to extensive production. In fact, disease rates tend to increase in intensive production systems, but careful interpretation is necessary because of the small articles from such systems. Therefore, interpretation of the results must be cautious for moderators who have few reports.

Small study effect and publication bias assessment

According to the results of the analysis of effect sizes against their standard errors, there is a publication bias for the log transformed prevalence for foot and mouth disease, which indicates a bias (Fig. 4). The contour-enhanced

Table 2 Pooled prevalence estimates of foot and mouth disease, stratified by sub-groups

Predictors	Pooled Prevalence			Heterogeneity			Test for subgroup differences (RE model)	
	Sample size	Cases	Prevalence (95% CI) (RE model)	I^2 (%)	τ^2	*P* value	(Cochran's Q)	*P* value
Overall prevalence	13,510	2705	21.39 [16.53– 26.68]	98	-	< 0.01	-	-
Agro-ecology								
Highland	4173	329	7.85 [4.94 – 12.24]	99	0.57	< 0.01		
Midland	3501	302	10.82 [6.34 – 17.23]	97	0.57	< 0.01	2.83	0.240
Lowland	5435	640	13.25 [8.45 – 19.23]	97	0.57	< 0.01		
Herd size								
Large herd	3731	451	10.82 [7.42 – 13.82]	98	0.21	< 0.01		
Medium herd	3349	300	8.18 [6.55 – 11.97]	96	0.21	< 0.01	8.05	0.020
Small herd	3345	216	5.86 [4.89 – 7.27]	94	0.21	< 0.01		
Production system								
Extensive	12,246	1931	15.24 12.16 – 20.33]	96	0.54	< 0.01		
Semi-intensive	2476	239	12.85 [7.65 – 21.05]	97	0.54	< 0.01	2.18	0.340
Intensive	1579	405	22.06 [12.79 – 37.32]	96	0.54	< 0.01		
Grazing system								
Communal grazing	7250	1049	40.42 [37.86 – 43.02]	94	0.41	< 0.01	0.63	0.430
Separate grazing	3928	969	19.51 [10.33 – 29.85]	98	0.41	< 0.01		
Movement history								
No movement	6427	374	4.63 [1.51 – 14.58]	89	1.49	< 0.01	1.54	0.210
Yes movement	4172	580	11.50 [5.27 – 22.28]	97	1.49	< 0.01		
Animal composition								
Mixed	4971	391	17.62 [9.28 – 29.23]	98	1.08	< 0.01	6.55	0.010
Not mixed	3867	218	3.58 [1.82 – 10.31]	98	1.08	< 0.01		
Cattle breed								
Cross	3268	523	7.54 [3.87 – 16.82]	99	1.37	< 0.01	2.69	0.100
Local	12,336	2024	15.1 [10.21 – 22.6]	99	1.37	< 0.01		
Age group of cattle								
> 3 years age	11,746	1781	19.52 [14.46 – 25.81]	97	0.49	< 0.01	35.6	< 0.01
≤ 3 years age	10,102	513	14.64 [11.93 – 18.86]	95	0.49	< 0.01		
Sex								
Female	10,329	1499	13.28 [10.77 – 16.19]	98	0.32	< 0.01	14.16	< 0.01
Male	11,249	890	7.31 [5.21 – 9.89]	96	0.32	< 0.01		

funnel plot is also used to examine how asymmetry patterns relate to statistical significance (Figs. 4A and 5). The Begg's and Egger's test, applied to the assessment of small study effects, showed small study bias ($P=0.074$ and $P=0.002$, respectively). Furthermore, there was evidence of missing studies that could be amalgamated by Duval and Tweedie's trim and fill method where they may fall on a funnel plot and visualize them in an effort to upturn the plot's symmetry (Fig. 4B).

Discussion

This is the first meta-analysis of pooled estimates of foot and mouth diseases in Ethiopia to our knowledge. In this meta-analysis, the data were collected from systematically reviewed publications and master's theses available in university repositories from 2007 to 2021. The review process was restricted to cattle of bifid ruminants to curtail heterogeneity between studies. This, on the other hand, limited the number of studies conducted on these animals. Almost 56 studies were excluded due to unfitting study designs, and inadequate sample size. Moreover, studies with analogous diagnostic techniques were included and the study design was selected to reduce variability. Furthermore, the absence of essential variables on articles and other moderators significantly reduced the number of studies included in the final meta-analysis. Therefore, the final systematic review and meta-analysis were conducted using only 27 studies.

Table 3 Univariable meta-regression on prevalence of Foot and Mouse Disease in Ethiopia

Predictors	Category	N	Odds ratio	95% CI	*P* value	R^2 (%)
Production system	Extensive	23	Ref.			
	Semi-intensive	5	3.01	1.43–6.32	0.0034	31.06
	Intensive	4	4.35	1.93–9.82	0.0004	
Breed of cattle	Local	25	Ref.			
	Cross	8	2.27	0.85–6.03	0.1008	0.00
Sex of animal	Male	23	Ref.			
	Female	22	2.07	1.19–3.61	0.0101	14.59
Herd size	Small	8	Ref.			
	Medium	8	1.52	0.21–1.32	0.6478	0.39
	Large	9	1.81	0.32–2.05	0.1677	
Age group	≤ 3 years	21	Ref.			
	> 3 years	24	3.77	2.12–6.68	0.0001	28.74
Grazing type	Separate	9	Ref			
	Communal	23	1.72	0.31–1.63	0.4286	0.00
Agro-ecology	Highland	8	Ref.			
	Midland	11	0.67	0.13–3.32	0.6210	0.00
	Lowland	6	0.86	0.22–3.39	0.8339	
Wildlife contact	No	15	Ref.			
	Yes	12	1.57	1.17–3.19	0.0227	18.64
Movement status	No history	13	Ref.			
	Had history	9	1.48	0.55–3.95	0.4389	3.68
Animal composition	Not mixed	13	Ref.			
	Mingled	14	1.86	1.28–2.73	0.0467	9.56

R^2: Amount of heterogeneity accounted for the observed variation

Based on the index of inverse variance ($I^2 = 98\%$), there was a significant level of true heterogeneity between reports. The detected variance is due to real differences between reports, and is used to explain the sources of variability and heterogeneity in the meta-regression analysis on the study-level variables, that is studied regions, production systems, herd size, breed, age category, herd composition, movement, and sex of cattle. The subsequent subgroup analysis on production system showed the prevalence varied considerably among production systems and estimates ranged from 12.8% in semi-intensive to 22.1% in intensive production; however, the variation was not statistically significant. Likewise, subgroup analysis on herd size showed statistically significant variation ($Q = 8.05$, $P = 0.02$) among herd size for prevalence estimates ranging from 5.86% in small herd size to 10.8% in large herds.

Table 4 Multivariable meta-regression on the prevalence of foot and mouth disease in Ethiopia

Predictors	Category	N	Odds ratio	95% CI	*P* value
Production system	Extensive	23	Ref.		
	Semi-intensive	5	2.07	1.48–4.38	0.0030
	Intensive	4	4.31	2.02–9.84	0.0000
Calf breed	Local	25	Ref.		
	Cross	8	2.44	1.73–7.43	0.1208
Sex of animal	Male	23	Ref.		
	Female	22	2.12	1.52–3.83	0.0090
Age group	≤ 3 years	21	Ref.		
	> 3 years	24	3.72	2.45–6.96	0.0003
Wildlife contact	No	15	Ref.		
	Yes	12	1.74	1.63–3.68	0.0300
Animal composition	Not mixed	13	Ref.		
	Mingled	14	1.94	1.42–2.92	0.0400

The pooled prevalence estimate of foot and mouth disease in cattle was 21.39% (95% CI 16.53—26.56), which is higher than a study conducted by Ayelet et al. (2012) to build epidemiological profile of the endemic occurrence of FMD in Ethiopia, which was estimated 10.5% of cattle in various regions have FMD. Most of the time, it is difficult for us to compare the present study estimates with reports from single studies that used almost similar farming systems. The observed pooled prevalence of FMD is extremely dangerous because it affects live animals, products, and their by-products since FMD is a transboundary and list A disease. As FMD is a forerunner disease,

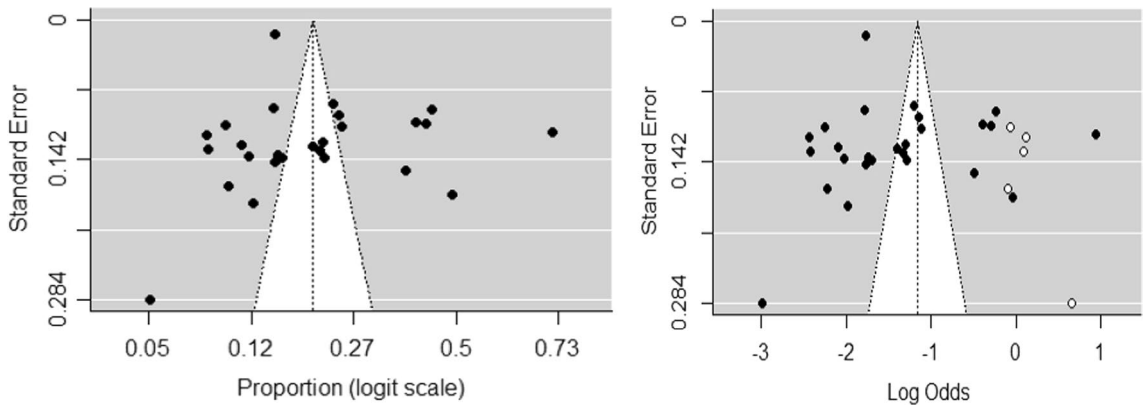

Fig. 4 Funnel (right-A) and missed study funnel plot (left-B) of the logit-prevalence of FMD in cattle in Ethiopia. It shows the number of studies missing from a meta-analysis due to the suppression of the most extreme results on one side of the funnel plot; it augments the observed data, so the funnel plot is more symmetric (white circle are augmented data)

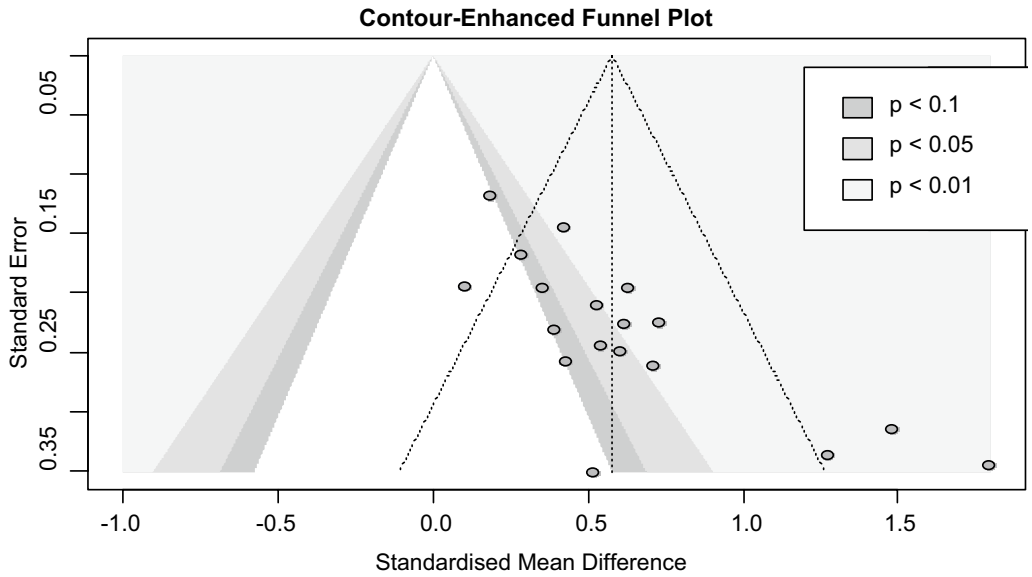

Fig. 5 Contour-enhanced figure plot showing the study bias and asymmetry of reports. The figure displays each study's estimated effect plotted against its SE and evaluates the relationship between study results and their precision (dot line plotted funnel plot)

it can severely affect trade worldwide. This is because it can threaten the livelihood of producers as well as the national economy derived from the livestock sector as a whole (Rufael et al. 2008).

Ethiopia is one of the countries in east Africa where foot and mouth disease is endemic, affected by five different serotypes (Mekonen et al. 2011; Dubie and Amare 2020; Dubie and Negash 2021). The research outputs reported by (Ayelet et al. 2009; Jemberu et al. 2016) in the country on FMD virus serotypes disclosed that aggregate existence is due to serotypes of O, A, C, SAT-2, and SAT-1, which have been diagnosed serologically and molecular methods during the period between 1981 and 2018. Based on our meta-analysis, we estimated a high prevalence of the disease nationwide, which calls for control and eradication measures. Pooled estimates of FMD reported in the current study are within the range of 5.6 to 42.7% (Abdela 2017). However, in most cases, it is not advisable to compare the pooled estimates with the reports from single studies even if they have an almost similar farming system. Similarly, the scarcity of nationwide survey reports also makes comparisons of our results difficult. Overall, this finding shows that FMD poses a serious threat in various regions of the country. This threat results in substantial economic losses due to the restriction of international trade, morbidity and mortality.

In subgroup analysis, some of moderators included in the study had a statistically significant effect on the prevalence of FMD. The prevalence of FMD in cattle at early age (ages less than and equal to three years) and adult (ages above three years) was 14.6% and 19.5%, respectively ($P < 0.01$). The low prevalence was observed among immature age groups due to fostering young animals separately from adults around the homestead. The statistical significance difference between age groups revealed the highest prevalence among cattle older than three years (19.5%), supporting the notion that with age, the chances of exposure to the disease increase (Lyons et al. 2014; Thrusfield et al. 2018). This is in line with the report of (Gelaye et al. 2009; Abunna et al. 2013; OIE 2021). The higher sero-prevalence of FMD in adult animals is likely due to the long lasting immunity caused by FMDV infection and carrier state (persistence of the virus) that lasts for years. The analysis also revealed an association between sex and pooled estimates of FMD in cattle with higher estimates among females (13.3%) than males (7.3%). The reason for the high prevalence of FMD in females compared to males is due to the fact that female cattle are kept for prolonged periods of time for breeding, where they are more likely to be FMD sero-prevalence than males.

Since the records reported deploying different agro-ecologies and systems of production that may include a variety of study populations from various areas in Ethiopia which are prone to variation between reports. The meta-regression on production system using extensive production as a reference revealed that FMD occurrences were 4.3 times higher in intensive production (Table 4). Intensive production may be associated with an increased occurrence of disease because of the close contact between animals in confined environments. This is because of the high rate of spreading of FMD virus particles through secretions since feeding and drinking points are neighboring or adjacent. Furthermore, the estimate observed in this analysis is in line with results reported by (Abunna et al. 2013) but greater than some reports (Jemberu et al. 2014; Azeb 2015).

This study provides the pooled estimate of foot and mouth disease prevalence in cattle; but it had limitations due to heterogeneity between reports and was limited to only 27 studies. This is supported by the funnel plot and Begg's and Egger's test statistics for possible publication bias and small studies. This indicates that there was likely evidence or a limitation in the study reporting prevalence. This might be a conservative estimate, which excludes workshop proceedings, unpublished studies, and unsuitable dissertations. As part of this research article, all undergraduate dissertations and theses from various academic institutions were excluded to avoid redundancy and less qualified works. Further, studies that were conducted for molecular characterization were excluded due to sample size limitations. The infectious nature of the FMD virus resulted in variance inflation and may also be a reason for the asymmetrical funnel plot observed and the strong skewness of the plot to its right (Fig. 4A). This study's limitations advocate balancing a wide range of studies with inclusion and exclusion criteria. This enabled us to present a more reliable sero-prevalence estimate of foot and mouth disease in Ethiopia that includes relevant studies.

Conclusions

This study has presented high estimates of prevalence of foot and mouth disease in Ethiopian cattle. This pooled prevalence estimate is considered dangerous since foot and mouth disease is transboundary and category A disease which affects the export of live animals and animal products. The subgroup analysis for herd size, animal composition, age group and sex of cattle identified as a potential statistically significant factors for foot and mouth disease in Ethiopia. Government and producers must therefore devise regular vaccination and management programs to control the pooled estimates and other moderators that predispose to highly contagious viruses. The existence of FMD is an effective barrier to accessing markets. This is because it is a significant determinant of international trade in livestock products. Since the disease is endemic in the country, there must be a prompt vaccination campaign with prevention alternatives, a steadfast control policy, and an aggressive eradication campaign.

Abbreviations

CI	Confidence interval
CSA	Central Statistical Authority
ELISA	Enzyme-linked immunosorbent assay
FMD	Foot and mouth disease
SAT	Southern African Territories
SNNPR	Southern Nation Nationalities Peoples Region

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Author contributions

ET and WS were participated in the study design, data collection and analysis, write up and proof reading of the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials

All data generated and analyzed during this study are included in this article [and its Additional file will be submitted upon request].

Declarations

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Competing interests
The authors declare that they have no conflict interests.

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