



REVIEW ARTICLE

Global Prevalence of Swine Foot-And-Mouth Disease Virus: A Systematic Review and Meta-Analysis

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ABSTRACT

Foot-and-mouth disease (FMD) is an acute, febrile, highly contagious animal disease caused by the foot-and-mouth disease virus (FMDV), which affects pigs, cattle and sheep. The overall infection rate and risk factors of FMDV in pigs around the world were meta-analyzed. A comprehensive search was conducted on Ovid Technologies (Ovid), CNKI, Wanfang, Embase, VIP Chinese Journal Database (VIP), Web of Science and other databases to search for relevant studies published so far. A random effects model was used to calculate combined seropositivity estimates with 95% confidence intervals (ci) and data from 15 countries and regions around the world were analyzed. The results showed that the total positive rate of swine FMDV was 4.17%. Among continents, Europe has the highest infection rate and Asia the lowest. The infection rate of boars was higher than that of sows. In the analysis of climate subgroups, the infection rate of countries and regions with tropical monsoon climate, it was the highest (55.15%). In the subgroup analysis of sampling time, the overall trend was downward. In the subgroup analysis of aquaculture management, the infection rate of free-range aquaculture (13.58%) was the highest. There are still many foot-and-mouth disease areas around the world. While protecting animal welfare, we should pay more attention to timely immunization of pig herds according to the immunization plan, promote the transition from free range to intensive farming, strengthen disinfection and cleaning work, reduce the incidence of foot-and-mouth disease and create more foot-and-mouth disease-free areas.

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INTRODUCTION

Foot-and-mouth disease (FMD) is a highly virulent contagious disease for livestock and wild cloven-hoofed animals and is seriously dangerous to animal husbandry production, causing significant economic losses around the world (Zhang *et al.*, 2024). The disease can spread rapidly over long distances and infects major livestock species such as pigs, cattle, sheep and other even-toed ungulates, with more than 70 susceptible species (Alexandersen and Mowat, 2005; Zai-xin, 2015). Foot and mouth disease virus belongs to the small RNA virus family (Picornaviridae) foot and mouth disease virus genus (Aphthovirus), is the first animal virus discovered by humans (Clemmons, *et al.*, 2021). Foot and mouth disease virus (FMDV) consists of a single-stranded, positive-stranded RNA genome of approximately 8,500 bases surrounded by four structural

proteins forming an icosahedral capsid (Zhengxin Yang, 2024) with a diameter of approximately 25-30 nm (Domingo *et al.*, 2002) and has seven O, A, C, Asia1, and SAT1, SAT2, and SAT3 serotypes (Li *et al.*, 2021), there is no cross-immunity between serotypes, but cross-immunity varies between subtypes within the same type, and complete cross-immunity cannot be guaranteed for all. FMDV infection causes vesicular lesions in the mouth, feet, and mammary glands, as well as severe systemic symptoms such as fever, salivation, and lameness (Kabir *et al.*, 2024). FMD is considered to be the most important constraint to international trade in animals and animal products due to its huge impact on the farming industry (Leforban, 1999). FMD epidemics affect the international trade of live animals and animal products in countries where FMD exists, it is still one of the important animal disease pathogens of economic concern (Brown *et al.*,

2021; Rodríguez-Habibe *et al.*, 2020). The International Organization for Animal Health (OIE) lists this disease at the top of the list of legally reported infectious diseases of animals, and it is one of the diseases that must be examined for international trade in live animals and animal products (Zai-xin, 2015). At present, most countries and regions of the world pay great attention to the prevention of FMD, and its main preventive means is the injection of FMD vaccine, but there are still some areas where FMD epidemics occur, which can cause great losses to people's production and life, so it is necessary to carry out a META analysis of the positive rate of pigs infected with FMDV in the world. Therefore, the present study was conducted to determine the FMDV positivity rate in pigs worldwide through systematic review and meta-analysis, and to assess the potential risk factors (sex, breed, age, geographic location, and climatic factors, etc.) for FMDV infection in pigs in some countries of the world.

MATERIALS AND METHODS

Establishment of the search formula: The meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher *et al.*, 2009). Literature related to foot-and-mouth disease published since the emergence of the disease. The databases searched included OVID, Embase, Web of Science, Chongqing VIP, CNKI and Wanfang. The final search formula was "TS = (foot-and-mouth disease or Foot and Mouth Disease or Foot-and-Mouth Diseases) AND TS = (pig or swine or Swine or Warthogs or Wart Hogs or Wart Hog or Phacochoerus)." We searched for articles using the keywords "pig" and "foot-and-mouth disease" simultaneously in OVID and Embase. In the Chinese databases, we used the corresponding Chinese words for retrieval: in CNKI and Wanfang databases, the subject terms were "pig," "prevalence," and "foot-and-mouth disease," while in the VIP database, the subject terms were "pig," "prevalence," and "foot-and-mouth disease." Endnote (X9.3.1; Clarivate, Philadelphia, PA, USA) was used to organize the information of the included literature.

Data extraction: Based on the title and abstract, a preliminary selection of the retrieved articles was made. Then, the articles were screened according to the following selection criteria: (1) the research purpose must be to investigate the positive rate of the FMDV in pigs; (2) the data must reflect the total sample size and the number of positive samples; (3) the study must be designed as a cross-sectional study; (4) articles published from the start of the literature search onwards must be included; (5) each sample must come from a single pig (not a mixed sample); (6) literature types such as reviews and pathological reports must be excluded.

We used standardized data collection methods to extract data, recording the following information: publication year, sampling year, first author, detection method, type of pig, feeding method, publication year, collection season, detailed geographical and climatic information, total sample size, number of positive samples, and the GDP of the sampling area for that year. Our database was created using Microsoft Excel (version 2409; Microsoft, Redmond, WA, USA).

Quality assessment: This analysis uses the quality assessment checklist by (Ding *et al.*, 2017) to evaluate the risk of bias in the included articles. The items examined were as follows: (1) was the research objective clearly described and stated? (2) was the period and location of the study clearly stated? (3) was the sample categorized into different species or orders? (4) was the sampling method described in detail? (5) was the diagnostic technique and procedure clearly pointed out? Scoring the item was based on a simple scale system ("2" for yes, "0" for no, or "1" for unsure). Therefore, a possible total score for each study ranged from 0 to 10.

Statistical analysis: We used the "meta" package in STATA software (version 17.0) for this analysis and to estimate the model. The Cochran's Q statistic was calculated to test for heterogeneity. An effect model was chosen based on the degree of heterogeneity of the retrieved studies. Correlation analysis was conducted for each group based on publication year to trace the sources of heterogeneity. The results of the overall meta-analysis are presented using a Forest plot. We chose a random effects model because of the heterogeneity in the selected articles.

In addition, we used the symmetry of the funnel plot to determine the bias in the included studies. The Egger test was employed to estimate whether there was publication bias in the included articles. We also used sensitivity analysis to assess the stability of our study. Subgroup analysis was conducted to further evaluate the possible sources of heterogeneity.

RESULTS

Search results and eligible studies: A total of 6,644 published studies were collected by searching 6 databases and relevant research references. Based on the inclusion and exclusion criteria, 27 studies were used for the meta-analysis (Fig. 1), and two additional papers were included through the snowball method. In total, there were 29 papers, 6 of which were of high quality (10 points), 20 papers were of medium quality (6 or 8 points), and the last 3 papers were of low quality (4 points)

Pooling and heterogeneity analysis: The research analyzed data from four continents, 15 countries and regions (Table 1 and Fig. 3). In the selected studies, the forest plot shows the detection rate of FMDV in pigs worldwide. In the subgroup analysis, due to the high level of heterogeneity in most subgroups, a random effects model was used to calculate the overall seroprevalence estimates for each subgroup (Fig. 2 and Table 2).

The positive rates of virus detection vary by country, with Europe having the highest rate (35.67%) and Asia the lowest (2.87%), while North America (11.32%) and Africa (14.42%) fall in between. Among the countries and regions, Vietnam has the highest positive rate for FMDV infection (92.86%), while South Korea has the lowest (0.85%). The infection rates for other countries and regions are as follows: Taiwan (3.98%), Ethiopia (2.33%), India (3.44%), South Africa (4.00%), Nigeria (17.37%), Canada (11.32%), China (5.18%), the UK (30.68%), Bhutan (6.83%), Kenya (51.71%), Israel (54.17%), and Malta (50.67%).

Table 1: Eligible cross sectional studies estimating FMDV in swine in Global.

Author(year)	No.tested	No.positive	Score	Prevalence
Woldemariam Fanos Tadesse(a) (2021)	426	9	10	0.0211268
Woldemariam Fanos Tadesse(b) (2021)	268	5	10	0.0186567
Woldemariam Fanos Tadesse(c) (2021)	158	4	10	0.0253165
Woldemariam Fanos Tadesse(d) (2021)	179	6	10	0.0335196
Dukpa, K.(a) (2011)	482	9	8	0.0186722
Dukpa, K.(b) (2011)	1143	73	8	0.063867
Dukpa, K. (2011)	117	37	8	0.3162393
Wee, S. H. (2008)	62232	523	8	0.008404
Park, J. H. (2013)	41	7	8	0.1707317
Sellers, R. F. (1990)	106	12	4	0.1132075
Wekesa Sabenzia N (2014)	191	101	8	0.5287958
Park, J. H.(a) (2014)	14	5	10	0.3571429
Siengsanam Lamont Jarunee (2021)	597	8	8	0.0134003
Sellers, R. F.(a) (1981)	309	21	6	0.0679612
Sellers, R. F.(b) (1981)	585	432	6	0.7384615
Neiffer, D. (2021)	100	4	8	0.04
Fakai, L. U.(a) (2015)	117	19	10	0.1623932
Fakai, L. U.(b) (2015)	133	26	10	0.1954887
Fakai, L. U.(c) (2015)	137	29	10	0.2116788
Fakai, L. U.(d) (2015)	113	16	10	0.1415929
Comfort O. Aiki-Raji(a) (2016)	127	52	10	0.4094488
Comfort O. Aiki-Raji(b) (2016)	237	116	10	0.4894515
Olufemi, O. T.(a) (2020)	163	8	8	0.0490798
Olufemi, O. T.(b) (2020)	110	9	8	0.0818182
Olufemi, O. T.(c) (2020)	286	19	8	0.0664336
Olufemi, O. T.(d) (2020)	173	12	8	0.0693642
Olufemi, O. T.(e) (2020)	175	8	8	0.0457143
Ehud eInekave(a) (2016)	24	13	8	0.5416667
Rout, M. (2017)	262	9	8	0.0343511
Sellers, R. F. (1973)	1944	285	4	0.1466049
Alexandersen, S. (2003)	734	537	6	0.7316076
Wilesmith, J. W.(a) (2003)	11	3	4	0.2727273
Vu Le T (2017)	378	351	8	0.9285714
Xv,Yang (a) (2016)	6949	228	6	0.0328105
Xv,Yang (b) (2016)	5944	76	6	0.012786
Xv,Yang (c) (2016)	7920	751	6	0.0948232
Li ,jin(a) (2017)	265	6	6	0.0226415
Li ,jin (b) (2017)	240	6	6	0.025
Yuan Cuixia (a) (2017)	250	12	10	0.048
Yuan Cuixia (b) (2017)	250	19	10	0.076
Lv, Qizhuang (2018)	389	102	8	0.2622108
Wu, Bo(a) (2018)	121	11	8	0.0909091
Wu, Bo(b) (2018)	87	6	8	0.0689655
Wu, Bo(c) (2018)	91	5	8	0.0549451
Wu, Bo(d) (2018)	69	9	8	0.1304348
Wu, Bo(e) (2018)	368	25	8	0.0679348
Hou Huili (2018)	90	38	6	0.4222222
Dou Siyuan (2014)	3076	118	8	0.0383615
Wang Hui (2018)	1352	10	8	0.0073964
Chung, W. B.(a) (2013)	5161	277	10	0.0536718
Chung, W. B.(b) (2013)	5061	241	10	0.047619
Chung, W. B.(c) (2013)	4521	137	10	0.030303
Chung, W. B.(d) (2013)	4551	113	10	0.0248297

Possible risk factors (gender, age, continent, country, climatic conditions, sampling season, detection methods, sampling year, management practices, type of virus infection) were further explored, and subgroup analyses were conducted. The results indicate that management practices, sampling year, climatic conditions, and pig production classification are risk factors.

The farming method of intensive management in farms (5.71%) has a lower infection rate of FMDV compared to free-range farming (13.58%). In the 20th century, the highest positive rate detected during the sampling period from January 1971 to December 1980 was 50.67%. In the 21st century, the highest infection rate detected during the

sampling period from January 2006 to December 2010 was 12.18%. The climatic conditions with the lowest positive rate are temperate monsoon climates (0.85%), while the three climatic types with higher positive rates are subtropical Mediterranean climate (50.67%), Mediterranean climate (54.17%) and tropical monsoon climate (55.15%). Among pig production classifications, the highest infection rate is found in fattening pigs (13.39%).

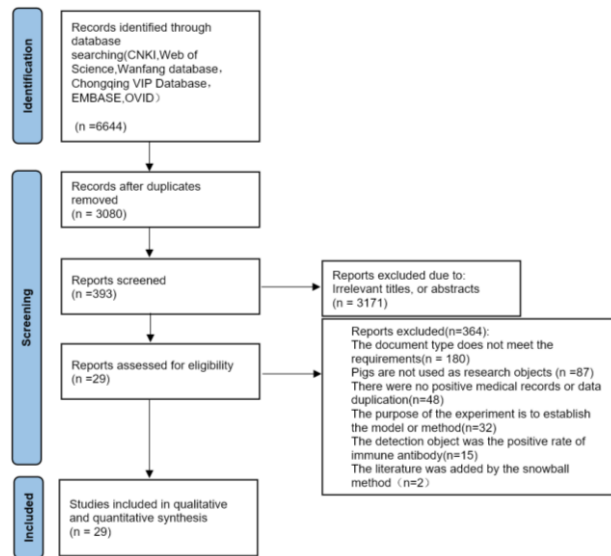


Fig. 1: Screening process for eligible articles.

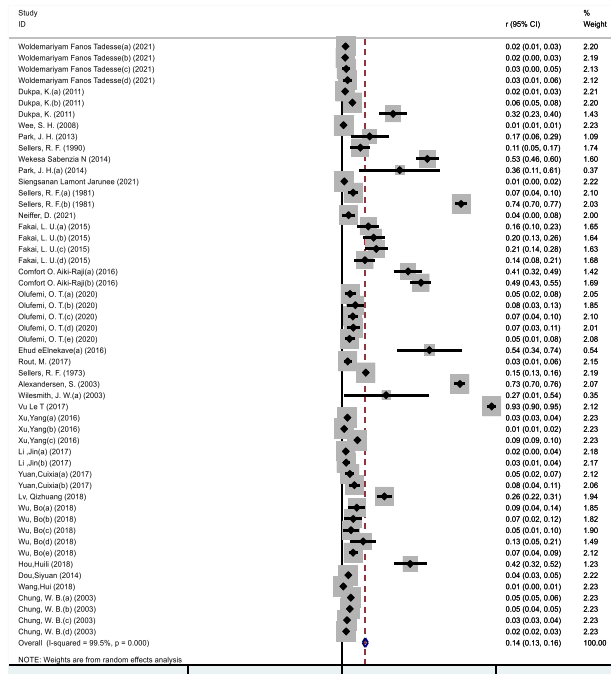


Fig. 2: Forest plot of the seroprevalence of FMDV in pigs worldwide.



Fig. 3: Global Map of FMDV positive rate in pigs.

Table 2: Pooled seroprevalence of FMDV infection in pigs worldwide according to several risk

Risk factor (number of studies)	Positive Rate (%)	No. tested	No. positive	r(95%CI)	P	I ² (%)
Variety				0.13(0.13,0.16)	0.000	99.50
Piglet (1)	6.80	309	21	0.07(0.04,0.10)	0.000	
Fattening pig (6)	13.39	9157	1226	0.19(0.02,0.36)	0.025	
Nursery pig (5)	2.68	13443	360	0.05(0.03,0.07)	0.000	
Gender				0.09(0.07,0.12)	0.000	97.70
Sow (7)	4.59	19932	915	0.08(0.06,0.10)	0.000	
Boar (3)	18.66	402	75	0.2(-0.01,0.40)	0.065	
Continent				0.14(0.13,0.16)	0.000	99.50
Europe (5)	35.67	3583	1278	0.39(0.09,0.69)	0.010	
North America (1)	11.32	106	12	0.11(0.05,0.17)	0.000	
Asia (29)	2.87	112031	3220	0.10(0.08,0.12)	0.000	
Africa (18)	14.42	3107	448	0.15(0.10,0.19)	0.000	
Country				0.14(0.13,0.16)	0.000	99.50
Korea (2)	0.85	62273	530	0.08(-0.08,0.24)	0.327	
Laos (1)	1.34	597	8	0.01(0.00,0.02)	0.004	
Ethiopia (4)	2.33	1031	24	0.02(0.01,0.03)	0.000	
India (1)	3.44	262	9	0.03(0.01,0.06)	0.002	
Taiwan, China (4)	3.98	19294	768	0.04(0.03,0.05)	0.000	
The Republic of South Africa (1)	4.00	100	4	0.04(0.00,0.08)	0.041	
China (16)	5.18	27461	1422	0.07(0.05,0.09)	0.000	
The Kingdom of Bhutan (3)	6.83	1742	119	0.11(0.04,0.17)	0.001	
Canada (1)	11.32	106	12	0.11(0.05,0.17)	0.000	
Nigeria (11)	17.73	1771	314	0.17(0.10,0.24)	0.000	
Britain (3)	30.68	2689	825	0.39(-0.08,0.36)	0.108	
Malta (2)	50.67	894	453	0.4(-0.25,1.06)	0.229	
Kenya (2)	51.71	205	106	0.49(0.34,0.63)	0.000	
Israel (1)	54.17	24	13	0.54(0.34,0.74)	0.000	
Vietnam (1)	92.86	378	351	0.93(0.90,0.95)	0.000	
Climate				0.14(0.13,0.16)	0.000	99.50
Monsoon climate of medium latitudes (2)	0.85	62273	530	0.08(-0.08,0.24)	0.327	
Temperate highland climate (4)	2.33	1031	24	0.02(0.01,0.03)	0.000	
Plateau continental climate (2)	2.38	505	12	0.02(0.01,0.04)	0.000	
Tropical, subtropical monsoon climate (5)	3.90	19891	776	0.03(0.02,0.05)	0.000	
Temperate continental climate (2)	4.09	3182	130	0.07(-0.00,0.14)	0.059	
Subtropical monsoon climate (12)	5.27	23790	1254	0.07(0.05,0.09)	0.000	
Subtropical climate (3)	6.83	1742	119	0.11(0.04,0.17)	0.001	
Savanna climate (12)	17.00	1871	318	0.16(0.10,0.22)	0.000	
Temperate maritime climate (3)	30.68	2689	825	0.39(-0.08,0.86)	0.108	
Continental monsoon climate (1)	42.22	90	38	0.42(0.32,0.52)	0.000	
Subtropical Mediterranean climate (2)	50.67	894	453	0.4(-0.25,1.06)	0.229	
Mediterranean climate (1)	54.17	24	13	0.54(0.34,0.74)	0.000	
Tropical monsoon climate (4)	55.15	845	466	0.46(-0.11,1.04)	0.114	
Season				0.17(0.15,0.20)	0.000	99.70
Summer (3)	1.10	62596	691	0.3(-0.06,0.67)	0.105	
Summer, Autumn (1)	1.28	5944	76	0.01(0.01,0.02)	0.000	
Spring (5)	4.96	21238	1053	0.06(0.04,0.08)	0.000	
Spring, summer (2)	6.20	500	31	0.06(0.03,0.09)	0.000	
Winter, spring (2)	6.58	14869	979	0.06(0.00,0.12)	0.040	
Annual (6)	10.15	1005	102	0.12(0.06,0.18)	0.000	
Autumn, winter and spring (1)	11.32	106	12	0.11(0.05,0.17)	0.000	
Autumn (1)	27.27	11	3	0.27(0.01,0.54)	0.042	
Winter (2)	70.19	775	544	0.45(-0.10,1.00)	0.105	
Spring, summer and autumn (1)	92.86	378	351	0.93(0.90,0.95)	0.000	
Detection method				0.15(0.13,0.18)	0.000	99.50
Clinical examination (4)	25.48	2944	750	0.27(-0.00,0.54)	0.054	
ELISA (38)	3.17	92804	2943	0.14(0.12,0.16)	0.000	
RT-PCR (2)	26.55	403	107	0.27(0.22,0.31)	0.000	
Immunochromatography (4)	18.00	500	90	0.18(0.14,0.21)	0.000	
PCR/RT-PCR (1)	0.74	1352	10	0.01(0.00,0.01)	0.002	
Sampling year				0.14(0.13,0.16)	0.000	99.50
1950.1-1970.12 (2)	14.49	2050	297	0.14(0.12,0.16)	0.000	
1971.1-1980.12 (2)	50.67	894	453	0.4(-0.25,1.06)	0.229	
2000.1-2005.12 (7)	2.23	82271	1831	0.14(0.10,0.18)	0.000	
2006.1-2010.12 (7)	12.18	2012	245	0.25(0.17,0.34)	0.000	
2011.1-2015.12 (13)	7.38	22822	1685	0.21(0.15,0.27)	0.000	
2016.1-2020.12 (19)	7.41	4250	315	0.07(0.05,0.10)	0.000	
1999.1-2016.12 (1)	4.00	100	4	0.04(0.00,0.08)	0.041	
2009.1-2012.12 (1)	3.84	3076	118	0.04(0.03,0.05)	0.000	
2013.1-2017.12 (1)	0.74	1352	10	0.01(0.00,0.01)	0.002	
Culture method				0.13(0.11,0.15)	0.000	99.20
Farm (27)	5.71	27392	1564	0.13(0.10,0.15)	0.000	
Slaughterhouse (9)	8.50	20847	1771	0.14(0.08,0.21)	0.000	
Wild animal (1)	0.74	1352	10	0.54(0.34,0.74)	0.000	
Farm, free range (2)	4.93	3166	156	0.15(-0.07,0.37)	0.182	

Free-ranging (2)	13.58	2253	306	0.05(0.03,0.08)	0.000
Virus type				0.2(0.15,0.25)	0.000
O (17)	8.51	23186	1974	0.21(0.16,0.27)	0.000
O、A、Asia1 (1)	1.34	597	8	0.01(0.00,0.02)	0.004

Table 3: Sensitivity analysis to evaluate the robust of the result estimates.

Study omitted	Estimate	[95% Conf. Interval]	
Woldemariam Fanos Tadesse(a) (2021)	0.14622279	0.12912996	0.16331563
Woldemariam Fanos Tadesse(b) (2021)	0.14623037	0.12916105	0.1632997
Woldemariam Fanos Tadesse(c) (2021)	0.14596853	0.12893584	0.16300121
Woldemariam Fanos Tadesse(d) (2021)	0.14576648	0.12873935	0.16279361
Dukpa, K.(a) (2011)	0.14631797	0.1292022	0.16343373
Dukpa, K.(b) (2011)	0.14520608	0.12815172	0.16226043
Dukpa, K. (2011)	0.14080895	0.12389315	0.15772476
Wee, S. H. (2008)	0.15202872	0.12987652	0.17418092
Park, J. H. (2013)	0.14305582	0.12614052	0.15997113
Sellers, R. F. (1990)	0.14389102	0.12691925	0.16086229
Wekesa Sabenzia N (2014)	0.13691427	0.1200912	0.15373734
Park, J. H.(a) (2014)	0.14255401	0.1257006	0.15940742
Siengsan Lamont Jarunee (2021)	0.14655263	0.12936226	0.163743
Sellers, R. F.(a) (1981)	0.14499482	0.12797985	0.16200979
Sellers, R. F.(b) (1981)	0.12925565	0.11339858	0.14511273
Neiffer, D. (2021)	0.14548536	0.12847923	0.16249149
Fakai, L. U.(a) (2015)	0.14302952	0.12607221	0.15998683
Fakai, L. U.(b) (2015)	0.14246902	0.12551863	0.1594194
Fakai, L. U.(c) (2015)	0.14220335	0.12525713	0.15914956
Fakai, L. U.(d) (2015)	0.14338348	0.12642041	0.16034654
Comfort O. Aiki-Raji(a) (2016)	0.13946905	0.12257757	0.15636053
Comfort O. Aiki-Raji(b) (2016)	0.13720972	0.12038596	0.15403348
Olufemi, O. T.(a) (2020)	0.14535579	0.12834332	0.16236826
Olufemi, O. T.(b) (2020)	0.14452460	0.12753928	0.16150992
Olufemi, O. T.(c) (2020)	0.14502201	0.12800761	0.16203641
Olufemi, O. T.(d) (2020)	0.14488454	0.12788211	0.16188697
Olufemi, O. T.(e) (2020)	0.14545127	0.12843478	0.16246775
Ehud eElnekave(a) (2016)	0.14117742	0.12432357	0.15803127
Rout, M. (2017)	0.14579827	0.12875999	0.16283655
Sellers, R. F. (1973)	0.14309712	0.12621651	0.15997774
Alexandersen, S. (2003)	0.12871008	0.11310284	0.14431732
Wilesmith, J. W. (2003)	0.14291145	0.12605807	0.15976483
Vu Le T (2017)	0.11888281	0.10565615	0.13210947
Xv,Yang (a) (2016)	0.14701525	0.12915527	0.16487523
Xv,Yang (b) (2016)	0.14902886	0.12986125	0.16819647
Xv,Yang (c) (2016)	0.14435624	0.12741737	0.16129511
Li,jin (a) (2017)	0.14611415	0.12905627	0.16317204
Li,jin (b) (2017)	0.14603573	0.12898719	0.16308426
Yuan,Cuixia (a) (2017)	0.14544781	0.12842392	0.1624717
Yuan,Cuixia (b) (2017)	0.14478426	0.12777782	0.1617907
Lv, Qizhuang (2018)	0.14089792	0.1239848	0.15781105
Wu, Bo(a) (2018)	0.14435128	0.1273673	0.16133525
Wu, Bo(b) (2018)	0.14474946	0.12776489	0.16173403
Wu, Bo(c) (2018)	0.14508586	0.12809214	0.16207958
Wu, Bo(d) (2018)	0.14355391	0.12660393	0.16050389
Wu, Bo(e) (2018)	0.14501344	0.12799507	0.1620318
Hou,Huili (2018)	0.13984899	0.12295991	0.15673808
Dou,Siyuan (2014)	0.14615485	0.12884737	0.16346233
Wang,Hui (2018)	0.14745756	0.12969917	0.16521595
Chung, W. B.(a) (2003)	0.14580043	0.1284992	0.16310167
Chung, W. B.(b) (2003)	0.14602698	0.12866055	0.16339341
Chung, W. B.(c) (2003)	0.14673893	0.12913429	0.16434357
Chung, W. B.(d) (2003)	0.14707262	0.1293076	0.16483764
Combined	0.14336223	0.12653632	0.16018814

Publication bias and sensitivity analysis: The funnel plot indicates that there may be publication bias in the studies we included (Fig. 4). The Egger test found $P < 0.05$ (Fig. 5), suggesting that there is publication bias in the included studies. After sensitivity analysis, the test results were not stable, and the heterogeneity originated from this literature (Vu, *et al.*, 2017).

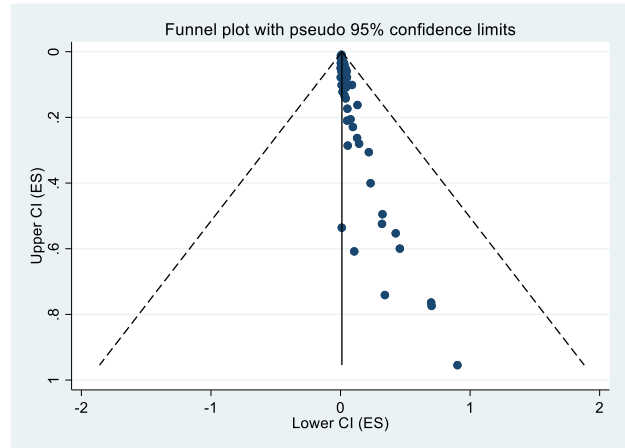


Fig. 4: Funnel plot for the publication bias test of the included studies.

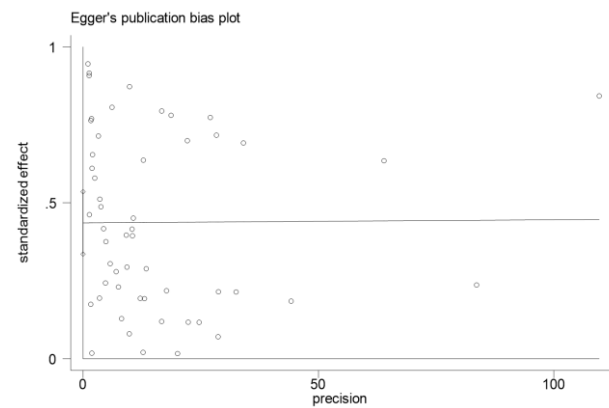


Fig. 5: Publication bias of included studies assessed using Eggers' test.

DISCUSSION

Foot-and-mouth disease (FMD) is an acute infectious disease caused by foot-and-mouth disease (FMD) virus, which is one of the most contagious livestock diseases in the world, with large regional epidemics in Africa, Asia, Europe, and North America, and a very high capacity for cross-regional transmission, as confirmed by epidemics in the United Kingdom and continental Europe in 2001, and in Japan and South Korea in 2000 (Knowles *et al.*, 2001). The epidemic has caused severe and sustained economic losses to the swine farming industry worldwide (van Maanen, 1990). FMDV belongs to the genus Foot and Mouth Disease Virus (FMDV) in the family of small RNA viruses (Belsham, 1993) and is a single-stranded positive-stranded RNA virus, which is mainly transmitted by direct contact, but can also be transmitted through indirect contact via contaminated transportation, staff, etc and where climatic conditions permit, by airborne transmission. Outbreaks of FMD usually cause significant economic losses to the country or region, mainly from the deaths of sick animals culled and reduced production capacity. Infected sows or pregnant pigs may suffer from abortion, stillbirths, or even long-term or permanent loss of productivity. Secondly, the economic losses incurred in the

fight against FMD also include the destruction of animals, compensation to farmers, vaccination, emergency vaccination, disinfection and cleaning of infected and non-infected areas.

Since the first clear record of foot-and-mouth disease in 1514, human beings have been acquainted with FMDV for more than 500 years, because the disease can cause great economic losses to people's production and life, most of the countries and regions attach great importance to foot-and-mouth disease epidemics, and according to the search statistics, the total prevalence rate of FMDV is 4.17% globally, of which the FMDV serotype is the O-type most common. In the subgroup analysis for the sampling time, the detection rates of FMDV in the sampling time periods of 1971.1-1980.12, 1950.1-1970.12, and 2006.1-2010.12 were 50.67, 14.49 and 12.18%, respectively, and as the sampling time period approached to the year of 2024, the virus detection rate of the time periods showed a decreasing trend in general. Trend. The higher detection rates in the time ranges of 1971.1-1980.12 and 1950.1-1970.12 were partly due to the fact that the means of detection at that time was clinical examination, and the clinical symptoms of FMD were similar to those of Senecavirus A (SVA) and swine vesicular disease virus (SVDV) (Chen, *et al.*, 2022), and there was a possibility of misdiagnosis, and the clinical examinations were not of high accuracy. The industrial production of vaccines was realized only after the 1950s through the successful cultivation of the virus in primary cells of the epithelium of the tongue of animals (Domingo *et al.*, 2002). The conversion of FMDV from adherent to suspension culture on BHK cells was achieved after the 1960s, so that further mass production of FMDV was possible, and the application of diethylenimine (BEI) and oil adjuvant in vaccine production in the 1970s led to the realization of the industrial mass production of FMDV inactivated vaccine (Barteling and Vreeswijk, 1991; Rodriguez and Gay, 2011). The increase in vaccine production while reducing the cost of vaccine production has made it possible to standardize the vaccination of pigs in captivity according to the immunization program on a large scale, which has enabled the subsequent reduction of the FMDV detection rate year after year, and greatly reduced the economic losses caused by FMD to people's production and life. In 2010, two papers from the Kenyan FMDV infection rate testing showed that the detection rate of FMDV in pigs was as high as 51.71% in the time period of 2010.4-2010.6, which could be attributed to the improper inactivation of inactivated vaccine used (Sangula *et al.*, 2011), tick-borne FMDV (Sang *et al.*, 2006), and transmission of FMDV from neighboring countries into the country (Balinda *et al.*, 2010) and so on. etc. Therefore, it is important to strengthen the use of the corresponding serotype vaccine and to cut off the transmission route of FMDV for the prevention and control of FMD epidemics.

In the subgroup analysis of the section on feeding conditions, we learned that the highest detection rate of FMDV was 13.58% in the free-range condition, while the detection rate was only 5.71% in the large-scale condition. Therefore, it can be concluded that the detection rate of FMDV is lower when the rearing method is more strict and more standardized. In the case of large-scale rearing, the airborne transmission of the virus is artificially isolated in some cases, as well as the indirect transmission routes such

as rats and ticks are cut off. We also calculated the GDP level of each country and region during the period when the samples were obtained and found that the detection rate of FMDV was positively correlated with the scale of farming in that country and region, and at the same time, negatively correlated with the GDP. This indicates that the higher the GDP, the better the ability of each farm to control its pigs, which can be immunized on time according to the immunization program, regularly disinfected, and the management of people and goods entering and leaving the farm is also more standardized. However, due to the large-scale management of the farm, the breeding density is large and once FMDV enters, it is very easy to have an epidemic outbreak. In the analysis of the included data, the infection rate of FMDV in wild boars was 0.74%, and the transmission of wild toxin may also be one of the causes of FMD outbreaks in artificially farmed pigs. Therefore, we should focus on epidemic prevention while changing the feeding management mode to farm scale feeding, immunize the herds as required, and do a good job of cleaning and elimination. FMDV may also cause long-term, asymptomatic infections in ruminants, "carrier" animals, which further complicates the situation of carrying the virus in the rearing environment (Zhu *et al.*, 2022).

In the subgroup analyses related to climatic conditions and sampling seasons, we found that the detection rate of FMDV infection in pigs was higher in tropical monsoon climate (55.15%), Mediterranean climate (54.17%), and subtropical Mediterranean climate (50.57%), which led to the judgment that FMDV spreads more readily in environments where the temperature and humidity are higher and where the moderately high temperature difference is more stable throughout the year. This was also confirmed in the subgroup analysis related to seasons, which showed that FMDV is more easily transmitted in spring and fall, according to past FMD-related studies. In the spring and fall seasons, a large temperature difference between day and night due to the receipt of summer and winter winds leads to a decrease in the resistance of pigs, while the change in temperature leads to an increase in rainfall and an increase in environmental humidity, which is more conducive to the propagation of viruses, bacteria, and other pathogens at suitable temperatures (Hagerman *et al.*, 2018) FMDV can contaminate the environment through aerosols and cause long-distance transmission events, so that it complicates the control of Foot-and-mouth disease (FMD) outbreaks (Brown *et al.*, 2022). It was also observed in the subgroup analysis regarding the seasons that the detection rate of FMDV in winter was as high as 70.19%. In winter, when the temperature is lower compared with spring and fall, the survival environment of pigs pays more attention to heat preservation, and there will be problems such as poor ventilation and higher breeding density, and at the same time, the low temperature is also more conducive to the survival and transmission of viruses, and most of the FMDV is transmitted by direct contact, therefore, in the environment of higher density, poor ventilation, and suitable temperature and humidity, FMDV is also easy to spread and cause outbreaks of epidemics.

In the age subgroup analysis, we categorized the pigs into piglets, nursery pigs, and fattening pigs according to the production mode, in which the highest FMDV detection rate of 13.39% was found in fattening pigs, and the lowest

FMDV detection rate of 2.68% was found in nursery pigs. In other related articles, nursery pigs are more susceptible to the disease because weaned piglets grow and develop quickly, and due to weaning and other factors such as weaning stress and lower levels of maternal antibodies lead to their higher susceptibility to the disease. However, this subgroup analysis concluded that, contrary to the conventional situation, the detection rate of FMDV in nursery pigs was the lowest among the pig group classifications, which may be due to the fact that nursery pigs are more susceptible to pathogen infections, which are more highly valued and more strictly regulated. Fattening pigs, on the other hand, are already at a relatively safe stage of growth, and during subsequent growth, antibody levels may be reduced due to poor FMD vaccination programs and lack of timely catch-up vaccination. Fattening pigs are older relative to nursery pigs, and may be exposed to more risk factors, and the likelihood of FMDV infection is elevated. In the sex subgroup analysis, the FMDV detection rate of sows (4.59%) was lower than that of boars (18.66%), the total sample size of sows data samples included was 49.5 times higher than that of boars, and the total number of FMDV detections in sows was 12.2 times higher than that of boars. Although the FMDV detection rate in sows was low compared to boars, the number of detections was much greater than the number of boars. The reasons for this phenomenon may be as follows: 1. The demand for sows is greater than that of boars in production life, resulting in an increase in the number of samples from sows; 2. As sows have reproductive functions, they need to be immunized with more types of vaccines than boars, which is likely to result in uneven immunization arrangements for sows, leading to a decrease in the number of immunizations; 3. Females have a lower immunity at specific times of the year (Foroutan-Rad *et al.*, 2016), which leads to the FMDV testing more frequently and increased detection rates.

In the subgroup analysis of detection methods, the highest detection rate was found using the RT-PCR (26.55%) method, followed by the clinical examination (25.48%) assay, and the ELISA method, which was applied most frequently, had a detection rate of 3.17%. Clinical diagnosis of FMD is sometimes difficult, e.g. in goats and sheep where the clinical manifestations are milder (Callens *et al.*, 1998). The period of literature related to the use of clinical examination is relatively early, the method of disease determination is primitive and prone to misjudgment due to the similarity of the symptoms of other disease onset, and the accuracy of the results of the clinical examination will be affected by the experience of the inspector (Osti *et al.*, 2019), and the maximum transmission of foot and mouth disease virus occurs after the animals show clinical symptoms, which increases the risk of transmission of foot and mouth disease virus from the inspector to the contact animals (Charleston *et al.*, 2011; Chase-Topping *et al.*, 2013), with the upgrading of detection methods, clinical examination of FMD methods were replaced by other methods. RT-PCR method is prone to aerosol contamination between samples during the experimental process, resulting in false positives and other situations such as mixing of samples, which may lead to a high detection rate of FMDV, lower accuracy of test results, and longer operation time, which is not a large

number of included in the analysis of the subgroup in this group. ELISA is a highly accurate assay that can visualize the viral content of the samples compared with RT-PCR. Due to the large number of samples tested simultaneously and the shorter operation time, the ELISA method included the largest number of samples in this subgroup analysis, and the data had a high degree of confidence. The 3ABC-ELISA method was used in the ELISA assay, which can differentiate between FMDV-infected animals and FMD-vaccinated animals, and the method is also effective in confirming the initial status of unvaccinated animals in FMD-free countries (De Diego *et al.*, 1997).

In the sensitivity test, the heterogeneity comes from this literature (Vu *et al.*, 2017) and the reason for its heterogeneity may be that in the data of this literature, the infection rate is too high, 92.86%, which is significantly higher than the infection rate of other samples.

In this meta-analysis, most of the included data are of medium to high quality, so it can be considered that this study reflects the situation of pig infections with FMDV in some countries and regions around the world. Sensitivity analysis also confirmed the reliability of the conclusions of this study.

The advantage of this study lies in the large total sample size, with a total of 6,646 articles retrieved, and the rigorous methodology, which discusses in detail the different detection rates caused by various subgroup factors. This study also has certain limitations. First, only six literature databases were searched, and the search methods and settings may have led to the omission of some relevant studies. Second, some subgroup analyses had relatively few data, and their analysis results may not be universally applicable. Furthermore, due to the lack of data in the included literature, the risk factors analyzed in this article may not be complete, such as whether different sampling sites could lead to varying viral loads, thereby affecting the detection rate of FMDV.

In summary, in recent years, the detection rate of FMDV infection in pigs has decreased globally, but FMD is still circulating globally. As pigs are the main source of meat for humans, and since vaccination is the main method of controlling FMD epidemics in FMD-endemic countries, more attention should be paid to the timely vaccination of FMD vaccines on a large scale and according to a schedule, and strict control of entry and exit of people and materials in the breeding area (Colenutt *et al.*, 2020), so as to further reduce the risk of FMDV infestation in pigs. Different climates, seasons and sampling years have a significant effect on the detection rate of FMDV infection in pigs. Meanwhile, in the detection process, more accurate detection methods should be used to reduce the possibility of misdetection and omission, so that researchers can have a more detailed picture of FMDV infection in pigs.

Conclusions: The overall positive rate of FMDV in pigs worldwide is about 4.17%, which is affected by season, climate, feeding and detection methods. The popularization of the vaccine, the standardization of the immunization program and the improvement of the biosafety level of large-scale pig farms may be the reasons for the decline of the detection rate of FMDV in pigs. However, in tropical and subtropical regions, the virus detection rate is relatively high, posing a great threat. In the future, more attention

should be paid to the risk factors such as asymptomatic pigs carrying the virus and the different amount of virus in different sampling sites to further reduce economic losses.

Authors contribution: MP conceptualization, validation, formal analysis, resources and writing—original draft; JL conceptualization, validation, investigation, data curation and writing—original draft; FZ methodology; XM software; YJ validation; WC r visualization; XW writing—review and editing, supervision; LT project administration, Funding acquisition.

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