



# Meta-analysis of seroprevalence and zoonotic infections of Middle East respiratory syndrome coronavirus (MERS-CoV): A one-health perspective

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## ABSTRACT

The zoonotic Middle East respiratory syndrome (MERS) is caused by an emerging beta-coronavirus (CoV). The majority of MERS studies have included scattered data from sub-Saharan Africa and the Middle East, and these data have not been analyzed collectively. In this work, a meta-analysis of these studies was conducted to coalesce these results, determine the prevalence and seroprevalence of MERS-CoV in camels and humans, and examine how zoonotic infection rates in dromedary camels are related to human infection rates. After extracting the collected data, the prevalence and seroprevalence at a 95% confidence interval (CI) using a fixed-effects inverse-variance meta-analysis was conducted. Thirteen studies were included. Eight studies included 2905 samples from dromedary camels, of which 1108 (38.14%) were positive for the virus. The prevalence was 8.75[–13.47, 30.98] at 95% CI in dromedary camels and 0.03[–35.23, 35.28] at 95% CI in humans. Ten studies included 7176 serum samples, 5788 (80.66%) of which were positive. The seroprevalence was 20.69[–4.60, 45.99] at 95% CI. The prevalence of MERS-CoV was moderate to high, but the seroprevalence was high. Despite the high prevalence of the virus in camel herds, zoonotic transmissions were not widespread. Further longitudinal and cross-sectional follow-up studies are recommended to provide solid control of MERS-CoV transmission.

## 1. Introduction

First identified in 2012 in Saudi Arabia [1], the Middle East respiratory syndrome (MERS) is caused by the coronavirus MERS-CoV. Primary MERS symptoms comprise cough, fever, and shortness of breath, and some patients develop pneumonia or gastrointestinal symptoms such as diarrhea. Currently, the disease has a fatality rate of 35%, although most MERS-CoV infections are asymptomatic and are only confirmed through laboratory testing [1]. Despite a majority of MERS-CoV infections being attributed to human–human transmission, there is scientific evidence linking dromedary camels to zoonotic MERS-CoV. In a recent study, researchers collected serum samples from 35 camel herders, 58 slaughterhouse workers, and 93 camel handlers in Kenya to determine the presence of MERS-CoV antibodies in these groups. The authors identified multiple potential risk factors among the slaughterhouse workers, including their cutting of the camel's throat and occasionally consuming the camel's blood [2].

These observations notwithstanding, previous research does not entirely corroborate the role of dromedary camels in MERS-CoV transmission, nor does it identify the route. Transmission of the virus requires

very close contact. As a result, most outbreaks have occurred among healthcare workers treating infected patients. The largest outbreaks have been recorded in the Republic of Korea, the United Arab Emirates, and Saudi Arabia [1].

The authors of one previous study attempted to identify the origins of MERS-CoV in a non-healthcare setting [3]. Almost half of a cohort of camel laborers in the Kingdom of Saudi Arabia was determined to have been previously infected with the virus. The participants all had well-documented histories of exposure to camels. Based on data collected via MERS-CoV-specific immunofluorescence and enzyme-linked immunosorbent assays, T-cell responses, and neutralizing antibody titers, the authors concluded that the dromedary camel was the most likely source of human infection [4]. The perplexing discovery is that, even though Africa is home to the greatest number of dromedary camels, and the MERS-CoV virus continues to be endemic among the camels there, there have been no reports of zoonotic transmissions within the continent.

Researchers compared MERS-CoV genetic variants from Burkina Faso, Nigeria, Morocco, and Ethiopia, to ascertain whether any variants had zoonotic potential [4]. Notably, the genetic and phenotypic virus variants acquired from West Africa were relevant to the zoonotic

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potential of those viruses. The relevance of human–animal interactions in the context of MERS-CoV infection is a subject of ongoing debate in the scientific community.

Regardless of the zoonotic uncertainty, most data indicate that dromedary camels are significant reservoirs of various coronaviruses, including MERS-CoV [5]. Of 891 samples, 584 (65.54%) tested positive for the MERS-CoV receptor-binding domain (RBD). The authors also determined the seroprevalence of MERS-CoV in camels using MERS-CoV nucleocapsid (NP) assays. They found that a larger number of MERS-CoV RBD positive samples were negative for MERS-CoV NP (91.78%), suggesting possible recombination events between MERS-CoV and a bat CoV in camels [5].

MERS-CoV and SARS-CoV, the sources of multiple human epidemics, are among the numerous zoonotic coronaviruses thought to persist in dromedary camels. One recent study included a thorough assessment of the incidence of two coronaviruses in dromedary camels to explore the function of animals as possible carriers of these viruses [6]. The results indicated that camels and bats were the largest reservoirs, thus suggesting their relevance in zoonotic transmission.

A limited number of studies have examined the presence of MERS-CoV in dromedary camels and its relationship to human infection. The majority of these studies have been scattered in sub-Saharan Africa and the Middle East. This meta-analysis used available peer-reviewed observational studies to coalesce these results and report the prevalence of MERS-CoV in camels and humans. MERS-CoV prevalence is also reported by species (camel and human) and area. The rate of MERS-CoV transmission between people and camels was determined using this pooled difference. The results will provide insight into the zoonotic transmission of coronaviruses and inform future primary research regarding transmission routes. Our results address questions regarding the prevalence of MERS-CoV infection, disease seroprevalence, and the relevance of zoonotic infections in dromedary camels in human infections.

## 2. Materials and methods

### 2.1. Protocol

This meta-analysis was conducted according to a Prospero protocol and following the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and the Cochrane Handbook for Systematic Reviews of Interventions. The protocol was prepared prior to beginning the meta-analysis.

### 2.2. Search strategy

A literature search was conducted in March 2022 by two independent investigators. Four electronic medical and scientific databases, PubMed, Medline, Scopus, and Web of Science, were searched for relevant studies. The search was conducted using keywords combined with medical subject heading (MeSH) terms, Boolean operators (AND and OR), truncations (\*), and field tags. In the literature search, specific search strings were developed from basic keywords common for this topic, such as “MERS-CoV”, with search alternatives “MERS”, “Middle East respiratory syndrome”, “Middle East respiratory syndrome coronavirus”, “CoV”, and “coronavirus”. A keyword search for humans included “camel workers”, “camel handlers”, and “camel slaughterhouse workers”. Finally, the keyword “camel” search alternatives were “dromedary camels”, “dromedaries”, and “*Camelus dromedarius*”. Reference lists of the retrieved articles, including systematic reviews and meta-analyses, were searched manually for potentially relevant publications that had not been published previously or not identified in the elaborate database search. These articles were advanced to the inclusion and exclusion stage, which was guided by predefined eligibility criteria (Supplementary file 1).

### 2.3. Eligibility criteria

Electronically available peer-reviewed articles were included in this study. The articles were subjected to the following inclusion criteria: 1) reported randomized controlled trials, clinical trials, or observational studies; 2) provided the prevalence or seroprevalence of MERS-CoV in any location worldwide; 3) assessed humans or dromedary camels; 4) included outcomes that provided insight into MERS-CoV virology and clinical traits. Studies including an animal interface between camels and humans as hosts of MERS-CoV were prioritized. Studies must have been published in English within the last 10 years. Foreign language studies were only considered if translated versions were available online.

### 2.4. Data extraction

Data were extracted into a standardized Excel sheet. The same two investigators who conducted the literature search were engaged in extracting information from the selected studies. A third party intervened in the event of a discrepancy. Extracted data were the characteristics of the selected studies, and these characteristics were included in the study identification (authors, location of the study, subjects involved in the study, and aim of the study). Results of these studies were also extracted in the form of prevalence, seroprevalence, and any other pooled data. Numerical results relevant to the meta-analysis were transformed into specific tables and reports in a synthesizable form, a manner that would allow the data to be examined by the analytical tool (STATA 16).

### 2.5. Analysis of results

A fixed-effects model meta-analysis and inverse-variance method were used to evaluate the prevalence and seroprevalence rates at a 95% confidence interval (CI). The standard measurement describing MERS-CoV distribution was standardized into positive and seropositive rates presented as dichotomous variables. In the meta-analysis, data were examined using StataMP Version 16.0 (STATA 16) to generate the effect size of MERS-CoV prevalence and seroprevalence. A literal analysis of the findings from the included studies was also conducted to create a link between the findings and consolidate independent primary results into a singular inference. The studies' heterogeneity was measured using the  $I^2$  statistic, which indicates how much of the variation in observed impact is attributable to variation in genuine effects rather than sampling error. Results were reported graphically on forest plots, and the publication bias of the studies was reported via funnel plot. Sub-group analyses of pooled data in terms of species (humans or camels) and geographic regions were also performed.

## 3. Results

### 3.1. Study selection

Because of the 10-year time limit for study eligibility, papers were published between April 2013 and March 2022, which encompassed nearly two years before MERS-CoV surfaced. As a result, non-relevant studies were eliminated. The electronic search identified 463 prospective papers, 38 of which were eliminated owing to publication time constraints prior to MERS-CoV emergence and 36 due to duplication. A manual search “hand search” of the remaining references revealed 13 additional studies that met the inclusion criteria, resulting in 402 articles. These articles were then submitted for a title and abstract screening to confirm whether they completely addressed the topic of the meta-analysis to completion. Manual screening conducted by the two independent investigators eliminated 249 studies and revealed 153 studies that potentially met full eligibility. The process of matching the studies with every criterion for eligibility for inclusion eliminated 97 studies, and 56 remained for final full-text screening. Finally, 43 studies from

this list were determined to be ineligible due to incomplete data, inappropriate methodology, specific outcomes assessed, or study design; the remaining 13 studies were included in the meta-analysis. Fig. 1 shows a PRISMA 2020 flow diagram for updated systematic reviews, which only includes searches for databases.

### 3.2. Study characteristics

Included articles presented studies conducted in Africa and Asia within the following countries: Saudi Arabia, Egypt, Qatar, Nigeria, Jordan, Sudan, Kenya, Senegal, Tunisia, Uganda, and Iraq. The included studies were published between 2013 and 2020, and dromedary camels were the subjects in most studies. Extracted virus prevalence and seroprevalence data are represented in Table 1, and transformed data are in Tables 2–4.

### 3.3. Prevalence of MERS-CoV

Eight studies [3,7–13] included the analysis results of tested the sera of 2905 dromedary camels. Of these, 1108 (38.14%) were positive for the presence of MERS-CoV. The studies generated a fixed effect size of 8.75[–13.47, 30.98] at a 95% confidence interval in dromedary camels and 0.03[–35.23, 35.28] at 95% CI in humans (Fig. 2).

### 3.4. Seroprevalence of MERS-CoV antibodies

Ten of the included studies [7,9–12,14–18] included the analysis results of 7176 serum samples, 5788 (80.66%) of which were positive for MERS-CoV antibodies. Meta-analysis results demonstrated a fixed effect size of 20.69[–4.60, 45.99] at a 95% confidence interval (Fig. 2).

## 4. Discussion

Although the consensus of the current literature is that dromedary camels serve as a reservoir for MERS-CoV the rate of zoonotic transmission is very low, indicating that most transmissions are likely between humans. In one of the studies included in the meta-analysis, of 30 people with routine exposure to camels (herders, handlers, and truck drivers), only 50% (15/30) were infected with MERS-CoV [3]. Farag et al. (2019) tested 18 humans working within a highly MERS-CoV positive environment, including camels, bats, donkeys, cows, goats, and sheep. Despite this potential for exposure, sera from all 18 individuals were negative [11]. In a cross-sectional surveillance study conducted in Kenya, Ommeh et al. (2018) found that only 20/486 (4.12%) camel workers from various counties tested seropositive for MERS-CoV compared to 792/1163 (69%) of camels [13].

Since MERS-CoV was first detected, substantial research has been devoted to categorizing the virus and identifying various human receptors. In this meta-analysis, our combined observations revealed that the seroprevalence was lower in African regions (3959 of 5137 samples, 77.07%) than in the Middle East (1829/2039, 89.70%). Tolah et al. (2020) found that the virus incidence rate in imported camels was lower than in local camels (154/1157, 13.3% versus 86/242, 35.5%) [12]. However, imported camels had higher seroprevalence (1085/1157, 93.8% versus 212/242, 87.6%) [12]. Therefore, improved surveillance and prevention measures are recommended to reduce the MERS-CoV spread from imported camels to local herds. One notable success in this regard is the use of preventive measures that curbed healthcare infections in the Arabian Peninsula between June and July 2014 [19].

The frequency of MERS-CoV infection is moderate, but seroprevalence is high in camels. This meta-analysis has demonstrated that despite

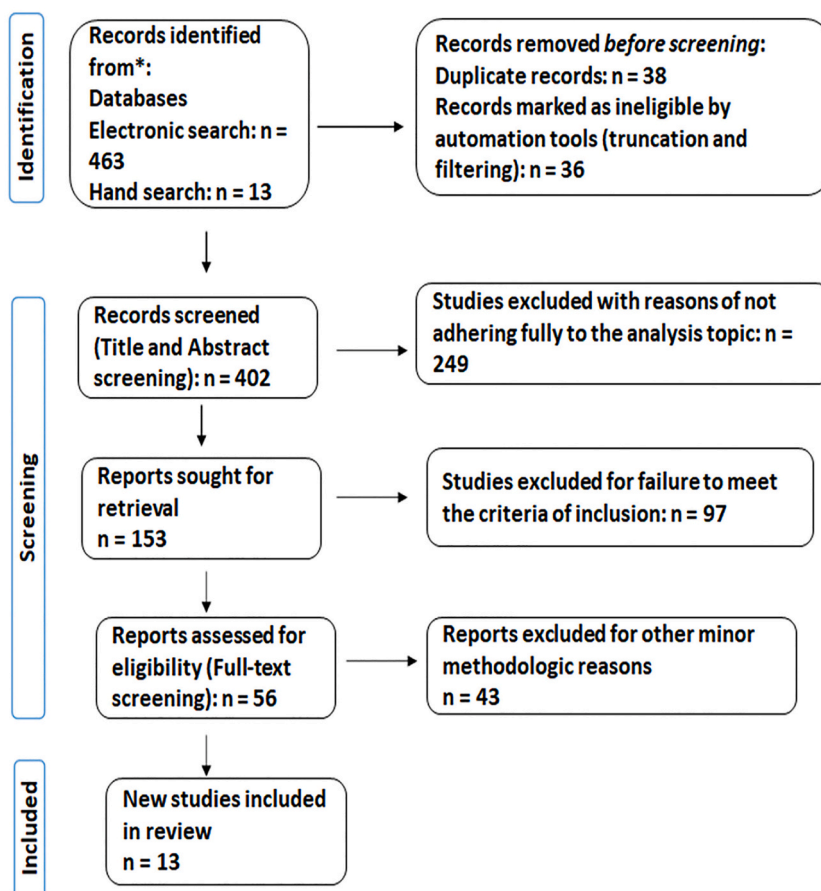


Fig. 1. PRISMA flow diagram of studies used in the current analysis.

**Table 1**  
The study characteristics comprising, the location, aim, subjects and results.

LOCATION	AIM	SUBJECTS	Results			Reference
			Prevalence (+ve Total)	Seroprevalence (+ve/Total; %)	Pooled Results	
Saudi Arabia	To investigate the prevalence of MERS-CoV among camel workers in Saudi Arabia.	Camel workers (humans)	15 30			[3]
Egypt	To assess the prevalence of MERS-CoV in imported camels.	Dromedary camels		871/1031; 84.5%	Seroprevalence: 614/692; 88.7% - imported camels, 257/339; 5.8% - local camels. 543/594; 91.4% - Sudan, 71/98; 72.4% - East Africa.	[14]
Qatar	Testing the presence of MERS-CoV in camels in connection with human infections.	Dromedary camels	5 14	14/14; 100%		[7]
Saudi Arabia	Assess historical and present MERS-CoV prevalence.	Dromedary camels		150/203; 74%	Seroprevalence: 93/98; 95% - adult camels, 57/104; 55% - juvenile camels.	[15]
Saudi Arabia	Investigate MERS-CoV infection within a herd of dromedary camels.	Dromedary camels	10 35			[8]
Nigeria	Investigate the detection rate of MERS-CoV in dromedary camels.	Dromedary camels	14 132	126/131;96%		[9]
Jordan	Determine the prevalence of MERS-CoV in two geographically separated herds of dromedary camels.	Dromedary camels	28 42	37/42; 89%		[10]
Saudi Arabia	A seroprevalence study to determine prevalence of MERS-CoV antibodies in dromedary camels.	Dromedary camels		280/310; 90.32%		[16]
Sudan & Qatar	Testing for prevalence of MERS-CoV infections in camels	Camel workers & Dromedary camels	CW: 0/18, DC: 3/90	CW: 0/18; 0%, DC: 146/154; 94.81%		[11]
Saudi Arabia	Assessing the prevalence study of MERS-CoV in imported and local dromedary camels.	Dromedary camels	241 1399	1297/1399; 92.7%	Seroprevalence: 1085/1157; 93.8% - imported camels, 212/242; 87.6% - local camels. 154 1157; 13.3% - imported camels, 86 242; 35.5%.	[12]
Africa & Middle East	Surveillance for MERS-CoV in Egypt, Senegal, Tunisia, Uganda, Jordan, Saudi Arabia, and Iraq.	Dromedary camels		2816/3821; 73.7%	Seroprevalence: 254/309 (82.2%)- live market herd, 129/187 (68.9%) - free herd, 474/924 (51.2%)- farm herd, 143/164 (87.1%)- quarantined herd, 401/449 (89.3%)- slaughterhouse herd.	[17]
Israel	Investigate the prevalence of MERS-CoV in dromedary camels.	Dromedary camels		51/71 (71.8%)	35/71; 49.3% - high neutralizing antibody titers (80–25,600), 16/71; 22.5% - low neutralizing antibody titers (20–40).	[18]
Kenya	A cross-sectional surveillance of humans and camels for MERS-CoV.	Camel workers & Dromedary camels	DC: 792 1163 CW: 20 486			[13]

**Table 2**  
Positivity rates in dromedary camels.

AUTHOR	Positive	Total
Alshukairi (2018)	15	30
Haagmans (2014)	5	14
Hemida (2014)	10	35
Chu (2015)	14	132
Van Doremalen (2017)	28	42
Farag (2019)	3	90
Tolah (2020)	241	1399
Ommeh (2018)	792	1163

**Table 3**  
Positivity rates in camel workers.

AUTHOR	Positive	Total
Farag (2019)	0	18
Ommeh (2018)	20	486

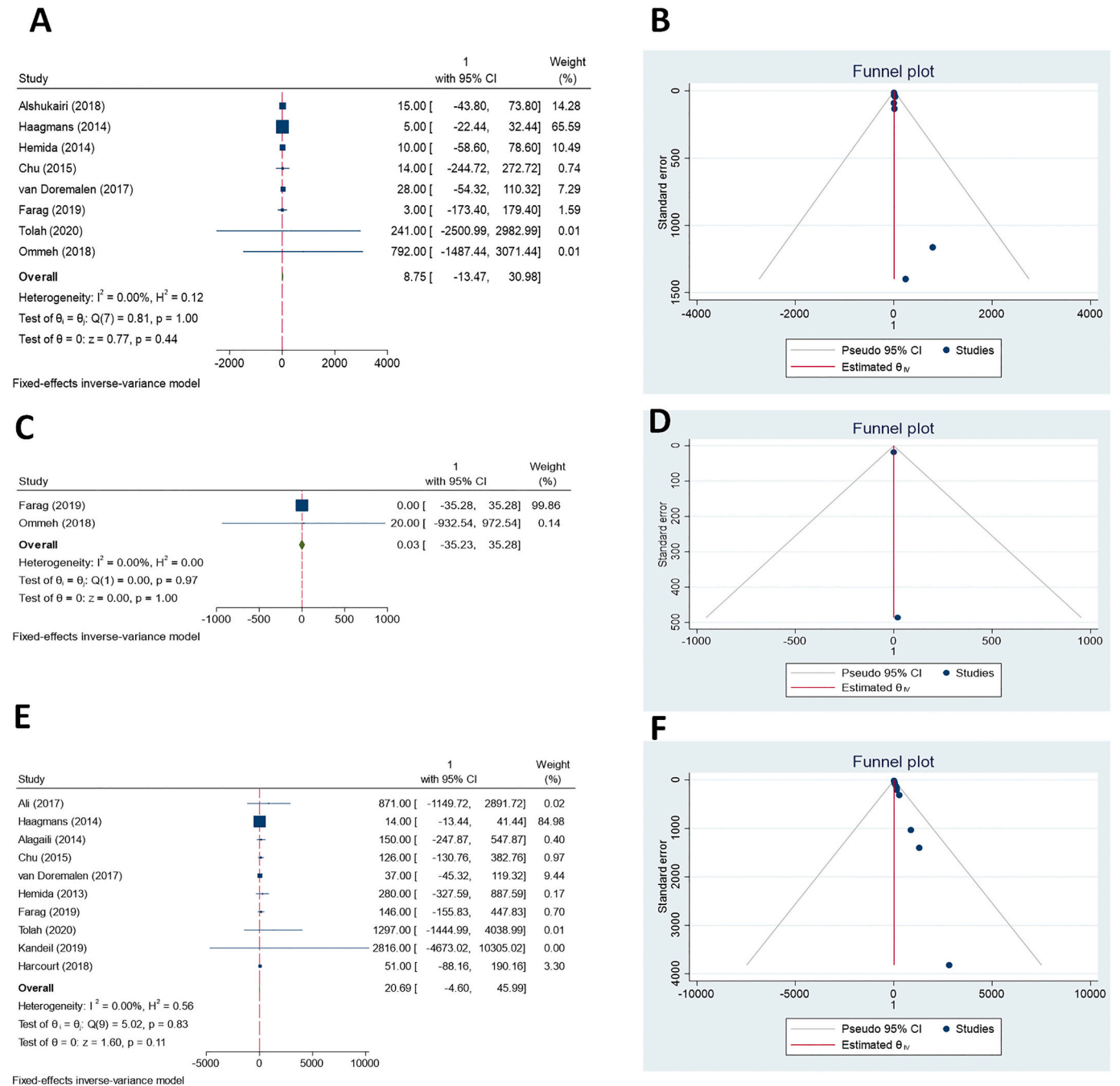
the high concentration of disease in camel herds, workers in the camel environment do not easily contract the disease. Camel-to-human transmissions are therefore not widespread. Given the possibility of human-human transmission, a clear line must be drawn between the

**Table 4**  
Seropositivity rates in dromedary camels.

AUTHOR	Seropositive	Total	Percentage
Ali (2017)	871	1031	84.50%
Haagmans (2014)	14	14	100.00%
Alagaili (2014)	150	203	74.00%
Chu (2015)	126	131	96.00%
Van Doremalen (2017)	37	42	89.00%
Hemida (2013)	280	310	90.32%
Farag (2019)	146	154	94.81%
Tolah (2020)	1297	1399	92.70%
Kandeil (2019)	2816	3821	73.70%
Harcourt (2018)	51	71	71.80%

contribution of zoonotic infection and interpersonal transmission to the reported MERS-CoV infection. Public health surveillance for MERS-CoV is needed in Africa and the Middle East, considering the rate of infection. Improved preventive measures should be implemented to reduce disease circulation in areas with high camel densities and regions where camel slaughtering is widespread, such as Saudi Arabia and East Africa.

A substantial number of camels included in the meta-analysis tested positive for MERS-CoV, while none or a small percentage of camel nasal or nasopharyngeal swabs tested positive for MERS-CoV RNA. Moreover, human serum samples did not demonstrate neutralizing potential



**Fig. 2.** Forest and funnel plots of seroprevalence and zoonotic infections of Middle East respiratory syndrome coronavirus. A) Forest plot showing the prevalence of MERS-CoV in dromedary camels. B) A standard funnel plot showing publication bias of the included studies of MERS-CoV in dromedary camels. C) Forest plot showing the prevalence of MERS-CoV in camel workers. D) A standard funnel plot showing publication bias of the included studies of MERS-CoV in camel workers. E) Forest plot showing seroprevalence of MERS-CoV in dromedary camels. F) A standard funnel plot showing publication bias of the included studies in seroprevalence of MERS-CoV in dromedary camels.

against MERS-CoV, as previously observed in other African countries [11]. Human MERS has only been documented in the Arabian Peninsula and only since 2012, despite the virus being detected in camels and travelers from this region since at least the early 1990s. Notably, no cases of zoonotic MERS illness have been reported in Africa or Asia, despite the presence of significant densities of MERS-CoV-infected dromedaries in these regions [20]. Although CoV's genomic variability is region-dependent, with clade B in the Arabian Peninsula and clade C in Africa, all known MERS-CoVs share >99% nucleotide identity. In Africa, certain clade C viruses have undergone progressive viral

protein deletions, which are thought to have a role in immune evasion in humans. However, their relevance in dromedary camels or the role of this species as a potential natural reservoir is unknown. With a few isolated exceptions, such deletions have not been detected in clade B viruses in the Arabian Peninsula. The persistence of deletions in accessory proteins may suggest that MERS-CoV has not yet fully adapted to the dromedary host [20]. These findings, in general, support the need for more follow-up studies to clarify the zoonotic transmission of MERS-CoV.

The expanding and often contradictory findings on the zoonotic



characteristics of MERS-CoV were evaluated in this meta-analysis. Several limitations were faced while writing a comprehensive systematic review and meta-analysis. Firstly, research on this issue was restricted in terms of the disease's global prevalence as well as the number and frequency of field trials. There were just a few trials for longitudinal and cross-sectional investigations. Long-term investigations to track disease progression and zoonosis are scarce. Second, observed variation might be due to differences in sample procedures, demographic characteristics, or intervention strategies.

The "One Health" perspective prioritizes human health and the avoidance of zoonotic illnesses, or diseases that may be transmitted from animals to humans. The World Health Organization (WHO) has defined the elements of one health track as monitoring across sectors, creating creative solutions that address the root causes and links between risks and outcomes, and enabling early control and containment of disease risks. MERS-CoV is seen as a prime illustration of the One Health concept. This is because animals, particularly dromedary camels, play significant roles in the virus's transmission and sustainability through contact with humans. The zoonotic pathway of MERS-CoV is challenged in this study. It was determined that zoonotic infection from camels was present. However, it contributes less than intended. However, other mysteries beyond MERS-CoV infection must be investigated. The large disparity between seropositive camels and the proportion of positive infection warrants additional investigation. This "One Health" notion includes the zoonotic pathway and its contribution.

## 5. Conclusions

MERS is a respiratory illness caused by an emerging beta-coronavirus. The potential human–camel zoonotic transmission of MERS-CoV is disputed. This meta-analysis examined findings related to this potential transmission route, reported the prevalence of MERS-CoV in camels and humans, and described how zoonotic infections from dromedary camels could influence human infections. Although the prevalence of MERS-CoV was found to be moderate, the seroprevalence was high. Despite the high MERS-CoV prevalence in camel herds, zoonotic transmissions from camels are rare, and there was no correlation between the number of seropositive camels and infected humans. More research is needed to characterize the zoonotic spread of MERS-CoV. In addition, the contribution of zoonotic and human-to-human routes is to be determined.

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## Data availability statement

Not applicable.

## Declaration of Competing Interest

The authors declare no conflict of interest.

## Data availability

All data in manuscript and supplementary materials

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.onehlt.2022.100436>.

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