

Systematic Review

MERS-CoV and SARS-CoV Infections in Animals: A Systematic Review and Meta-Analysis of Prevalence Studies

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Abstract

Introduction: Coronaviruses are zoonotic viruses that include human epidemic pathogens such as the Middle East Respiratory Syndrome virus (MERS-CoV), and the Severe Acute Respiratory Syndrome virus (SARS-CoV), among others (e.g., COVID-19, the recently emerging coronavirus disease). The role of animals as potential reservoirs for such pathogens remains an unanswered question. No systematic reviews have been published on this topic to date.

Methods: We performed a systematic literature review with meta-analysis, using three databases to assess MERS-CoV and SARS-CoV infection in animals and its diagnosis by serological and molecular tests. We performed a random-effects model meta-analysis to calculate the pooled prevalences and 95% confidence interval (95%CI).

Results: 6,493 articles were retrieved (1960-2019). After screening by abstract/title, 50 articles were selected for full-text assessment. Of them, 42 were finally included for qualitative and quantitative analyses. From a total of 34 studies (n=20,896 animals), the pool prevalence by RT-PCR for MERS-CoV was 7.2% (95%CI 5.6-8.7%), with 97.3% occurring in camels, in which pool prevalence was 10.3% (95%CI 8.3-12.3). Qatar was the country with the highest MERS-CoV RT-PCR pool prevalence, 32.6% (95%CI 4.8-60.4%). From 5 studies and 2,618 animals, for SARS-CoV, the RT-PCR pool prevalence was 2.3% (95%CI 1.3-3.3). Of those, 38.35% were reported on bats, in which the pool prevalence was 14.1% (95%CI 0.0-44.6%).

Discussion: A considerable proportion of infected animals tested positive, particularly by nucleic acid amplification tests (NAAT), an essential condition that highlights the relevance of individual animals as reservoirs of MERS-CoV and SARS-CoV. In this meta-analysis, camels and bats were found to be positive by RT-PCR in over 10% of the cases for both; thus, suggesting their relevance in the maintenance of wild zoonotic transmission.

Keywords: Coronavirus; SARS-CoV; MERS-CoV; serology; molecular diagnosis; reservoir; public health.

Introduction

Rationale

Since 2002, the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), became an important zoonotic pathogen, after the recorded epidemics of SARS taking place in China and other countries accross East Asia. A decade later, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), originating in Saudi Arabia, emerged as the second most relevant zoonotic coronavirus (de Wit, van Doremalen, Falzarano, & Munster, 2016; Gumel et al., 2004; Srikantiah et al., 2005). Currently, SARS-CoV, taxonomically, shares species level with other SARS-related coronaviruses whithin the subgenus *Sarbecovirus*. The subgeneruses *Embecovirus*, *Hibecovirus*, *Merbecovirus*, and *Nobecovirus*, are all included whithin the genus *Betacoronavirus* (order *Nidovirales*; suborder *Cornidovirineae*; family *Coronaviridae*; subfamily *Coronavirinae*) (D. Katterine Bonilla-Aldana, Villamil-Gómez, Rabaan, & Rodriguez-Morales, 2020; Gorbalenya, 2020; Ksiazek et al., 2003; Q. Li et al., 2020; Millan-Oñate et al., 2020; Phan et al., 2020 doi 10.1056/NEJMc2001272; Pongpirul, Pongpirul, Ratnarathon, & Prasithsirikul, 2020); while the MERS-CoV is part of the subgenus *Merbecovirus* (D. Katterine Bonilla-Aldana et al., 2020; Gorbalenya, 2020; Ksiazek et al., 2003; Q. Li et al., 2020; Millan-Oñate et al., 2020; Phan et al., 2020 doi 10.1056/NEJMc2001272; Pongpirul et al., 2020).

As expected with other coronaviruses, SARS and MERS CoVs share many ecological and zoonotic aspects, as well as several clinical, epidemiological and management features of disease. (Al-Tawfiq, Zumla, & Memish, 2014; D. K. Bonilla-Aldana et al., 2020; Chan et al., 2020 doi 10.1016/S0140-6736(20)30154-9; N. Chen et al., 2020 doi 10.1016/S0140-6736(20)30211-7; Huang et al., 2020; World Health Organization, 2020a, 2020b). Structurally, these viruses are positive-strand RNA enveloped viruses isolated from bats which share a high degree of sequence homology with human isolates, suggesting their role as likely natural hosts and reservoirs (D. K. Bonilla-Aldana et al., 2019; Mattar & González, 2018; Millan-Oñate et al., 2020; Plowright et al., 2017; A. J. Rodriguez-Morales, D. K. Bonilla-Aldana, et al., 2020). The aforementioned raises the issue on the role and implications of animals as natural hosts and reservoirs for these viruses (Al-Tawfiq et al., 2014; N. Chen et al., 2020 doi 10.1016/S0140-6736(20)30211-7; Huang et al., 2020; Yin & Wunderink, 2018). Thus, a better understanding on the frequency and transmission dynamics across the wild, suburban, and urban settings, from animals to humans (spillover) is of utmost importance (Lu et al., 2020; McCloskey & Heymann, 2020; Mohd, Al-Tawfiq, & Memish, 2016; Monchatre-Leroy et al., 2017; Murdoch & French, 2020; Peeri et al., 2020). Despite multiple studies, conducted mainly in humans, animal studies are still scarce, particularly addressing in a concise manner all available evidence on the prevalence of SARS-CoV and MERS-CoV in different animal hosts (Dhama et al., 2020; Fan, Zhao, Shi, & Zhou, 2019; Guarner, 2020; Harypursat & Chen, 2020; Ji, Wang, Zhao, Zai, & Li, 2020; X. Li, Song, Wong, & Cui, 2020; X. Li, J. Zai, et al., 2020).

Such findings would be of extreme importance to extrapolate in light of the ongoing expanding epidemics of the third highly relevant zoonotic coronavirus (SARS-CoV-2), currently causing the Coronavirus Disease 2019 (COVID-19), which is also believed to have originated from animals (Ramadan & Shaib, 2019; Salata, Calistri, Parolin, & Palu, 2019; Wang & Eaton, 2007; Wong, Li, Lau, & Woo, 2019; Xiao et al., 2020), mostly bats in China (Bastola et al., 2020; Holshue et al., 2020; Pongpirul et al., 2020; Silverstein, Stroud, Cleghorn, & Leis, 2020). For these reasons, we carried out a systematic review and meta-analysis in order to consolidate what has been found from each study assessing infection in animals with MERS-CoV and SARS-CoV by serological and molecular techniques.

Objectives

- To summarize the frequency of infection of animals reported on currently available observational studies for MERS-CoV and SARS-CoV.
- To examine the differences between the pool prevalences by technique, animals, and countries.
- To compare the significant differences in the frequency of infection between SARS-CoV and MERS-CoV in animals by main serological and molecular techniques.

Methods

Protocol

This protocol follows the recommendations established by the PRISMA statement (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

Eligibility criteria

We included published peer-reviewed articles that reported infection in animals with serological or molecular confirmation of SARS-CoV or MERS-CoV. For serological tests, we considered enzyme-linked immunosorbent assay (ELISA), Indirect Immunofluorescence test (IFI), immunofluorescence antibody test (IFAT), pseudoparticle neutralization test (ppNT), microneutralization test (mNT), and the MERS-COV antigen assay (MERS-CoV Ag assay). For molecular based testing, Reverse Transcription Polymerase Chain Reaction (RT-PCR); and the Reverse Transcription Loop-Mediated Isothermal Amplification (RT-LAMP) were included. Article language limit was not set, and we included publications from January 1, 2002, until the date the search was finalized and completed (February 1, 2020). Review articles, opinion articles, and letters not presenting original data were excluded from the study, as well as studies reporting on cases with incomplete information.

Information sources and Search Strategy

We conducted a systematic review using Medline/PubMed, Scopus, and Web of Sciences. The search terms used were as follows: “coronavirus,” “SARS coronavirus 2019”, “SARS-CoV,” “MERS coronavirus 2019,” “MERS-CoV.” The searches were concluded by February 1, 2020, and four different researchers independently evaluated search results.

Study Selection

Results of the initial search strategy were first screened by title and abstract. The full texts of relevant articles were examined for inclusion and exclusion criteria (Figure 1). When an article reported duplicate information from the same patient, the information of both reports was combined in order to obtain complementary data, counting only as a single case. Observational studies that reported the frequency of animals infected due to SARS-CoV or MERS-CoV were included for quantitative synthesis (metanalysis).

Data collection process and data items:

Data extraction forms including information on the type of publication, the publishing institution, country, year and date of publication, as well as the number of infected animals assessed by serological or molecular tests, were filled independently by four investigators. A fifth researcher checked the article list and data extractions to ensure there were no duplicate articles or duplicate information of the same study and also resolved discrepancies about study inclusion.

Assessment of methodological quality and risk of bias:

For quality assessment, we used the Quality Appraisal of Case Series Studies Checklist of the IHE and specifically the critical appraisal tool to assess the quality of cross-sectional studies (AXIS) (Downes, Brennan, Williams, & Dean, 2016; Institute of Health Economics (IHE), 2014). Publication bias was assessed using a funnel-plot. A random-effects model was used to calculate the pooled prevalence and 95% CI, given variable degrees of data heterogeneity, and given the inherent heterogeneity in any systematic review of studies from the published literature. In addition, Egger’s test was performed.

Statistical approach

Unit discordance for variables was resolved by converting all units to a standard measurement for that variable. Percentages and means \pm standard deviation (SDs) were calculated to describe the distributions of categorical and continuous variables, respectively. Since individual patient information was not available for all patients, we report weighted means and SDs. The baseline data were analyzed using the Stata version 14.0, licensed for Universidad Tecnológica de Pereira.

The meta-analyses were performed using Stata, and the software Open Meta[Analyst](Wallace et al., 2012) and Comprehensive Meta Analysis ve.3.3® licensed for Universidad Tecnológica de Pereira. Pooled prevalences and their 95% confidence intervals (95% CIs) were used to summarize the weighted effect size for each study grouping variable using the binary random-effects model (the weighting took into consideration the sample sizes of the individual studies), except for median age, where a continuous random-effect model was applied (DerSimonian-Laird procedure) (Kontopantelis & Reeves, 2012; Viechtbauer, 2010). A random-effects meta-analysis model involves an assumption that the effects being estimated in the different studies are not identical, but follow some distribution. For random-effects analyses, the pooled estimate and 95% CIs refer to the center of the distribution of pooled prevalence but do not describe the width of the distribution. Often the pooled estimate and its 95% CI are quoted in isolation as an alternative estimate of the quantity evaluated in a fixed-effect meta-analysis, which is inappropriate. The 95% CI from a random-effects meta-analysis describes uncertainty in the location of the mean of systematically different prevalence in the different studies.

Measures of heterogeneity, including Cochran’s Q statistic, the I² index, and the tau-squared test, were estimated and reported. We performed subgroup analyses by techniques, animals, and countries. And meta-analyses for each of the variables of interest. Publication bias was assessed using a funnel-plot. A random-effects model was used to calculate the pooled prevalence and 95% CI, given variable degrees of data heterogeneity, and given the inherent heterogeneity in any systematic review of studies from the published literature.

Results

Study Selection and Characteristics:

A total of 6,493 articles were retrieved using the search strategy. After screening by abstract and title, 50 articles were finally selected for full-text assessment. Of these, eight were excluded due to lack of information on molecular diagnosis, and 42 were finally included for final qualitative and quantitative meta-analysis (Figure 1). The main characteristics of the included studies are shown in Table 1.

Our review included 42 studies that were published between January 1, 2002, and December 31, 2019, most of them from Kenya (18%), Saudi Arabia (16%), Egypt (10%), and Qatar (10%) (Table 1), including a total of 23,807 animals assessed by RT-PCR, and 8,604 by ELISA, 37 studies for MERS-CoV and 5 for SARS-CoV. All the studies were cross-sectional (Tables 1-2). We analyzed 16 variables for the meta-analyses (Table 3). Publication bias was assessed with a funnel plot for the standard error by logit event, with no evidence of bias for MERS (Figure S1) but with evidence for SARS (Figure S2). Additionally, the Egger test suggested that there was no notable evidence of publication bias on MERS (P=0.6708), but significant for SARS (P=0.0103).

Individual study characteristics:

The mean of the number of included animals for RT-PCR per study was 384, 374 for ELISA, with positive rates ranging from 0 to 100% in both coronaviruses (Tables 1-2).

Serological findings:

Regarding the ELISA, the pool prevalence for MERS-CoV derived from 15 studies, including 7,648 animals, was 73.0% (95%CI 63.8-82.2%) (Table 3). In the case of SARS-CoV, with seven studies, with 947 animals, it was 3.0% (95%CI 0.4-5.5%) (Table 3) (Figure S3).

The results for MERS-CoV with the IFI/IFAT techniques were similar, 83.9% (95%CI 66.0-100.0%) (no significant difference with the ELISA) (Table 3). Not enough studies with these techniques were available for meta-analyses of SARS-CoV. However, for SARS-CoV, the pool prevalence with the Western Blot, from 2 studies, with 44 animals, was 65.0% (95%CI 0.0-100.0%). Similarly, for MERS-CoV, there were not enough studies with Western Blot available for meta-analyses (Table 3) (Figure S3).

Molecular findings:

Regarding the RT-PCR, the pool prevalence for MERS-CoV derived from 34 studies, including 20,896 animals, was 7.2% (95%CI 5.6-8.7%) (Table 3). From the total number of animals, 97.3% corresponded to camels, in which pool prevalence was 10.3% (95%CI 8.3-12.3). In the case of SARS-CoV, with 2,618 animals in from 5 studies, the RT-PCR pool prevalence was 2.3% (95%CI 1.3-3.3). Of them, 38.35% were bats, in which the pool prevalence was 14.1% (95%CI 0.0-44.6%) (Table 3) (Figure S3).

Comparing the findings by countries, Kenya, Qatar, Saudi Arabia, United Arab Emirates, and Egypt, reported three or more studies for MERS-CoV in animals using RT-PCR (Table 3). The highest prevalence was found in Qatar, with five studies, including 177 animals, with 32.6% (95%CI 4.8-60.4%), followed by United Arab Emirates (UAE), with four studies, including the highest number of animals, 8,166, for a pool prevalence of 16.0% (95%CI 5.8-26.2%) (no significant differences between both countries). Saudi Arabia yielded 15.4% and Egypt 7.7%. The lowest pool prevalence derived from Kenya, with 13 studies and 3,830 animals, with 0.4% (95%CI 0.2-0.6%), significantly lower than Qatar and UAE (Table 3) (Figure S3).

Discussion

A considerable number of studies have shown that the proportion of infected animals testing positive by molecular techniques, is an essential condition to consider the relevance of individual animals as reservoirs of MERS-CoV and SARS-CoV (Baharoon & Memish, 2019; D. K. Bonilla-Aldana et al., 2020; de Groot et al., 2013; Gumel et al., 2004; Yin & Wunderink, 2018). In this meta-analysis, positivity amongst camels and bats by RT-PCR was found in more than 10% of the evaluated animals, suggesting their possible role and importance in the maintenance of wild zoonotic transmission (Azhar et al., 2014).

In 2012, the MERS-CoV was first detected in humans, and it wasn't until mid-2016 that 1,733 laboratory-confirmed human cases and 628 deaths were reported to the World Health Organization (WHO) from 27 countries (Munyua et al., 2017). The majority of these cases were reported from the Arabian Peninsula, but imported cases to other countries have also caused significant hospital-linked outbreaks, such as in South Korea, in 2015. Severe respiratory disease and death rate was higher in infections among older patients and those with preexisting conditions. Dromedary camels have been identified as potential reservoir for the virus following the detection of the virus in camels in Saudi Arabia, Oman, and Qatar, and the detection of high seroprevalence levels of MERS-CoV antibodies in camel populations from a broader range of countries including countries in the Middle East and Africa. Most MERS-CoV infections in humans are not linked to camel exposure and are thought to be due to human-to-human transmission, particularly in health-care settings. Low frequency of camel-to-human infections is supported by the fact that MERS-CoV seroprevalence among the general human population in Saudi Arabia is less than 0.5%, with significantly higher seropositivity amongst camel shepherds (2.3%) and slaughterhouse workers (3.6%) (Munyua et al., 2017). Nevertheless, results from 20 studies have shown that prevalence in camels is approximately 10.3%, ranging from 8.3 to 12.3 (95%CI); thus, incriminating camels instead as potential animal reservoirs.

According to the Food and Agriculture Organization (FAO), the world population of camels in 2001 was 19 million, of which, 17 million were dromedary camels, and approximately 65% of these were found in the eastern African countries of Sudan, Somalia, Ethiopia, and Kenya (Munyua et al., 2017). Kenya was found in this systematic review to have a pool prevalence of 0.4% for MERS-CoV, considering more than 3,800 animals. Even though the majority of dromedary camels are in Africa, no cases of MERS-CoV in humans have been reported in Africa, except for a cluster of three family members in Tunisia, back in 2013, which was linked to an imported index case with no history of exposure to camels (Abroug et al., 2014). Such findings may be related to the low frequency of infection among camels, as observed revealed in this systematic review. In such contexts, comparative genomic and phylogenetic studies focusing on viral sequences derived both, from human hosts and dromedaries are essential to trace and link possible zoonotic transmission of MERS-CoV from dromedaries to humans (Al Hammadi et al., 2015).

A retrospective study carried out in Kenya detected MERS-CoV antibodies in more than 90% of camels from different regions of the country (Corman et al., 2014; Munyua et al., 2017). A more recent study that analyzed > 1,000 human sera among pastoralists who did not keep camels reported two likely asymptomatic (< 0.2%) positive human cases for MERS-CoV by neutralizing antibodies detection (Liljander et al., 2016; Munyua et al., 2017). In order to better understand the risk of transmission between camels and humans living in close contact, more studies are needed, including more serosurvey or seroprevalence investigations amongst camels and humans within the same households to determine the prevalence of MERS-CoV antibodies as well as to determine the frequency of infection by molecular techniques and also establish which are the possible risk factors associated with seropositivity in camels and humans. Studies involving follow-up of herds of camels from time of calving through the first year of life with serial blood samples together with oral and rectal or fresh fecal swabs would better help define the ecology of the MERS-CoV-like virus infecting these animals and provide virus isolates for genetic characterization (Hemida et al., 2013). Another concerning issue is that the MERS-CoV is not only shed by nasal secretions and feces, but also from milk (viral RNA), raising the possibility of food-borne transmission of MERS-CoV (Reusken, Farag, et al., 2014). In addition, a high proportion of camels presenting for slaughter in some studies show evidence for nasal MERS-CoV shedding (Farag et al., 2015) thus increasing the likelihood of potential airborne transmission.

Evidence suggests that MERS-CoV was present and circulating in camels some decades ago before MERS emerged causing epidemics in the Middle East, as found in a study assessing blood samples from 1992, finding low frequency antibodies (4.5%) in the Rift Valley of Kenya (Corman et al., 2014). In another retrospective study surveying countries in Africa, (Somalia, Sudan, and Egypt) it was found that 189 archived serum samples from camels tested positive for MERS-CoV antibodies, as far as 1983, with 80% in Somalia and 86.7% in Sudan in 1984 and 85.2% in Somalia and 81.4% in 1997 in Egypt (Muller et al., 2014). Also, camels have tested positive to MERS-CoV by serological and molecular-based methods (including genome sequencing) in different studies outside the Arabian Peninsula, and across Africa (Reusken, Messadi, et al., 2014) (Chu et al., 2014). In those countries, imported infected camels have also been a matter of concern, even in recent years (Al Hammadi et al., 2015). For that reason, studies have also been carried in Australia and Japan (Hemida et al., 2014). However, preliminary data suggest that nor Australian or Japanese dromedaries are exempt of MERS-CoV infection, demanding further confirmatory studies (Hemida et al., 2014; Shirato et al., 2015).

In addition to camels, the role of other animals in MERS transmission remains largely unknown. Molecular investigations have suggested that bats in Saudi Arabia are infected with several alphacoronaviruses and betacoronaviruses. A virus isolated from 1 bat showed 100% shared nucleotide identity to a human virus from an index case-patient. An increasing body of research suggests that bats may play a role in human infection (Memish et al., 2013). A wide range of CoV species are known to circulate among bats in Saudi Arabia (Memish et al., 2013). Although the prevalence of CoVs was high ($\approx 28\%$ of fecal samples), MERS CoV was found in only one bat (Memish et al., 2013). A 3.5% MERS CoV infection rate ($n = 29$; 95% CI 0–20%) in *Taphozous perforatus* bats is low compared with that for severe acute respiratory syndrome-like CoV in rhinolophid bats in China (10%–12.5%) but consistent with CoV prevalence among bats in Mexico (Anthony et al., 2013; Memish et al., 2013). Bats are reservoirs of several viruses that can cause human disease, including rabies, Hendra, Nipah, Marburg, severe acute respiratory syndrome CoV, Ebola, rabies, and even some arboviral diseases, such as dengue and Venezuelan Equine Encephalitis viruses (Calderon, Guzman, Mattar, Rodriguez, Acosta, et al., 2019; Calderon, Guzman, Mattar, Rodriguez, Martinez, et al., 2019; Lau et al., 2005; W. Li et al., 2005; Memish et al., 2013; Poon et al., 2005; Smith & Wang, 2013). Although, in the current systematic review, we were not able to find enough prevalence studies of MERS-CoV in bats for a meta-analysis, we did find more studies relating bats to SARS-CoV, in which 14% a pool prevalence was found after analyzing more than 1000 specimens. Cross-species transmission from bats to humans can be direct, through contact with infected bats or their excreta, or facilitated by intermediate hosts (Khan et al., 2012), probably also in MERS-CoV, but especially for SARS-CoV.

Bat CoVs are typically host specific; however, MERS-related CoVs have reportedly been found in many bat families, including *Vespertilionidae*, *Molossidae*, *Nycteridae*, and *Emballonuridae*

(sheath-tailed bats) in Africa, the Americas, Asia, and Europe (Memish et al., 2013). In addition to bats and camels, the presence of MERS-CoV in other animals has been investigated, including the alpaca (*Vicugna pacos*), a native *Camelidae* species from South America and a close descendent of the vicuña, which has proved naturally susceptible to MERS-CoV infection. Such findings prompt future studies in order to determine the role of alpacas as additional livestock reservoir for MERS-CoV (Reusken et al., 2016) in other areas of the Middle East. In a study carried out in Qatar, an endemic area for MERS, alpacas were found positive to MERS-CoV-specific antibodies with reciprocal titers ranging from 49 to 773 (Reusken et al., 2016). These findings raise essential questions regarding the possibility that certain areas of South America would be suitable for MERS-CoV transmission and established endemicity, as well as for other zoonotic coronaviruses. In these same lines, the genus *Vicugna* which includes the *V. vicugna* (vicuña), another South American camelid, also deserves further investigation regarding its possible susceptibility to infection by MERS-CoV and other coronaviruses. In some countries of South America, the llama, another camelid, widely used as a meat and pack animal by Andean cultures since the Pre-Columbian era, could also prove susceptible to MERS-CoV infection demanding careful investigation.

In Saudi Arabia, other animals have also been scrutinized resulting negative to MERS-CoV, as is the case for sheep, goats, cattle, and chicken (Hemida et al., 2013). Similar results have been found in Egypt, assessing not only sheep, goats, but also water buffalos and cows, testing also negatively (Perera et al., 2013). In that same study (Perera et al., 2013), more than 93% of camels tested positive for antibodies by ppNT and mNT, exhibiting a high prevalence.

In contrast, a study in Egypt following on serum microneutralisation assay (mnT) found that one serum sample from a sheep (1/51, 2%) revealed 1:640 neutralizing titer (M. Ali et al., 2017). This same study found negative results from other domestic animals such as cattle, goats, donkeys, buffalo, and horses, but also bats. Using the mnT, they found 84% positivity in camels, with RT-PCR positive confirmation of around 4% (M. Ali et al., 2017). Sheeps were also found to test negative for MERS-CoV in a study from the United Arab Emirates (Muhairi et al., 2016).

Interestingly also primates, such as the *Papio anubis*, rodents such as *Acomys kempis*, *Acomys percivalli*, *Elephantulus rufescens*, *Gerbillus robustus*, *Aethomys shindei*, *Myomyscus brodermani*, *Grammonys dolichorus*, and *Saccostomus meamsi*, were screened for MERS-CoV in a study from Kenya, testing all negative by RT-PCR (Gambo, 2018). Unfortunately, the authors of this study did not assess blood samples of those animals by serological tests. In a similar study from Kenya, using IFI/IFAT, authors found seropositivity rates as high as 94% in camels (Corman et al., 2014).

Data derived from a longitudinal study in camels performed in Saudi Arabia, provided evidence for reinfection of previously seropositive camels, suggesting that prior infection does not provide complete immunity from reinfection, a finding that is relevant to camel vaccination strategies as a means to prevent zoonotic transmission (Hemida et al., 2017). These results may be of interest for MERS-CoV and other coronaviruses in humans, as is the case of Coronavirus Disease 2019 (COVID-19), in which there is also concern for possible reinfections in humans throughout the ongoing 2020 outbreak in China. In the specific case of MERS-CoV in camels, it appears that infections do not elicit long-lasting (mucosal) immunity (Frag et al., 2015; Kiambi et al., 2018).

Besides reinfection, co-infection with other coronaviruses is also a matter of pressing concern. In a 2019 study, results revealed the occurrence of MERS-CoV and HKU8r-CoV co-circulation in camels. The study also suggested the possibility of circulation of a recombinant coronavirus virus with the spike of MERS-CoV and the nucleocapsid of an HKU8r-CoV in Kenya. However, the authors failed to provide molecular evidence of an HKU8r-CoV or a putative recombinant virus (Zhang et al., 2019).

In contrast to MERS-CoV, SARS-CoV has also been detected in studies from different animals, besides bats (Tang et al., 2006), in China, and other countries such as Kenya (Muller et al., 2007; Tong et al., 2009), but also from pigs, implicating such species in possible zoonotic transmission (W. Chen et al., 2005). A study in China reported on the isolation of SARS-CoV from a pig during a survey aimed to determine possible routes of viral transmission short after the SARS epidemic,

finding that the animal was in close contact with humans in a suburban area and its extended farming villages, Xiqing County of Tianjin, where a SARS outbreak occurred in late spring of 2003(W. Chen et al., 2005).

The results of this systematic review highlight the importance of animals as reservoirs for coronavirus and their intimate link as zoonotic diseases, as for the case of MERS and SARS. Also, the increasing need for more field studies aimed to understand the main epidemiological features, ecological / environmental aspects, and the role of wild and domestic animals as drivers of these emerging viral infections(Biscayart et al., 2020; Holshue et al., 2020; Rodriguez-Morales, MacGregor, Kanagarajah, Patel, & Schlagenhauf, 2020). Despite a growing volume of literature, further studies on many aspects of related to MERS-CoV and SARS-CoV are needed. Moreover, with the recent emergence of SARS-CoV-2 causing the COVID-19 epidemics, studies aimed at evaluating the role of animals reservoirs such as bats, camels and other domestic animals as well as wild game, including pangolins, birds, snakes, and other reptiles and mammals, would be highly relevant, as to drawing the landscape on the origin of these coronaviruses as zoonotic pathogens, (A. J. Rodriguez-Morales, D. K. Bonilla-Aldana, et al., 2020; A. J. Rodriguez-Morales, K. MacGregor, et al., 2020), and their potential for global expansion (Bastola et al., 2020; Malik et al., 2020; Alfonso J. Rodriguez-Morales et al., 2020; A. J. Rodriguez-Morales, K. MacGregor, et al., 2020).

Limitations

This review has several limitations. First, still few studies are available for inclusion, especially for SARS-CoV(Cui, Li, & Shi, 2019; World Health Organization, 2018). It would be better to include as many more studies not only from the Middle East but especially from East Asia. Second, more detailed information on the collected and sample animals, particularly regarding their clinical findings and conditions during collection, was unavailable in most studies at the time of analyses; however, the data in this review permit a first synthesis of the frequency of infection due to MERS-CoV and SARS-CoV in animals, although the need to be more detailed for the last one.

Conclusions

Infection with MERS-CoV and SARS-CoV is considered crucial in animals given their reported frequency (Cui et al., 2019; Wang & Anderson, 2019). These results, as mentioned, not only have implications for MERS-CoV and SARS-CoV but also for the novel SARS-CoV-2, causing the COVID-19. Additional research is needed to elucidate multiple aspects of transmission, reinfection, coinfection, and many other ecological aspects of the disease, including the role of environmental aspects related to their natural cycles. Future research should focus on developing studies that contribute to fully characterizing and defining the determinants of coronavirus zoonotic spillover and their linkages to make operational contributions for risk assessment(Plowright et al., 2017).The phenomenon of cross-species spillover is the defining characteristic of pathogens that transmit from vertebrate animals to humans, zoonoses, as is the case of MERS-CoV, SARS-CoV, and SARS-CoV-2. The public health burden imposed by zoonoses includes outbreaks of those pathogens that can lead to even to larger outbreaks, as currently with the ongoing COVID-19. Camels and bats are essential confirmed hosts of MERS-CoV and SARS-CoV, respectively. The role of other animals remains an entirely unanswered question, but a link between these viruses and other mammals remains a latent possibility.

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Figure 1. Study selection and characteristics.

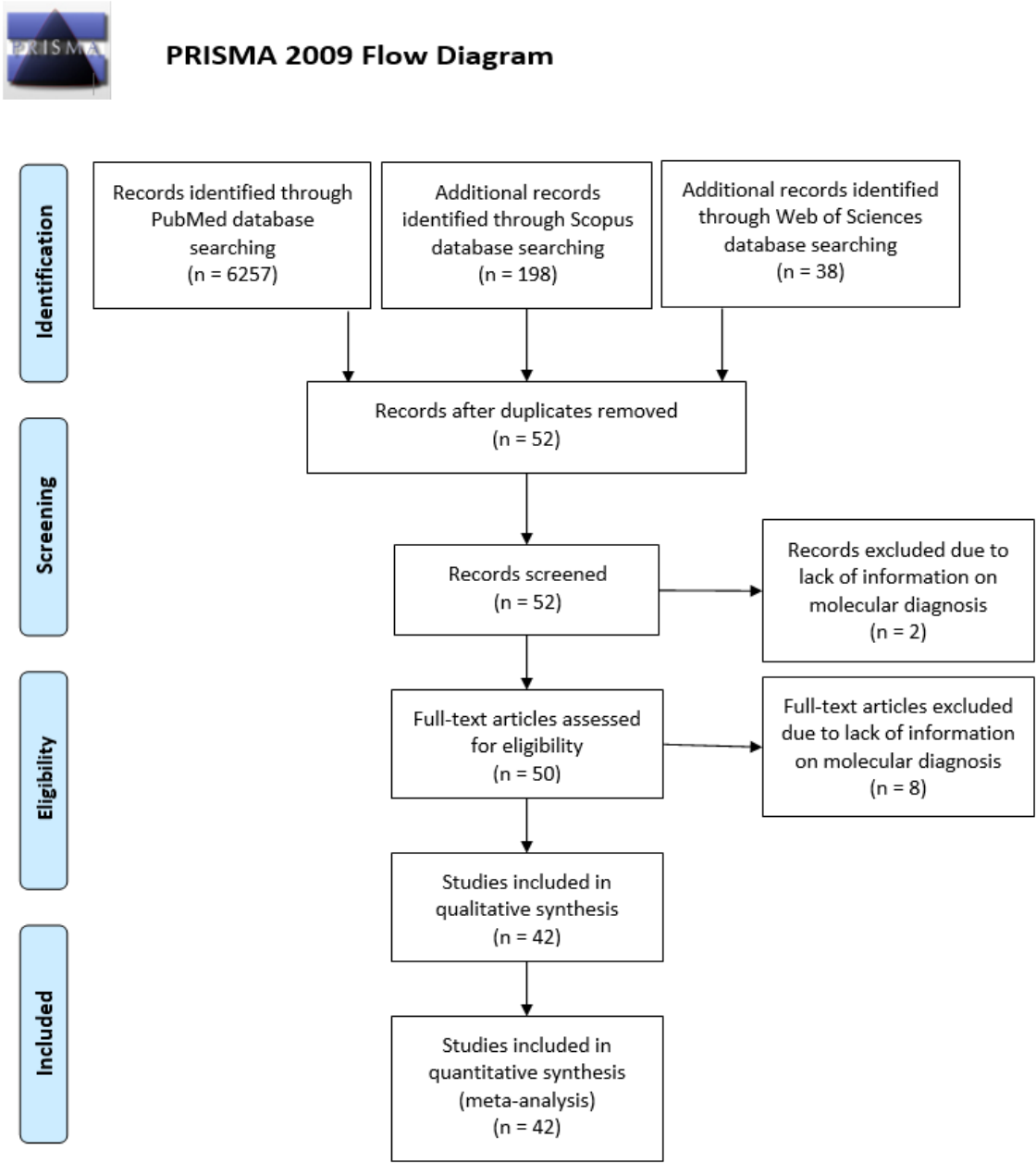


Table 1.Characteristics of the included studies on MERS and SARS on animals.

Study	Journal	Year*	Country	Study Type	Animals evaluated	Laboratory Techniques																		Ref
						ELISA		IFI/IFAT		RT-PCR		ppNT		Protein MicroArray		mNT		RT-LAMP		Western Blot		Rapid MERS-CoV Ag assay		
						N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	
MERS studies																								
No Serologic Evidence of Middle East Respiratory Syndrome Coronavirus Infection among Camel Farmers Exposed to Highly Seropositive Camel Herds: A Household Linked Study, Kenya, 2013	Am J Trop Med Hyg. 2017 Jun;96(6):1318-1324.	2017	Kenya	S	Camels	879	791	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	(Mun yua et al., 2017)
Middle East Respiratory Syndrome Coronavirus in Bats, Saudi Arabia	Emerg Infect Dis. 2013 Nov;19(11):1819-23.	2013	Saudi Arabia	P	Bats	-	-	-	-	29	1	-	-	-	-	-	-	-	-	-	-	-	-	(Me mish et al., 2013)
Antibodies against MERS Coronavirus in Dromedary Camels, Kenya, 1992-2013	Emerg Infect Dis. 2014 Aug;20(8):1319-22. doi	2014	Kenya	S	Dromedary camels	774	228	228	213	-	-	-	-	-	-	-	-	-	-	-	-	-	-	(Cor man et al., 2014)
Geographic Distribution of MERS Coronavirus among Dromedary Camels, Africa	Emerg Infect Dis. 2014 Aug;20(8):1370-4	2014	Tunisia	P	Dromedary camels	-	-	-	-	-	-	-	-	-	204	99	-	-	-	-	-	-	-	(Reus ken, Mess adi, et al., 2014)
			Ethiopia	P	Dromedary camels	-	-	-	-	-	-	-	-	188	182	-	-	-	-	-	-	-	-	
			Nigeria	P	Dromedary camels	-	-	-	-	-	-	-	-	358	336	-	-	-	-	-	-	-	-	
MERS Coronavirus neutralizing antibodies in Camels, Eastern Africa, 1983-1997	Emerg Infect Dis. 2014 Dec;20(12):2093-5.	2014	Somalia	S	Dromedary camels	86	72	-	-	-	-	-	-	-	-	86	70	-	-	-	-	-	-	(Mull er et al., 2014)
			Sudan	S	Dromedary camels	60	52	-	-	-	-	-	-	-	-	60	49	-	-	-	-	-	-	
			Egypt	S	Dromedary camels	43	35	-	-	-	-	-	-	-	-	43	34	-	-	-	-	-	-	
MERS Coronaviruses in Dromedary Camels, Egypt	Emerg Infect Dis. 2014 Jun;20(6):1049-53	2014	Egypt	P	Dromedary camels	-	-	-	-	110	4	-	-	-	-	-	-	-	-	-	-	-	-	(Chu et al., 2014)
Asymptomatic MERS-CoV Infection in Humans Possibly Linked to Infected Dromedaries Imported from Oman to United Arab Emirates, May 2015	Emerg Infect Dis. 2015 Dec;21(12):2197-200	2015	United Arab Emirates	P	Dromedary camels	-	-	-	-	5	5	-	-	-	-	-	-	-	-	-	-	-	-	(Al Ham madi et al., 2015)
MERS-CoV Infection of Alpaca in a Region Where MERS-CoV is endemic	Emerg Infect Dis. 2016 Jun; 22(6): 1129–1131.	2016	Qatar	P	Dromedary camels	-	-	-	-	15	0	-	-	15	15	-	-	-	-	-	-	-	-	(Reus ken et al., 2016)
				P	<i>Vicugna pacos</i>	-	-	-	-	10	0	-	-	10	9	-	-	-	-	-	-	-	-	
Serologic Evidence for MERS-CoV Infection in Dromedary Camels, Punjab, Pakistan, 2012–2015	Emerg Infect Dis. 2017 Mar;23(3):550-551.	2017	Pakistan	S	Dromedary camels	565	315	-	-	-	-	-	-	-	-	565	223	-	-	-	-	-	-	(Saqi b et al., 2017)
Middle East Respiratory Syndrome Coronavirus Antibodies in Dromedary Camels, Bangladesh, 2015	Emerg Infect Dis. 2018 May;24(5):926-928.	2018	Bangladesh	P	Dromedary camels	55	17	-	-	55	0	55	17	-	-	-	-	-	-	-	-	-	-	(Is la m et al., 2018)
Systematic, active surveillance for Middle East respiratory syndrome coronavirus in camels in Egypt	Emerg Microbes Infect. 2017 Jan 4;6(1):e1.	2017	Egypt	P	Dromedary camels	-	-	-	-	2825	435	-	-	-	-	2541	1808	-	-	-	-	-	-	(M. A. Ali et

						Laboratory Techniques																Rapid MERS-CoV Ag assay		Ref	
						ELISA		IFI/IFAT		RT-PCR		ppNT		Protein MicroArray		mNT		RT-LAMP		Western Blot					
						N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)		
High Prevalence of Middle East Respiratory Coronavirus in Young Dromedary Camels in Jordan	Vector Borne Zoonotic Dis. 2017 Feb;17(2):155-159.	2016	Jordan	P	<i>Acomyskempis</i>	-	-	-	-	30	0	-	-	-	-	-	-	-	-	-	-	-	-	-	(van Doremale et al., 2017) (Thwiny, Ham ed, & Nazz al, 2018) (Om meh et al., 2018) (Zoh aib et al., 2018) (Yus of et al., 2015) (Muh airi et al., 2016)
				P	<i>Acomysperci valli</i>	-	-	-	-	29	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Elephantulus rufescens</i>	-	-	-	-	6	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Gerbilliscus robustus</i>	-	-	-	-	20	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Aethomyshin dei</i>	-	-	-	-	60	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Myomyscus b rodernani</i>	-	-	-	-	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Grammonys dolichorus</i>	-	-	-	-	7	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	<i>Saccostomus meamsi</i>	-	-	-	-	8	0	-	-	-	-	-	-	-	-	-	-	-	-	-	
Seroepidemiological study of Middle East Respiratory Syndrome(MERS) virus infection in Iraqi dromedary camels	Veterinarski Arhiv 88(2):191-200	2018	Iraq	S	Dromedary camels	180	153	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	(van Doremale et al., 2017) (Thwiny, Ham ed, & Nazz al, 2018) (Om meh et al., 2018) (Zoh aib et al., 2018) (Yus of et al., 2015) (Muh airi et al., 2016)		
Genetic Evidence of Middle East Respiratory Syndrome Coronavirus (MERS-Cov) and Widespread Seroprevalence among Camels in Kenya	Virol Sin. 2018 Dec;33(6):484-492.	2018	Kenya	P	Dromedary camels	1163	792	-	-	1163	11	-	-	-	-	-	-	-	-	-	-	-	(Zoh aib et al., 2018) (Yus of et al., 2015) (Muh airi et al., 2016)		
Countrywide Survey for MERS-Coronavirus Antibodies in Dromedaries and Humans in Pakistan	Virol Sin. 2018 Oct;33(5):410-417.	2018	Pakistan	P	Dromedary camels	1050	794	-	-	2050	22	-	-	-	-	-	-	-	-	-	-	-	(Zoh aib et al., 2018) (Yus of et al., 2015) (Muh airi et al., 2016)		
Prevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels in Abu Dhabi Emirate, United Arab Emirates	Virus Genes. 2015 Jun;50(3):509-13.	2015	United Arab Emirates	P	Dromedary camels	-	-	-	-	7803	126	-	-	-	-	-	-	-	-	-	-	-	(Yus of et al., 2015) (Muh airi et al., 2016)		
Epidemiological investigation of Middle East respiratory syndrome coronavirus in dromedary camel farms linked with human infection in Abu Dhabi Emirate, United Arab Emirates	Virus Genes. 2016 Dec;52(6):848-854.	2016	United Arab Emirates	P	Dromedary camels	-	-	-	-	324	42	-	-	-	-	-	-	-	-	-	-	-	(Muh airi et al., 2016)		
The prevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) antibodies in dromedary camels in Israel	Zoonoses Public Health. 2018 Sep;65(6):749-754.	2018	Israel	S	sheep Dromedary camels	-	-	-	-	34	0	-	-	-	-	-	-	-	-	-	-	-	-	(Harcourt et al., 2018)	
SARS studies																									
SARS-associated Coronavirus Transmitted from Human to Pig	Emerg Infect Dis. 2005 Mar;11(3):446-8.	2005	China	P	Pigs	110	2	-	-	14	1	-	-	-	-	-	-	-	-	7	2	-	-	(W. Chen	

						Laboratory Techniques																		Ref		
						ELISA		IFI/IFAT		RT-PCR		ppNT		Protein		mNT		RT-LAMP		Western Blot		Rapid				
														MicroArray								MERS-CoV	Ag assay			
Study	Journal	Year*	Country	Study Type	Animals evaluated	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)	N	n(+)			
Coronavirus Antibodies in African Bat Species	Emerg Infect Dis. 2007 Sep;13(9):1367-70.	2007	South Africa	P	Cattle	60	0	-	-	22	0	-	-	-	-	-	-	-	-	-	-	-	-	et al., 2005)		
				P	Dogs	20	0	-	-	14	0	-	-	-	-	-	-	-	-	-	-	-	-	-		
				P	Cats	11	0	-	-	11	0	-	-	-	-	-	-	-	-	-	-	-	-	-		
				P	Chickens	11	0	-	-	11	0	-	-	-	-	-	-	-	-	-	-	-	-	-		
				P	Ducks	30	0	-	-	22	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
				P	Bats	705	47	37	12			-	-	-	-	-	-	-	-	37	36	-	-	(Muller et al., 2007)		
Detection of Novel SARS-like and other Coronaviruses in Bats from Kenya	Emerg Infect Dis. 2009 Mar;15(3):482-5.	2009	Kenya	P	Bats	-	-	-	-	19	6	-	-	-	-	-	-	-	-	-	-	-	-	(Tong et al., 2009)		
Prevalence and Genetic Diversity of Coronaviruses in Bats from China	J Virol. 2006 Aug;80(15):7481-90.	2006	China	P	Bats	-	-	-	-	985	3	-	-	-	-	-	-	-	-	-	-	-	-	(Tang et al., 2006)		
Molecular Detection and Characterization of Coronavirus Infection in Olive Baboons (Papio Anubis), Bats and Rodents in Laikipia County, Kenya	Univ of Nairobi Res Arch 2018	2017	Kenya	P	Papioanubis	-	-	-	-	130	0	-	-	-	-	-	-	-	-	-	-	-	-	(Gambo, 2018)		
					Chaerephon sp	-	-	-	-	188	0	-	-	-	-	-	-	-	-	-	-	-	-	-		
					Scotophiluss p	-	-	-	-	14	0	-	-	-	-	-	-	-	-	-	-	-	-	-		
					Acomyssp	-	-	-	-	30	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Acomyssp	-	-	-	-	29	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Elephantulus rufescens	-	-	-	-	6	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Gerbilliscus robustus	-	-	-	-	20	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Aethomyshin dei	-	-	-	-	60	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Myomyscusb rodermani	-	-	-	-	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Grammonys dolichorus	-	-	-	-	7	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
					Saccostomus meamsi	-	-	-	-	8	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

*Year of publication; ELISA, enzyme-linked immunosorbent assay; IFI, Indirect Immunofluorescence; IFAT, immunofluorescence antibody test; RT-PCR, reverse transcription-polymerase chain reaction; ppNT,pseudoparticleneutralization;mNT, microneutralization test; RT-LAMP, Reverse transcription loop-mediated isothermal amplification.MERS-CoV Ag assay, MERS-COV antigen assay. P, prevalence, S, seroprevalence.

Table 2. Positive results for MERS-CoV and SARS-CoV in animals in the included studies by different techniques.

						%								
Study	Journal	Year*	Country	Study Type	Animals evaluated	ELISA	IF/IFAT	RT-PCR	ppNT	Protein MicroArray	mNT	RT-LAMP	Western Blot	Rapid MERS-CoV Ag assay
MERS Studies														
No Serologic Evidence of Middle East Respiratory Syndrome Coronavirus Infection among Camel Farmers Exposed to Highly Seropositive Camel Herds: A Household Linked Study, Kenya, 2013	Am J Trop Med Hyg. 2017 Jun;96(6):1318-1324.	2017	Kenya	S	Camels	90.0								
Middle East Respiratory Syndrome Coronavirus in Bats, Saudi Arabia	Emerg Infect Dis. 2013 Nov;19(11):1819-23.	2013	Saudi Arabia	P	Bats			3.4						
Antibodies against MERS Coronavirus in Dromedary Camels, Kenya, 1992-2013	Emerg Infect Dis. 2014 Aug;20(8):1319-22. doi	2014	Kenya	S	Dromedary camels	29.5	93.4							
Geographic Distribution of MERS Coronavirus among Dromedary Camels, Africa	Emerg Infect Dis. 2014 Aug;20(8):1370-4	2014	Tunisia	P	Dromedary camels					48.5				
			Ethiopia	P	Dromedary camels					96.8				
			Nigeria	P	Dromedary camels					93.9				
MERS Coronavirus neutralizing antibodies in Camels, Eastern Africa, 1983-1997	Emerg Infect Dis. 2014 Dec;20(12):2093-5.	2014	Somalia	S	Dromedary camels	83.7					81			
			Sudan	S	Dromedary camels	86.7					82			
			Egypt	S	Dromedary camels	81.4					79			
MERS Coronaviruses in Dromedary Camels, Egypt	Emerg Infect Dis. 2014 Jun;20(6):1049-53	2014	Egypt	P	Dromedary camels			3.6						
Asymptomatic MERS-CoV Infection in Humans Possibly Linked to Infected Dromedaries Imported from Oman to United Arab Emirates, May 2015	Emerg Infect Dis. 2015 Dec;21(12):2197-200	2015	United Arab Emirates	P	Dromedary camels			100.0						
MERS-CoV Infection of Alpaca in a Region Where MERS-CoV is endemic	Emerg Infect Dis. 2016 Jun; 22(6): 1129–1131.	2016	Qatar	P	Dromedary camels			0.0		100.0				
				P	Vicugna pacos			0.0		90.0				
Serologic Evidence for MERS-CoV Infection in Dromedary Camels, Punjab, Pakistan, 2012–2015	Emerg Infect Dis. 2017 Mar;23(3):550-551.	2017	Pakistan	S	Dromedary camels	55.8					39			
Middle East Respiratory Syndrome Coronavirus Antibodies in Dromedary Camels, Bangladesh, 2015	Emerg Infect Dis. 2018 May;24(5):926-928.	2018	Bangladesh	P	Dromedary camels	30.9		0.0	30.9					
Systematic, active surveillance for Middle East respiratory syndrome coronavirus in camels in Egypt	Emerg Microbes Infect. 2017 Jan 4;6(1):e1.	2017	Egypt	P	Dromedary camels			15.4			71			
Longitudinal study of Middle East Respiratory Syndrome coronavirus infection in dromedary camel herds in Saudi Arabia, 2014–2015	Emerg Microbes Infect. 2017 Jun 21;6(6):e56.	2017	Saudi Arabia	P	Dromedary camels			3.0						
Detection of distinct MERS-Coronavirus strains in dromedary camels from Kenya, 2017	Emerg Microbes Infect. 2018 Nov 28;7(1):195.	2018	Kenya	P	Dromedary camels			0.3						
Serological evidence of MERS-CoV and HKU8-related CoV co-infection in Kenyan camels	Emerg Microbes Infect. 2019;8(1):1528-1534	2019	Kenya	S	Dromedary camels	65.5								
Middle East Respiratory Syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia, 2010 to 2013	Euro Surveill. 2013 Dec 12;18(50):20659.	2013	Saudi Arabia	S	Dromedary camels				18.1					

						%								
Study	Journal	Year*	Country	Study Type	Animals evaluated	ELISA	IFI/IFAT	RT-PCR	ppNT	Protein MicroArray	mNT	RT-LAMP	Western Blot	Rapid MERS-CoV Ag assay
Seroepidemiology for MERS coronavirus using microneutralisation and pseudoparticle virus neutralisation assays reveal a high prevalence of antibody in dromedary camels in Egypt, June 2013	Euro Surveill. 2013 Sep 5;18(36):pii=20574.	2013	Egypt	S	sheep				0.0					
				S	goats				0.0					
				S	cattle				0.0					
				S	chicken				0.0					
				S	Goat						0.0			
Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels, Oman, 2013	Euro Surveill. 2014 Apr 24;19(16):20781.	2014	Oman	S	Sheep						0.0			
				S	Water buffalo						0.0			
				S	Cow						0.0			
				S	Dromedary camels				98.2		94			
				P	Dromedary camels			6.6						
Sero-epidemiology of MERS coronavirus in Saudi Arabia (1993) and Australia (2014) and characterization of assay specificity	Euro Surveill. 2014 Jun 12;19(23). pii: 20828.	2015	Australia	S	Dromedary camels				0.0		0.0			
Middle East respiratory syndrome coronavirus (MERS-CoV) RNA and neutralising antibodies in milk collected according to local customs from dromedary camels, Qatar, April 2014	Euro Surveill. 2014 Jun 12;19(23). pii: 20829.	2014	Saudi Arabia	S	Dromedary camels				90.1					
			Qatar	P	Dromedary camels	100.0		21.2						
Cross-sectional surveillance of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels and other mammals in Egypt, August 2015 to January 2016	Euro Surveill. 2017 Mar 16;22(11). pii: 30487	2017	Egypt	P	Dromedary camels			3.8			84.5			
				P	domestic animals:cattle, sheep, goats, donkeys, buffalo, horses						0.7			
				P	bats						0.0			
High proportion of MERS-CoV shedding dromedaries at slaughterhouse with a potential epidemiological link to human cases, Qatar 2014	Infect Ecol Epidemiol. 2015 Jul 15;5:28305.	2015	Qatar	P	Dromedary camels			59.0						
The prevalence of Middle East respiratory Syndrome coronavirus (MERS-CoV) infection in livestock and temporal relation to locations and seasons	J Infect Public Health. 2018 Nov - Dec;11(6):884-888.	2018	Saudi Arabia	P	Dromedary camels			56.4						27.9

						%								
Study	Journal	Year*	Country	Study Type	Animals evaluated	ELISA	IFI/IFAT	RT-PCR	ppNT	Protein MicroArray	mNT	RT-LAMP	Western Blot	Rapid MERS-CoV Ag assay
Sero-prevalence of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) specific antibodies in Dromedary Camels in Tabuk, Saudi Arabia	J Med Virol. 2018 Aug;90(8):1285-1289.	2018	Saudi Arabia	S	Dromedary camels	84.2								
Middle East respiratory syndrome coronavirus infection not found in camels in Japan	Jpn J Infect Dis. 2015;68(3):256-8.	2015	Japan	P	Dromedary camels			0.0				0.0		
Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study	Lancet Infect Dis. 2013 Oct;13(10):859-66.	2013	Spain	S	Dromedary camels					14.3				
Middle East respiratory syndrome coronavirus in dromedary camels: an outbreak investigation	Lancet Infect Dis. 2014 Feb;14(2):140-5.	2014	Oman	S	Dromedary camels					100.0				
			Qatar	P	Dromedary camels		100.0	78.6						
Evidence for Camel-to-Human Transmission of MERS Coronavirus	N Engl J Med. 2014 Jun 26;370(26):2499-505	2014	Saudi Arabia	P	Dromedary camels	11.1	100.0	11.1						
Serological Evidence of MERS-CoV Antibodies in Dromedary Camels (Camelus dromedaries) in Laikipia County, Kenya	PLoS One. 2015 Oct 16;10(10):e0140125.	2015	Kenya	S	Dromedary camels					46.9				
Epidemiological study of Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia, April–May 2015	Rev Sci Tech. 2018 Dec;37(3):985-997.	2018	Saudi Arabia	P	Dromedary camels	80.5		2.4						
Molecular Detection and Characterization of Coronavirus Infection in Olive Baboons (Papio Anubis), Bats and Rodents in Laikipia County, Kenya	Univ of Nairobi Res Arch 2018	2018	Kenya	P	Papioanubis			0.0						
				P	Chaerephonsp			0.0						
				P	scotophilussp			0.0						
				P	Acomyskempis			0.0						
				P	Acomyspercivalli			0.0						
				P	Elephantulusrufescens			0.0						
				P	Gerbilliscus robustus			0.0						
				P	Aethomyshindei			0.0						
				P	Myomyscusbrodernani			0.0						
				P	Grammonysdolichorus			0.0						
				P	Saccostomusmeamsi			0.0						
High Prevalence of Middle East Respiratory Coronavirus in Young Dromedary Camels in Jordan	Vector Borne Zoonotic Dis. 2017 Feb;17(2):155-159.	2016	Jordan	S	dromedary camels	82.2								

						%								
Study	Journal	Year*	Country	Study Type	Animals evaluated	ELISA	IFI/IFAT	RT-PCR	ppNT	Protein MicroArray	mNT	RT-LAMP	Western Blot	Rapid MERS-CoV Ag assay
Seroepidemiological study of Middle East Respiratory Syndrome (MERS) virus infection in Iraqi dromedary camels	VeterinarskiArhiv 88(2):191-200	2018	Iraq	S	Dromedary camels	85.0								
Genetic Evidence of Middle East Respiratory Syndrome Coronavirus (MERS-Cov) and Widespread Seroprevalence among Camels in Kenya	Viol Sin. 2018 Dec;33(6):484-492.	2018	Kenya	P	Dromedary camels	68.1		0.9						
Countrywide Survey for MERS-Coronavirus Antibodies in Dromedaries and Humans in Pakistan	Viol Sin. 2018 Oct;33(5):410-417.	2018	Pakistan	P	Dromedary camels	75.6		1.1						
Prevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels in Abu Dhabi Emirate, United Arab Emirates	Virus Genes. 2015 Jun;50(3):509-13.	2015	United Arab Emirates	P	Dromedary camels			1.6						
Epidemiological investigation of Middle East respiratory syndrome coronavirus in dromedary camel farms linked with human infection in Abu Dhabi Emirate, United Arab Emirates	Virus Genes. 2016 Dec;52(6):848-854.	2016	United Arab Emirates	P	Dromedary camels			13.0						
The prevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) antibodies in dromedary camels in Israel	Zoonoses Public Health. 2018 Sep;65(6):749-754.	2018	Israel	P S	sheep Dromedary camels		49.3	0.0			71.8			
SARS Studies														
SARS-associated Coronavirus Transmitted from Human to Pig	Emerg Infect Dis. 2005 Mar;11(3):446-8.	2005	China	P	Pigs	1.8		7.1					28.6	
				P	Cattle	0.0		0.0						
				P	Dogs	0.0		0.0						
				P	Cats	0.0		0.0						
				P	Chickens	0.0		0.0						
				P	Ducks	0.0		0.0						
Coronavirus Antibodies in African Bat Species	Emerg Infect Dis. 2007 Sep;13(9):1367-70.	2007	South Africa	P	Bats	6.7	32.4						97.3	
Detection of Novel SARS-like and other Coronaviruses in Bats from Kenya	Emerg Infect Dis. 2009 Mar;15(3):482-5.	2009	Kenya	P	Bats			31.6						
Prevalence and Genetic Diversity of Coronaviruses in Bats from China	J Virol. 2006 Aug;80(15):7481-90.	2006	China	P	Bats			0.3						
Molecular Detection and Characterization of Coronavirus Infection in Olive Baboons (<i>Papio Anubis</i>), Bats and Rodents in Laikipia County, Kenya	Univ of Nairobi Res Arch 2018	2017	Kenya	P	<i>Papioanubis</i>			0.0						
					<i>Chaerephonsp</i>			0.0						
					<i>Scotophilussp</i>			0.0						
					<i>Acomys</i> sp			0.0						
					<i>Acomys</i> sp			0.0						

						%								
Study	Journal	Year*	Country	Study Type	Animals evaluated	ELISA	IFI/IFAT	RT-PCR	ppNT	Protein MicroArray	mNT	RT-LAMP	Western Blot	Rapid MERS-CoV Ag assay
					<i>Elephantulusrufescens</i>			0.0						
					<i>Gerbilliscus robustus</i>			0.0						
					<i>Aethomysshindei</i>			0.0						
					<i>Myomyscusbrodernani</i>			0.0						
					<i>Grammonysdolichorus</i>			0.0						
					<i>Saccostomusmeamsi</i>			0.0						

*Year of publication; ELISA, enzyme-linked immunosorbent assay; IFI, Indirect Immunofluorescence; IFAT, immunofluorescence antibody test; RT-PCR, reverse transcription-polymerase chain reaction; ppNT,pseudoparticleneutralization; mNT, microneutralization test; RT-LAMP, Reverse transcription loop-mediated isothermal amplification. MERS-CoV Ag assay, MERS-COV antigen assay. P, prevalence, S, seroprevalence.

Table 3. Meta-analysis outcomes (random-effects model)*.

Coronavirus, technique, animals, countries	Number of Studies	Pool Prevalence (%)	95%CI	n	Q [†]	I ² [‡]	t ² [§]	p
<i>MERS Studies</i>								
ELISA	15	73.0	63.8-82.2	7,648	1271.924	98.899	0.032	<0.001
IFI/IFAT	4	83.9	66.0-100.0	322	53.402	94.382	0.031	<0.001
RT-PCR	34	7.2	5.6-8.7	20,896	1719.949	98.081	0.001	<0.001
Camels	20	10.3	8.3-12.3	20,330	1705.777	98.89	0.011	<0.001
Qatar	5	32.6	4.8-60.4	177	110.178	96.37	0.01	<0.001
United Arab Emirates	4	16.0	5.8-26.2	8,166	100.376	97.01	0.01	<0.001
Saudi Arabia	5	15.4	0.0-37.2	2,509	799.239	99.5	0.01	<0.001
Egypt	3	7.7	0.0-16.5	4,013	175.581	98.86	0.01	<0.001
Kenya	13	0.4	0.2-0.6	3,830	7.724	0.0	0.01	<0.001
ppNT	9	26.8	6.2-47.4	1,066	6788.447	99.882	0.099	<0.001
Protein MicroArray	8	73.1	56.1-90.2	1,265	957.284	99.269	0.059	<0.001
mNT	15	41.8	21.0-62.6	4,837	9678.135	99.855	0.167	<0.001
<i>SARS Studies</i>								
ELISA	5	3.0	0.4-5.5	947	19.327	68.955	0.001	<0.001
RT-PCR	5	2.3	1.3-3.3	2,618	78.037	66.682	0.001	<0.001
Bats	2	14.1	0.0-44.6	1,004	77.578	88.37	0.005	0.003
Western-Blot	2	65.0	0.0-100.0	44	15.815	93.677	0.221	<0.001

* 95% CI = 95% confidence interval. † Cochran’s Q statistic for heterogeneity. ‡ I² index for the degree of heterogeneity. § Tau-squared measure of heterogeneity.
ELISA, enzyme-linked immunosorbent assay; IFI, Indirect Immunofluorescence; IFAT, immunofluorescence antibody test; RT-PCR, reverse transcription-polymerase chain reaction; ppNT, pseudoparticle neutralization; mNT, microneutralization test.

Supplemental Materials.

Figure S1. Funnel-plot for the Standard Error by Logit Event rate to assess for publication bias on MERS studies.

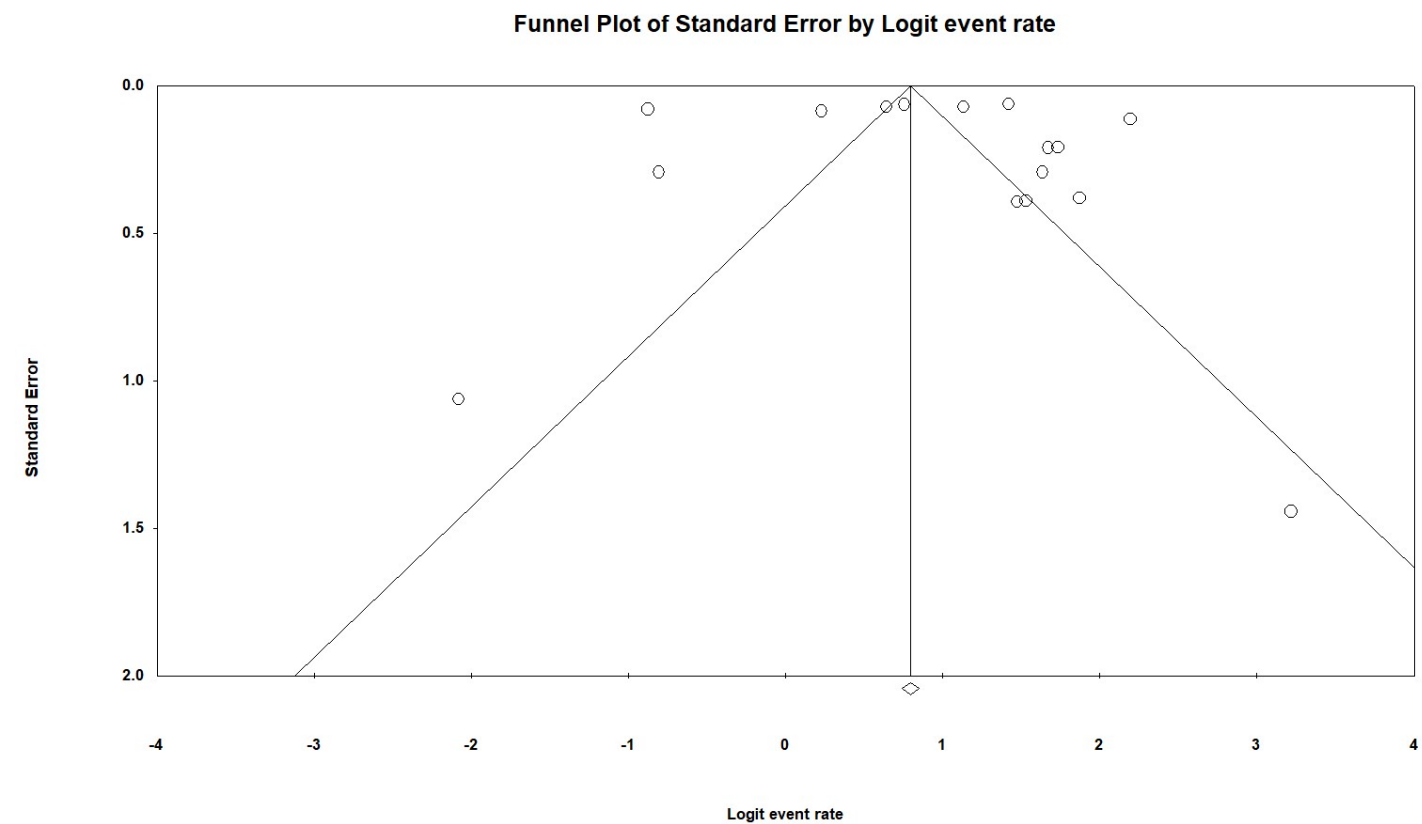


Figure S2. Funnel-plot for the Standard Error by Logit Event rate to assess for publication bias on SARS studies.

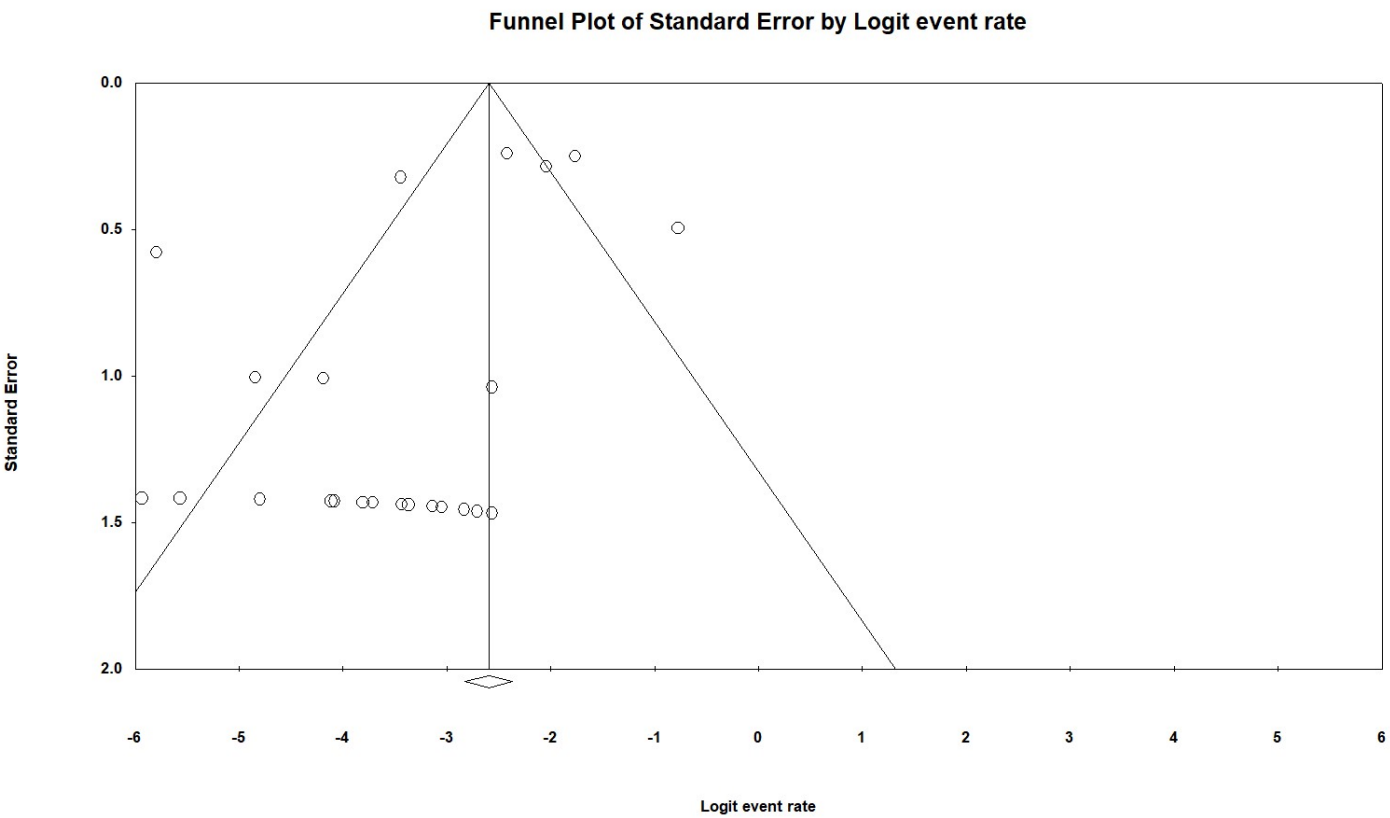
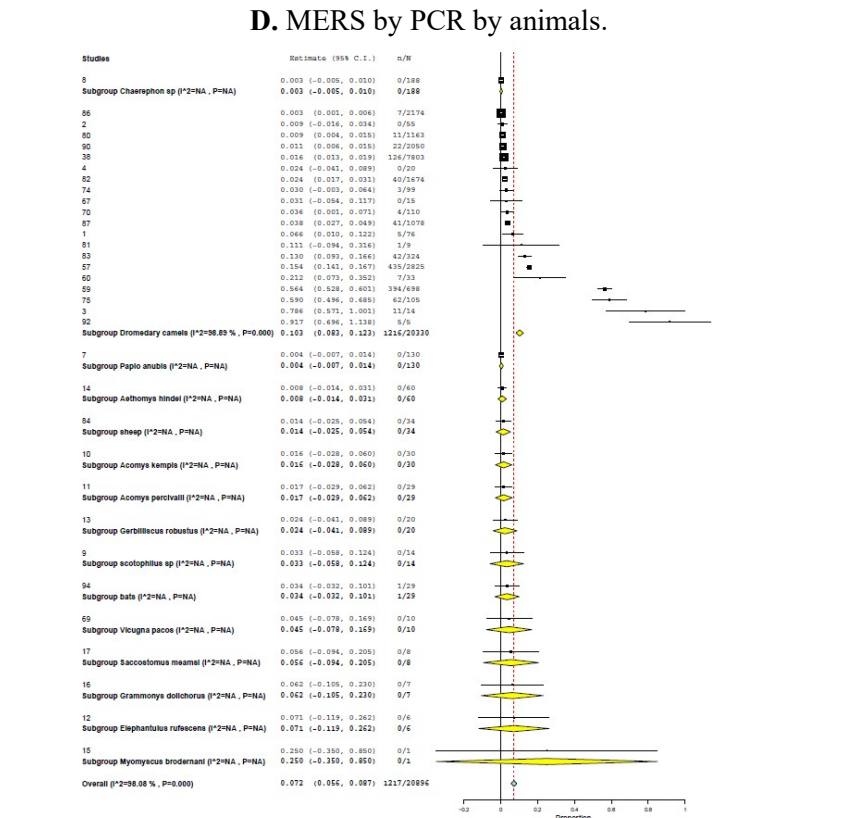
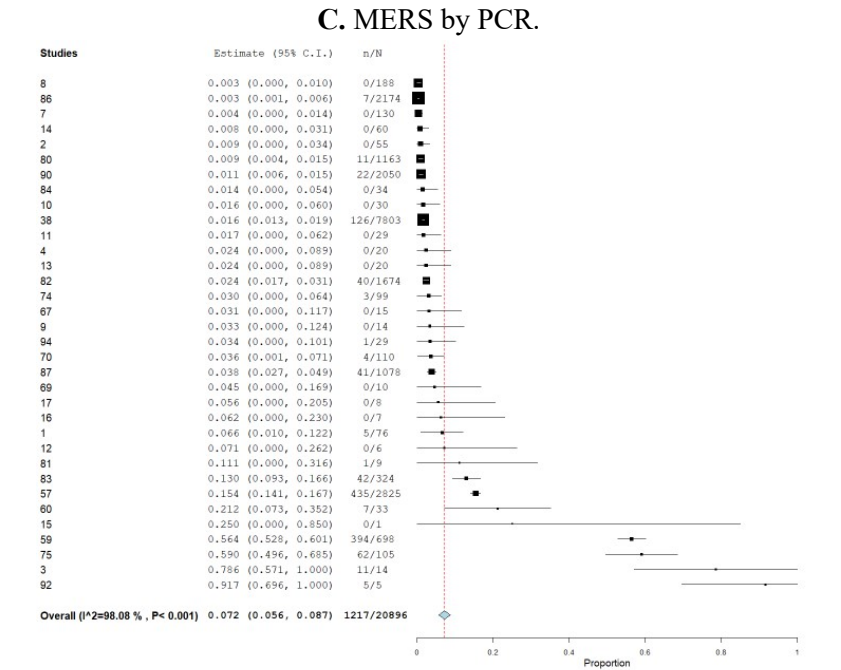
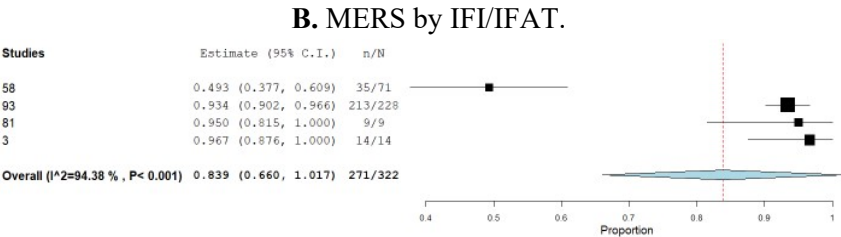
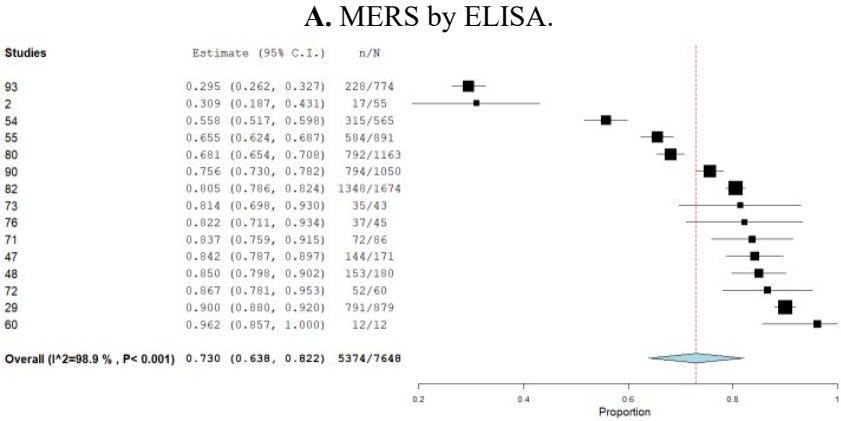
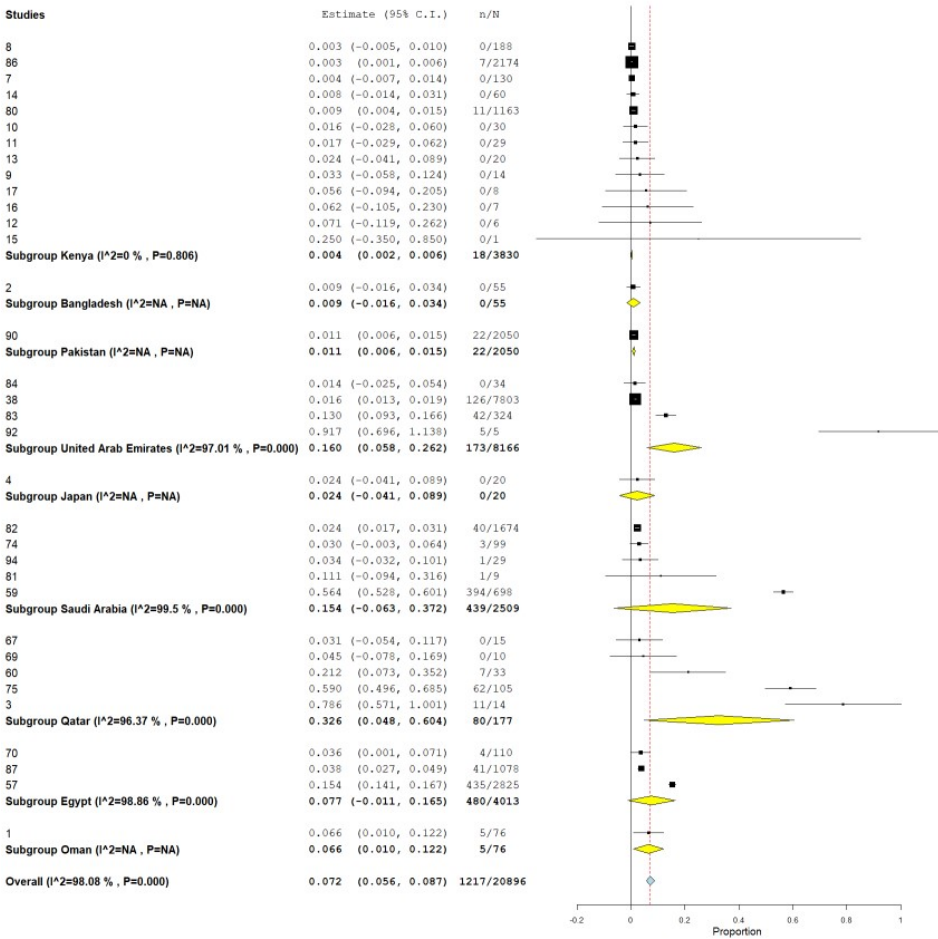


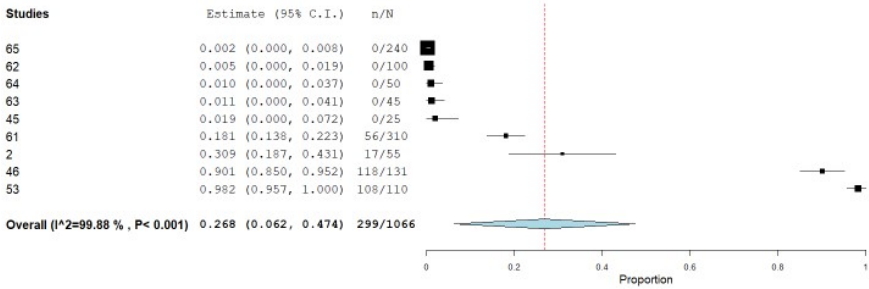
Figure S3. Pool prevalences forest plots of findings described in Table 3.



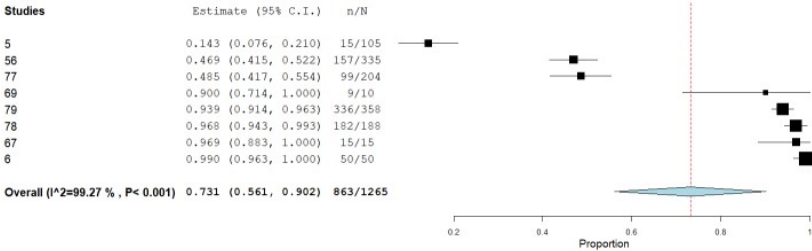
E. MERS by PCR by countries.



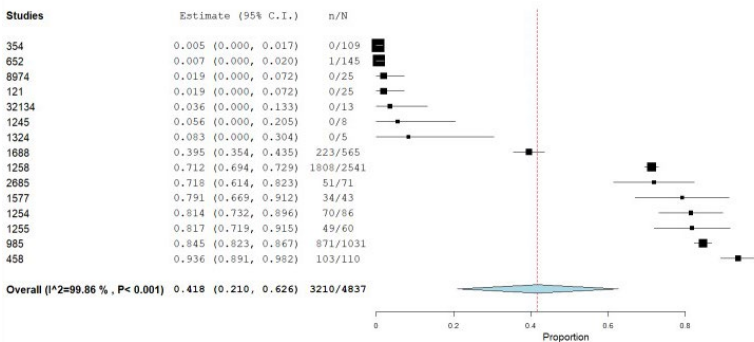
F. MERS by ppNT.



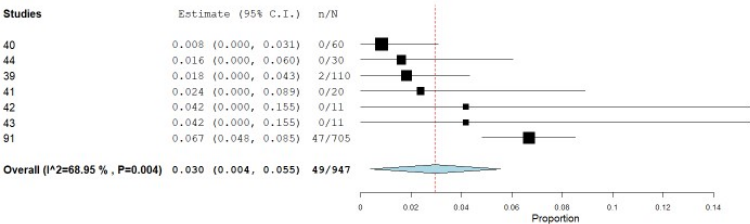
G. MERS by Protein MicroArray.



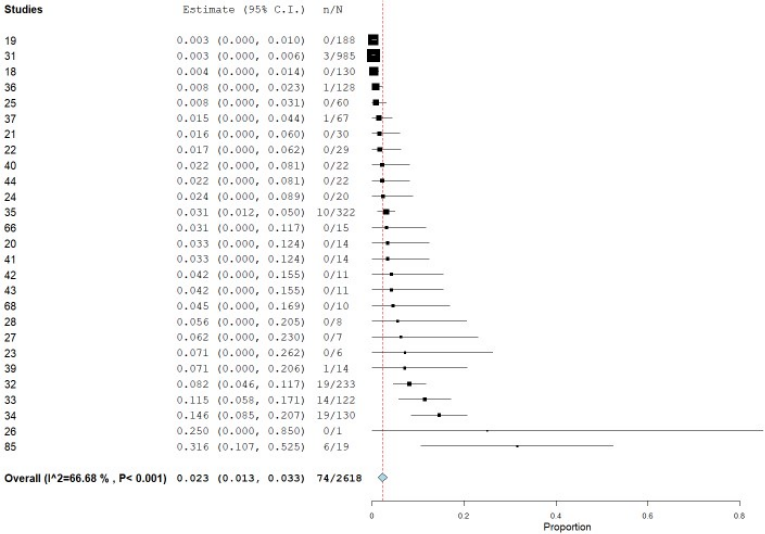
H. MERS by mNT.



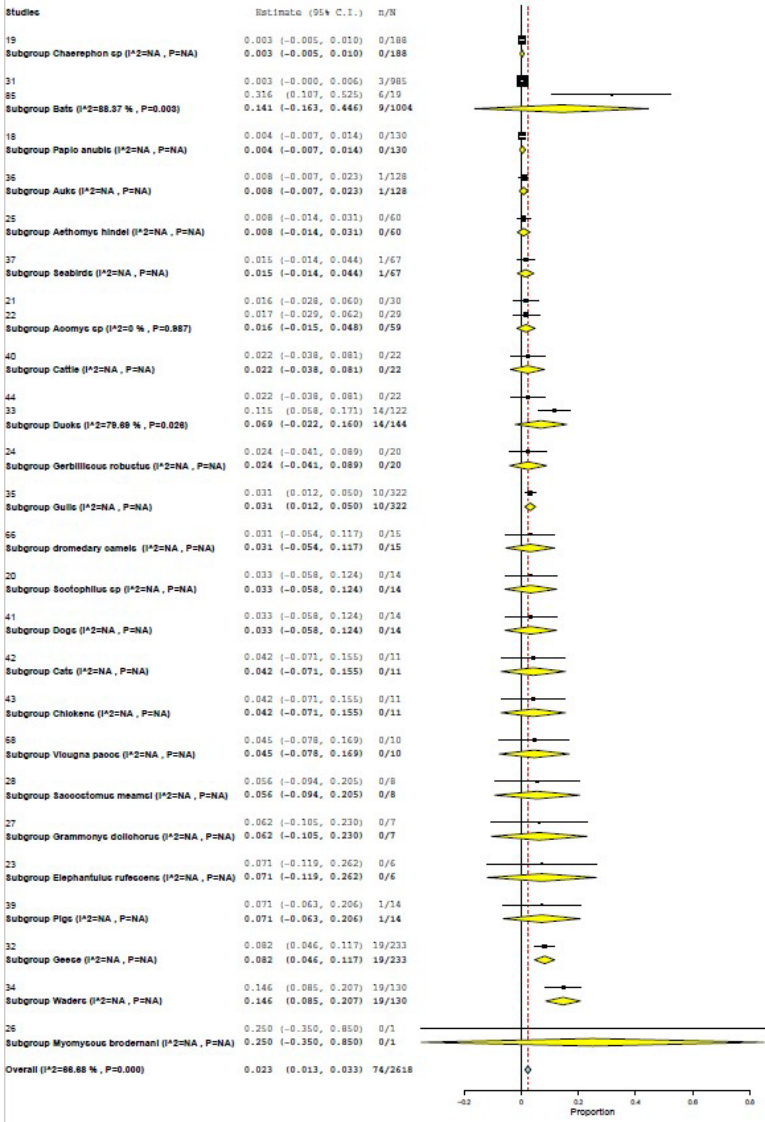
I. SARS by ELISA.



J. SARS by RT-PCR.



K. SARS by RT-PCR by animals.



L. SARS by Western Blot.

