

HUMAN EMERGING RESPIRATORY PATHOGENS BULLETIN

MONTHLY SITUATIONAL ANALYSIS OF EMERGING RESPIRATORY DISEASES AFFECTING HUMANS

Issue No 015 April 2018

IN THIS BULLETIN

AVIAN INFLUENZA A(H7N9)

In March 2018, there have been no new cases of H7N9 reported. A total of 1567 human cases of avian influenza A(H7N9), including at least 613 deaths, have been reported globally since 2013, with 1564 cases reported in wave 5 and three cases reported in wave 6. The three cases reported in the current wave (wave 6) have been spread across China. Two travel-related cases were reported in Canada in January 2015.

AVIAN INFLUENZA A(H5N1)

In March 2018, no new cases of H5N1 were reported to the World Health Organization (WHO). A total of 860 cases, including 454 deaths, have been reported globally since 1997. One fatal travel-related case of A(H5N1) was reported in Canada in January 2014.

AVIAN INFLUENZA A(H9N2)

In March 2018, three new cases of H9N2 were reported, all from China from Anhui Province, Guangdong Province, and Beijing. Globally, 45 cases, including 1 death, have been reported since 1998.

AVIAN INFLUENZA A(H5N6)

In March 2018, no new cases of H5N6 were reported to the WHO. There have been a total of 19 cases, including 9 deaths, reported globally since 2014, with all cases occurring in China.

AVIAN INFLUENZA A(H7N4)

In March 2018, no new cases of H7N4 were reported to the WHO. The only human case reported so far was in China in February 2018.

REASSORTANT INFLUENZA A(H1N2)

In March 2018, a case was infected with a new reassortant A(H1N2) virus in the Netherlands. The virus is made of 2 genes from A(H1N1)pdm09 and 6 genes from A(H3N2). The case is a 1 year and 7 month old male.

UPDATE ON HUMAN EMERGING RESPIRATORY PATHOGEN PUBLIC HEALTH EVENTS (AS OF MARCH 31, 2018)

NOVEL INFLUENZA[1]	[N CUMULATIVE CASES[2] (DEATHS), CFR%[3]]
A(H7N9)	[1567 (613), 39%]
A(H5N1)	[860 (454), 53%]
A(H9N2)	[45 (1), 2%]
A(H5N6)	[19 (9), 47%]
A(H7N4)	[1 (0), 0%]
H3N2v	[434 (1), <1%]
H1N2v	[13 (0), 0%]
H1N1v	[22 (0), 0%]
MERS-CoV[1]	
Global case count	[2183 (760), 35%]
Saudi Arabia	[1828 (726), 40%]

[1]**Date of 1st Reported Case of Human Infection:** MERS-CoV: February 2013 (retrospective case finding September 2012). A(H7N9): March 2013. A(H5N1): 1997. A(H9N2): 1998. A(H5N6): 2014. A(H7N4): February 2018 (retrospective case finding December 2017). H3N2v with M gene from pH1N1: 2011. H1N2v: 2005. H1N1v: 2005.

[2]**Cumulative Case Counts:** updated using data reported by the World Health Organization (avian and swine influenza, MERS CoV), and the United States Centers for Disease Control and Prevention (US CDC) (swine influenza).

[3]**Case Fatality Rate:** The proportion of cases that resulted in death.

SWINE ORIGIN INFLUENZAS A(H3N2)v, A(H1N2v), and A(H1N1)v

In March 2018, there have been no new cases of H3N2v. One locally-acquired case of H3N2v was reported in Canada in December 2016.

In March 2018, there have been no new cases of H1N2v. Since 2005, there have been a total of 13 confirmed cases of H1N2v in the United States, with four cases occurring in 2017.

In March 2018, no new cases of H1N1v were reported to the WHO. There have been a total of 22 cases reported globally since 2005, with only one case reported in 2018.

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Canada

MIDDLE EAST RESPIRATORY SYNDROME- CORONAVIRUS (MERS-COV)

In March 2018, 17 new cases of Middle East Respiratory Syndrome (MERS) were reported. The majority of new cases were reported from Saudi Arabia (n=16). A total of 2183 cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV), including at least 760 deaths, have been reported globally since 2012. Further information can be found in the *in depth analysis* section below.

IN DEPTH ANALYSIS

HUMAN RESPIRATORY DISEASE ASSOCIATED WITH MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-CoV)

Risk to Canada

The Public Health Agency of Canada (PHAC) has conducted a risk assessment for MERS-CoV. To date, no cases have been reported in Canada and the public health risk posed by MERS-CoV to Canadians is considered **low** based on the available information at this time. Additional cases of MERS-CoV infections are expected to be reported from the Middle East and it is likely that cases will continue to be exported to other countries by individuals who might acquire infection following exposure to an animal (camels) or human source. Human-to-human transmission of the virus has been low and self-limited to only a few generations of infection with occasional amplification in health care settings. Thus, it is important that health care facilities, research laboratories, and public health professionals remain vigilant in the systematic implementation and adherence of infection prevention and control (IPC) measures.

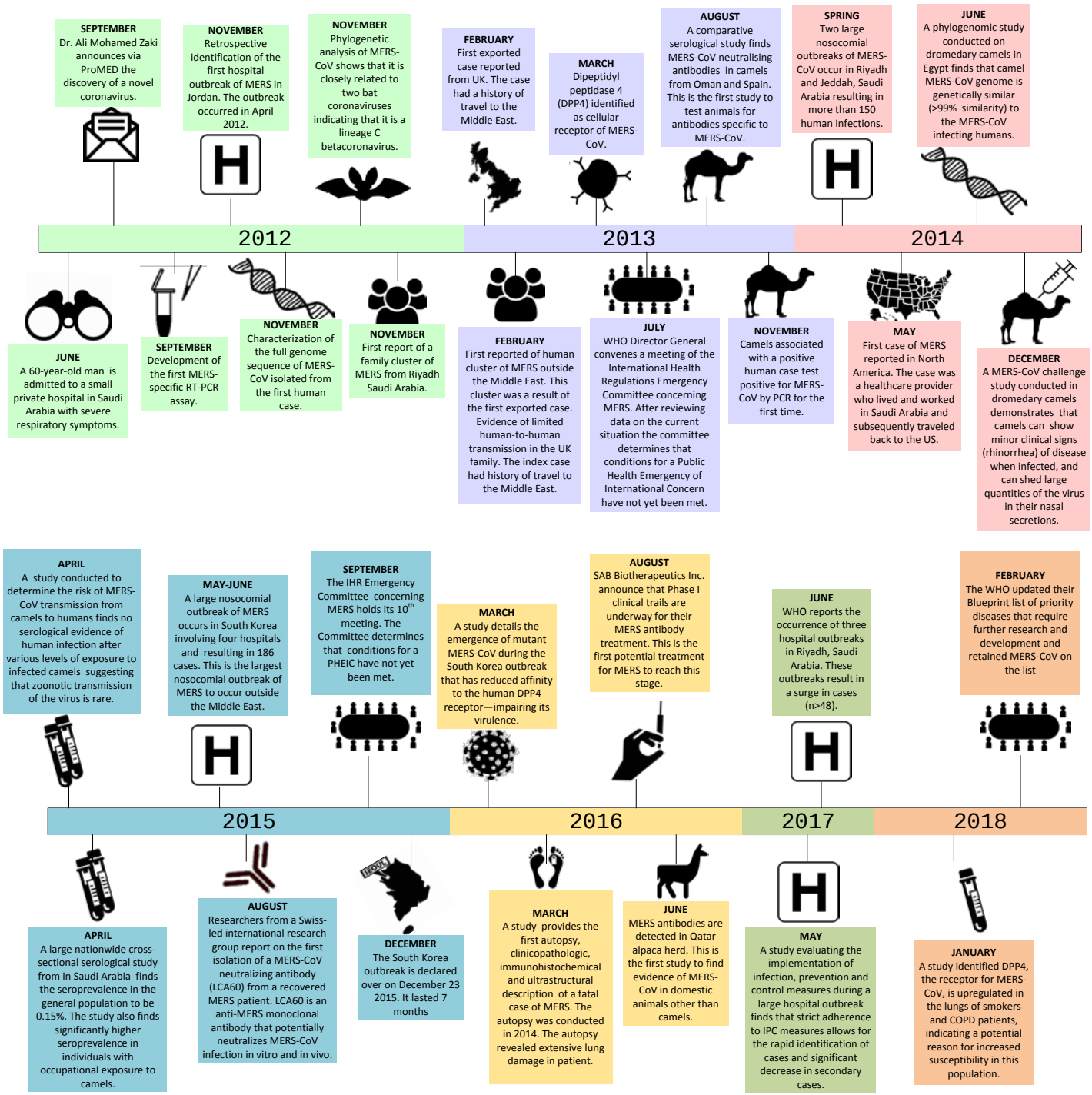
Guidance documents including a public health notice, a travel health notice, IPC guidelines, a biosafety advisory, case and contact management guidelines, and case definitions can be found on the Government of Canada website for MERS-CoV.

BACKGROUND

On June 13, 2012, a 60 year old Saudi man was admitted to a private hospital in Jeddah, Saudi Arabia, after reporting respiratory symptoms like cough, expectoration, shortness of breath, and fever (1,2). Eleven days after admission, on June 24, 2012, he died of progressive respiratory and renal failure (1). The investigation into the etiological agent responsible for his condition began at the laboratory attached to the hospital. After two months of testing clinical isolates from the patient for multiple viruses (influenza virus A, influenza virus B, parainfluenza virus, paramyxovirus, hantavirus, enterovirus and adenovirus), the isolate was tested for coronavirus using a pancoronavirus RT-PCR (3). The test was positive, but negative for SARS specific primers, suggesting the discovery of a novel coronavirus (3). On September 20th, 2012, after further confirmation by another laboratory (the Erasmus Medical Center), the discovery of a novel coronavirus was announced through ProMED (3,4). This coronavirus, the etiological agent for Middle East Respiratory Syndrome (MERS), was eventually named Middle East Respiratory Syndrome Coronavirus (MERS-CoV), the 6th strain of human coronavirus discovered (5).

Since that time, over 2000 cases have been reported globally. Family clusters and hospital outbreaks have occurred both within the Middle East and elsewhere, and the cases have spread from the region to some other countries [Figure 1] (6). There has also been important progress in laboratory diagnostics, virus characterization, vaccine development, and understanding of the clinical course of illness and the mechanism of transmission [Figure 1]. This in-depth analysis provides a summary of the descriptive epidemiology of human infection with MERS-CoV since its emergence in 2012, with a focus on the demographic, geographic and temporal distribution of reported cases, as well as a review of the clinical symptoms, sources of exposure, and virus characteristics.

Figure 1. Middle East Respiratory Syndrome (MERS) epidemic: a timeline of major events (2012-2018).



Note: This timeline is not meant to include all developments regarding the MERS epidemic. Instead, selected items are intended to demonstrate important research advancements and epidemiological milestones in the ongoing epidemic (4,7-23,59,84).

SOURCE OF EXPOSURE

Primary cases of MERS are associated with zoonotic transmission from camels. Though research suggests that MERS-CoV emerged from bats, multiple studies on the emergence and transmission of MERS-CoV point to the role of camels as a reservoir and primary source of zoonotic infection due to the high prevalence of MERS-CoV antibodies in camels across the Arabian Peninsula and North and Eastern Africa (47,62-65). The detection of MERS-CoV by RT-PCR in respiratory secretions, urine, feces and milk of dromedary camels, and demonstration of similarities in the genomic sequence of viruses isolated from infected individuals and camels (47,62-65) further support the role of camels in zoonotic transmission of MERS-CoV. These findings also highlight the importance of focusing prevention and control measures on camels. Challenge studies conducted in camels suggest that infection of MERS-CoV in dromedary camels results in mild respiratory disease with mild to no signs of illness (19). To date, despite the number of reported zoonotic cases, only 14 camel outbreaks of MERS have been reported to the World Organization for Animal Health (OIE) signifying that outbreaks in camel herds are likely to go undetected and allow for an ongoing risk of transmission to humans (66). Based on sero-epidemiological studies carried out in other livestock, alpacas are the only other domestic livestock in which MERS-CoV-specific antibodies have been identified; however, no human cases with exposure to alpacas have been reported (23).

Although the route of camel to human transmission is not fully understood, zoonotic infections of MERS likely occur through direct or indirect contact with camels or camel-related products (e.g. raw milk) (31). Serological studies that compare the presence of MERS-CoV antibodies in individuals with and without contact to dromedary camels have left a conflicting picture about the role of camel exposure in the zoonotic transmission of MERS. Some studies have found no serological evidence of MERS-CoV infections in humans with various levels of exposure to dromedary camels (21,67,68). These findings suggest that zoonotic transmission is rare (21,67,68). However, other studies have found a significantly higher seroprevalence of MERS-CoV antibodies in camel-exposed individuals compared to the general population, suggesting a greater risk of MERS-CoV infection among individuals exposed to camels (22,69). Based on the available information to date, further studies are needed to fully understand how human-animal interactions contribute to the transmission of MERS-CoV.

Human-to-human transmission of MERS-CoV has largely been associated with nosocomial outbreaks; however, household transmission has also been reported (10,70). Nosocomial outbreaks of MERS have played an important role in increasing the magnitude of reported cases. To date large scale hospital outbreaks have been reported in Saudi Arabia, United Arab Emirates, and South Korea (42,71,72). Lack of IPC measures (e.g. overcrowding, delays in isolation of cases, lack of knowledge of MERS case definitions amongst healthcare workers) along with intra- and inter-hospital transmission, super spreaders, and asymptomatic cases are factors that have contributed to these hospital outbreaks in the past (73). A study published in 2017 evaluating the implementation of IPC measures during a large hospital outbreak found that strict adherence to IPC measures allowed for rapid identification of cases and a significant decrease in secondary cases, which may explain why recent outbreaks in Saudi Arabia were quickly contained (27,28,74).

VIRUS CHARACTERISTICS

MERS- CoV is a single stranded RNA virus belonging to the Coronaviridae family (2,75). Though caused by the same genera of coronavirus as SARS, MERS-CoV is distinct in that it belongs to lineage C whereas SARS belongs to lineage B. Entry of MERS-CoV into host cells is mediated by its spike (S) protein binding to the host cell receptor, dipeptidyl peptidase 4 (DPP4) (76). DDP4 is a surface cell protein that is mainly expressed in the human respiratory tract, but is also extensively expressed on epithelial cells in the kidneys, small intestine, liver, prostate, and activated leukocytes (55). In the case of SARS, extensive mutations in the virus resulted in its ability to adapt to the human cell receptor angiotensin-converting enzyme 2 (ACE 2) which allowed for increased human-to-human transmission (77). Though sequenced viral isolates from camels and humans indicate that MERS-CoV has undergone recombination and genetic changes since its introduction to humans in 2012, none of these viral mutations have allowed more efficient adaptation to the human cell receptor DPP4 (78). In fact, analysis of viral isolates with a mutation in the receptor binding domain from the South Korea outbreak showed reduced affinity to human DPP4 (79). Given the magnitude of South Korea outbreak, these findings further convolute the role of the S protein and DPP4 in the human adaptation of this virus. Overall, the coronaviruses possess the abilities of efficient mutation and recombination, and a propensity to cross host species and adapt to a new environment. These abilities raise concerns that MERS-CoV would gain virulence and an enhanced ability to transmit from human-to-human. However, sustained human-to-human transmission has not occurred in the general population. Potential hotspots of animal-to-human and human-to-human transmission need to be monitored on an on-going basis.

CLINICAL MANIFESTATIONS

Human infection with MERS-CoV results in a wide range of clinical manifestations, from asymptomatic infection to severe clinical disease (2). Common clinical symptoms include fever, cough and shortness of breath that can rapidly progress to severe acute pneumonia, acute respiratory distress syndrome, septic shock, multi-organ failure and death (2,56). In some instances, cases have experienced gastrointestinal symptoms of abdominal pain, vomiting and diarrhea (2). In comparison to human illness with other coronaviruses such as Severe Acute Respiratory Syndrome (SARS) (global CFR 14%-15%), MERS has a high case fatality rate of 35% among all cases reported globally and 40% in cases reported from Saudi Arabia (6,32,57). Studies assessing risk factors for disease severity and mortality have found that pre-existing health conditions, older age, sex (being male) and co-infection with other bacterial or viral agents to be significant risk factors for increased odds of mortality and disease severity (56,58).

Pediatric Cases

Based on case information available to date, pediatric cases of MERS are rare (34,60,61). Thus far, approximately 2% of all cases have occurred in the pediatric population (individual ≤ 18 years of age) and the case fatality rate is 2.5%. In 2016 Al-Tawfiq et al., published a study that aimed to summarize both the epidemiological and clinical characteristics of pediatric cases reported from June 2012 to April 19, 2016 (n=31) (60). Of the cases for which clinical information was available (n=29), 45% were asymptomatic and 7% presented with mild respiratory symptoms (60). Of the cases for which information on source of exposure was available (n=15), 68% acquired their infection through household contact (60). Although the number of pediatric cases is low it is important to remain viligiant in the documentation of the clinical presentation to better understand whether the clinical picture in this population differs from that of the general population.

EVENT SUMMARY: JANUARY TO MARCH 2018

Between January 1, 2018 and March 31, 2018, 54 cases of MERS including 5 deaths (CFR=36%) of the individuals with known outcomes were reported to the World Health Organization (WHO) and by the Kingdom of Saudi Arabia's Ministry of Health (KSA MOH) (24). The case count and case fatality rates were comparable to those reported during the same time period in 2016 and 2017, but substantially lower than in 2015 and 2014 (25). The age and sex distribution of cases has remained relatively consistent with previous years: most cases were male (75%), and the median age was 59 years (range 5 years to 89 years). Geographically, cases were less dispersed than previous years with only three countries (Malaysia, Saudi Arabia, and Oman) reporting cases to date. The case reported from Oman was locally acquired, while the case reported from Malaysia was imported from Saudi Arabia – the country with the majority of reported cases (26). Of the cases for which exposure information was available (n=5), 29% reported exposure to camels while 21% reported exposure to a positive MERS case, giving a similar proportion of secondary[1] cases to primary[2] cases reported to the WHO this year so far. Between January 1 and March 31, 2018, one nosocomial outbreak was reported in a private hospital in the Hafr Albatin region of Saudi Arabia, while a cluster of nosocomial infections was detected in a health facility in the Riyadh region of Saudi Arabia (27,28).

GLOBAL EPIDEMIOLOGICAL ANALYSIS

Since the emergence of MERS-CoV in 2012, 2183 human infections including at least 760 deaths (CFR =35%) have been reported from 27 countries (6,32). The epidemiological analyses of the MERS-CoV to date reflect sporadic zoonotic infections with amplified human to human transmission in health care settings. Overall, two-thirds of the reported cases (66%) have occurred in men with the median age of 54 years (range of 9 months to 109 years). Though cases of MERS continue to be reported each year, there has been a decline in the number of reported cases and the case fatality rate since 2014 [Table 1] (29). Given the association between amplified human-to-human transmission and outbreaks in health care settings, strict adherence to infection prevention and control (IPC) measures is likely the main driver for the observed reduction in the incidence of cases according to the WHO (30).

Table 1. Epidemiologic characteristics of MERS cases reported between January – December 2013 to 2017 and January – March 2018.

Characteristics	2013	2014	2015	2016	2017	2018
Number of reported cases (CFR %)	188 (53)	758 (38)	672 (33)	251 (29)	250 (29)	54 (36)
Median age (range) in years	51 (2-94)	48 (4-99)	54 (9 months-109)	54 (18-94)	53 (10-88)	59 (5-89)
% Male	65	65	65	73	72	75
Number of countries reporting cases	10	17	12	7	5	3
% Healthcare workers	20	26	10	13	17	4

Note: Data for epidemiological characteristics of MERS cases from 2013-2016 were sourced from the WHO Regional Office for the Eastern Mediterranean (EMRO) January-February 2017 MERS Situation update and compared to data retrieved from WHO Disease Outbreak News (DON) on July 6th on MERS cases reported from Jan-Jun 2017 data. Epidemiological characteristics for cases reported from June 2017-March 2018 were based on data retrieved from WHO DON on March 15th and cases reported by the

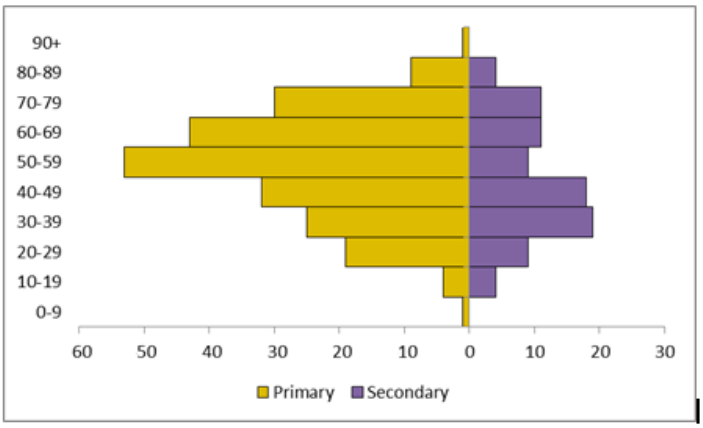
[1] Secondary cases are cases with a history of contact with a positive MERS case
[2] Primary cases are cases with no history of contact with a positive MERS case

Kingdom of Saudi Arabia (KSA) Ministry of Health (MOH) up until the end of March 2018. Data reported in this table are subject to change as a result of ongoing investigations and updated analysis (24,29,32).

AGE AND SEX DISTRIBUTION

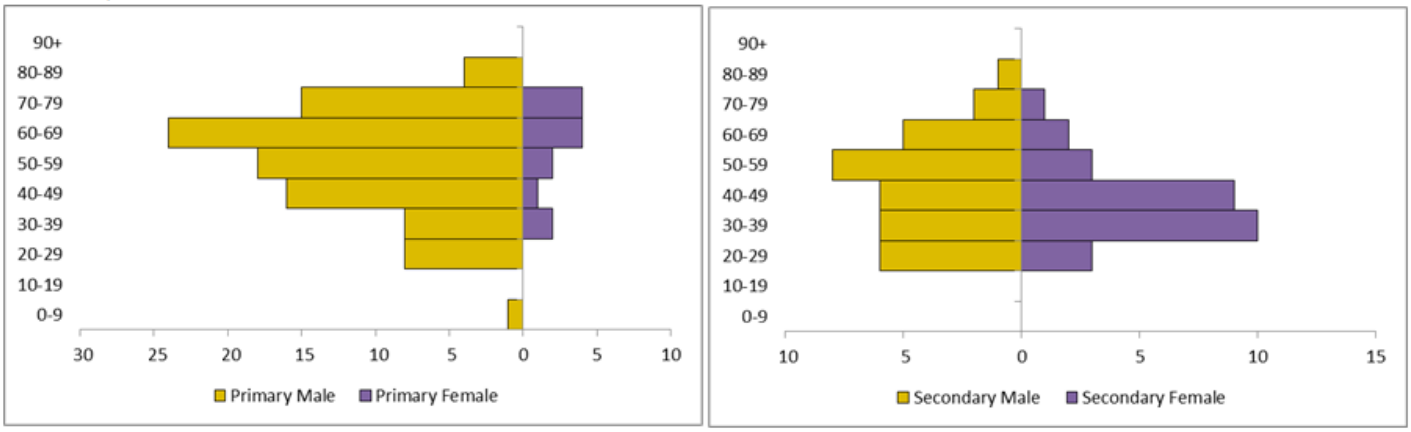
Overall, the age-sex distribution of cases is skewed towards older men [Figure 2]. However, further investigation of exposure type reveals distinctive age-sex patterns between primary and secondary cases [Figure 3] (31). Exposure and demographic information was available for 109 primary cases and 62 secondary cases (total=171) reported by the WHO Disease Outbreak News (DON) and the KSA MOH between January 1, 2017 and March 31, 2018 (24,32). Primary cases were skewed towards older men: a significantly higher proportion of primary cases were male (88%) and aged 50 years and older (67%). In contrast, secondary cases had a more balanced age-sex distribution: there was no significant difference between the proportion of males to females or between age groups (25). Further, secondary cases had a significantly lower mean age, compared to primary cases (46 years vs. 56 years). The observed age-sex pattern in primary cases – people infected through direct contact with camels – is hypothesized to be due socio-cultural behaviours, such as camel rearing being an activity popular among middle-aged and retired men (31).

Figure 2. Comparison of the age distribution of primary to secondary MERS cases reported worldwide between January 1, 2017 and March 31, 2018.



Note. Data displayed on this graph represent a subset of cases reported by the WHO DON and the Kingdom of Saudi Arabia Ministry of Health. Data reported in this figure are subject to change as a result of ongoing investigations and updated analysis (32).

Figure 3. Age and sex distribution of primary and secondary MERS cases reported worldwide between January 1, 2017 and March 31, 2018

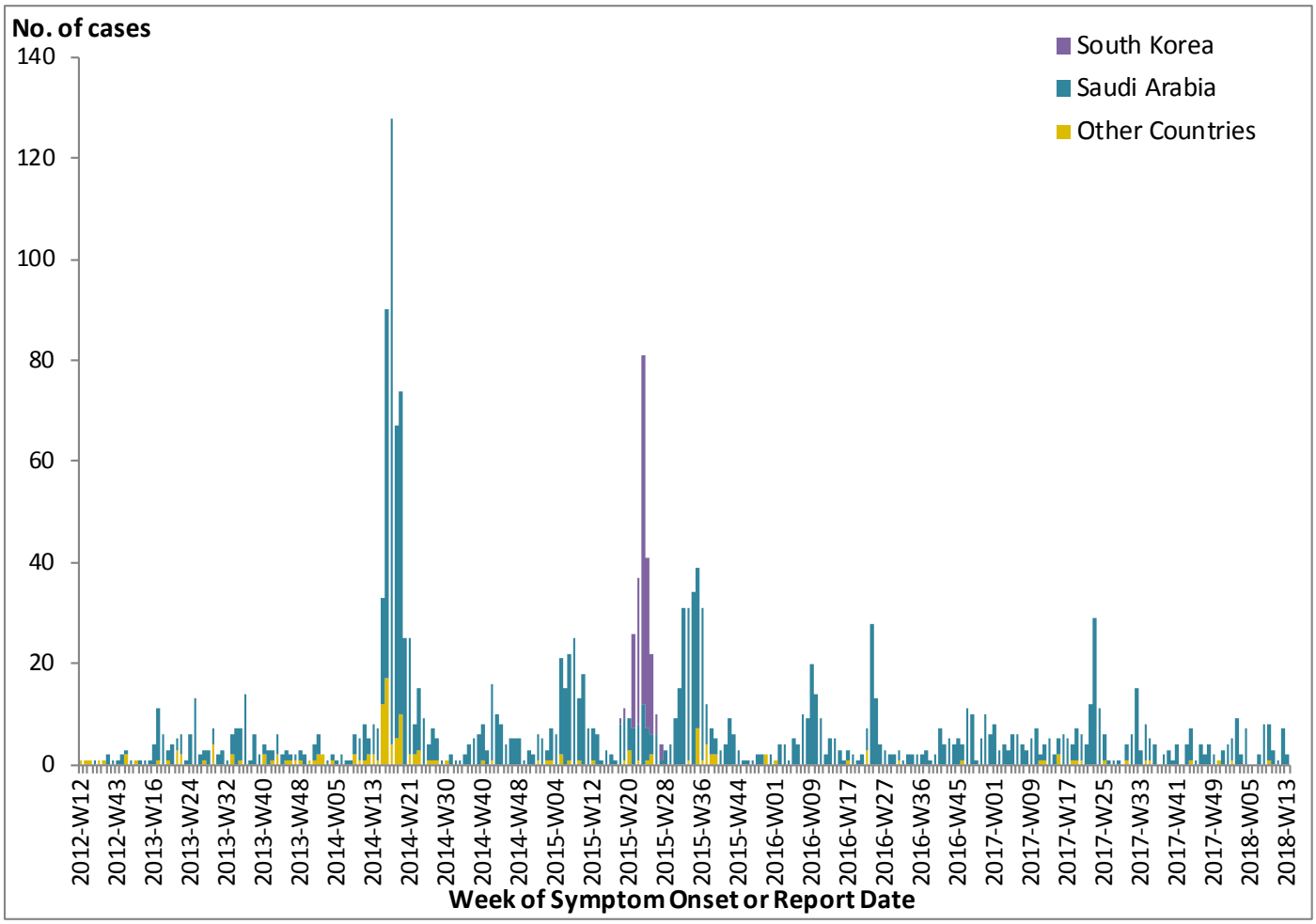


Note. Data displayed on this graph represent a subset of cases reported by the WHO DON and the KSA MOH. Data reported in this figure are subject to change as a result of ongoing investigations and updated analysis (32).

TEMPORAL DISTRIBUTION

The overall temporal distribution of the MERS epidemic can be characterized by multiple intermittent peaks that correspond to large-scale or simultaneously occurring hospital outbreaks. Between 2014 and June 2016, these peaks occurred every 12 to 26 weeks, on average [Figure 3]. However, between 2016 and 2017, there was a 52-week period between peak activity and there has been no peak in activity in 2018 thus far. The recent increased duration between peak activity, resulting in low but ongoing activity, suggests that there have been improvements in the implementation of IPC measures and a decrease in hospital-acquired cases since 2015 as noted by the WHO (28, 30).

Figure 4. Global count of human cases of MERS by week of symptom onset or earliest recorded date and location of report, March 2012 to March 31, 2018.

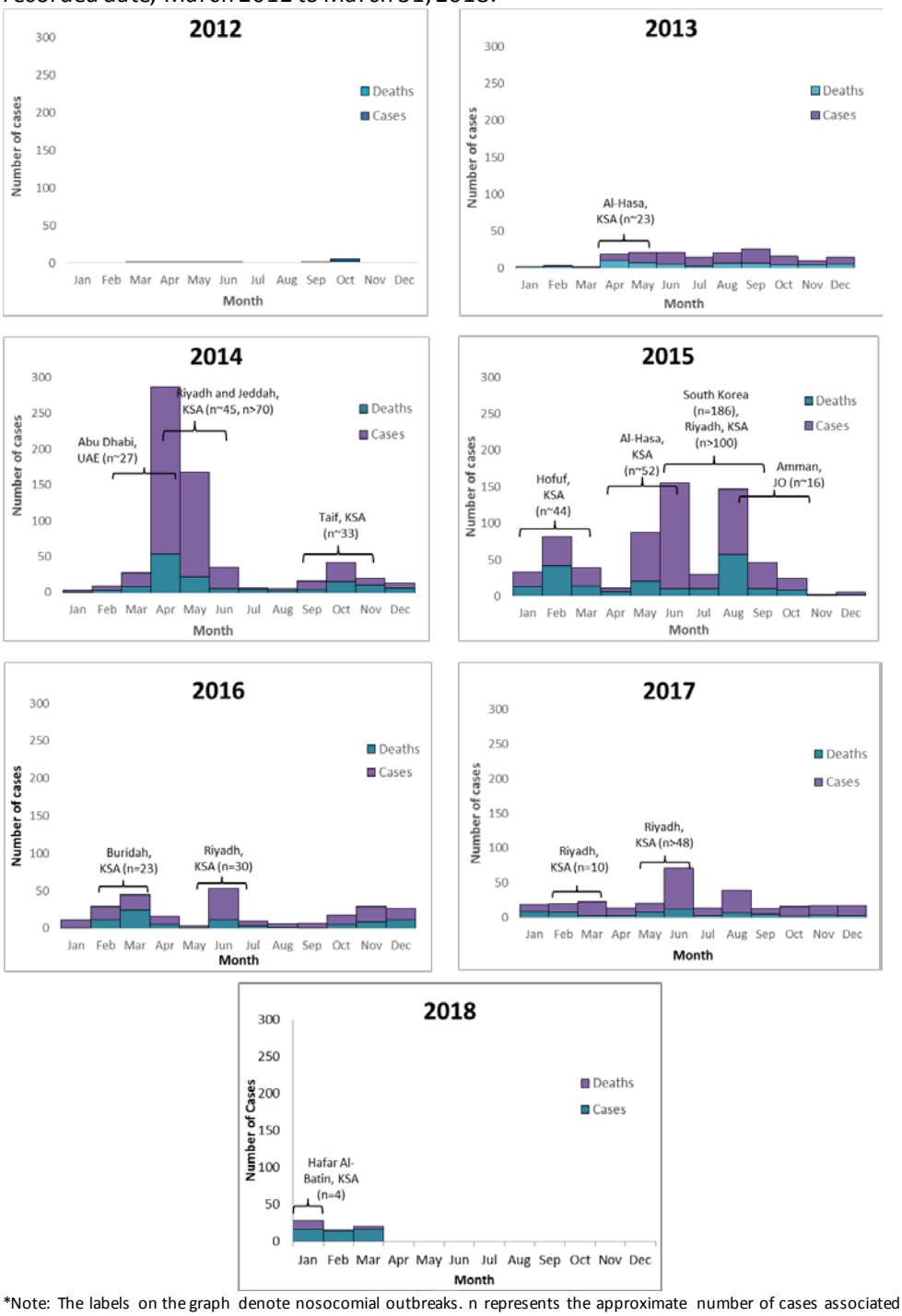


Prepared by the Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, using data compiled from Global Public Health Intelligence Network (GPHIN), the WHO, and the Kingdom of Saudi Arabia's Ministry of Health.

Early analysis of the temporal distribution of MERS cases between 2012 and 2014 suggested a seasonal pattern with cases increasing from March to April each year. At the time, this seasonal pattern had been linked to the calving and weaning patterns of camels; however, this pattern has not been observed since 2014 (33). Analysis of the temporal distribution of annual MERS cases reported since 2014 demonstrates that the majority of cases (approximately 61% to 84%) occur during the first 6 months of the year, with peaks corresponding with reported hospital outbreaks that involve more than 20 cases

[Figure 5]. Further analysis of the temporal distribution of primary and secondary cases may help determine whether MERS truly exhibits seasonality.

Figure 5. Temporal distribution of MERS cases, deaths and nosocomial outbreaks* by month of symptom onset or earliest recorded date, March 2012 to March 31, 2018.



*Note: The labels on the graph denote nosocomial outbreaks. n represents the approximate number of cases associated with the outbreak. The bracket does not reflect the actual duration of the outbreak but the approximate time period when the majority of cases occurred or were reported. KSA= Kingdom of Saudi Arabia, JO =Jordan and UAE =United Arab Emirates (8,27,34-46).

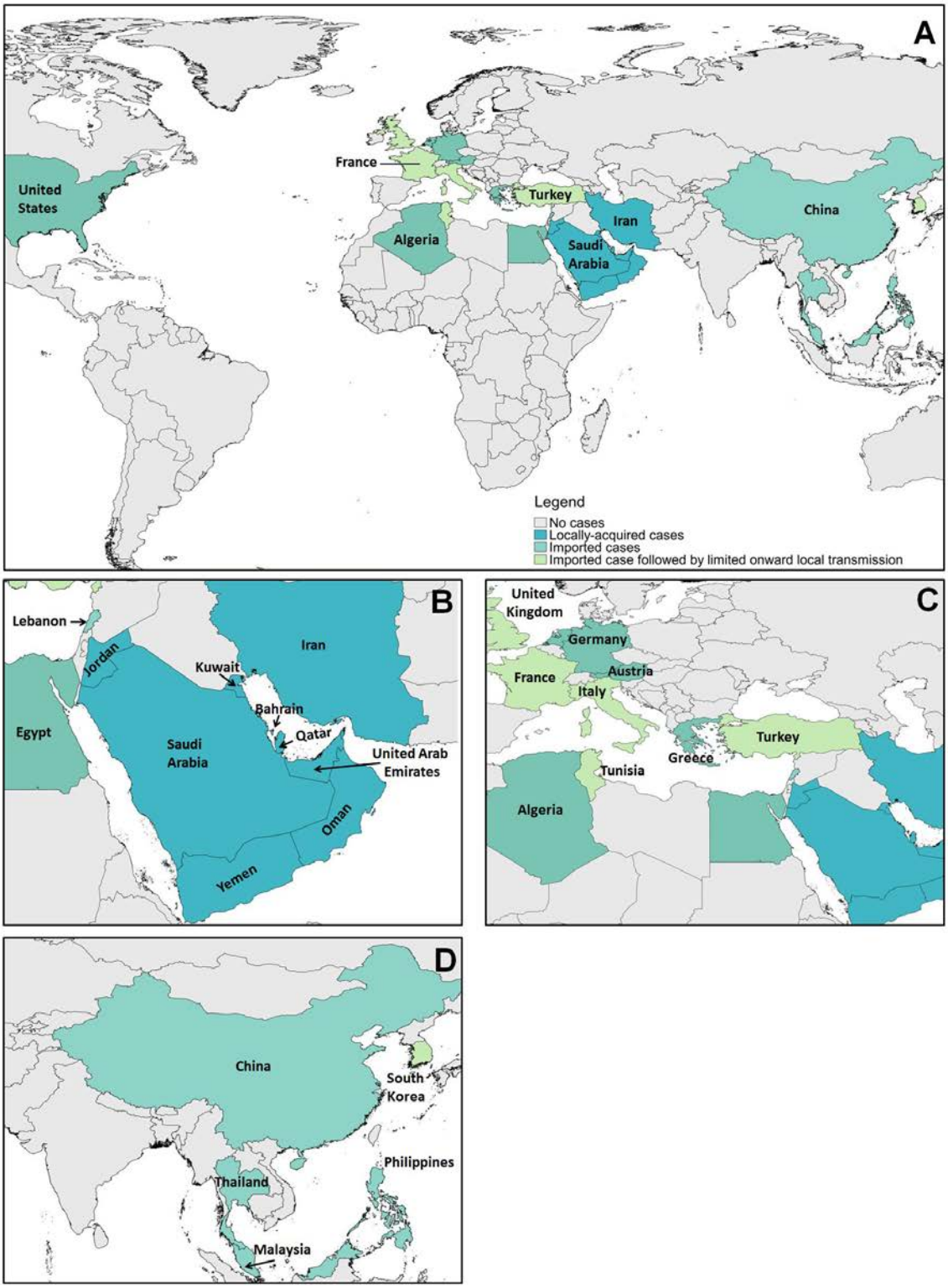
GEOGRAPHICAL DISTRIBUTION

To date, 27 countries located in the Middle East, Northern Africa, Europe, North America and Asia have reported imported and locally-acquired cases of MERS [Figure 6] (6). The majority of cases (n=1845, 90%), have been reported from countries within the Arabian Peninsula with 92% of those cases reported from Saudi Arabia. Research on the human-animal interactions and the circulation of MERS-CoV in dromedary camels suggest that in addition to the dromedary camel population within the Arabian Peninsula, economic, cultural, and recreational practices specific to the area—such as the movement towards more intensive camel farming clustered around cities—are the cause for the observed concentration of cases (31,33,47-50).

Currently, the majority of the world's dromedary camel population (>60%) is located in the Greater Horn of Africa (GHA); a region that regularly exports camels to countries in the Arabian Peninsula (48). Though serological studies conducted on dromedary camels from multiple countries in Africa (Egypt, Ethiopia, Nigeria, Somalia, Sudan) have demonstrated that camels in these areas have high seroprevalence of MERS-CoV, no local zoonotic infections with MERS have been reported from any country in Africa; only 6 cases have been reported from countries in Africa and all cases have been imported or linked to an imported case from the Middle East (47). Additionally, a study on the circulation of coronavirus species in Saudi Arabia found that local camels had significantly higher carrier rates than imported camels (49). Lineage testing identified MERS-CoV found in African camels is genetically different from MERS-CoV found in camels and humans in the Middle East (48,83). This evidence suggests that zoonotic MERS cases seen in Saudi Arabia and other countries in the Arabian Peninsula are connected to factors specific to the Arabian Peninsula and Saudi Arabia.

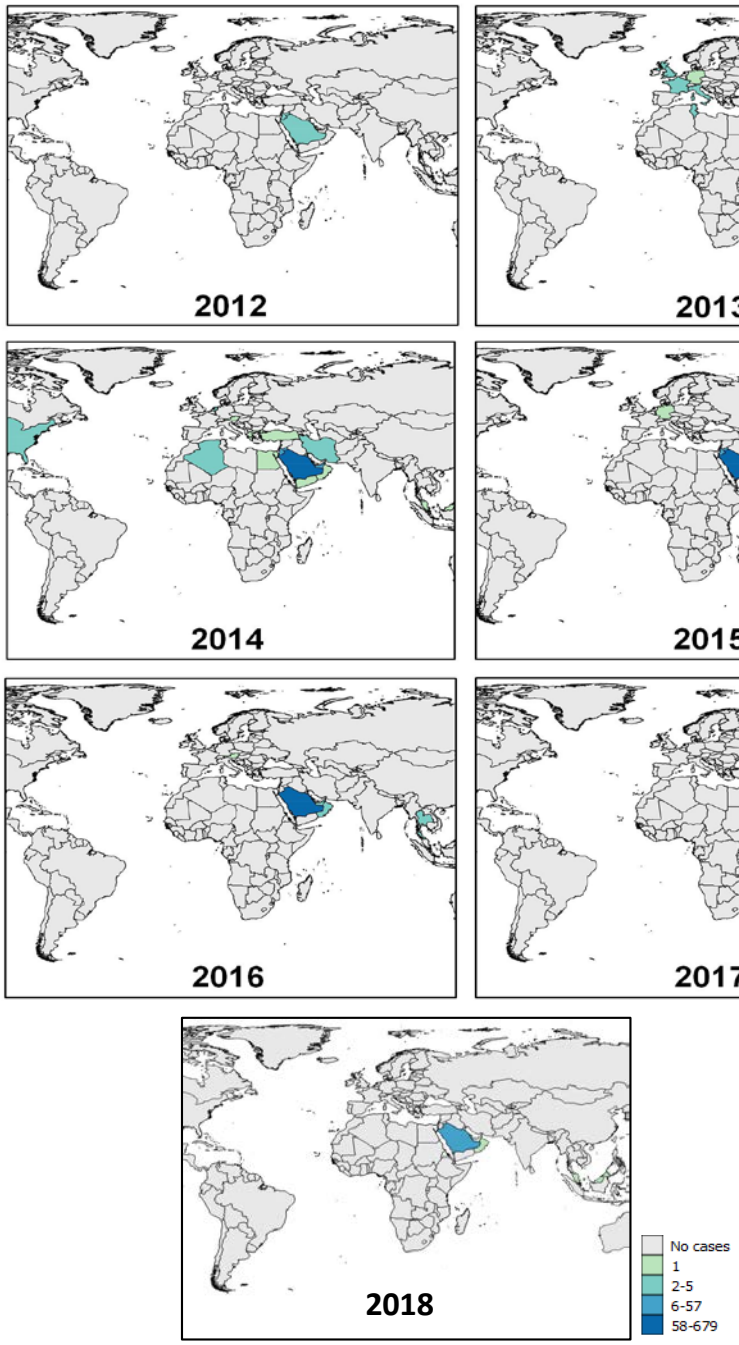
Given that MERS-CoV has been endemic in Saudi Arabia dromedary camels for over two decades and that the virus is widespread within the Arabian Peninsula, further cases are expected to be reported and exported from these areas (51). Countries like India and Bangladesh, with a large volume of citizens that travel to Saudi Arabia for religious pilgrimages, have been identified as potential high-risk areas for MERS-CoV importation (52,53). To date the largest number of cases to be reported from outside the Middle East occurred in South Korea in 2015: the majority of the 186 reported cases were associated with a large multi-hospital outbreak (54). Overall, cases were the most geographically dispersed in the 2014 season when 17 countries reported cases [Figure 7].

Figure 6. Geographical distribution of reported MERS cases between March 2012 and March 31, 2018. (A) Globally, (B) the Arabian Peninsula, (C)Europe, Northern Africa and the Middle East, and (D) Asia.



Note: Map was prepared by Centre for Immunization and Respiratory Infectious Diseases (CIRID) using information compiled by the World Health Organization (24).

Figure 7. Spatial distribution of human cases of MERS between March 2012 and March 31, 2018



Note: Map was prepared by Centre for Immunization and Respiratory Infectious Diseases (CIRID) using information compiled by the World Health Organization and the KSA MOH (24,32,39).

VACCINES AGAINST MERS-CoV

No vaccine or effective antiviral treatment is currently available for MERS-CoV. Research is underway and many candidate vaccines targeted for humans are under development. These candidates use a wide range of platforms including whole virus vaccine (live attenuated and inactivated), vectored-virus vaccines, DNA vaccine, and protein-based vaccines, with many of the viruses targeting the S (envelope) protein or the DPP4 receptor binding domain (RBD) of the S protein (80). Thus far, only one candidate vaccine has advanced to clinical development: a DNA-only vaccine called GLS-5300 that generated protective MERS-CoV antibodies in mice, camels and monkeys, and advanced to Phase 1 human clinical trials in February 2016 (81). This candidate vaccine has also been tested and reduced virus shedding in dromedary camels (81). The DNA-based vaccines directed at inducing anti S responses also induce protection in non-human primates (80). As the spike protein (specifically S1) is highly divergent among different CoVs, the neutralizing antibodies only provide homotypic protection. In contrast, the amino acid sequence of the spike protein, specifically of S2 domain, is conserved with minimal variability among MERS-CoV strains. Additionally, the circulating MERS-CoV strains also lack significant variation in the serological reactivity. As the S2 domain protein is more conserved among coronaviruses, the adaptive immune response directed against S2 protein can potentially constitute the basis for the development of an vaccine capable of inducing heterotypic protection against circulating MERS-CoV strains. Additionally, a modified vaccinia Ankara based vaccine that reduced virus shedding and generated protective antibodies and mucosal immunity is currently scheduled for a Phase 1 safety trial (82).

LIMITATIONS

This in-depth analysis of MERS-CoV is subject to several limitations. The majority of data in this report represent laboratory-confirmed cases of MERS-CoV reported in the Kingdom of Saudi Arabia. Very limited data are available about cases' clinical manifestation, diagnosis, treatment and comorbidities. There is the possibility of unknown selection biases as the primary cases are only detected following presentation with illness. The asymptomatic primary cases or cases with limited access to health care remain undetected. It remains challenging to interpret risk factors for the acquisition of MERS-CoV particularly in the absence of evidence from extensive case-control epidemiology studies.

CONCLUSION

In 2015, the WHO created a Blueprint list of priority diseases that pose major public health risks and require further research and development. Both the original list and the update provided in February 2018 deemed MERS-CoV a potential public health emergency (59). Since the emergence of MERS in 2012, human cases, predominantly from countries within the Arabian Peninsula, continue to be reported. Transmission patterns of the disease have remained consistent with repeated introductions in the human population occurring through zoonotic transmission followed by amplified human to human transmission in health care settings. A better understanding of the transmission of MERS-CoV in healthcare settings is required, especially of the exposures that result in human-to-human transmission, the potential role of asymptomatic infected health-care workers, and the possible role of environmental contamination, in order to mitigate the risk of nosocomial outbreaks. Though the number of cases reported annually appears to be on the decline, it is clear that continued research and surveillance is needed to further bridge the gaps in knowledge surrounding the virus origin and characteristics, transmission of this disease in the community, the exact mode of zoonotic transmission, and potential environmental sources of disease.

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