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The epidemiology of Middle East respiratory syndrome coronavirus in the Kingdom of Saudi Arabia, 2012–2015

Abdullah J. Alsahafi [a,*], Allen C. Cheng [b]

[a] Department of Epidemiology and Preventive Medicine, Monash University, Alfred Centre, 99 Commercial Rd, Melbourne, VIC 3004, Australia
[b] Infection Prevention and Healthcare Epidemiology Unit, Alfred Health, Melbourne, Australia

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SUMMARY

Objectives: The aim of this study was to review the epidemiology of cases of Middle East respiratory syndrome coronavirus (MERS-CoV) reported in the Kingdom of Saudi Arabia from 2012 when the first MERS-CoV was confirmed up to July 2015.
Methods: MERS-CoV data were obtained from the Saudi Ministry of Health for the period 2012 to July 2015. Descriptive statistics were used to summarize the results regarding the risk factors and mortality of MERS-CoV infection.
Results: In this series, the risk factors and outcomes of 939 cases of MERS-CoV occurring in the last 3 years are described. The majority of the affected patients were aged ≥40 years (n = 657; 70%). Of the 657 patients aged ≥40 years, 377 (57.3%) died.
Conclusions: The case-fatality ratio was found to increase significantly with age. It ranged from 12.5% in those aged ≤19 years to 86.2% in those aged ≥80 years. The results confirmed the association between severe MERS-CoV illness and patients with a pre-existing health morbidity. The duration from symptom onset to admission was not statistically associated with the disease outcome.

1. Introduction

Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in the Kingdom of Saudi Arabia in 2012.[1,2] Although MERS-CoV is thought to be a zoonosis, probably involving dromedary camels,[3] clusters due to human-to-human transmission are well recognized.[4–6] Locally acquired cases have been reported primarily in countries of the Middle East including Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, United Arab Emirates, and Yemen; imported cases (or import-related cases) have also occurred in Algeria, Austria, China, Egypt, France, Germany, Greece, Italy, Malaysia, Netherlands, Philippines, South Korea, Thailand, Tunisia, Turkey, UK, and the USA.[7]

The aim of this study was to review the epidemiology of cases of MERS-CoV in the Kingdom of Saudi Arabia prior to July 2015.

2. Methods

Data were obtained from the Saudi Ministry of Health for the period 2012 to July 2015. Cases were defined as patients with a positive nucleic acid test for MERS-CoV, whether diagnosed due to clinical presentation because of illness, or active surveillance in known contacts. Primary cases were defined as patients who were diagnosed with MERS-CoV following presentation for medical care, and secondary cases were patients who were tested as a contact of a known case, whether in a household, as an inpatient in hospital, or as a healthcare worker caring for a case.

Descriptive statistics were used to summarize the results. Proportions were compared between groups using the Chi-square test, and continuous variables were compared using the Mann–Whitney test or Kruskal–Wallis test, as appropriate. Univariate and a multivariate logistic regression models were used to determine risk factors for mortality, excluding asymptomatic patients and those for whom medical morbidities or the outcome were not ascertained. Statistical tests were performed using Stata 14 for Windows (StataCorp, College Station, TX, USA).

This study was approved by the Ministry of Health of the Kingdom of Saudi Arabia.

3. Results

During the period 2012 to July 2015, 939 cases of MERS-CoV were reported to the Saudi Ministry of Health. Of these,

* Corresponding author. Tel.: +61 406548300.
E-mail address: Abdullah.sahafi@monash.edu (A.J. Alsahafi).

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624 patients (66%) were male, 33% were elderly (>60 years), and 3.2% were children (<20 years) (Table 1). Compared to the other groups, a higher proportion were female in the group of healthcare workers. The largest proportion of cases were from the Riyadh region (n = 369; 39.3%), followed by Jeddah (n = 195; 20.8%) and the Eastern region (n = 125; 13.3%). The majority of cases in Riyadh (n = 197; 53.4%) and Jeddah (n = 197; 91.8%) occurred in 2014, while most cases in the Eastern region (n = 67; 53.6%) were reported in 2015.

Primary cases and secondary case hospital inpatients were older than household contacts and secondary case healthcare workers (Figure 1).

The distribution of MERS-CoV cases in the Kingdom of Saudi Arabia from September 2012 to July 2015 by month of symptom onset showed no specific constant seasonal pattern. Most of the cases occurred during the first 6 months of the year (Figure 2).

3.1. Clinical presentation

The location of diagnosis was reported for 788 patients. Of these, 329 patients were diagnosed following presentation with illness. Of the remaining 459 patients who were diagnosed as contacts, 114 were contacts of known cases in the community, 174 were inpatient contacts of known cases, and 171 were healthcare worker contacts (Table 1). Of the secondary cases, 93 were asymptomatic; this proportion was highest in healthcare workers (32%), followed by household cases (23%).

3.2. Risk factors

Medical comorbidities were reported in 421 patients (Table 1). Overall, 351 patients (44%) had one or more comorbidity; the proportion with comorbidities was higher in patients who were >60 years of age and those who were secondary cases in hospital inpatients. Diabetes was common in all groups (53% overall).

3.3. Mortality

The case-fatality ratio increased with age, with a mortality of 12.5% in children aged <20 years rising to 86% in elderly patients aged >80 years. In the univariate analysis of patients for whom complete data were available and excluding asymptomatic cases, acquisition as a hospital inpatient, hypertension, renal disease, cardiac disease, and cancer were positively associated with mortality (Table 2). On multivariate analysis, age >80 years, cardiac disease, and cancer were independently associated with mortality. Compared to primary cases, mortality was lower in household cases and healthcare workers. The duration from symptom onset to admission was not statistically associated with the disease outcome.

MERS cases were notified to the Saudi Ministry of Health (MOH) from different regions of the Kingdom. The present data showed that 564 (65.1%) patient cases were notified within 7 days after the onset of symptoms, while 301 (34.8%) patient cases were notified at >7 days after symptom onset (Table 1).

4. Discussion

In this series, the risk factors and outcomes of more than 900 cases of MERS-CoV occurring over 3 years are described. These represent 60% of the 1570 cases reported worldwide.

A distinct clinical profile was found in the different populations based on their likely location of acquisition, which reinforces the association of chronic comorbidity and severe infection. While previous studies have noted a lower mortality in secondary cases consistent with a detection bias in primary cases,[8] it was found that the case fatality varied in the different groups with secondary infection. Patients who presented with primary infection were more severely unwell but had a similar mortality as hospital inpatients who acquired the infection in hospital. Healthcare workers and household contacts had a lower mortality, reflecting a

Table 1
Characteristics of MERS-CoV cases in the Kingdom of Saudi Arabia prior to July 2015, by location of acquisition

	Primary	Secondary			Unknown	Total	p-Value[a]
		Household	Inpatient	HCW			
Number[b]	329	114	174	171	151	939	
Year							<0.001
2012	3 (0.9%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (0.5%)	
2013	38 (11.6%)	26 (22.8%)	40 (23.0%)	26 (15.2%)	6 (4.0%)	136 (14.5%)	
2014	168 (51.1%)	55 (48.2%)	73 (42.0%)	127 (74.3%)	134 (88.7%)	557 (59.3%)	
2015	120 (36.5%)	31 (27.2%)	61 (35.1%)	18 (10.5%)	11 (7.3%)	241 (25.7%)	
Age group, years							<0.001
≤19	7 (2.1%)	16 (14.0%)	4 (2.3%)	0 (0.0%)	5 (3.3%)	32 (3.4%)	
20–39	52 (15.8%)	40 (35.1%)	25 (14.4%)	104 (60.8%)	29 (19.2%)	250 (26.6%)	
40–59	135 (41.0%)	41 (36.0%)	53 (30.5%)	62 (36.3%)	54 (35.8%)	345 (36.7%)	
60–79	112 (34.0%)	15 (13.2%)	71 (40.8%)	5 (2.9%)	50 (33.1%)	253 (26.9%)	
≥80	23 (7.0%)	2 (1.8%)	21 (12.1%)	0 (0.0%)	13 (8.6%)	59 (6.3%)	
Male	250 (76.0%)	80 (70.2%)	124 (71.3%)	71 (41.5%)	99 (65.6%)	624 (66.5%)	<0.001
Resident of KSA	236 (71.7%)	92 (80.7%)	144 (82.8%)	29 (17.0%)	112 (74.2%)	613 (65.3%)	<0.001
Comorbidities							
Diabetes	116/198 (58.6%)	19/38 (50.0%)	49/99 (49.5%)	10/34 (29.4%)	30/52 (57.7%)	224/421 (53.2%)	0.014
Hypertension	96/198 (48.5%)	13/38 (34.2%)	58/99 (58.6%)	6/34 (17.6%)	27/52 (51.9%)	200/421 (47.5%)	0.001
Renal disease	22/198 (11.1%)	2/38 (5.3%)	31/99 (31.3%)	1/34 (2.9%)	12/52 (23.1%)	68/421 (16.2%)	0.001
Pulmonary disease	19/198 (9.6%)	0/38 (0.0%)	11/99 (11.1%)	2/34 (5.9%)	5/52 (9.6%)	37/421 (8.8%)	0.18
Cardiac disease	37/198 (18.7%)	8/38 (21.1%)	34/99 (34.3%)	3/34 (8.8%)	15/52 (28.8%)	97/421 (23.0%)	0.004
Cancer	9/198 (4.5%)	1/38 (2.6%)	9/99 (9.1%)	0/34 (0.0%)	4/52 (7.7%)	23/421 (5.5%)	0.13
Other chronic disease	46/198 (23.2%)	2/38 (5.3%)	32/99 (32.3%)	4/34 (11.8%)	14/52 (26.9%)	98/421 (23.3%)	0.003
Presentation: asymptomatic	0/325 (0.0%)	25/110 (22.7%)	4/172 (2.3%)	56/170 (32.9%)	8/147 (5.4%)	93/924 (10.1%)	0.001
Notification from symptom onset >7 days	146/317 (46.1%)	28/99 (28.3%)	38/167 (22.8%)	27/146 (18.5%)	62/137 (45.3%)	301/866 (34.8%)	0.001
Died	184/325 (56.6%)	18/110 (16.4%)	132/172 (76.7%)	15/170 (8.8%)	76/147 (51.7%)	425/924 (46.0%)	0.001

MERS-CoV, Middle East respiratory syndrome coronavirus; HCW, healthcare worker; KSA, Kingdom of Saudi Arabia.

[a] p-Values represent results of the Chi-square test for the null hypothesis of no difference in proportions across groups, excluding patients with an unknown source of acquisition.

[b] Denominator unless reported otherwise.

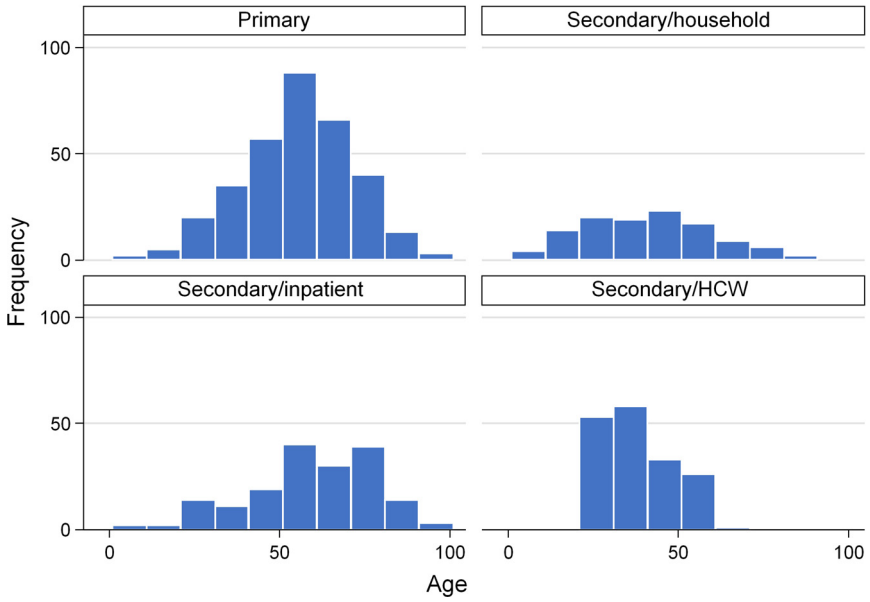

Figure 1. Age distribution of MERS-CoV cases reported in the Kingdom of Saudi Arabia during the period 2012 to July 2015, by location of acquisition.

lower severity of illness in these populations who were previously well.

The present findings confirm the association between comorbidities in patients and severe illness.[9–11] Previous studies have defined obesity, diabetes, and renal disease as risk factors when comparing cases to test-negative hospital-based controls with respiratory illnesses.[8–10] Diabetes was very common across all groups, including healthcare workers. The high prevalence of renal disease in hospital inpatients reflects the wards in which nosocomial outbreaks occurred.

Patients with secondary infections were detected by active surveillance and therefore are more likely to reflect the full spectrum of illness. Of note, a significant proportion of household infections and healthcare worker infections were reported to be asymptomatic, and previous cases have been noted to have prolonged viral shedding.[5,12–14] Similar to a previous study, it was found that acute disease (with a short duration of symptoms at the time of hospital admission) was not associated with increased mortality.[11] It was reassuring to find that the majority of cases were admitted within a week, as early diagnosis is required to ensure that control measures are effective.[15] A small proportion who were asymptomatic was noted; the clinical significance of asymptomatic infection, and particularly the potential for transmission, is not yet known.

There were several limitations in reviewing this public health database. The data reported here represent almost 90% of the 1045 laboratory-confirmed cases of MERS-CoV reported in the Kingdom of Saudi Arabia, but the reasons for the missing data are not apparent. Available clinical data on diagnosis and treatment were scarce, and a significant proportion had missing data on comorbidities. As primary cases were detected following presentation with illness, unknown selection biases may be present. It is not possible to comment on risk factors for the acquisition of MERS-CoV without a control group without infection.

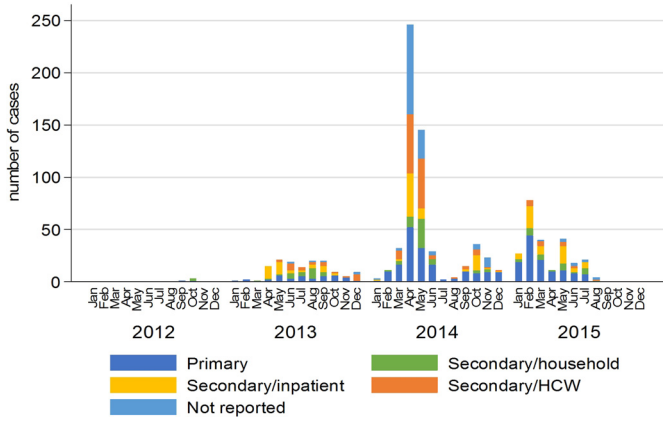

Figure 2. Distribution of MERS-CoV cases in the Kingdom of Saudi Arabia during the period 2012 to July 2015, by month of onset of symptoms.

Table 2
Factors associated with mortality in 403 symptomatic MERS-CoV cases in the Kingdom of Saudi Arabia for the period 2012 to July 2015, for whom comorbidities and the outcome were ascertained

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age group, years		
≤19	0.40 (0.04, 3.95)	0.37 (0.03, 3.95)
20–39	0.54 (0.30, 0.96)	0.64 (0.32, 1.27)
40–59	1	1
60–79	2.44 (1.51, 3.93)	1.49 (0.87, 2.56)
≥80	6.51 (2.38, 17.82)	4.07 (1.41, 11.78)
Male	0.93 (0.60, 1.45)	0.78 (0.45, 1.34)
Comorbidities		
Diabetes	1.43 (0.96, 2.11)	0.86 (0.49, 1.52)
Hypertension	2.34 (1.56, 3.49)	1.41 (0.80, 2.48)
Renal disease	1.84 (1.06, 3.18)	1.06 (0.56, 2.03)
Pulmonary disease	1.38 (0.68, 2.79)	1.10 (0.48, 2.54)
Cardiac disease	3.86 (2.25, 6.60)	2.80 (1.52, 5.16)
Cancer	6.46 (1.89, 22.10)	5.98 (1.64, 21.79)
Location of acquisition		
Primary	1	1
Secondary/household	0.24 (0.10, 0.58)	0.25 (0.09, 0.68)
Secondary/inpatient	3.32 (1.90, 5.82)	2.61 (1.41, 4.82)
Secondary/HCW	0.10 (0.03, 0.35)	0.17 (0.05, 0.59)
Unknown	1.20 (0.63, 2.26)	1.02 (0.50, 2.06)

MERS-CoV, Middle East respiratory syndrome coronavirus; OR, odds ratio; CI, confidence interval; HCW, healthcare worker.

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Conflict of interest: All authors declare that they have no competing interests.

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