JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Brief Original Article

No molecular evidence of MERS-CoV circulation in Jeddah, Saudi Arabia between 2010–2012: a single-center retrospective study

Reem Jamal Alamoudi[1], Leena Esam Azhar[2], Dareen Hussein Alamoudi[2], Dena Hussein Alamoudi[2], Ahmed Majdi Tolah[1], Rowa Yousef Alhabbab[1,3], Esam Ibraheem Azhar[1,3], Anwar Mohammed Hashem[1,4]

[1] Special Infectious Agents Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia
[2] Student Research and Innovation Unit, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[3] Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia
[4] Department of Medical Microbiology and Parasitology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Introduction: Middle East respiratory syndrome coronavirus (MERS-CoV) is an emerging zoonotic viral pathogen and a serious public health concern. The virus was first reported in Saudi Arabia in 2012 and continues to be endemic in the region. Most of the initial MERS-CoV cases in 2012 and early 2013 were sporadic, and it remains unclear whether MERS-CoV was circulating before 2012 or not. Therefore, we tried here to find any molecular evidence of MERS-CoV circulation in humans before or during 2012 in the city of Jeddah, Saudi Arabia.
Methodology: We examined 349 archived respiratory samples collected between January 2010 and December 2012 from patients with acute respiratory illnesses from the city of Jeddah in Western Saudi Arabia. All samples were screened for MERS-CoV by real-time RT-PCR targeting the upstream E-gene (UpE) and the open reading frame 1 a (ORF1a).
Results: All tested samples which were originally found negative for influenza A H1N1 virus were also found to be negative for MERS-CoV.
Conclusions: These results suggest that circulation of MERS-CoV was uncommon among patients with acute respiratory symptoms in Western Saudi Arabia between 2010 and 2012.

Key words: MERS-CoV; Jeddah; Saudi Arabia.

J Infect Dev Ctries 2018; 12(5):390-393. doi:10.3855/jidc.9523

(Received 17 June 2017 – Accepted 12 February 2018)

Introduction

In September 2012, the first case of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was reported after the death of a patient (patient zero) suffering from severe respiratory illness in Jeddah, Saudi Arabia [1]. This case was initially admitted to a hospital back in June 13, 2012, with symptom onset starting 7 days before. On September 23, 2012, a second confirmed case was reported in London from a Qatari patient who had travel history to Saudi Arabia [2]. Interestingly, retrospective study from Jordan confirmed MERS-CoV circulation in Zarqa region as early as April 2012 causing several infections with at least 2 deaths [3]. As of March 25, 2017, there is a total of 1,917 laboratory confirmed MERS cases and 684 associated deaths (>35%) from 27 countries [4]. So far, Saudi Arabia has reported more than 82% of the cases (1581 laboratory confirmed cases) with local death rate exceeding 41% (659 deaths) [5].

The majority of the reported MERS-CoV cases were due to direct human-to-human transmissions particularly with poor infection control measures. Nonetheless, several epidemiological studies have demonstrated the widespread of MERS-CoV in dromedary camels (*Camelus dromedarius*) in Africa and the Arabian Peninsula as early as 1983 and 1993, respectively [6,7]. Furthermore, other studies have provided strong evidences of MERS-CoV transmission from camels-to-humans [8-10], suggesting that dromedaries are most likely the reservoir host for MERS-CoV and an important source of human infections. However, most of initial MERS cases in 2012 and early 2013 were sporadic, and it remains unclear whether MERS-CoV was circulating before 2012 or not. Therefore, we tried here to find any

molecular evidence of MERS-CoV infection in humans that might have occurred before or during 2012.

Methodology

Samples

A total of 349 archived respiratory samples collected between January 2010 and December 2012 from patients with acute respiratory illnesses (Table) at the King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia were retrieved. All samples were collected originally for influenza A H1N1 screening at the Special Infectious Agents Unit (SIAU), King Fahd Medical Research Center (KFMRC) before the emergence of MERS-CoV in Saudi Arabia. These samples were found to be negative for influenza A viruses and were stored at -80°C since their collection. Samples included throat and nasopharyngeal swabs, tracheal, nasopharyngeal and endotracheal tube aspirates, bronchial wash, and bronchial alveolar lavage.

RNA extraction and MERS-CoV RT-PCR

Viral RNA was extracted using QIAamp Viral RNA mini kit (Qiagen, Hilden, Germany) according to manufacturer's instructions from all samples, eluted in 40 µL and stored at -80°C until use. Extracted RNA from all samples was tested for MERS-CoV upstream E-gene (UpE) and open reading frame 1 a (ORF1a) using real time RT-PCR as previously described [9]. Positive and negative (no-template control) controls were always included during testing.

Results

In order to determine whether MERS-CoV was circulating in the city of Jeddah before or during 2012, a total of 349 archived respiratory samples (Table) from patients with acute respiratory tract infections collected between January 2010 and December 2012 were retrieved. Most of the samples were collected during the winter season starting from October to late March (Table). Samples were from 204 males and 145 female patients with the majority of them being from patients

Table 1. Summary of demography characteristics of patients with upper respiratory tract infection.

Year	2010 n = 91	2011 n = 62	2012 n = 196	Total n = 349
	Number (%)			
Months				
January	6 (6.6)	23 (37.1)	15 (7.7)	44 (12.6)
February	17 (18.7)	11 (17.7)	22 (11.2)	50 (14.3)
March	11 (12.1)	9 (14.5)	12 (6.1)	32 (9.2)
April	8 (8.8)	6 (9.7)	7 (3.6)	21 (6.0)
May	2 (2.2)	2 (3.2)	20 (10.2)	24 (6.9)
June	2 (2.2)	1 (1.6)	2 (1.0)	5 (1.4)
July	0 (0.0)	0 (0.0)	2 (1.0)	2 (0.6)
August	1 (1.1)	5 (8.1)	1 (0.5)	7 (2.0)
September	2 (2.2)	3 (4.8)	2 (1.0)	7 (2.0)
October	12 (13.2)	0 (0.0)	27 (13.8)	39 (11.2)
November	10 (11.0)	0 (0.0)	42 (21.4)	52 (14.9)
December	20 (22.0)	2 (3.2)	44 (22.4)	66 (18.9)
Gender				
Male	53 (58.2)	37 (59.7)	114 (58.2)	204 (58.5)
Female	38 (41.8)	25 (40.3)	82 (41.8)	145 (41.5)
Sample				
Nasopharyngeal swab	25 (27.5)	41 (66.1)	139 (70.9)	205 (58.7)
Throat swab	62 (68.1)	14 (22.6)	13 (6.6)	89 (25.5)
Endo tracheal tube aspirate	2 (2.2)	2 (3.2)	27 (13.8)	31 (8.9)
Nasopharyngeal aspirate	0 (0.0)	4 (6.5)	12 (6.1)	16 (4.6)
Tracheal aspirate	2 (2.2)	1 (1.6)	3 (1.5)	6 (1.7)
Bronchial alveolar lavage	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.3)
Bronchial wash	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.3)
Age group (years)				
0–14	30 (33.0)	33 (53.2)	141 (71.9)	204 (58.5)
15–34	35 (38.5)	14 (22.6)	30 (15.3)	79 (22.6)
35–65	18 (19.8)	8 (12.9)	21 (10.7)	47 (13.5)
> 66	8 (8.8)	7 (11.3)	4 (2.0)	19 (5.4)

within the age range of 0-14 years (204 samples). None of the samples tested here was positive for MERS-CoV UpE or ORF1a regions, suggesting that there is sparse evidence of MERS-CoV circulation in Jeddah during or before 2012.

Discussion

MERS-CoV is a reminder of the severe acute respiratory syndrome-CoV (SARS-CoV) which first emerged in China in late 2002 and caused more than 8000 laboratory-confirmed cases and ~9.6% mortality rate in 37 countries. Unlike SARS-CoV which disappeared within a couple of years from its introduction, MERS-CoV continues to be endemic in the Arabian Peninsula since its emergence with high potential to cause global spread as recently observed in South Korea [11]. Nonetheless, the progression pattern of the two viruses seems to be somewhat similar in terms of their initial sporadic introduction, eventual establishment, and sustained dissemination in humans [12,13]. Indeed, MERS-CoV started by causing sporadic infections in mid 2012 which then progressed to a sustained human-to-human transmission causing several hospital and household outbreaks with global spread in some occasions [4,11].

In the case of SARS-CoV, it was suggested that it might have been circulating at a very low level in an adaptation window period in humans before it was first reported in November 2002 from the first index patient in China [12]. Similarly, the temporal and spatial pattern of early known index MERS cases as well as the high endemicity of MERS-CoV in dromedaries in several countries in the Middle East and Africa most probably for more than 30 years [6-10] suggest that there might have been several introduction points or spill-overs from camels to humans. However, our data here as well as previously reported seroepidemiological results [13,14] failed to document any molecular or serological evidence of MERS-CoV circulation in humans during or before 2012 in at least three regions in Saudi Arabia (Jeddah, Makkah and Jazan regions).

A recent large molecular surveillance study from Saudi Arabia on more than 57,000 suspected MERS cases showed an incidence rate of 0.7% (384 patients) during the study period, suggesting a very low prevalence among humans [15]. Interestingly, while most testing was done in wintertime, the majority of the positive cases were during the months of May and August most probably due to ongoing hospital outbreaks [15]. Nevertheless, it was shown that infections can occur all year-round but at very low rate mostly due to horizontal transmission rather than direct contact with camels. The results of this study clearly suggest that direct transmission of MERS-CoV from camels to humans remains a rare event regardless of the continuous exposure and high prevalence of MERS-CoV in camels highlighting several unanswered questions. Therefore, understanding where, how and when MERS-CoV cases actually started, why MERS cases peaked very shortly and suddenly after the first few reports in the Arabian Peninsula, and whether human MERS cases are mainly restricted to the Arabian Peninsula but not other countries where seropositive dromedaries are very common could help us not only to better understand MERS-CoV epidemiology but also to reduce or prevent its transmission.

The current study has several limitations. First, the sample size is small mostly due to our inability to obtain more archived samples from other hospitals or regions as samples are usually maintained and stored for few months only before their disposal, and we were only able to retrieve samples from 3-year period. Second, samples were collected from patients admitted or presented to one tertiary hospital in the city of Jeddah only. Third, most of the samples were from patients under the age of 14 years which seems to be the least affected age group by MERS-CoV. Therefore, it might be more appropriate to conduct further large-scale epidemiological and serological studies to actually get better understanding of MERS-CoV emergence in humans. However, such studies might be difficult to conduct in the absence of continuous and active sentinel surveillance programs not only for MERS-CoV but also for other pathogens in the region.

Conclusions

MERS-CoV infections in the community has been sporadic since its first detection in 2012. This study as well as previous reports suggest that MERS-CoV was uncommon in humans in several cities in Saudi Arabia between 2010 and 2012, and that human cases were most probably due to isolated spill-overs from camels to humans. However, further studies with larger number of samples are clearly required to better understand the possible circulation of MERS-CoV before its emergence.

Acknowledgements

This project was funded by the Deanship of Scientific Research (DSR), King Abdulaziz University (KAU), Jeddah, under grant no. (G-484-140-37). The authors, therefore, acknowledge with thanks DSR for technical and financial support.

References

1. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA (2012) Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 367: 1814–1820.
2. World Health Organization (2012) Novel coronavirus infection — update — revised interim case definition. Geneva: World Health Organization Available: http://www.who.int/csr/don/2012_09_29/en/index.html. Accessed: 15 March 2017.
3. Al-Abdallat MM, Payne DC, Alqasrawi S, Rha B, Tohme RA, Abedi GR, Al Nsour M, Iblan I, Jarour N, Farag NH, Haddadin A, Al-Sanouri T, Tamin A, Harcourt JL, Kuhar DT, Swerdlow DL, Erdman DD, Pallansch MA, Haynes LM, Gerber SI; Jordan MERS-CoV Investigation Team (2014) Hospital-associated outbreak of Middle East Respiratory Syndrome Coronavirus: a serologic, epidemiologic, and clinical description. Clin Infect Dis 59: 1225-1233.
4. World Health Organization (2017) Middle East respiratory syndrome coronavirus (MERS-CoV). Available: http://www.who.int/emergencies/mers-cov/en/ Accessed: 15 March 2017.
5. Saudi ministry of health command and control center (2017) Statistics Available: http://www.moh.gov.sa/en/ccc/pressreleases/pages/default.aspx Accessed: 15 March 2017.
6. Müller MA, Corman VM, Jores J, Meyer B, Younan M, Liljander A, Bosch BJ, Lattwein E, Hilali M, Musa BE, Bornstein S, Drosten C (2014) MERS coronavirus neutralizing antibodies in camels, Eastern Africa, 1983-1997. Emerg Infect Dis 20: 2093-2095.
7. Hemida MG, Perera RA, Al Jassim RA, Kayali G, Siu LY, Wang P, Chu KW, Perlman S, Ali MA, Alnaeem A, Guan Y, Poon LL, Saif L, Peiris M (2014) Seroepidemiology of Middle East respiratory syndrome (MERS) coronavirus in Saudi Arabia (1993) and Australia (2014) and characterisation of assay specificity. Euro Surveill 19: 20828.
8. Memish ZA, Cotten M, Meyer B, Watson SJ, Alsahafi AJ, Al Rabeeah AA, Corman VM, Sieberg A, Makhdoom HQ, Assiri A, Al Masri M, Aldabbagh S, Bosch BJ, Beer M, Müller MA, Kellam P, Drosten C (2014) Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, 2013. Emerg Infect Dis 20: 1012-1015.
9. Azhar EI, El-Kafrawy SA, Farraj SA, Hassan AM, Al-Saeed MS, Hashem AM, Madani TA (2014) Evidence for camel-to-human transmission of MERS coronavirus. N Engl J Med 370: 2499-2505.
10. Alagaili AN, Briese T, Mishra N, Kapoor V, Sameroff SC, Burbelo PD, de Wit E, Munster VJ, Hensley LE, Zalmout IS, Kapoor A, Epstein JH, Karesh WB, Daszak P, Mohammed OB, Lipkin WI (2014) Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. M Bio 5: e00884-14.
11. Park SH, Kim YS, Jung Y, Choi SY, Cho NH, Jeong HW, Heo JY, Yoon JH, Lee J, Cheon S, Sohn KM (2016) Outbreaks of Middle East respiratory syndrome in two hospitals initiated by a single patient in Daejeon, South Korea. Infect Chemother 48: 99-107.
12. Xu RH, He JF, Evans MR, Peng GW, Field HE, Yu DW, Lee CK, Luo HM, Lin WS, Lin P, Li LH, Liang WJ, Lin JY, Schnur A (2004) Epidemiologic clues to SARS origin in China. Emerg Infect Dis 10: 1030–1037.
13. Memish ZA, Alsahly A, Masri MA, Heil GL, Anderson BD, Peiris M, Khan SU, Gray GC (2015) Sparse evidence of MERS-CoV infection among animal workers living in Southern Saudi Arabia during 2012. Influenza Other Respir Viruses 9: 64-67.
14. Aburizaiza AS, Mattes FM, Azhar EI, Hassan AM, Memish ZA, Muth D, Meyer B, Lattwein E, Müller MA, Drosten C (2014) Investigation of anti-MERS Coronavirus antibodies in blood donors and abbatoir workers in Jeddah and Makkah, Kingdom of Saudi Arabia, fall 2012. J Infect Dis 209: 243–246.
15. Saeed AA, Abedi GR, Alzahrani AG, Salameh I, Abdirizak F, Alhakeem R, Algarni H, El Nil OA, Mohammed M, Assiri AM, Alabdely HM, Watson JT, Gerber SI (2017) Surveillance and testing for Middle East respiratory syndrome coronavirus, Saudi Arabia, April 2015-February 2016. Emerg Infect Dis 23: 682-685.

Corresponding author

Anwar Hashem, PhD
Special Infectious Agents Unit, King Fahd Medical Research Center, King Abdulaziz University, P.O. Box 80205, Jeddah 21589, Saudi Arabia
Phone: +966 12 6400000, EXT 21033
Email: amhashem@kau.edu.sa

Conflict of interests: No conflict of interests is declared.