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Screening for Middle East respiratory syndrome coronavirus among febrile Indonesian Hajj pilgrims: A study on 28,197 returning pilgrims

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K Shimizu⁴ and Y Mori⁴

Abstract

There were 211,000 Indonesian Hajj pilgrims going to Mecca through 11 main airports in 2015 who were at risk of contracting the Middle East respiratory syndrome coronavirus (MERS-CoV). We aimed to find out whether there was any occurrence of MERS-CoV by performing screening on 28,197 returning pilgrims. Those with a body temperature of > 38 °C and respiratory symptoms were sent to the airport clinic to have an oropharyngeal swab and a bacterial culture. Fifteen pilgrims had fever (> 38 °C) accompanied by respiratory symptoms; of these, 12 patients were diagnosed with upper and lower respiratory tract infections and three patients with pneumonia. However, none of them were found to be infected with MERS-CoV. The bacterial cultures showed evidence of normal flora growth.

Keywords

MERS-CoV, pilgrims, screening, Indonesia

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Introduction

Hajj (pilgrimage) is a mandatory religious ritual required by all able Muslims once in their lifetime. The pilgrimage is considered the largest annual religious gathering with up to three million participants from around the world. The pilgrims should perform a series of physically demanding religious rituals in about 5–6 days in the city of Mecca and surrounding places that could potentially affect their health (Hashim et al., 2016), in addition to unpredictable weather conditions.

Since 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV) has become endemic in the Kingdom of Saudi Arabia (KSA) and other Arabian Peninsula countries. To date, there have been 1905 of reported MERS-CoV cases with 677 deaths from 27 countries (World Health Organization, 2017). MERS-CoV symptoms range from mild influenza-like symptoms to severe acute respiratory disease (Memish et al., 2013). Multiple outbreaks have been reported in hospitals and community settings with possible human transmission (Assiri et al., 2013; Oboho

et al., 2015), yet the virus reservoirs and disease transmission are not fully understood. In confirmed cases of the infection, the mortality rate can be as high as 45% with chronic morbidities or existing diseases as the prominent risk characteristics (Center for Disease Control and

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Prevention, 2013; Cho et al., 2016; Perlman, 2013). Moreover, physical exhaustion of pilgrims and crowded conditions may be related to the outbreaks of this virus.

Indonesia contributes to the annual religious gathering as a country with the highest number of Hajj pilgrims with up to 211,000 people attending annually. They depart from 11 official airports as embarkation points, one of which is Juanda airport in Surabaya, East Java. Surabaya port also represents one of the biggest embarkation points in the country, with nearly 30,000 pilgrims departing in 2015. Previous reports suggested that > 50% of the pilgrims departing from Surabaya are at high risk of contracting infectious diseases (Kantor Kesehatan Pelabuhan Surabaya, 2013). Therefore, early detection in pilgrims is an important preventive action to tackle the spread of MERS-CoV to their communities upon completing the pilgrimage. This study aimed to screen all pilgrims returning to Indonesia at the Surabaya debarkation point in the 2015 Hajj season.

Methods

Ethics

This study has been reviewed and approved by local ethics commissions. All investigated participants were also provided with written informed consent prior to investigation.

Screening procedures

We administered the screening protocol on all pilgrims arriving at the Surabaya debarkation point during the 2015 Hajj season. Every returning pilgrim at the airport had to pass through a thermal detector upon arrival. Pilgrims with body temperature of > 38 °C accompanied by respiratory symptoms such as cough and dyspnoea were quarantined, had their details recorded and an oropharyngeal swab was taken by trained personnel. Should there be an acute condition, pilgrims were directly hospitalised at the designated hospital, while those with mild symptoms could return home and for follow-up after the laboratory tests were completed. For those with body temperature < 38 °C, a report had to be made to the nearest primary healthcare centre or hospital if they experienced a body temperature increase (> 38 °C) which was accompanied by respiratory symptoms within ten days of their return to the country. In this study, a thermal body scanner was tested and calibrated before use.

Case definitions

Early diagnosis was made based on clinical presentation upon case detection. A MERS-CoV case was defined if the real-time polymerase chain reaction (RT-PCR) test of the pharyngeal swab was positive for MERS-CoV. Other bacterial infections were investigated based on the pharyngeal swab culture.

Laboratory test for MERS-CoV

The MERS-CoV from the oropharyngeal swab specimen was tested using the RT-PCR technique by means of RNA extraction from the specimen of oropharyngeal swab. The benefit of RT-PCR testing has been described elsewhere (Wacker and Godard, 2005). The bacterial culture of the swab was conducted at an accredited laboratory of microbiology in Surabaya.

In the RT-PCR technique, extraction of RNA from swab samples was performed using a Qiaamp MinElute Virus Spin Kit (Qiagen, Tokyo, Japan) following the manufacturer's manual at the Biosafety Level 3 laboratory facility. Examination for the presence of the MERS-CoV genomes in the swab was carried out by one-step TaqMan RT-PCR using a QuantiTect Probe RT-PCR Kit (Qiagen, Tokyo, Japan). The reaction mixture was made up with 5 µL of template RNA, with each primer at a final concentration of 0.6 gM, probe 0.1 µM and QuantiTect probe RT-PCR mix. The mixture was then subjected to a one-step assay with an ABI model 7300 Instrument by using the following amplification conditions: step 1 = RT for 30 min at 50 °C; step 2 = 15 min at 95 °C to activate 7aq polymerase; and step 3 = 45 cycles of 15 s at 94 °C and 75 s at 56 °C. Primers and TaqMan probes were designed according to Corman et al. (2012). Synthetic RNAs of upE and Orfla sequences were used as a positive control with permission (National Institute of Health, 2015).

Results

There were 28,197 Hajj pilgrims returning to Indonesia through Juanda airport between October and December 2015 who passed through the body thermal detector. Of these, 15 pilgrims were detected to have a body temperature > 38 °C with respiratory symptoms such as cough, flu and sore throat, and thus were further investigated. The age range of those investigated was 40–80 years (8 men, 7 women).

Of the 15 pilgrims investigated, 12 were clinically diagnosed with upper respiratory tract infection, while three others were diagnosed with pneumonia. Those with pneumonia were sent directly to the local hospital while the remaining 12 pilgrims were sent home. Three patients had a co-morbidity of hypertension and one pilgrim had both hypertension and coronary heart disease.

The RT-PCR test showed no evidence of MERS-CoV infection among 15 oropharyngeal swab samples. Bacteria were detected in nine swab cultures. Detailed findings are shown in Table 1.

Discussion

The objective of this study was to detect MERS CoV-infected Hajj pilgrims at Surabaya debarkation point, who

Table 1. Case finding of 15 pilgrims with fever.

Case No.	Sex	Age	Medical History	Respiratory Infection	MERS-CoV	Bacterial Growth
1	Male	55	Hypertension	URTI	Negative	No bacterial growth
2	Male	61	Hypertension	URTI	Negative	No bacterial growth
3	Female	40	-	URTI	Negative	No bacterial growth
4	Male	83	Hypertension, heart disease	Pneumonia	Negative	<i>Corynebacterium urealyticum</i>
5	Female	66	-	URTI	Negative	<i>Staphylococcus epidermidis</i>
6	Male	41	-	URTI	Negative	<i>Staphylococcus aureus</i>
7	Male	62	-	LRTI	Negative	No bacterial growth
8	Male	63	Hypertension	Acute pharyngitis	Negative	No bacterial growth
9	Female	48	-	URTI	Negative	<i>Corynebacterium ulcerans</i>
10	Female	71	-	LRTI	Negative	<i>Corynebacterium ulcerans</i>
11	Male	46	-	URTI	Negative	<i>Corynebacterium ulcerans</i>
12	Male	40	-	URTI	Negative	No bacterial growth
13	Female	78	-	URTI	Negative	<i>Corynebacterium ulcerans</i>
14	Female	65	-	Pneumonia	Negative	<i>Corynebacterium matruchotii</i>
15	Female	86	-	Pneumonia with suspected MERS-CoV	Negative	<i>Streptococcus viridans</i>

URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection; MERS-CoV, Middle East respiratory syndrome coronavirus.

could potentially carry infection to Indonesia. This was conducted on all Hajj pilgrims arriving at the debarkation point of Surabaya airport, 28,197 pilgrims in total.

In this study, 15 Hajj pilgrims were found to have fever (body temperature > 38°C) accompanied by respiratory symptoms. The PCR test from oropharyngeal swab specimens did not reveal the presence of MERS-CoV in the tested samples. The pilgrims have been instructed by the physicians to report to the MERS-CoV team if they had fever within ten days of their return. None of them reported symptoms within the time frame.

The result of this study is similar to an early detection of MERS-CoV done in 2012 by Gautret et al. (2013) on French Hajj pilgrims using the RT-PCR method with no evidence of MERS-CoV infection detected. Another serosurvey of MERS-CoV was done in Germany on 123 people with negative result (Buchholz et al., 2013).

All of the patients investigated had fever captured by the thermal detector. The thermal detector may have a sensitivity of up to 90% in detecting body temperature (Priest et al., 2011). However, there is also a varying degree of sensitivity according to the site of the body, with the eyes and forehead having the highest correlation to the actual body

temperature (Ng et al., 2004). In addition, thermal detection of body temperature may be affected by ambient air temperature and location of measurement (Liu et al., 2004). Antipyretic use before scanning may also yield a false-negative result.

The bacteria recovered from the swabs of pyrexial patients predominantly reflected normal flora. This was in line with a study performed at Jeddah airport on pilgrims from 13 countries where virus and bacteria were the predominant pathogens (Memish et al., 2015). Tuberculosis has also been identified among patients admitted to hospitals during the Hajj (Al-Tawfiq et al., 2013). However, given the incubation time of the disease, it is challenging to identify such cases in a rapid survey during short period of time.

Study limitations

A recent meta-analysis suggested most respiratory symptoms from returning of Hajj pilgrim was caused by viral infection other than MERS or SARS coronavirus (Gautret et al., 2016). We did not perform specific investigation of other common respiratory virus and thus limit this study in explaining etiological aspects of the investigated cases.

The method of using the thermal body detector may have some limitations in detecting MERS-CoV as the disease may not always present with fever. In addition, pilgrims could have taken an antipyretic before arrival. Despite those limitations, the study protocol also includes a subsequent monitoring by means of pilgrims' self-report upon ten days of arrival involving local health authorities and public healthcare centres. This may reduce the risk of missing MERS-CoV, especially in those pilgrims without fever.

Conclusion

In this study, there was no evidence of MERS-CoV infection among 28,197 Hajj pilgrims returning at Surabaya debarkation point in 2015 presenting with fever. Given the large number of Indonesian Hajj pilgrims annually, constant surveillance involving all debarkation points is needed for early prevention of MERS-CoV spread.

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