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Surveillance of the MERS Coronavirus Infection in Healthcare Workers after Contact with Confirmed MERS Patients: Incidence and Risk Factors of MERS-CoV Seropositivity

Chung-Jong Kim¹, Won Suk Choi², Younghee Jung³, Sungmin Kim⁴, Hee Yun Seol⁵, Heung Jeong Woo⁶, Young Hwa Choi⁷, Jun Seong Son⁸, Kye-Hyung Kim⁹, Yeon-Sook Kim¹⁰, Eu Suk Kim¹¹, Sun Hee Park¹², Ji Hyun Yoon¹³, Su-Mi Choi¹⁴, Hyuck Lee¹⁵, Won Sup Oh¹⁶, Soo-Young Choi¹⁷, Nam-Joong Kim¹⁸, Jae-Phil Choi¹⁹, So Yeon Park²⁰, Jieun Kim²¹, Su Jin Jeong²², Kkot Sil Lee²³, Hee Chang Jang²⁴, Ji Young Rhee²⁵, Baek-Nam Kim²⁶, Ji Hwan Bang²⁷, Jae Hoon Lee²⁸, ShinAe Park²⁹, Hyo Youl Kim³⁰, Jae Ki Choi³¹, Yu-Mi Wi³², Hee Jung Choi¹*¹

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21 Department of Internal Medicine, Hanyang University Guri Hospital
22 Department of Internal Medicine, Gangnam Severance Hospital
23 Department of Internal Medicine, Myongji Hospital
24 Department of Internal Medicine, Chonnam National University Hospital
25 Department of Internal Medicine, Dankook University Hospital
26 Department of Internal Medicine, Inje University Sanggye Paik Hospital
27 Department of Internal Medicine, Borame Medical Center
28 Department of Internal Medicine, Wonkwang University Hospital
29 Department of Family Medicine, Seobuk Hospital Seoul Metropolitan Government
30 Department of Internal Medicine, Wonju Severance Christian Hospital
31 Department of Internal Medicine, College of Medicine, the Catholic University of Korea, Bucheon St. Mary’s Hospital
32 Department of Internal Medicine, Samsung Changwon Hospital
Conflicts of Interest: None

Key Words: Middle East Respiratory Syndrome, Healthcare Personnel, Incidence, IgG, Personal protective equipment

Running title: MERS incidence in Healthcare Personnel

Study registration: Clinicaltrials.gov (identifier No.: NCT02497885).

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Abstract

Objectives: Given the mode of transmission of Middle East Respiratory Syndrome (MERS), healthcare workers (HCWs) in contact with MERS patients are expected to be at risk of MERS infections. We evaluated the prevalence of MERS coronavirus (CoV) immunoglobulin G (IgG) in HCWs exposed to MERS patients, and calculated the incidence of MERS-affected cases in HCWs.

Methods: We enrolled HCWs from hospitals where confirmed MERS patients had visited. Serum was collected 4–6 weeks after the last contact with a confirmed MERS patient. We performed an enzyme-linked immunosorbent assay (ELISA) to screen for the presence of MERS-CoV IgG, and an indirect immunofluorescence test (IIFT) to confirm MERS-CoV IgG. We used a questionnaire to collect information regarding the exposure. We calculated the incidence of MERS-affected cases by dividing the sum of PCR-confirmed and serology-confirmed cases by the number of exposed HCWs in participating hospitals.

Results: In total 1169 HCWs in 31 hospitals had contact with 114 MERS patients, and among the HCWs 15 were PCR-confirmed MERS cases in study hospitals. Serologic analysis was performed for 737 participants. ELISA was positive in five participants and borderline for seven. IIFT was positive for two of these 12 participants (0.3%). Among the participants who did not use appropriate personal protective equipment (PPE), seropositivity was 0.7% (2/294), compared to 0% (0/443) in cases with appropriate PPE use.

Conclusions: The incidence of MERS infection in HCWs was 1.5% (17/1169). The seroprevalence of MERS-CoV IgG among HCWs was higher among participants who did not use appropriate PPE.
Introduction

Middle East Respiratory Syndrome (MERS) is an emerging infectious disease, first described in Saudi Arabia [1, 2], and mainly found within the Middle Eastern region [3]. Only a few cases have been reported outside the Middle East [4-6], and no epidemic event outside the Middle East was seen before 2015. However, that year, the largest single-nation outbreak outside of Saudi Arabia occurred in South Korea over 45 days, with 186 confirmed MERS patients including 38 deaths [7, 8]. Because the main mode of transmission of MERS is respiratory droplet and the most of MERS transmission is occurred in nosocomial setting, healthcare workers (HCWs) in contact with confirmed MERS patients are at high risk of MERS infections [3, 9, 10]. In South Korea, among the 186 laboratory-confirmed MERS patients, 39 cases (21.0%) were medical professionals or HCWs [8, 11].

The spectrum of clinical manifestations of MERS was diverse, and some patients, including a number of affected HCWs, showed relatively mild symptoms. Therefore, it was suspected that asymptomatic or undetected MERS infection may present in some of the HCWs who had been involved in managing confirmed MERS patients. One previous study reported that 25% of MERS coronavirus (MERS-CoV) polymerase chain reaction (PCR) positive patients were asymptomatic, and among these, 64% were HCWs [3]. Moreover, the period in which MERS-CoV is present in respiratory specimens is unknown, because the viral shedding mechanism is still ambiguous even in confirmed MERS patients, and the PCR positivity rate of asymptomatic patients is unknown as yet. Therefore, we aimed to evaluate the seroprevalence of MERS-CoV IgG in HCWs exposed to MERS patients, and calculate the incidence of MERS affected cases in HCWs. Furthermore, we aimed to identify risk factors of MERS infection in HCWs.
Methods

Population

We enrolled HCWs from participating hospitals where confirmed MERS patients had visited or been treated. The participating HCWs included doctors, nurses, nursing assistants, radiologic technologists, patient transporters, and patient caregivers. Others were also included in the study if they had had direct contact with confirmed MERS patients. This study did not use mandatory surveillance, and only those who agreed to participate in the study were enrolled. HCWs who were already diagnosed as PCR-confirmed MERS were not included in serologic assay, but included in calculating the incidence.

Definitions

We included as participants only individuals who had been in direct contact with confirmed MERS patients. Direct contact was defined as any of the following: i) sharing conversations with a confirmed MERS patient within a 2-meter reach, ii) staying with a patient in a closed room for longer than 5 minutes, or iii) direct contact with respiratory or gastrointestinal secretions from a patient. Environmental factors and air circulation conditions were not considered because these varied markedly among the hospitals.

Study hospitals were divided into two groups: MERS-referral hospitals are those to which PCR-confirmed MERS patients were referred for management, whereas MERS-affected hospitals are those where patients suspected to have MERS had visited prior to confirmation of their diagnosis. That is, patients who had fever and respiratory symptoms visited MERS-affected rather than MERS-referral hospitals, and if MERS was confirmed by means of MERS-CoV PCR, these patients were transferred to designated MERS-referral hospitals. In some of the hospitals initially visited by patients, suspected cases were admitted and managed following laboratory confirmation of MERS. These hospitals, serving as a
single stop for patients, were defined as MERS-affected in this study.

Some participating HCWs were quarantined or under contact surveillance after contact with a confirmed MERS patient. The decision between quarantine and contact surveillance was made by national Epidemic Intelligence Service officers dispatched to specific hospitals, according to the national guidelines. In brief, if the HCW was a close contact with MERS patients without appropriate protection, the case was placed under quarantine. If casual contact occurred, the case was placed under contact surveillance [12]. HCWs who were quarantined were confined at home or in a quarantine facility for 14 days. If respiratory symptoms or fever developed in quarantined HCWs, MERS-CoV PCR in respiratory specimen was performed twice in a 48-hour period, according to the national guidelines, in each institution [12]. HCWs who were placed under contact surveillance were monitored daily for fever and respiratory symptoms for 14 days, but were not prohibited from working in hospitals.

The definition of appropriate personal protective equipment (PPE) was drawn from previous recommendations [12-15]. Appropriate PPE was defined as use of all of the following: i) N95 respirator or powered air purifying respirator (PAPR), ii) isolation gown (coverall), iii) goggles or face shield, and iv) gloves. If any part of the PPE was missing, that was considered to be exposure without appropriate PPE.

We defined aerosol-generating procedures (AGP) as follows: suction of airway, application of high-flow \( O_2 \) instrument, bronchoscopy, intubation, and/or cardiopulmonary resuscitation. In cases in which AGP were performed, only PAPR, not an N95 respirator, was considered appropriate PPE [12].

Sample Collection and Survey

We collected the serum of participants to identify the presence of MERS-CoV IgG.
Further, we used a questionnaire survey to gather information regarding the HCWs’ demographic characteristics and extent of exposure. The survey questionnaire was based on a WHO questionnaire [16].

Serum was collected 4–6 weeks after the last contact with confirmed MERS patients.

**Laboratory Procedures**

We performed an enzyme-linked immunosorbent assay (ELISA) (Euroimmun, Lübeck, Germany) to screen for the presence of MERS-CoV IgG. In cases in which the optical density of the ELISA exceeded a predefined cutoff value (>50% of the reference value), we performed an indirect immunofluorescence test (IIFT) (Euroimmun) to confirm MERS-CoV IgG and quantify antibody titers. The cutoff ELISA values were 80% of the reference value for a positive and 50% for borderline result. Serum was diluted 100-fold, according to the protocol suggested by the manufacturer. Antibody titer measurement was conducted by two-fold dilution from 1:100 to 1:3200.

**Statistical Analysis**

The data were analyzed using SPSS Version 20.0. We compared MERS-referral and MERS-affected hospitals using the chi-squared test and the Mann–Whitney U test. All tests were two-sided, and a p-value of 0.05 or less was considered significant.

Incidence was calculated as follows: Incidence of MERS-infected cases = (the number of PCR-confirmed MERS cases in participating hospitals + the number of serology-confirmed MERS cases in participating hospitals) / total number of MERS exposed HCWs in participating hospitals.

**Study Approval**

8
All participants enrolled in the study voluntarily, and written informed consent was acquired before participation. The study protocol was approved by the institutional review board of Ewha Womans University Mokdong Hospital in Seoul, South Korea (EUMC 2015-07-002).
Results

Baseline Characteristics

Eighteen MERS-affected hospitals and 13 MERS-referral hospitals participated in the study (Figure 1). A total of 114 cases of MERS patients were managed in the participating hospitals. A total 1169 HCWs had contact with MERS patients in study hospitals, of whom 603 were in MERS-affected hospitals, and 566 were in MERS-referral hospitals. Among these, 15 were diagnosed as PCR-confirmed MERS cases during quarantine, all of whom were in MERS-affected hospitals. Four-hundred and seventeen HCWs did not agree to participate in the study. Therefore, 737 HCWs were enrolled in the study (Figure 2). Of these participants, doctors accounted for 19.4%, nurses 69.1%, and radiologic technologists 2.3% (Table 1). In MERS-affected hospitals, 62.4% of participants were quarantined, whereas only 2.5% of participants in MERS-referral hospitals were quarantined. The baseline characteristics of participants are shown in Table 1.

ELISA and IIFT

The ELISA result was positive in 5/737 (0.7%) participants, and borderline in 7/737 (0.9%) participants. The IIFT was positive in 2 among the 12 participants who showed borderline or positive results on the ELISA (0.3% of the total) (Table 2). Quantitative IIFT showed that the titer of antibody was 1:400 and 1:800, respectively.

Calculation of Incidence

We found 2 seropositive cases among 737 participants. Therefore, seroprevalence of MERS-CoV IgG among HCWs exposed to MERS patients, who were asymptomatic or symptomatic with negative MERS-CoV PCR was 0.3%. Based on the 15 cases of PCR-confirmed MERS cases in our study hospitals, we assumed that at least 17 healthcare workers were affected by
MERS, and the incidence was at least 1.5% (17/1169). Five of these cases were males, and 12 were females.

Symptoms Reported by Participants and Extent of Exposure

Overall, 221 (30.0%) participants out of 737 reported one or more symptoms within 4 weeks of contact with PCR-confirmed MERS patient. Generalized symptoms (177/737, 24.0%), including fever (82/737, 11.1%), fatigue (82/737, 11.1%), and myalgia (68/737, 9.2%) were frequently reported. Respiratory symptoms were reported in 13.6%, and gastrointestinal symptoms in 7.5% of participants.

Total duration of contact with MERS patients, and mean duration of contact with MERS patients in a day were both significantly longer in MERS-referral hospitals. Two hundred and ninety-four participants had been exposed to one or more PCR-confirmed MERS patients without at least one form of appropriate PPE. Exposure to AGP without PAPR occurred in 122 participants (Table 3).

Among the participants who on even one occasion did not use appropriate PPE, 0.7% (2/294) were seropositive, compared to 0% among those who used it appropriately every time. Among participants who were exposed to AGP, 0.8% (1/122) were seropositive among those who had been exposed without PAPR even once, whereas 0.2% (1/615) were seropositive among those who had been exposed only with PAPR (Table 4).
Discussion

In this study, we evaluated the seroprevalence of MERS-CoV among HCWs who had had contact with MERS patients. We found 2 asymptomatic or subclinical MERS infection in HCWs, both of them were exposed without appropriate PPE. Overall prevalence of MERS-CoV seropositivity was 0.3% (2/737); especially, among the participants who did not use appropriate PPE, 0.7% (2/294) was seropositive. Considering fifteen PCR-confirmed MERS cases among HCWs in study hospital, the incidence of MERS affected cases among 1169 exposed HCWs was at least 1.5%.

MERS-CoV seroprevalence among populations other than confirmed MERS patients are limited. Recently, it was reported that seroprevalence of MERS-CoV IgG among the general population of Saudi Arabia was 0.15%, and that of the high-risk population was 2.3–3.6% [17]. This suggests that a number of cases of asymptomatic or mild infection may be present in the high-risk population. However, there are not sufficient MERS-CoV IgG seroprevalence data among HCWs with which we can compare our results. In SARS-affected areas in 2003, seroprevalence among HCWs by using a confirmatory test ranged from 0 to 1.04% [18], suggesting that undetected or asymptomatic cases were present after the SARS epidemic. Our study found a similar proportion of MERS subclinical infection among HCWs.

To prevent MERS infection in HCWs, use of PPE is emphasized. In general, isolation gown and gloves are recommended as a contact precaution, and surgical mask is recommended as a droplet precaution [19]. Although MERS is known to be transmitted by droplet and by direct contact, use of appropriate PPE, including N95 respirator and isolation gown, has been emphasized in preventing MERS infection [12-15]. In our study, only participants who were exposed to MERS patients without appropriate PPE had IgG antibody against MERS-CoV. This was also found in PCR-confirmed MERS-infected HCWs. Among the 39 PCR-confirmed MERS-infected HCWs [8, 11], we reviewed the 15 patients who were
affiliated with our study’s participating hospitals (unpublished data). We found that 14 of these patients were exposed without N95 respirator. Therefore, in our participating hospitals, almost all MERS-infected HCWs were related to not using appropriate PPE. There were two exceptional cases, who had used isolation gown and N95 respirator following guidelines [14], but eventually were infected with MERS. These cases were both exposed to AGP, intubation of MERS patient (seropositive case in our study), and cardiopulmonary resuscitation of MERS patient (PCR-confirmed MERS case). Although the fitting test was not performed in either case, we guess that N95 respirator is less efficient in AGP for high viral burden patients. Consequently, appropriate use of PPE is important in protection of MERS, and when performing AGP, more efficient respirators might be necessary [12].

In previous studies, the presence of MERS-CoV IgG was confirmed by a neutralizing assay such as a plaque reduction neutralization test [17] or microneutralization assay [20]. Müller et al. reported that only 10% of samples that received positive ELISA results for antibody to S1 antigen were positive in the neutralization assay [17]. In their study, however, the IIFT was well correlated with the neutralization assay. Their report showed that the ELISA alone was useful in screening for presence of MERS-CoV IgG but not in confirming it, whereas the IIFT could substitute the neutralization assay. In another recent report, the correlation of MERS-CoV ELISA and neutralization assay was strong in PCR-confirmed MERS patients [21]. Therefore, our protocol, composed of screening by MERS-CoV S1 ELISA and confirming by IIFT, may be robust to detect true seropositive samples.

Our study has some limitations that should be reflected. First, the optimal timing of serum collection for MERS testing is unknown. It is unknown how long serum antibodies persist in MERS-infected patients. Moreover, recent studies have shown that confirmed MERS patients with mild symptoms had only borderline serum IgG levels 32 days after
diagnosis [22]. Thus, some of the negative ELISA results in our participants may have been false negatives.

Second, since this work was for research purposes only, participation was not mandatory but voluntary. Therefore, not all HCWs exposed to MERS patients were enrolled. Approximately 48 hospitals and 61 clinics in South Korea were affected by MERS, and 30 hospitals were designated as MERS-referral hospitals. Among these institutions, only 31 hospitals participated in this study; and in these hospitals, only 63.0% of HCWs (75.2% in MERS-affected hospitals and 49.5% in MERS-referral hospitals) in participating institutions who had been potentially exposed to confirmed MERS patients participated.

Third, the estimated incidence of MERS-affected HCWs could be underestimated by two reasons. First, because 35.7% (417/1169) of HCWs did not agree to be enrolled in the study, some seropositive cases may be missing. Second, two hospitals where large clustered cases developed did not participate in our study, and the incidence of MERS affected cases in these hospitals may be higher than others. These hospitals included one that was visited by the first Korean MERS-infected patient, and another at which the largest super-spreading event occurred. In those hospitals, HCWs were not prepared for such a high risk of infection, and appropriate PPE was not used during the management of patients in early period of outbreak. Therefore, seroprevalence would be expected to be higher in those hospitals than others.

In conclusion, the seroprevalence of MERS-CoV IgG in HCWs after contact with MERS patients in participating hospitals was found to be 0.3%, and among the participants who did not use appropriate PPE, 0.7%. The calculated incidence of MERS-affected cases in HCWs was at least 1.5%. The seroprevalence of MERS-CoV IgG was higher among the participants who did not use appropriate PPE.
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Conflicts of Interest: None
**Figure legends**

Figure 1. Geographic distribution of the participating 31 hospitals in South Korea

Abbreviation. MERS, Middle east respiratory syndrome

Figure 2. The STROBE flow chart of participating population

Abbreviation. MERS, Middle east respiratory syndrome; PCR, polymerase chain reaction; ELISA, Enzyme-linked immunosorbent assay; IIFT, indirect immunofluorescence test
Reference


9. Al-Tawfiq JA, Perl TM. Middle East respiratory syndrome coronavirus in healthcare


Table 1. Baseline characteristics of enrolled participants.

<table>
<thead>
<tr>
<th></th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male, n (%))</td>
<td>160 (21.7%)</td>
<td>51 (18.2%)</td>
<td>109 (23.9%)</td>
<td>0.072</td>
</tr>
<tr>
<td>Age (mean (±SD), range)</td>
<td>33.0 (±8.5), 18–67</td>
<td>33.8 (±8.6), 18–58</td>
<td>32.6 (±8.5), 22–67</td>
<td>0.037</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctor</td>
<td>143 (19.4%)</td>
<td>46 (16.4%)</td>
<td>97 (21.2%)</td>
<td></td>
</tr>
<tr>
<td>Nurse</td>
<td>509 (69.1%)</td>
<td>201 (71.8%)</td>
<td>308 (67.4%)</td>
<td></td>
</tr>
<tr>
<td>Nursing assistant</td>
<td>13 (1.8%)</td>
<td>3 (1.1%)</td>
<td>10 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Radiologic technologist</td>
<td>17 (2.3%)</td>
<td>3 (1.1%)</td>
<td>14 (3.1%)</td>
<td></td>
</tr>
<tr>
<td>Patient transporter</td>
<td>12 (1.6%)</td>
<td>0</td>
<td>12 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Clerical officer/security guard</td>
<td>8 (1.1%)</td>
<td>1 (0.4%)</td>
<td>7 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>35 (4.7%)</td>
<td>26 (9.3%)</td>
<td>9 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Doctor, department*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>108 (76.6%)</td>
<td>42 (93.3%)</td>
<td>66 (68.8%)</td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>9 (6.4%)</td>
<td>2 (4.4%)</td>
<td>7 (7.3%)</td>
<td></td>
</tr>
<tr>
<td>Emergency medicine</td>
<td>23 (16.3%)</td>
<td>0</td>
<td>23 (24.0%)</td>
<td></td>
</tr>
<tr>
<td>Location of exposure†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency room</td>
<td>79 (10.7%)</td>
<td>9 (3.2%)</td>
<td>70 (15.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ward</td>
<td>411 (55.8%)</td>
<td>232 (82.9%)</td>
<td>179 (39.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>186 (25.2%)</td>
<td>41 (14.6%)</td>
<td>145 (31.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outpatient department</td>
<td>40 (5.4%)</td>
<td>5 (1.9%)</td>
<td>35 (7.7%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Abbreviation: MERS, Middle East respiratory syndrome; SD, standard deviation.

* One participant, a doctor of Oriental medicine, is excluded from department classification.

† Some participants were exposed at multiple sites.
Table 2. Participants’ laboratory results for ELISA and IIFT by serum.

<table>
<thead>
<tr>
<th></th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ELISA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD 50–79%</td>
<td>7 (0.9%)</td>
<td>2 (0.7%)</td>
<td>5 (1.2%)</td>
<td></td>
</tr>
<tr>
<td>OD over 80%</td>
<td>5 (0.7%)</td>
<td>1 (0.4%)</td>
<td>4 (0.9%)</td>
<td>0.655</td>
</tr>
<tr>
<td>IIFT positive</td>
<td>2 (0.3%)</td>
<td>0</td>
<td>2 (0.4%)</td>
<td>0.528</td>
</tr>
</tbody>
</table>

Abbreviations: MERS, Middle East respiratory syndrome; ELISA, enzyme-linked immunosorbent assay; OD, optical density; IIFT, indirect immunofluorescence test
Table 3. Extent of exposure to MERS-confirmed patients among enrolled participants.

<table>
<thead>
<tr>
<th>Duration of contact with MERS patients (days)*</th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3</td>
<td>284 (43.0%)</td>
<td>13 (5.5%)</td>
<td>271 (64.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4–7</td>
<td>89 (13.5%)</td>
<td>13 (5.5%)</td>
<td>76 (18.0%)</td>
<td></td>
</tr>
<tr>
<td>8–14</td>
<td>90 (13.6%)</td>
<td>61 (25.6%)</td>
<td>29 (6.9%)</td>
<td></td>
</tr>
<tr>
<td>15–30</td>
<td>107 (16.2%)</td>
<td>65 (27.3%)</td>
<td>42 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>&gt;31</td>
<td>4 (0.9%)</td>
<td>86 (36.1%)</td>
<td>4 (0.9%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean duration of contact with MERS patients per day (hours)†</th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.5</td>
<td>221 (33.5%)</td>
<td>39 (14.4%)</td>
<td>182 (46.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0.5–1</td>
<td>105 (15.9%)</td>
<td>47 (17.4%)</td>
<td>58 (14.9%)</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>86 (13.0%)</td>
<td>53 (19.6%)</td>
<td>33 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>2–6</td>
<td>113 (17.1%)</td>
<td>80 (29.6%)</td>
<td>33 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>6–12</td>
<td>121 (18.3%)</td>
<td>44 (16.3%)</td>
<td>77 (19.7%)</td>
<td></td>
</tr>
<tr>
<td>&gt;12</td>
<td>14 (2.1%)</td>
<td>7 (2.6%)</td>
<td>7 (1.8%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospitals in contact with case with super-spreading event‡</th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>255 (34.6%)</td>
<td>56 (20.0%)</td>
<td>199 (43.5%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure without appropriate PPE§</th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>294 (39.9%)</td>
<td>53 (18.9%)</td>
<td>241 (52.7%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure without PAPR during aerosol-generation procedure§</th>
<th>Total (N=737)</th>
<th>MERS-referral hospital (N=280)</th>
<th>MERS-affected hospital (N=457)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>122 (16.6%)</td>
<td>47 (16.8%)</td>
<td>75 (16.4%)</td>
<td>0.894</td>
</tr>
</tbody>
</table>
Abbreviations: PPE, personal protective equipment; PAPR, powered air purifying respirator.

Abbreviations: MERS, Middle East respiratory syndrome; PPE, personal protective equipment; PAPR, powered air purifying respirator

* Data were missing for 42 and 35 participants in MERS-referral and MERS-affected hospitals, respectively.
† Data were missing for 10 and 67 participants in MERS-referral and MERS-affected hospitals, respectively.
‡ Case with super-spreading event: confirmed MERS patient who infected more than 5 people.
§ Not all 737 participants were exposed to aerosol-generating procedures.
Table 4. Use of personal protective equipment and seropositivity in MERS-exposed healthcare workers*.

<table>
<thead>
<tr>
<th>Extent of exposure</th>
<th>Seropositive (N=2)</th>
<th>Seronegative (N=735)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure without appropriate PPE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (0.7%)*</td>
<td>292 (99.3%)*</td>
<td>0.159</td>
</tr>
<tr>
<td>Never</td>
<td>0</td>
<td>443 (100%)*</td>
<td></td>
</tr>
<tr>
<td><strong>Exposure without PAPR during aerosolized procedure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (0.8%)*</td>
<td>121 (99.2%)*</td>
<td>0.304</td>
</tr>
<tr>
<td>Never or do not perform such procedures</td>
<td>1 (0.2%)*</td>
<td>614 (99.8%)*</td>
<td></td>
</tr>
</tbody>
</table>

*Percentage in parentheses is proportion of each serostatus according to exposure status.

Abbreviations: MERS, Middle east respiratory syndrome; PPE, personal protective equipment; PAPR, powered air purifying respirator
Healthcare workers contact with MERS patients in study hospitals
N=1169

MERS-affected Hospital
n=603

MERS-referral Hospital
n=566

Eligible population of serology assay
n=1154

MERS-affected Hospital
n=588

MERS-referral Hospital
n=566

Not agree to participate
n=417

MERS-affected Hospital
n=146

MERS-referral Hospital
n=286

Participants for serology assay
n=737

MERS-affected Hospital
n=457

MERS-referral Hospital
n=280

PCR-confirmed MERS patients
n=15

ELISA
positive=5

IIFT
positive=2

ELISA
borderline=7

IIFT
positive=0