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Original Research Article

Transmission of Middle East respiratory syndrome coronavirus infections among healthcare personnel in the Middle East: A systematic review

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Abstract

Purpose: *To undertake a systematic review of the high mortality rate of Middle East respiratory syndrome coronavirus infections (MERS-CoV) among healthcare personnel in the Middle East.*
Methods: *To conduct this systematic review various electronic databases were searched for earlier recorded studies. Prisma guidelines were used to shortlist the studies based on the inclusion and exclusion criterion. Finally, twelve studies were selected and analysed for the systematic review.*
Results: *Twelve articles were selected after filtering 184 articles on Coronavirus. The studies chosen for this systematic review which outline the transmission information of MERS-CoV among health care personnel. A majority of studies were from Saudi Arabia, as the prevalence of Mers-CoV in Saudi Arabia is higher than in other countries in the region. Mers-CoV transmission into humans was mainly expected from infected dromedary camels.*
Conclusion: *The results indicate that the use of infection control procedures and protocols, which include ensuring that all persons with respiratory infection symptoms adhere to respiratory hygiene, hand hygiene, and cough etiquette, would minimize the infection rate among HCPs. The required consumables for maintaining hand hygiene should be readily available to all HCPs.*

Keywords: *Middle East respiratory syndrome coronavirus (MERS-CoV), Systematic review, healthcare-associated infections, Coronaviruses, Health care personnel*

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INTRODUCTION

The Middle East respiratory syndrome (MERS) is a recently described virus in humans [1,2]. Numerous cases in many countries around the world have been reported like Qatar, United Arab Emirates, Oman, and Austria, but Saudi Arabia is the primary source [2,3].Coronaviruses generally effectuated mild upper respiratory illnesses [1]. The occurrence of severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) has drawn universal recognition on the clinical importance of coronaviruses (4).

The signs and symptoms in most cases are flu-like syndromes, but in more severe cases life-threatening disease occurs, like SARS and pneumonia [5,6]. However, coronaviruses constitute a significant cause of the Middle East respiratory syndrome (MERS) which occurs not just in humans but also found in a range of farm animals including chicken. MERS is reported to be found in camels which serves as a reservoir for the virus [7].

Middle East respiratory syndrome coronavirus (MERS-CoV) is similar to other viruses which spread from infected human secretions, such as sneezing, coughing, because its human-to-human transmission [8]. A close contact with infected people who recently travelled from the Middle East or nearby area had become a significant cause for spreading of coronavirus infection [9]. Hospital settings also play a crucial role in coronavirus transmission [10,11]. The first case of MERS-CoV was initially detected in the year 2012-June, presented as a respiratory tract infection in Jeddah city in Saudi Arabia who later died of renal failure and pneumonia [12].

From the beginning of 2017 till Jan-2018 101 cases of MERS-CoV infections in the Middle East were reported, out of which 6.93 % of recorded cases were among in healthcare personnel (HCP's), and the rest 93.07 % cases were of those patients who were not HCP's but had recent healthcare exposure [13]. The current understanding of the epidemiology of MERS-CoV transmission and infection control procedure is based on the experiences with the other viruses. [2]. However, the pathway through which the virus spreads is not currently well understood.

The objective of this systematic review was first to summarize the transmission of MERS-CoV, with an aim to identify a problem approach which could prevent in spreading of this virus. The author suggests the use of recommended personal protective equipment and execution of infection control procedures can help in protecting HCP's.

The primary objective was to determine the human-to-human transmission of MERS-CoV in health care personnel. A secondary objective was to identify and characterize epidemiological and clinical characteristics of persons with healthcare-associated infections and to understand the factors contributing in spreading of MERS-CoV transmission within the healthcare settings. In this review, the known risk of transmission within health care settings were discussed, and relevant recommendations to prevent the transmission of MERS-CoV were presented.

METHODS

Various electronic databases were searched, including PubMed, Science Direct and Google Scholar, for earlier reported studies on the subject. A systematic review was conducted on the shortlisted studies based on the inclusion and exclusion criterion of the study following Prisma guidelines with consideration on four pre-defined themes (clinical characteristics/epidemiology, reservoirs/origins, virology and therapeutics prevention) for published studies.

Search eligibility criteria

Recent studies done on MERS-CoV in the English language which fulfilled the review criteria were selected for the systematic review of MERS-CoV transmission in HCP's.

Search keywords

Keywords used were ''coronavirus'', ''MERS-CoV'', in combination with "human studies", ''transmission'', randomized controlled trials (RCT), case-control designs, prospective or retrospective cohort designs.

This effort resulted in 184 relevant studies primarily based on "MERS-CoV in the Middle East" and secondly in studies since 2010, of these, 12 articles were selected for this study.

Primary search - databases for data collection

All types of databases and other journal websites, like Google Scholar, PubMed, Emerging infectious diseases, BMC Public health, The New England Journal of Medicine, American Journal of Infection Control, Journal of Epidemiology and Global Health, Journal of Infection and Public Health, and European Society of Clinical Microbiology and Infectious Diseases, were used for primary search.

The extracted data from these journals includes authors' name, type of study, publication year, number of patients, sample size and level of study. The outcomes of interest included measures of morbidity and mortality rate. The end result recorded in the chosen studies included improvement of symptoms, infectious complications and death.

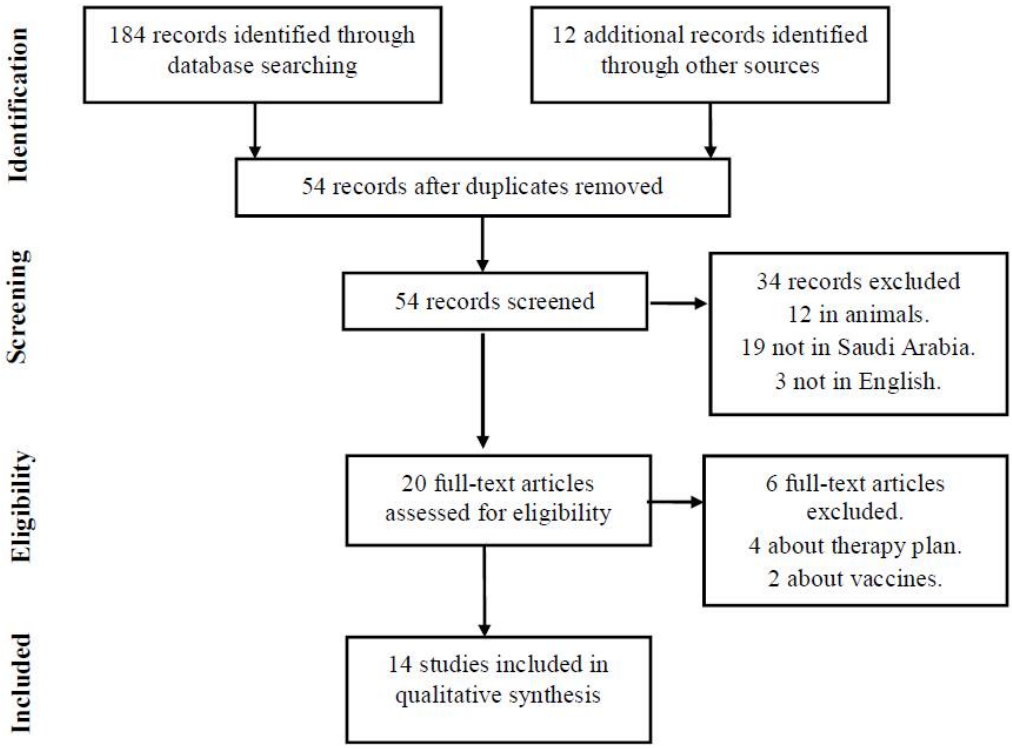

Figure 1: Prisma flowchart which summary of the included and excluded studies for the systematic review

Secondary search - databases for data collection

After the primary search was concluded on the cited references in the articles, primary screening of the articles was mainly concentrated on the scanning of the title and the abstract. Articles which passed the primary screening were read in full detail for the final inclusion of articles (Figure 1).

Studies with full-text were only included in the review and not just abstract. Studies which discussed the vaccine therapy of MERS-CoV were excluded. Studies on MERS-CoV in different countries other than the Middle East were also excluded. Similarly, articles based only on MERS-CoV in children, in non-health care personnel and studies in animals were also filtered out. After filtering these categories, only twelve studies are left. The method used here is a qualitative systemic review.

A wide range of environmental, medical and scientific databases was searched to extract relevant citations and to identify primary studies on MERS-CoV in health care facilities.

Assessment of study quality

Clinical studies included in this review were critically appraised by evaluating the study design, transmission allocation, possibility of bias in the selection of the control group and consistency in reporting the study outcomes.

Included studies in this review are tabulated narratively and were grouped by a systematic strategy. Details of the included study were presented including year of publication, author's name, type of study, number of patients, number of males, number of females, level of study, and the studies are arranged according to the principal signs and symptoms of MERS-CoV.

RESULTS

A total of twelve articles were selected after filtering 184 articles on Coronavirus. The studies chosen for this systematic review are summarized in Table 1. Table 2 outlines the transmission information of these studies in healthcare personnel.

A total of ten articles were from Saudi Arabia from different cities mostly from Jeddah, one from United Arab Emirates (Abu Dhabi) and one from Arabian Peninsula. Majority of studies were from Saudi Arabia, as the prevalence of Mers-CoV in Saudi Arabia is high compared to other countries. Mers-CoV transmission into humans was mainly expected from infected dromedary camels [1]. Out of 12 selected studies, 3 were questionnaire-based survey results [4,6,11]. The

Table 1: Summary of all studies on transmission of MERS-CoV Infection among HCP's in Middle-East

Study	Type of study	Number of participants	Male	Female	Level of study
Memish *et al* [1]	A cross-sectional study (Observational study)	7	0	7	Low
Hall *et al* [2]	Case report	48	27	29	Low
Hunter JC et al [3]	Retrospective	19	11	8	Low
Khan et al [4]*	A cross-sectional study (Observational study)	153	85	68	Low
Oboho *et al* [5]	Retrospective	78	NR	NR	Low
Khalid *et al* [6]*	A cross-sectional (Observational study)	117	28	89	Low
Shalhoub *et al* [7]	Primary case	1	0	1	Low
Maltezou *et al* [8]	Review study	155	NR	NR	Moderate
Sherbini *et al* [9]	Retrospective	5	NR	NR	Low
Memish *et al* [10]	Prospective descriptive study	19	4	15	NR
Rabaan *et al* [11]*	A cross-sectional (Observational study)	607	269	338	NR
Alraddadi *et al* [12]	Cohort study	250	NR	NR	NR

NR=not reported *Questionnaire

signs and symptoms of Mers-CoV infections are standard in all the twelve articles. A single study mentioned the history of a patient of travelling from Amman, Jordan before getting infected; so it illustrates the pathway of transmission from camel to human then to HCP [3].

Another study reported a healthy outcome after HCP contact with the pathogen resulted in a negative test for MERS-CoV infections. Three studies have shown smoking as a risk factor, however it is unclear that diabetes, asthma or obesity has any association with acquiring MERS-CoV infection among HCP. Most of the studies have a total duration of exposure of pathogen between less than an hour to 4 h with the exception of one study. Symptoms are reported to appear after 14 days for first exposure to the pathogen. However, changing linen, feeding, bathing, lifting, giving medicines, placing IV or other catheters are the major tasks performed by HCP's causing transmission of the MERS-CoV infection. Studies reported that personal protective equipment used by HCP's were masks and gloves. Table 1 included the name of the first author, type of study (case report, primary case, observational study, retrospective study, prospective descriptive study and review study), number of patients and the level of each study. Missing information from any studies is marked as "NR", meaning not reported.

Table 2-4 summarises the data on risk factors, exposure history, touched patient (direct or indirect), type of exposures to the patient (the activity that leads to the transfer of pathogen), presence during high-risk procedure, use of personal protective equipment. In the end, the outcome of HCP's as healthy or diseased was presented. Nahid *et al* included five HCP's, three of them were staff nurses, and the other two were clinicians [9].

DISCUSSION

Globally it has been a lot of concern about the transmission of the MERS-CoV [14]. Due to a high mortality rate of MERS-CoV, this systematic review was conducted to summarize the available studies in the scope of transmission of coronavirus in health-care personnel for prevention of coronavirus infection based on previous reports [15].

The noticeable growth in the number of patients infected with MERS-CoV in the Middle East could be illustrated by secondary human-to-human transmission, rather than by an unexpected increase of primary cases in the community [16].

Studies discussed the risk factors like diabetic mellitus, smoking, and asthma (13). After filtering out major risk factors of HCP's by excluding those with a history of exposure to dromedary camels, proximity of health care personnel to patients, handling of human biological fluids, such as respiratory secretions, urine, sputum, feces, or blood found to increase the possibility of transmission of MERS-CoV infections among HCP's [17.

Three articles discuss diabetes mellitus as a risk factor and other three about smoking [18. However, the chronic disease increase the risk of

Table 2: Transmission information summary of studies on transmission of Middle East Respiratory Syndrome Coronavirus Infection among HCP's in the Middle East

Study	Risk factor	Exposure history (Total Duration of exposure/s)	Touched patient	Type of exposure/s to patient	Presence during high-risk procedure (aerosol generating)	Use of personal protective equipment	Outcome
Memish et al. (1)	1=Diabetes out of 7 female patients	<1hrs =4 1-5hrs =4	0	Change linen =4 Feeding =4 Bathing =3 Lifting =4 Give meds =4 Place IV or other catheters =5	Intubation =5 Airway suctioning =4 Sputum induction =2	Regular mask =5 -Respirator (n95 or equivalent) =3 Eye protection =0 -Gloves =4 -Gowns =7 Hand hygiene=NR	Diseased (N=7/7)
Hall et al. (2)	Underlying illness =6 Smoking =6 overweight or obese =24	<1hrs =28 1-4hrs =8 >or=5 =12	41	Touched patient's bedding, equipment, or body fluids =30 Collected clinical specimens = 19 Emptied bedpan =11 Came within 1 m of patient =43	Airway suction =24 Nebulizer treatment = 14 Sputum induction = 11 Bronchoscopy =4 Intubation =3	Gloves =45 Mask =42 Gown =19 eye protection =0 N95 mask =16 hand hygiene =48	Healthy
Hunter et al. (3)	Diabetes mellitus =1 Obese =1 Hypertension =5 Hyperlipidemia =4 Asthma =2 Ischemic heart disease =1	<10 min =1 10–30 min =6 >30 min =2 Unknown =5	14	Patient examination =7 Procedure with potential aerosol generation‡ =5 Patient transport =3 Radiograph =1 Clerical =1 Unknown =1	Manipulation of cannula or oxygen mask (n = 3), administration of inhaler or nebulizer treatment (n = 2), intubation (n = 1), suctioning before intubation (n = 1); healthcare workers could perform >1 of these patient care activities.	Any mask=6 Surgical mask=5 N95 respirator=2 Gloves=4 Gown=3 Gown gloves, and surgical mask or N95 respirator=3 Eye protection=NR	Diseased

Table 3: Transmission information summary of studies on transmission of Middle East Respiratory Syndrome Coronavirus Infection among HCP's in the Middle East

Study	Risk factor	Exposure history (Total Duration of exposure/s)	Touched patient	Type of exposure/s to patient	Presence during high-risk procedure (aerosol generating)	Use of personal protective equipment	Outcome
Khan et al (4)	NR	NR	NR	NR	NR	NR	Healthy
Oboho et al (5)	NR	A person with severe respiratory illness of unknown cause during the 14 days before the onset of illness is admitted to the hospital	NA	NA	NA	NA	Diseased
Khalid et al. (6)	NR	NR	NR	NR	NR	NR	Healthy
Shalhoub et al. (7)	smoker	2day	NR	Performed standard nursing care that included taking vital signs, intravenous access, accompanying the patient to the radiology department, inserting peripheral and inserting a urinary catheter	NR	NR	Diseased
Maltezou et al. (8)	NR	4 of them <1hrs	NR (direct and indirect)	2 of them in the hemodialysis unit	NR	13 of them don't use personal protective equipment apart from gloves	Diseased and one of them died

Table 4: Transmission information summary of studies on transmission of Middle East Respiratory Syndrome Coronavirus Infection among HCP's in the Middle East

Study	Risk factor	Exposure history (Total Duration of exposure/s)	Touched patient	Type of exposure/s to patient	Presence during high-risk procedure (aerosol generating)	Use of personal protective equipment	Outcome
Sherbini et al. (9)	**NR**	**NR**	**close contact**	**NR**	**NR**	**NR**	**Diseased**
Memish et al. (10)	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**Diseased**
Rabaan et al. (11)	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**Healthy**
Alraddadi et al. (12)	Co-morbidity=8 Asthma=2 Diabetes mellitus=3 Allergic rhinitis=5 Smoking=10	NR	direct contact= 250	Bathing =7 Feeding =6 Lifting positioning =14 Emptying bedpan =8 Changing linen =11 Providing injection =10 Placing intravascular device =10 Performing hemodialysis =2 Taking medical history =6 Performing physical exam =9 Drawing blood =11 Collecting respiratory laboratory specimens=9	The highest attack rate (29.4 %) is among radiology technicians, followed by respiratory therapists (3.2 %), nurses (9.4%) and physicians.	Gloves =18 Gown =11 Eye protection Direct contact =1 Aerosol-generating procedure =3 Nose and mouth covering with N95 respirator or medical mask Direct patient contact =11 Aerosol-generating procedures =8 Medical mask Direct patient contact =9 Aerosol-generating procedures =5 N95 respirator Direct patient contact =6 Aerosol-generating procedures =5	7=healthy

NR=not reported *Questionnaire

acquiring this infection and one study suggested categorizing HCP with diabetes mellitus as a high-risk group [19. One study indicates that the current threat of transmission within health car facilities remains small and that the recommended infection control measures are adequate.

Majority of studies mentioned the exposure time to infect HCP's by less than one hour, an exception to 2 studies which reported higher exposure time or multiple exposure occasions. Transmission of the pathogen from human-human doesn't take much time and is through droplet transmission, as it is reported that performing an activity related to a respiratory system like the aerosol generation is highly likely infect a HCP [20]. In another single study, due to

In fact, most of the studies showed the need for the use of various personal protective equipment like gloves and mask and suggested this may lead to protect the people from the viruses [2]. One study mentioned that the use of N95 mask is less compared to the regular mask because it's more expensive, but the protection is adequately even with regular mask.

The questionnaire studies state that the safety of HCP is its primary concern. In the survey Khan MU *et al* [4], it showed that majority of HCP were well aware of the precautionary measures and hygienic issues to get prevented from transmission of pathogens. However, Ali et al. focused on the hospital infrastructure and its design which is also a significant factor for spreading the infection [11].

Finally, this study concludes infection prevention program and good practices to be followed by the management of hospitals to minimize the spread of MERS-CoV infections and protect staff, patients, and visitors to hospitals.

CONCLUSION

Health care personnel (HCPs) are at high risk of transfer of MERS-CoV from infected patients through the secondary human-to-human transmission. The HCPs in most of the studies showed good attitude and knowledge of MERS. The infection prevention program and proper procedures that were used might contribute in demonstrating lack of transmission. Nonetheless, rapid identification of high-risk patients with MERS-CoV and implementation of infection control precautions can help protect HCPs. Provision of supporting healthcare facilities to prevent the transmission and to improve the safety and protection of HCPs remain a priority. lack of appropriate following the infection control measures, some HCP's had to face maximal exposure [21]. Not a single article stated remain animal-human transmission except one, but it's not clearly identified.

Most of the studies here confirm that direct contact of the equipment related to the infected person by HCP results in strong association with transmission of MERS-CoV Infections [22]. Nurses have high chances of getting infected when compared to others as they are mostly involved in activities such as hemolysis and drawing blood. Several studies pointed towards the possible cross-contamination through contaminated surfaces and medical devices in use by HCP [21].

However, face masks, gloves and gowns should be used during all procedures, especially aerosol generation procedure. In general, infection control procedures should be strictly adhered to, and HCPs with chronic disease conditions such as diabetes and asthma ideally should be kept away from infected patients.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

I declare that Syed Ata ur Rahman did this systematic review and the author will bear all liabilities pertaining to claims relating to the content of this article

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